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BODY-MASS INDEX AND MORTALITY IN A PROSPECTIVE COHORT OF U.S. ADULTS

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ABSTRACT

Background Body-mass index (the weight in kilograms divided by the square of the height in meters) is known to be associated with overall mortality. We investigated the effects of age, race, sex, smoking status, and history of disease on the relation between body-mass index and mortality.

Methods In a prospective study of more than 1 million adults in the United States (457,785 men and 588,369 women), 201,622 deaths occurred during 14 years of follow-up. We examined the relation between body-mass index and the risk of death from all causes in four subgroups categorized according to smoking status and history of disease. In healthy people who had never smoked, we further examined whether the relation varied according to race, cause of death, or age. The relative risk was used to assess the relation between mortality and body-mass index.

Results The association between body-mass index and the risk of death was substantially modified by smoking status and the presence of disease. In healthy people who had never smoked, the nadir of the curve for body-mass index and mortality was found at a body-mass index of 23.5 to 24.9 in men and 22.0 to 23.4 in women. Among subjects with the highest body-mass indexes, white men and women had a relative risk of death of 2.58 and 2.00, respectively, as compared with those with a body-mass index of 23.5 to 24.9. Black men and women with the highest body-mass indexes had much lower risks of death (1.35 and 1.21), which did not differ significantly from 1.00. A high body-mass index was most predictive of death from cardiovascular disease, especially in men (relative risk, 2.90; 95 percent confidence interval, 2.37 to 3.56). Heavier men and women in all age groups had an increased risk of death.

Conclusions The risk of death from all causes, cardiovascular disease, cancer, or other diseases increases throughout the range of moderate and severe overweight for both men and women in all age groups. The risk associated with a high body-mass index is greater for whites than for blacks. (N Engl J Med 1999;341:1097-105.)

THE relation between body weight and mortality remains controversial. Important unresolved questions concern the shape of the curve relating the two variables; the optimal weight for longevity; whether the optimal weight varies according to age, race, or sex; and whether the increased death rates often observed among very lean people are causal or an artifact of leanness due to smoking or concurrent illness. Debate about the potential hazards of excessive leanness has received disproportionate attention in a culture in which obesity is far more prevalent.

Much of the vast literature examining the relation between body weight and mortality[1-16] supports the hypothesis of a curvilinear relation, in which the risk is increased among the very heavy and the very lean. However, many of the studies that found increased risk to be associated with leanness have been criticized[17,18] for failing to exclude smokers and people with concurrent illness. Several prospective studies that excluded smokers and those with existing disease have challenged the notion of a curvilinear relation, suggesting that, overall, death rates increase linearly with increasing adiposity, with no excess risk among the very lean.[8,10,12,15]

Other areas of controversy pertain to whether the optimal weight for longevity increases with age or varies according to race. Past weight guidelines have recommended a higher maximal weight (for height) with increasing age.[19] There is disagreement, however, as to whether this practice is justified[18]; the Department of Agriculture's 1995 *Dietary Guidelines for Americans*[20] did not include age-specific recommendations. Contributing to the controversy are the findings that the relative risk of death associated with adiposity decreases with increasing age[3,10,11,14,15] and

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that the optimal weight for longevity may be higher in older populations.[1,2,13] Although relatively few cohort studies have examined the effects of adiposity on mortality among blacks,[2,4,21-26] the available literature suggests that adiposity may be a less important predictor of mortality among blacks than among whites, particularly among women.

To investigate further the risk of death associated with body weight in men and women and to determine whether this risk varies according to smoking and disease status, race, cause of death, and age, we examined the association between body-mass index and death rates in a large, prospective cohort of U.S. adults.

METHODS

Study Population

The study subjects were selected from the 1,184,657 participants in the Cancer Prevention Study II, a prospective study of mortality among men and women in the United States that was begun by the American Cancer Society in 1982.[27] Participants were identified and enrolled by more than 77,000 volunteers in all 50 states, the District of Columbia, and Puerto Rico. Families were enrolled if at least one household member was 45 years of age or older, and all enrolled members were at least 30 years old. The average age of the participants at enrollment was 57 years. In 1982, the participants completed a confidential questionnaire that was mailed to them; they provided information on demographic characteristics, personal and family history of cancer and other diseases, various aspects of behavior, environmental and occupational exposures, and diet.

