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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.)

WHETHER 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*[1] 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,*[2] 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,[3,4] 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

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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.[3] 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.[5]

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.[6] 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 base-line 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 vs. 1811 per 100,000 person-years for men [P<0.001] and 2147 vs. 1159 per 100,000 person-years for women [P<0.001]). The mean age-adjusted body-mass index was the same for the excluded and the included men (25.5) and only slightly higher among the excluded women than among the included women (24.8 vs. 24.7, P<0.001).

Table 1. Subjects Excluded from or Included in the Study Cohort.

	Men	Women
Initial cohort (no.)	92,769	376,380
Subjects excluded (%)*		
Questionnaire completed by proxy	15.4	5.3
Missing data on height or weight	4.8	7.4
Missing data on ≥1 covariate	2.4	3.7
≤0.05th percentile or ≥99.95th percentile for height, weight, or BMI†	0.2	0.2
Involuntary weight loss >10 lb (4.5 kg) in past 2 yr	1.2	1.9
Died in first year of follow-up	0.6	0.3
History of cancer other than skin cancer	0.9	2.7
History of heart disease or stroke	4.6	3.9
Sick or in poor health‡	2.9	4.7
Pregnant	—	0.3
Subjects included (no.)	62,116	262,019

*Percentages show the proportions of white subjects 30 years old or older at base line who had never smoked who were excluded from the study, in sequence.

†Subjects with values ≤0.05th percentile or ≥99.95th percentile were excluded. Among men, we excluded those whose weight was below 101 lb (46 kg) or 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) below 14.9 or above 43.4. Among women, we excluded those whose weight was below 85 lb (39 kg) or above 270 lb (123 kg), those 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.

‡The subjects in this category responded affirmatively to the question "Are you sick at the present time?" or reported that their health had been "poor" within the past month, rather than "fair" or "good."

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).[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 <90 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.[8,9]

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.[10] 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.[11] 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 5259 deaths due to cardiovascular disease per 100,000 person-years in the group with body-mass indexes of 19.0 to 21.9, as compared with 5227 per 100,000 person-years in the group with indexes of 29.0 to 31.9.

The distributions of several characteristics associated with longevity and body-mass index varied with age. Younger subjects were more highly educated, more likely to report a high level of physical activity, and more likely to drink alcoholic beverages than were older subjects (data not shown).

The relative risks of death from all causes (Fig. 1) and death from cardiovascular disease (Fig. 2) according to body-mass-index category were estimated in models that included age, education, physical activity, and alcohol consumption as covariates. Separate analyses were conducted for the six age groups, with the body-mass-index category 19.0 to 21.9 used as the reference category. Relative-risk estimates are not reported for groups defined by age and 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 BASE LINE IN THE STUDY COHORT OF HEALTHY WHITE MEN AND WOMEN WHO HAD NEVER SMOKED.

VARIABLE*	AGE (YR) 30–44	45–54	55–64	65–74	75–84	≥85	TOTAL
Men							
No. of subjects	9,981	25,736	16,583	7,917	1,771	128	62,116
No. of deaths	272	1,812	2,887	3,159	1,251	117	9,498
No. of deaths from CVD	117	1,040	1,818	2,126	868	93	6,062
Person-yr of follow-up	120,870	306,198	187,845	79,998	14,497	741	710,149
Mean body-mass index	25.6	25.8	25.6	25.1	24.0	23.2	25.6
Women							
No. of subjects	55,935	98,539	70,407	30,801	5,912	425	262,019
No. of deaths	1,145	4,108	7,201	8,251	3,615	380	24,700
No. of deaths from CVD	217	1,280	3,710	5,389	2,654	309	13,559
Person-yr of follow-up	676,870	1,176,539	816,270	331,523	53,413	2652	3,057,268
Mean body-mass index	23.8	24.7	25.2	25.0	24.1	23.4	24.7

*CVD denotes cardiovascular disease.

