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ORIGINAL ARTICLE

Body mass index and all-cause mortality in a nationwide US cohort

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Objective: To investigate whether the nature of the relationship between body mass index (BMI (kg/m^2)) and all-cause mortality is direct, J- or U-shaped, and whether this relationship changes as people age.
Design: Prospective nationwide cohort study of US radiologic technologists (USRT).
Subjects: Sixty-four thousand seven hundred and thirty-three female and 19 011 male certified radiation technologists.
Methods: We prospectively followed participants from the USRT study who completed a mail survey in 1983–1989 through 2000. During an average of 14.7 years of follow-up or 1.23 million person-years, 2278 women and 1495 men died. Using Cox's proportional-hazards regression analyses, we analyzed the relationship between BMI and all-cause mortality by gender and by age group (<55 years; ⩾55 years). We also examined risk in never-smokers after the first 5 years of follow-up to limit bias owing to the confounding effects of smoking and illness-related weight loss on BMI and mortality.
Results: Risks were generally J-shaped for both genders and age groups. When we excluded smokers and the first 5 year of follow-up, risks were substantially reduced in those with low BMIs. In never-smoking women under the age of 55 years (excluding the initial 5-year follow-up period), risk rose as BMI increased above 21.0 kg/m^2, whereas in older women, risk increased beginning at a higher BMI (⩾25.0 kg/m^2). Among younger men who never smoked (excluding the initial 5-year follow-up period), risk began to rise above a BMI of 23.0 kg/m^2, whereas in older men, risk did not begin to increase until exceeding a BMI of 30.0 kg/m^2.
Conclusions: In younger/middle-aged, but not older, women and men, mortality risks appear directly related to BMI. The more complicated relationship between BMI and mortality in older subjects suggests the importance of assessing whether other markers of body composition better explain mortality risk in older adults.
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Keywords: body mass index; mortality; age factors; smoking; risk factors; prospective studies

Introduction

In recent years, many prospective epidemiologic studies have evaluated the relationship between mortality and body mass index (BMI) (weight adjusted for height (kg/m^2)),[1–20] which is commonly considered a surrogate for body fat. Study findings vary as to whether the relationship is best described as direct, J- or U-shaped, the latter two characterizations suggesting higher risks among both heavier and leaner individuals. Moreover, results are inconsistent as to whether the relationship between BMI and mortality changes as people age.

Some of the divergent findings may reflect inherent difficulties with observational studies. Principal among them are the confounding effects of smoking behavior and serious illness, both of which are associated with higher mortality and lower BMI.[21,22] Thus, a low BMI may reflect a healthy lifestyle (i.e., balanced caloric intake and physical activity), as well as smoking or illness. Understanding the effects of BMI on mortality may require taking into account tobacco use and the potential effects of weight loss owing to existing illnesses.[21,22]

Only a few large studies have assessed BMI and longevity among never-smokers who do not have serious medical conditions at baseline and have survived some period beyond baseline to account for illness-related weight loss.[10,14] The US Radiologic Technologists (USRT) study

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population assessed here is a large cohort that draws male and female medical radiation workers from all 50 states, who have provided baseline information related to smoking behavior and health status, and have been followed for an average of 14.7 years. In this analysis, we examined prospectively (1983–2000) the association between BMI and mortality from all causes in women and in men of all ages combined (22–92 years), in two broad age groups, and in black subjects separately.

Methods

Study population

The USRT study, an ongoing collaboration of the US National Cancer Institute, University of Minnesota, and the American Registry of Radiologic Technologists (ARRT) has followed up a nationwide cohort of 146 022 radiologic technologists residing in the United States and certified by ARRT for at least 2 years between 1926 and 1980. Detailed information on the methods has been provided elsewhere.[23,24]

Briefly, during 1983–1989, all subjects located alive ($n=132\,519$) were mailed a baseline questionnaire, which collected self-reported information on weight, height, education, smoking and alcohol behavior, as well as work history, demographic, reproductive and medical history, and other personal information. The evaluation of mortality risk was limited to subjects who responded to the first questionnaire (1983–1989), were cancer free (except for non-melanoma skin cancer) and reported no history of myocardial infarction at baseline to limit confounding owing to illness ($n=86\,059$, after excluding 4218 with prior cancer/myocardial infarction). We also excluded less than 3% ($n=2315$) of participants who reported insufficient information to calculate a BMI. The final study population included 64 733 women and 19 011 men, a total of 83 744 subjects. Eligible cases were those who died as reported by the Social Security Death Mortality File or the National Death Index (NDI-Plus) before December 31, 2000. This study was approved by the Institutional Review Boards of the National Cancer Institute and the University of Minnesota.