Deaths that occurred between the month of enrollment and December 31, 1996, were ascertained through personal inquiries by volunteers in September 1984, September 1986, and September 1988 and then through linkage with the National Death Index.[28] As of December 31, 1996, a total of 20.1 percent of the participants had died, 79.7 percent were still living, and 0.2 percent had had follow-up truncated on September 1, 1988, because of insufficient data for linkage with the National Death Index. Death certificates or codes for cause of death were obtained for 98.6 percent of all deaths.

In the questionnaire, participants were asked to give their current weight, weight one year previously, and height (without shoes). We excluded from the analysis participants with extreme values for height or weight (those at or below the 0.1 percentile and those at or above the 99.9 percentile) or for whom these values were not known. In addition, we excluded participants for whom we did not have information on race or who were not white or black. We also excluded participants for whom smoking status and prior weight were unknown. After these exclusions, 457,785 men and 588,369 women were eligible for participation in our study. A total of 113,517 men and 88,105 women in this population died during the 14 years of follow-up.

Body-Mass Index

We categorized body-mass index (the weight in kilograms divided by the square of the height in meters), which we used as our measure of adiposity, as lower than 18.5, 18.5 to 20.4, 20.5 to 21.9, 22.0 to 23.4, 23.5 to 24.9, 25.0 to 26.4, 26.5 to 27.9, 28.0 to 29.9, 30.0 to 31.9, 32.0 to 34.9, 35.0 to 39.9, and 40.0 or higher. We created these 12 categories to allow a detailed examination of the association between body-mass index and mortality across a wide range of body-mass values without a priori assumptions about the shape of the dose–response curve. In addition, combinations of these categories correspond to the cutoff points proposed by the World Health Organization for what it terms the normal range (a body-mass index between 18.5 and 24.9), grade 1 overweight (between 25.0 and 29.9), grade 2 overweight (between 30.0 and 39.9), and grade 3 overweight (40.0 or higher).[29]

End Points

Death from all causes was the primary end point in these analyses. In addition, we examined the association between body-mass index and death due to cardiovascular disease (codes 390 through 459 of the *International Classification of Diseases, Ninth Revision* [ICD-9]), cancer (ICD-9 codes 140 through 208), and all other causes.[30]

Subgroups

From the cohort of 1,046,154 men and women, we established four mutually exclusive subgroups categorized according to smoking status and history of disease — current or former smokers with a history of any of the following: cancer (but not nonmelanoma skin cancer), heart disease, stroke, respiratory disease (chronic bronchitis, emphysema, or asthma), current illness (of any type), or a weight loss of at least 10 lb (4.5 kg) in the previous year; current or former smokers with no history of disease at enrollment; those who had never smoked and who had a history of dis-

TABLE 1. COHORTS IN THE ANALYSIS OF OVERALL MORTALITY AND BODY-MASS INDEX.*

COHORT	MEN (N=457,785)	MEN WHO DIED (N=113,517)	WOMEN (N=588,369)	WOMEN WHO DIED (N=88,105)
		number		
Current or former smokers with a history of disease	123,586	48,893	95,109	22,351
Current or former smokers with no history of disease	216,788	42,925	170,979	19,313
Nonsmokers with a history of disease	33,035	9,986	104,424	23,647
Nonsmokers with no history of disease	84,376	11,713	217,857	22,794

*Nonsmokers had never smoked. Subjects with a history of disease reported one or more of the following at enrollment: cancer (except nonmelanoma skin cancer), heart disease, stroke, respiratory disease (chronic bronchitis, emphysema, or asthma), current illness (of any type), or a weight loss of at least 10 lb (4.5 kg) in the previous year.

ease at enrollment; and those who had never smoked and who had no history of disease at enrollment (Table 1). For each of the four subgroups, we examined the association between body-mass index and overall mortality according to sex.

In the 81,468 white men, 2908 black men, 208,710 white women, and 9147 black women who had never smoked and had no disease, we further examined whether the association between body-mass index and mortality varied according to race, cause of death, or age. For these analyses, we combined categories of body-mass index, if necessary, to avoid having fewer than 15 deaths in a category.