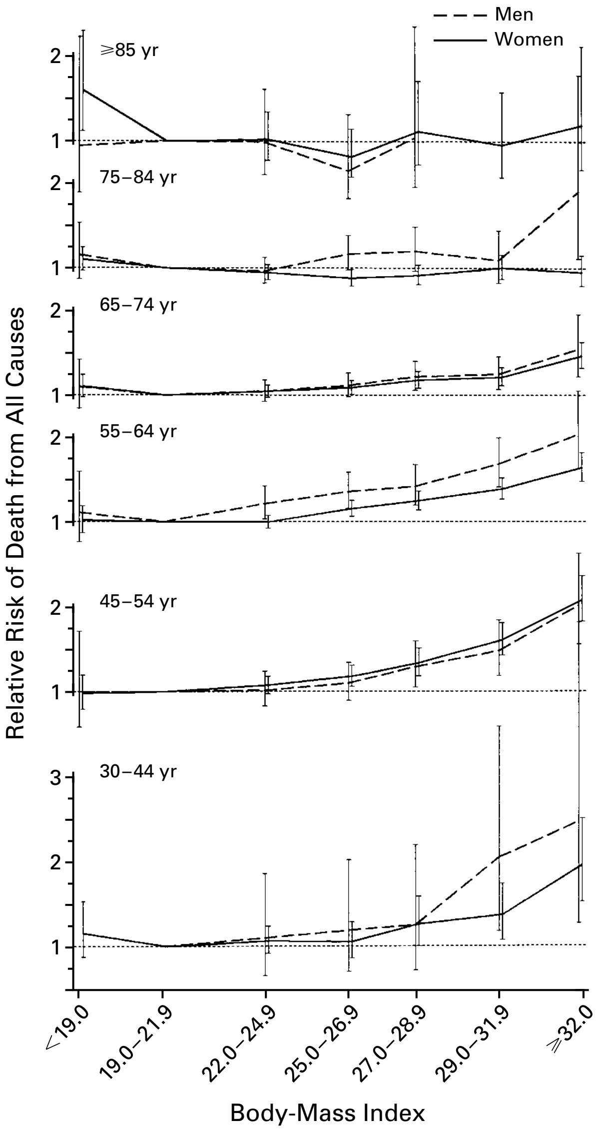

Figure 1. Relative Risk of Death from Any Cause According to Age Group and Body-Mass-Index Category among Healthy White Men and Women Who Had Never Smoked.

All relative risks were adjusted for age, education, physical activity, and alcohol consumption. The reference category was made up of subjects with body-mass indexes of 19.0 to 21.9. The bars represent 95 percent confidence limits. Relative-risk estimates are not shown for age–body-mass-index groups with five or fewer deaths.

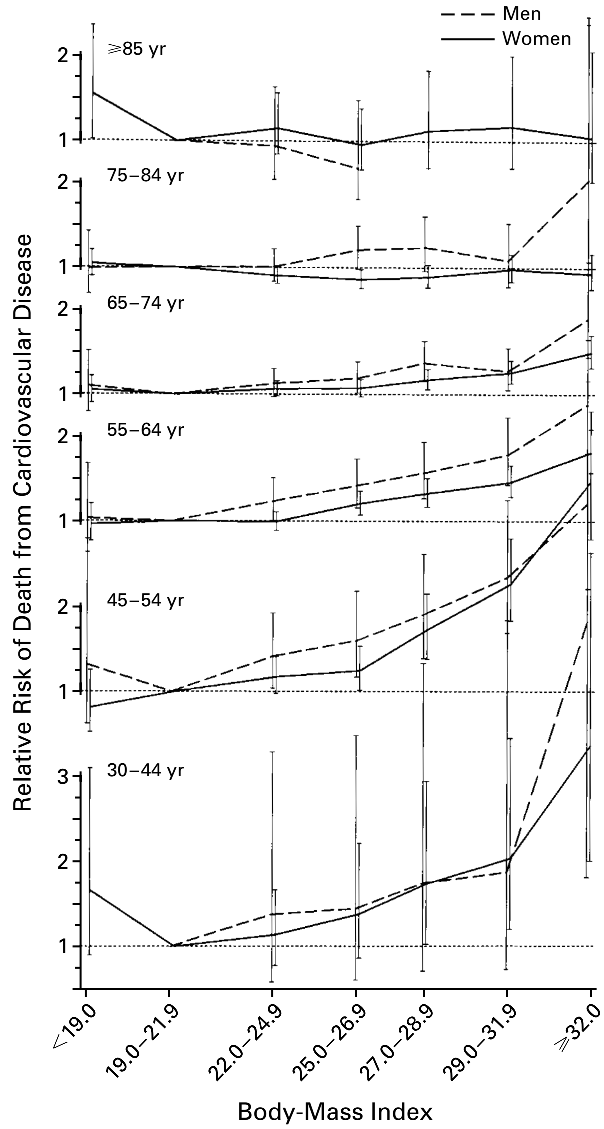

Figure 2. Relative Risk of Death from Cardiovascular Disease According to Age Group and Body-Mass-Index Category among Healthy White Men and Women Who Had Never Smoked.

All relative risks were adjusted for age, education, physical activity, and alcohol consumption. The reference category was made up of subjects with body-mass indexes of 19.0 to 21.9. The bars represent 95 percent confidence limits. Relative-risk estimates are shown for age–body-mass-index groups with five or fewer deaths.