Risk factors

Public health guidelines refer to a BMI between 18.5 and 24.9 kg/m^2 as normal, between 25.0 and 29.9 kg/m^2 as overweight and $\geqslant 30.0\,kg/m^2$ as obese.[25,26] A BMI below 18.5 kg/m^2 is referred to as 'underweight'. In this study, BMI was calculated from self-reported weight and height, with eight categories, in which the lowest ($<18.5\,kg/m^2$) covers levels considered 'underweight', the next three categories (18.5–20.9, 21.0–22.9 and 23.0–24.9 kg/m^2) comprise the range of a normal BMI, the following two (25.0–26.9 and 27.0–29.9 kg/m^2) span the indices characterized as overweight and the highest two (30.0–34.9 and $\geqslant 35\,kg/m^2$) reflect obesity. Race groupings were white, black and other/unknown. We assessed educational attainment as radiation technology program (2 years), one or more years of college/graduate school and other. For smoking history, we summarized smoking levels using duration, categorized in groups: never-smoker; <10 years; 10–19 years; 20–29 years; and 30+ years. Alcohol consumption was assessed from responses to a question about levels of current consumption: '[h]ow many drinks of alcoholic beverage (beer, wine, or liquor) do you usually have in a typical week?' with grouped responses as 0, <1–6, 7–14 and >14 drinks/week.

Statistical analyses

Participants were followed from the return date of the baseline questionnaire until death or December 31, 2000, whichever occurred first. We used Cox's proportional-hazards regression analyses to compute relative risks (RRs) with 95% confidence intervals (CIs), using age (beginning at completion of the first questionnaire) as the time scale,[27] and stratifying at baseline for birth cohort in 5-year intervals to control for secular trends. In all analyses, a BMI of 21.0–22.9 kg/m^2, the middle category within the normal range, was selected as the referent category. Missing information was coded to unknown in separate variables.

In multivariate models, we included established factors related to mortality risk, including education, race, and smoking and alcohol behavior, as reported on the baseline questionnaire. To avoid confounding by smoking behavior more completely, we also assessed risk among subjects who reported they had never smoked as of the baseline questionnaire. Subjects were characterized as 'never' having smoked, if they reported smoking fewer than 100 cigarettes in their lifetime. In addition, to reduce the confounding effect of weight loss at baseline owing to ill health, we also separately examined the effects of BMI in never-smokers by excluding deaths that occurred in the first 5 years of follow-up. We did not include occupational radiation exposure in the model because the surrogate for historic ionizing radiation exposure that we have found most consistently related to specific cancers and cardiovascular disease, year first worked as a radiation technologist, was not associated with all-cause mortality risk.

To evaluate the effects of age on risk associated with BMI, we examined risk among women and men stratified by a commonly used cut-point for age, under the age of 55 years, and aged 55 years and older at baseline,[6,10,11,14] and separately in these age groups, among never-smokers who had survived 5 years of follow-up. We assessed the assumption of hazard proportionality within the two age groups and found no interaction between age and BMI in either men or women within the two age groups, thus limiting the need for further subgroup analysis. Presenting the results by these age groups also allows comparison with results from many other studies. We also assessed separately the relationship between BMI and mortality in black subjects.

Results

Most of the participants in the study were under the age of 55 years at the beginning of follow-up (94% of women and 88% of men) (Table 1). More than three-fourths of study participants are women, and less than 40% of women and 60% of men attended college. The large majority is white, with fewer than 4 and 10% of women and men, respectively, identifying themselves as belonging to other racial/ethnic groups. During an average of 14.7 years of follow-up or 1.23 million person-years, 2278 women and 1495 men died.

Mortality risks of women

In the multivariate analysis of all women (Table 2), risk was J-shaped, that is, lowest and similar across the range of normal BMIs (18.5–24.9 kg/m^2), but elevated in those who were 'underweight' as well as those overweight or obese. When we restricted the analysis to never-smoking women, the relationship between BMI and mortality remained J-shaped, with similar risks spanning the normal weight range. When we examined risk separately in never-smoking women beyond the first 5 years of follow-up, we observed a more direct relationship between BMI and mortality, with the lowest risk at the lean end of the normal weight spectrum (BMI = 18.5–20.9 kg/m^2), and only marginally higher risks among the 'underweight'.