Statistical Analysis

We calculated age-adjusted death rates for each category of body-mass index and standardized these rates to the age distribution of the entire male or female study population. We computed summary rate ratios (the death rate in a category of body-mass index divided by the corresponding rate in the reference category [body-mass indexes between 23.5 and 24.9]) and the rate differences (the death rate in a category minus that in the reference category); we used approximate variance formulas to calculate 95 percent confidence intervals.[31]

We also used a Cox proportional-hazards model[32] to compute relative risk and to adjust for other potential risk factors reported at base line. We adjusted Cox models for exact age at enrollment, level of education and physical activity, alcohol use, marital status, current use of aspirin, a crude index of fat consumption,[33] vegetable consumption, and (in women) use of estrogen-replacement therapy. All relative risks are from the multivariate Cox models unless otherwise noted.

RESULTS

Effect of Smoking Status and History of Disease

The relation between body-mass index and death from all causes differed according to smoking status and the presence or absence of a history of disease (Fig. 1). Obesity was most strongly associated with an increased risk of death among those who had never smoked and who had no history of disease, whereas leanness was most strongly associated with an increased risk of death among current or former smokers with a history of disease. For current or former smokers with no history of disease and for those who had never smoked and who had a history of disease, the pattern was intermediate.

The absolute risk of death varied substantially among these four subgroups. The age-standardized rates of death from all causes were lowest among those who had never smoked and who had no history of disease (at a body-mass index between 23.5 and 24.9, there were 962 deaths per 100,000 men per year and 682 deaths per 100,000 women per year), highest among current or former smokers with a history of disease (2896 deaths per 100,000 men per year and 1796 deaths per 100,000 women per year), and intermediate among those who were current or former smokers with no history of disease (1559 deaths per 100,000 men per year and 1023 deaths per 100,000 women per year) or those who had never smoked and who had a history of disease (1819 deaths per 100,000 men per year and 1266 deaths per 100,000 women per year).

Among subjects who had never smoked and who had no history of disease, the highest mortality rates were among the heaviest men (relative risk, 2.68; 95 percent confidence interval, 1.76 to 4.08) and women (relative risk, 1.89; 95 percent confidence interval, 1.62 to 2.21). There were much smaller increases in risk among the leanest men (relative risk, 1.28; 95 percent confidence interval, 1.04 to 1.58) and women (relative risk, 1.36; 95 percent confidence interval, 1.26 to 1.48). The nadir of the curve of body-mass index and mortality was at a body-mass index between 23.5 and 24.9 in men and 22.0 and 23.4 in women. Relative risks were not significantly different from 1.00 for the range of body-mass index between 22.0 and 26.4 in men and 20.5 and 24.9 in women.