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

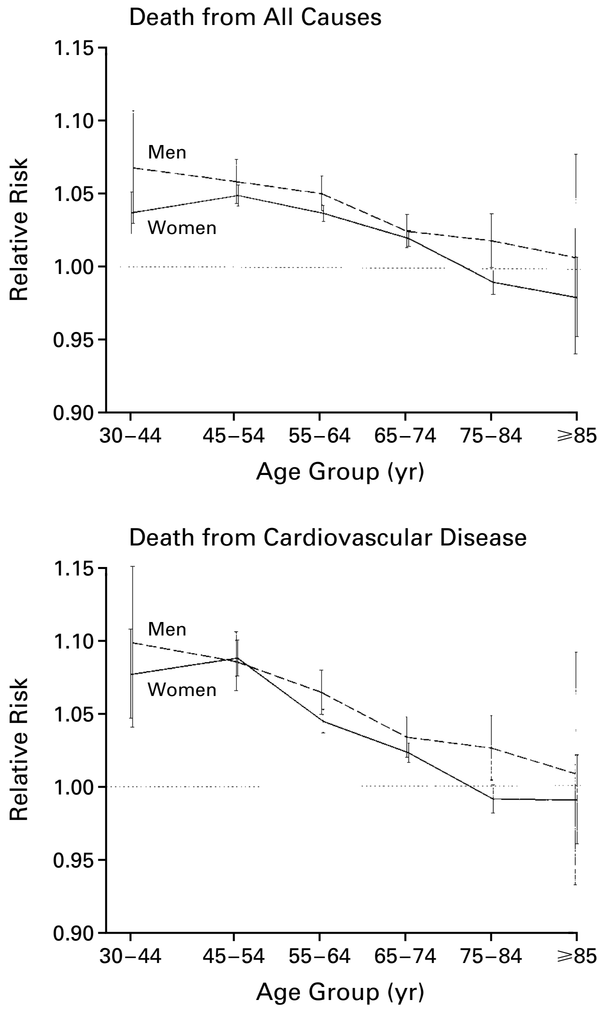

Figure 3. Relative Risk of Death from Any Cause and from Cardiovascular Disease Associated with an Increment of 1.0 in Body-Mass Index among White Men and Women Who Had Never Smoked, According to Age Group.

Relative risks are from separate models tested within the age groups, with body-mass index entered as a continuous variable. All relative risks were adjusted for age, education, physical activity, and alcohol consumption. The bars represent 95 percent confidence limits. Among men, the test for trend was significant for mortality from all causes ($P<0.01$) and for mortality from cardiovascular disease ($P<0.001$). In women, the test for trend was significant for mortality from all causes ($P<0.05$) and for mortality from cardiovascular disease ($P<0.01$).

men, body-mass index was significantly associated with mortality from all causes and from cardiovascular disease in all but the oldest age group.

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, <0.01 and <0.001, respectively). The relative risk tended to increase between the youngest two age groups among women, but overall the relative risk associated with higher levels of body-mass index also declined with age for both mortality from all causes and mortality from cardiovascular disease (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.

Table 3. Body-Mass Index (BMI) and Body Weight Associated with 20 Percent and 50 Percent Increases in Mortality from All Causes and Mortality from Cardiovascular Disease (CVD).

Group	20% Increase				50% Increase			
	Mortality from All Causes		Mortality from CVD		Mortality from All Causes		Mortality from CVD	
	BMI*	weight (lb)†	BMI*	weight (lb)†	BMI*	weight (lb)†	BMI*	weight (lb)†
70-in. men								
30–44 yr	23.8	166	22.9	160	27.2	189	25.3	177
45–54 yr	24.2	169	23.2	162	28.1	196	26.0	181
55–64 yr	24.7	172	23.9	167	29.1	203	27.5	192
65–74 yr	28.2	197	26.5	185	37.0	258	33.2	232
75–84 yr	30.5	213	28.1	196	42.1	294	36.7	256
64-in. women								
30–44 yr	26.0	152	23.5	137	32.1	187	26.5	155
45–54 yr	24.8	145	23.2	135	29.4	171	25.8	151
55–64 yr	25.9	151	25.2	147	32.0	187	30.3	177
65–74 yr	29.9	174	29.0	169	40.8	238	38.7	226

*A body-mass index of 21.0 was used as the reference value.

†For men, a height of 70 in. (178 cm) and a weight of 146.5 lb (67 kg) were used as the reference value. For women, a height of 64 in. (163 cm) and a weight of 122.5 lb (56 kg) were used as the reference value. These values correspond to a body-mass index of 21.0. Values were not estimated for men and women ≥85 years of age and for women 75 to 84 years of age, since the slopes were either negative or so small that the calculated body-mass index associated with a 20 percent increase in risk was outside the physiologic range.

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 Study[14] and Waaler's Norwegian study[15] 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 17,159 women[16] and 22,995 men[17] 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 underreport 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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