In black women, we found that mortality risks were generally somewhat higher than in the total group of women. The multivariate RRs of death according to BMI categories, using the same groupings and reference level for BMI as indicated in Table 2, were: 1.75 (95% CI = 0.45–6.84),

Table 1 Baseline selected demographic and other characteristics in the USRT study cohort[a]

Characteristics	*Female deaths*		*Female study population*		*Male deaths*		*Male study population*	
	No. = 2278	*%*	*No. = 64 733*	*%*	*No. = 1495*	*%*	*No. = 19 011*	*%*
Age at baseline (years)[b]								
<35	264	11.6	31 031	47.9	156	10.4	6724	35.4
35–44	436	19.1	21 546	33.3	285	19.1	7093	37.3
45–54	498	21.9	8165	12.6	288	19.3	2978	15.7
55–64	397	17.4	2579	4.0	400	26.8	1541	8.1
65+	683	30.0	1412	2.2	366	24.5	675	3.6
Race								
White	2155	94.6	62 277	96.2	1335	89.3	17 200	90.5
Black	74	3.3	1461	2.3	74	5.0	725	3.8
Other/unknown	49	2.1	995	1.5	86	5.8	1086	5.7
Education[c]								
Radiation Technology Program (2 years)	1150	50.5	38 602	59.6	465	31.1	6008	31.6
⩾1 years college/graduate school	840	36.9	22 488	34.7	770	51.5	11 376	59.8
Other/unknown	288	12.6	3643	5.6	260	17.4	1627	8.6
Residence at baseline								
Northeast	491	21.6	16 919	26.1	327	21.9	4024	21.2
South	597	26.2	16 183	25.0	430	28.8	5436	28.6
Midwest	663	29.1	20 738	32.0	341	22.8	5089	26.8
West	527	23.1	10 880	16.8	395	26.4	4459	23.5
Unknown	0	0	13	<0.1	2	0.1	3	<0.1
Smoking duration (years)								
Never-smoker	850	37.3	32 749	50.6	365	24.4	7293	38.4
<10	147	6.5	9319	14.4	103	6.9	2462	13.0
10–19	277	12.2	13 061	20.2	220	14.7	4501	23.7
20–29	322	14.1	6169	9.5	234	15.7	2681	14.1
30+	613	26.9	2677	4.1	518	34.7	1673	8.8
Unknown (smoking status or years)	69	3.0	689	1.1	55	3.7	346	1.8
Alcohol intake (drinks/week)								
0	617	27.1	11 235	17.4	355	23.8	3569	18.8
<1–6	1303	57.2	47 557	73.5	790	52.8	11 826	62.2
7–14	278	12.2	4900	7.6	239	16.0	2614	13.8
>14	54	2.4	656	1.0	104	7.0	876	4.6
Unknown	26	1.1	359	0.6	7	0.5	119	0.6

[a]Restricted to respondents to first survey (baseline) questionnaire who at baseline were cancer free (other than non-melanoma skin cancer) and reported never having had a myocardial infarction. [b]As of the time subjects responded to the first questionnaire (1983–1989). [c]Subjects were placed in the 'highest' educational category applicable, with college ranked after radiological training.

Table 2 RR of all-cause mortality by BMI in women and men[a]

	BMI (kg/m²)							
	<18.5	18.5–20.9	21.0–22.9	23.0–24.9	25.0–26.9	27.0–29.9	30.0–34.9	35.0+
All women (median age = 35 at baseline)								
No. of women	2813	19 447	16 734	10 808	5740	4694	3012	1245
No. of deaths	133	472	494	417	261	261	154	86
RR	1.64	1.09	1.0	1.03	1.15	1.38	1.25	2.10
95% CI	1.35–1.98	0.96–1.24	—	0.90–1.18	0.99–1.34	1.18–1.60	1.04–1.50	1.67–2.65
Women who never smoked								
No. of deaths	43	163	180	156	109	105	59	35
RR	1.55	0.99	1.0	1.02	1.30	1.36	1.10	2.14
95% CI	1.10–2.17	0.80–1.23	—	0.82–1.26	1.02–1.65	1.07–1.74	0.82–1.49	1.48–3.09
Women who never smoked and excluding first 5 years of follow-up								
No. of deaths	25	132	155	131	93	93	50	33
RR	1.05	0.94	1.0	1.00	1.30	1.40	1.07	2.37
95% CI	0.68–1.61	0.74–1.19	—	0.79–1.26	1.00–1.69	1.08–1.82	0.77–1.47	1.62–3.48
All men (median age = 37 at baseline)								
No. of men	120	1029	3045	4678	4552	3573	1639	375
No. of deaths	16	115	236	374	302	262	146	44
RR	1.34	1.43	1.0	0.98	079	0.88	1.19	1.84
95% CI	0.80–2.23	1.14–1.79	—	0.83–1.16	0.67–0.94	0.74–1.05	0.96–1.46	1.33–2.56
Men who never smoked								
No. of deaths	4	22	57	98	66	62	41	15
RR	0.90	1.13	1.0	1.01	0.71	0.84	1.42	2.82
95% CI	0.32–2.55	0.68–1.88	—	0.73–1.41	0.49–1.02	0.58–1.22	0.94–2.15	1.58–5.04
Men who never smoked and excluding first 5 years of follow-up								
No. of deaths	2	16	42	73	57	50	37	14
RR	0.62	1.13	1.0	1.01	0.80	0.87	1.70	3.46
95% CI	0.15–2.62	0.62–2.05	—	0.69–1.50	0.53–1.20	0.57–1.32	1.08–2.67	1.86–6.43