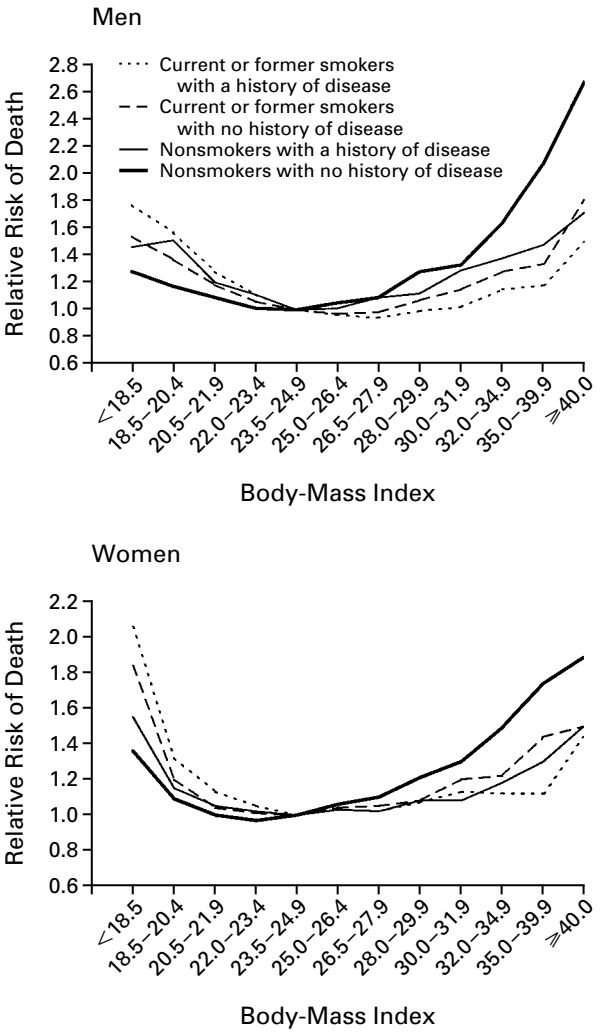

Figure 1. Multivariate Relative Risk of Death from All Causes among Men and Women According to Body-Mass Index, Smoking Status, and Disease Status.

The four subgroups are mutually exclusive. Nonsmokers had never smoked. The reference category was made up of subjects with a body-mass index of 23.5 to 24.9.

TABLE 2. RATES AND RELATIVE RISKS OF DEATH FROM ALL CAUSES AMONG SUBJECTS WHO HAD NEVER SMOKED AND WHO HAD NO HISTORY OF DISEASE, ACCORDING TO BODY-MASS INDEX, RACE, AND SEX.*

GROUP	BODY-MASS INDEX											
	<18.5	18.5–20.4	20.5–21.9	22.0–23.4	23.5–24.9	25.0–26.4	26.5–27.9	28.0–29.9	30.0–31.9	32.0–34.9	35.0–39.9	≥40.0
White men												
No. of deaths	93	305	734	1,523	2,085	2,250	1,738	1,338	592	398	153	19
Person-yr of follow-up	5,438	19,847	61,863	148,107	216,788	239,158	181,735	125,967	56,682	32,878	11,079	1,315
Age-standardized rate†	1,270	1,133	1,022	953	956	1,007	1,058	1,255	1,300	1,619	2,076	2,065
Multivariate RR‡	1.26	1.19	1.09	1.01	1.00§	1.04	1.09	1.28	1.32	1.66	2.17	2.58
95% CI	1.02–1.56	1.05–1.34	1.00–1.18	0.94–1.07	—	0.98–1.10	1.02–1.16	1.19–1.37	1.21–1.45	1.49–1.85	1.84–2.56	1.64–4.06
White women												
No. of deaths	680	2,054	3,003	3,344	3,133	2,522	2,173	1,913	1,225	953	462	144
Person-yr of follow-up	55,362	314,575	495,542	507,570	422,903	302,692	261,253	215,245	130,432	95,505	48,414	14,372
Age-standardized rate†	923	732	671	653	673	727	755	837	908	1,083	1,216	1,399
Multivariate RR‡	1.36	1.10	1.00	0.97	1.00§	1.07	1.10	1.21	1.30	1.53	1.76	2.00
95% CI	1.25–1.48	1.04–1.16	0.95–1.05	0.93–1.02	—	1.01–1.13	1.04–1.17	1.14–1.28	1.22–1.39	1.42–1.65	1.60–1.94	1.69–2.36
			≤21.9	22.0–23.4	23.5–24.9	25.0–26.4	26.5–27.9	28.0–29.9	30.0–31.9	≥32.0		
Black men												
No. of deaths			36	51	63	87	78	87	46	37		
Person-yr of follow-up			2,704	3,752	5,866	6,455	6,661	6,311	3,515	3,339		
Age-standardized rate†			1,568	1,273	1,169	1,447	1,402	1,511	1,601	1,632		
Multivariate RR‡			1.25	1.02	1.00§	1.20	1.13	1.28	1.29	1.35		
95% CI			0.81–1.94	0.69–1.52	—	0.86–1.68	0.81–1.59	0.92–1.79	0.87–1.90	0.89–2.06		
	<18.5	18.5–20.4	20.5–21.9	22.0–23.4	23.5–24.9	25.0–26.4	26.5–27.9	28.0–29.9	30.0–31.9	32.0–34.9	35.0–39.9	≥40.0
Black women												
No. of deaths	25	53	86	109	143	128	158	167	139	91	64	25
Person-yr of follow-up	1,424	5,350	9,489	14,498	15,628	14,905	16,170	16,258	11,730	9,978	5,606	2,449
Age-standardized rate†	1,182	1,078	937	854	959	853	935	1,041	1,155	1,009	1,340	1,216
Multivariate RR‡	1.66	1.07	1.05	0.92	1.00§	0.90	0.97	1.08	1.17	1.02	1.29	1.21
95% CI	1.07–2.58	0.77–1.48	0.80–1.38	0.72–1.19	—	0.71–1.15	0.77–1.22	0.86–1.35	0.92–1.48	0.78–1.33	0.95–1.74	0.78–1.86

*At enrollment the subjects had no history of the following: cancer (except nonmelanoma skin cancer), heart disease, stroke, respiratory disease (chronic bronchitis, emphysema, or asthma), current illness (of any type), or a weight loss of at least 10 lb in the previous year. RR denotes relative risk, and CI confidence interval.

†The rate is per 100,000 person-years, directly standardized to the age distribution of the entire male or female study population.

‡The Cox proportional-hazards model was used, with adjustment for age, level of education, physical activity, alcohol use, marital status, aspirin use, fat consumption, vegetable consumption, and use of estrogen-replacement therapy (in women).

§The reference category was made up of subjects with a body-mass index of 23.5 to 24.9.

Effect of Race

Among subjects who had never smoked and who had no history of disease the association between a high body-mass index and an increased risk of death from all causes was stronger in whites than in blacks (Table 2). At the highest level of body-mass index, white men and women had relative risks of 2.58 and 2.00, respectively. In contrast, the association between a high body-mass index and an increased risk of death appeared more moderate among black men (relative risk, 1.35; 95 percent confidence interval, 0.89 to 2.06). However, the small numbers of deaths among black men limited our analysis of risk at very high levels of body-mass index. In black women, a small (20 to 30 percent) increase in risk was found only at the highest levels of body-mass index (35.0 or higher), and it was not statistically significant. Extreme leanness was associated with some increase in overall mortality in all subgroups (Table 2).

Effect of Cause of Death

The shape of the mortality curve differed according to the cause of death among subjects who had never smoked and who had no history of disease (Fig. 2). The relation between body-mass index and the risk of death from cancer was positive and showed no elevation in risk among the leanest persons. The curve for the risk of death from cardiovascular disease was J-shaped; for the risk of death from all other causes, the curve was U-shaped. The J-shaped and U-shaped curves were explained primarily by an increased risk of death among lean men and women as a result of cerebrovascular disease, pneumonia, and diseases of the central nervous system (data not shown). A high body-mass index was most predictive of death from cardiovascular disease, especially in men (relative risk, 2.90; 95 percent confidence interval, 2.37 to 3.56). Significantly increased risks of death from cardiovascular disease were found at all body-mass indexes of more than 25.0 in women and 26.5 in men.

Effect of Age

A high body-mass index was associated with increased risk of death from all causes at all ages among both men and women who had never smoked and who had no history of disease (Table 3). Although the relative increase in risk associated with a high body-mass index declined with increasing age (to a 50 percent increase in men 75 years of age or older and to a 40 to 50 percent increase in women 75 or older), the absolute increase in death rates associated with a high body-mass index was greatest in elderly men and women. The excess risk for the heaviest men and women who were 75 or older, expressed as the difference in rates, was 2230 deaths per 100,000 men per year and 1652 deaths per 100,000 women per year. The nadir of the curve was within the range of body-mass index from 20.5 to 24.9 for all six groups categorized according to age and sex.

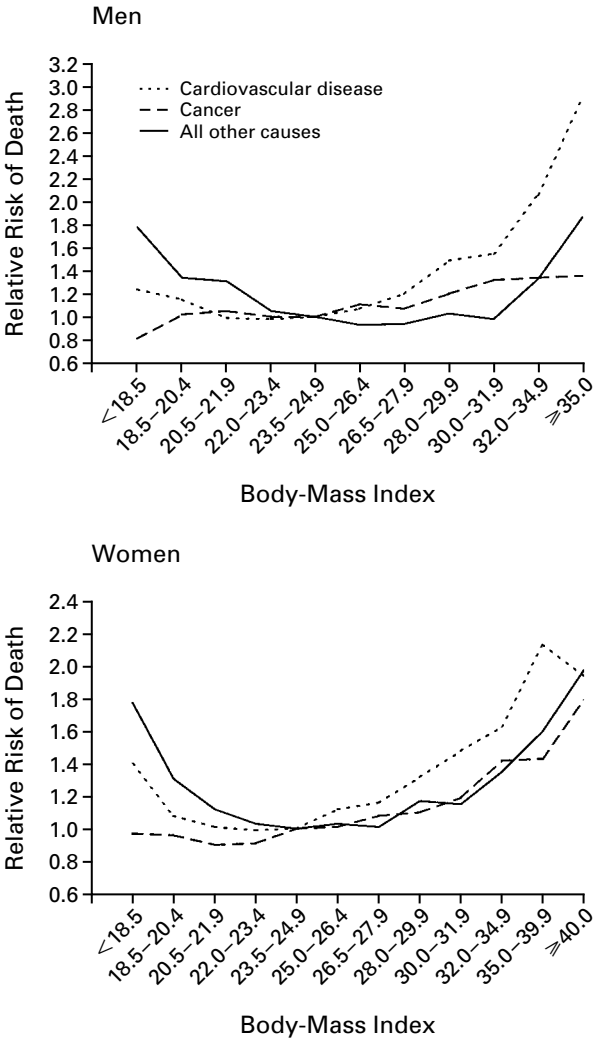

Figure 2. Multivariate Relative Risk of Death from Cardiovascular Disease, Cancer, and All Other Causes among Men and Women Who Had Never Smoked and Who Had No History of Disease at Enrollment, According to Body-Mass Index.

The reference category was made up of subjects with a body-mass index of 23.5 to 24.9.

DISCUSSION

In this large, prospective study, the lowest rates of death from all causes were found at body-mass indexes between 23.5 and 24.9 in men and 22.0 and 23.4 in women; relative risks were not significantly elevated for the range of body-mass indexes between 22.0 and 26.4 in men and 20.5 and 24.9 in women. Death rates increased throughout the range of moderate and severe overweight for both men and women, but less so for blacks, particularly black women. The

TABLE 3. RATES AND RELATIVE RISKS OF DEATH FROM ALL CAUSES AMONG SUBJECTS WHO HAD NEVER SMOKED AND WHO HAD NO HISTORY OF DISEASE, ACCORDING TO BODY-MASS INDEX, SEX, AND AGE.*

GROUP	BODY-MASS INDEX										
	<20.5	20.5–21.9	22.0–23.4	23.5–24.9	25.0–26.4	26.5–27.9	28.0–29.9	30.0–31.9	32.0–34.9	≥35.0	
Men											
Age 30–64 yr											
No. of deaths	43	106	212	306	417	322	289	157	124	56	
Age-standardized rate†	348	325	263	250	301	296	367	432	557	659	
Multivariate RR‡	1.34	1.27	1.06	1.00§	1.19	1.15	1.41	1.62	2.05	2.30	
95% CI	0.97–1.84	1.02–1.58	0.89–1.26	—	1.02–1.38	0.98–1.34	1.20–1.65	1.34–1.97	1.66–2.53	1.72–3.06	
Age 65–74 yr											
No. of deaths	77	135	356	568	661	562	473	222	152	80	
Age-standardized rate†	1089	816	854	898	941	1038	1270	1370	1798	2767	
Multivariate RR‡	1.21	0.90	0.96	1.00§	1.04	1.12	1.34	1.42	1.85	2.75	
95% CI	0.95–1.53	0.74–1.08	0.84–1.09	—	0.93–1.16	1.00–1.26	1.19–1.52	1.22–1.66	1.54–2.22	2.17–3.49	
Age ≥75 yr											
No. of deaths	289	518	1006	1274	1259	932	663	259	146	49	
Age-standardized rate†	4564	4344	3956	3924	4024	4206	4840	4687	5393	6154	
Multivariate RR‡	1.16	1.12	1.01	1.00§	1.01	1.06	1.21	1.16	1.31	1.53	
95% CI	1.02–1.32	1.01–1.24	0.93–1.09	—	0.94–1.09	0.97–1.15	1.10–1.33	1.01–1.32	1.10–1.55	1.15–2.04	

	<18.5	18.5–20.4	20.5–21.9	22.0–23.4	23.5–24.9	25.0–26.4	26.5–27.9	28.0–29.9	30.0–31.9	32.0–34.9	35.0–39.9	≥40.0
Women												
Age 30–64 yr												
No. of deaths	70	337	490	489	394	362	329	282	201	165	112	54
Age-standardized rate†	232	177	161	163	163	217	221	224	257	268	335	513
Multivariate RR‡	1.44	1.07	0.99	1.00	1.00§	1.31	1.33	1.33	1.51	1.53	1.86	2.70
95% CI	1.11–1.85	0.93–1.24	0.87–1.13	0.88–1.14	—	1.14–1.51	1.15–1.54	1.14–1.55	1.28–1.79	1.27–1.84	1.51–2.30	2.03–3.60
Age 65–74 yr												
No. of deaths	79	369	614	714	772	595	557	580	367	338	180	51
Age-standardized rate†	594	531	503	498	595	598	636	796	836	1111	1299	1434
Multivariate RR‡	0.99	0.91	0.86	0.84	1.00§	0.99	1.04	1.28	1.32	1.71	1.99	2.09
95% CI	0.78–1.25	0.80–1.03	0.77–0.96	0.76–0.93	—	0.89–1.10	0.94–1.16	1.15–1.43	1.17–1.50	1.51–1.95	1.69–2.34	1.57–2.78
Age ≥75 yr												
No. of deaths	556	1401	1985	2250	2110	1693	1445	1218	796	541	234	64
Age-standardized rate†	4051	3124	2848	2732	2711	2837	2960	3209	3514	3939	4348	4363
Multivariate RR‡	1.44	1.16	1.06	1.01	1.00§	1.04	1.07	1.15	1.25	1.36	1.53	1.41
95% CI	1.31–1.58	1.09–1.25	1.00–1.13	0.96–1.08	—	0.97–1.10	1.00–1.15	1.07–1.23	1.15–1.35	1.23–1.49	1.33–1.75	1.10–1.81

*The subjects had no history of the following conditions: cancer (except nonmelanoma skin cancer), heart disease, stroke, respiratory disease (chronic bronchitis, emphysema, or asthma), current illness (of any type), or a weight loss of at least 10 lb in the previous year. RR denotes relative risk, and CI confidence interval.

†The rate is per 100,000 person-years, directly standardized within the specified age range of the male or female study population.

‡The Cox proportional-hazards model was used, with adjustment for age, level of education, physical activity, alcohol use, marital status, aspirin use, fat consumption, vegetable consumption, and use of estrogen-replacement therapy (in women).

§The reference category was made up of subjects with a body-mass index of 23.5 to 24.9.

risk of death increased with an increasing body-mass index in all age groups and for all categories of causes of death.

As expected,[17] the shape and magnitude of the association between body-mass index and mortality were substantially modified by a history of both smoking and disease, factors that are predictive of leanness and poor survival. Limiting the primary analyses to subjects who had never smoked and who had no history of disease at enrollment greatly reduced the apparent elevation in the risk of death among lean persons, increased the risk among heavy persons, and shifted downward the body-mass index level associated with the lowest risk of death. Among current or former smokers with a history of disease, the prospective effect of body-mass index on the risk of illness and death cannot be separated from the effect of smoking and disease on the body-mass index. Public health recommendations regarding optimal body-mass index are therefore most valid when they are based on studies of healthy persons who have never smoked.

We found, as did previous studies,[2,21-24,26] that obesity was least strongly associated with the risk of death from any cause among black women. Among black women, we found a small (approximately 20 to 30 percent) increase in risk for those with a body-mass index of 35.0 or higher, in contrast to the risk among the heaviest white women, which was increased by approximately 75 to 100 percent. Although black women tend to have a relatively central and abdominal distribution of body fat as compared with white women,[21,34] some evidence suggests that the central distribution of fat in black women may have a weaker effect on atherogenic risk factors such as levels of cholesterol, triglycerides, and sex hormone–binding globulin and degree of peripheral insulin resistance.[34] Our findings in black men parallel the findings of other studies[2,21,26] in showing moderate (approximately 20 to 35 percent) increases in mortality at body-mass index levels of 25.0 or higher. However, there were insufficient numbers of black men in our cohort who had a body-mass index of 32.0 or higher for us to evaluate the effect of extreme adiposity in these men.

The cause of death modified the relation between body-mass index and the risk of death in both men and women. The heaviest men and women had a 40 to 80 percent increase in the risk of dying from cancer, and there was no evidence of an increased risk among the leanest subjects, findings consistent with the results of studies in animals that showed that dietary restriction can dramatically decrease the incidence of tumors and the rate of tumor growth.[35] In contrast to the fairly linear relation found in the risk of death from cancer, a curvilinear relation was found for the risks of death from cardiovascular disease and death from other causes. These findings were explained primarily by an increased risk of death among lean men and women as a result of cerebrovascular disease, pneumonia, and diseases of the central nervous system. In other prospective studies, leanness has been associated with an increased risk of respiratory disease[14] and cerebrovascular disease.[14,36]

A high body-mass index was associated with higher rates of death from all causes among both men and women in all age groups, including those 75 years or older. Although the relative risk of death declined with increasing age, the absolute risk of death associated with adiposity increased substantially with increasing age and was highest in the oldest age groups. These age-specific findings are similar to the recently published results of an earlier study of an American Cancer Society cohort, the Cancer Prevention Study I.[15] When we used either absolute or relative measures of risk, our data indicated that heavier men and women have an increased risk of death at all ages. The optimal body-mass index for longevity fell between 20.5 and 24.9 for men and women of all ages. These data offer support for the use of a single recommended range of body weight throughout life.

Despite our best efforts to control for bias from antecedent disease, it is likely that we were unable to eliminate such bias completely. Thus, the increased risk of death from specific causes that was associated with leanness in this and other studies may reflect preexisting, but unrecognized, disease processes, even after careful exclusions have been made. Also, although we had information on recent weight loss, we were unable to control for long-term weight loss. Several investigators have suggested that there is an association between illness-related weight loss over a period of many years and the subsequent risk of death in very thin persons and that controlling for recent weight loss may be insufficient.[3,13]

Although an understanding of the risk associated with leanness is of scientific interest, in terms of public health, of greater concern is the excess risk of death due to obesity. Nearly one third (32.6 percent) of adults in the United States meet the World Health Organization's definition of grade 1 overweight (a body-mass index between 25.0 and 29.9), and 22.3 percent meet the criteria for grade 2 and grade 3 overweight (a body-mass index of 30.0 or higher).[37] In contrast, only 7.7 percent of adults in the United States have a body-mass index lower than 20.0, and only 1.5 percent have a body-mass index lower than 18.0.[37]

The measure of adiposity that we used in our study has several limitations. We used self-reported weight and height at enrollment to calculate body-mass index, a widely used[37] index of weight adjusted for height. Although self-reported weight and height are highly correlated with measured weight and height,[38] a small, generally systematic, error exists — an overestimation of height and an underestimation of weight, especially at higher weights.[38] Thus, our measure of

body-mass index probably underestimated the true body-mass index of overweight persons (e.g., a body-mass index of 27 calculated from self-reported weight and height is likely to have been closer to a true value of 28). We had no direct measure of adiposity or of lean body mass, and we had no measure of central adiposity, such as the ratio of waist circumference to hip circumference. Although the body-mass index is highly correlated with more direct measures of body fat in most populations,[39] it may be a less useful indicator of adiposity among the elderly, who tend to have a shift of fat from peripheral to central sites with a concomitant increase in waist-to-hip ratio but no increase in body-mass index.[40] Folsom et al.[5] found the waist-to-hip ratio to be a better predictor of the risk of death than the body-mass index in a prospective cohort of older women in Iowa.

The large size of our cohort allowed us to follow, for a 14-year period, more than 300,000 apparently healthy people who had never smoked and to investigate the relation between body-mass index and the risk of death across a wide range of body-mass–index values and according to age, race, sex, and cause of death. In addition, we were able to control for other potential confounders of the relation.

In summary, our findings support the well-established increase in the risk of death associated with severe overweight as well as a gradient of increasing risk associated with moderate overweight. The consistency of our findings in men and women and in all age groups also argues for the use of a single recommended range of body weight throughout life.

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