[a]Restricted to subjects who responded to the baseline questionnaire and were cancer free (other than non-melanoma skin cancer) and had no history of myocardial infarction at that time. RR estimated using Cox's proportional-hazards regression with age as the time-scale, stratified at baseline by birth cohort in 5-year intervals. Multivariate risks adjusted for smoking duration, alcohol consumption, race and education. Missing information was coded in a separate category.

1.95 (0.79–4.84), 1.0 (reference), 1.18 (0.50–2.78), 0.84 (0.28–2.46), 1.64 (0.69–3.94), 1.24 (0.43–3.53) and 3.38 (1.16–9.91). When assessing risk in black women who never smoked and excluding the first 5 years of follow-up, case numbers were small, yet the pattern of risks remained similar (data not shown).

In assessing risks in the total group of never-smoking women who were under the age of 55 years at baseline (after excluding the first 5 years of follow-up) (Table 3), we again found a relatively direct relationship between BMI and mortality, with the lowest risks associated with the leanest BMI in the normal range. There was no difference in risk between those considered underweight (BMI $<18.5\,kg/m^2$) and most of the spectrum of a normal BMI (21.0–24.9 kg/m^2). Compared to the reference group, risks rose 30–55% among overweight women. Although there was no increase in risk at the low end of obesity, very obese women, with a BMI above 35.0 kg/m^2, had a nearly twofold elevated risk.

When we examined never-smoking women aged 55 years and older (again excluding early follow-up), there was a J-shaped relationship between BMI and mortality, with the lowest risks associated with a BMI between 21.0 and 24.9 kg/m^2 (Table 3). Among the overweight and those at the low end of obesity, risks were elevated about 30%. Risks, however, rose more than threefold among the very obese ($BMI = 35.0+\ kg/m^2$).

Mortality risks of men

In the multivariate analysis of all men (Table 2), the lowest risks were associated with BMIs considered overweight ($BMI = 25.0–29.9\,kg/m^2$). When we separately examined men who never smoked, risk remained lowest in the overweight group. When we restricted the analysis to follow-up beyond the first 5 years in never-smoking men, the relationship between BMI and mortality was not substantially changed.

In black men, mortality risks followed the general pattern for all men, although there were no cases classified as 'underweight'. Risks by BMI category, excluding the first 'underweight' group, were: 2.12 (0.66–6.79), 1.0 (reference),

Table 3 RR of all-cause mortality by BMI in women and men by age[a]

	BMI (kg/m^2)							
	<18.5	*18.5–20.9*	*21.0–22.9*	*23.0–24.9*	*25.0–26.9*	*27.0–29.9*	*30.0–34.9*	*35.0+*
Women <55 years (median age = 34 at baseline)								
No. of women	3658	18 792	15 831	9954	5200	4231	2851	1225
No. of deaths	59	262	273	215	131	137	73	48
RR	1.65	0.97	1.0	1.07	1.19	1.48	1.21	1.95
95% CI	1.25–2.19	0.81–1.14	—	0.90–1.28	0.97–1.47	1.21–1.82	0.93–1.57	1.43–2.66
Women <55 years (never-smokers; excl. 5 years)								
No. of women	1375	9697	7765	4988	2588	2141	1543	628
No. of deaths	12	65	81	60	44	45	18	15
RR	1.01	0.74	1.0	1.00	1.30	1.55	0.81	1.75
95% CI	0.55–1.86	0.53–1.02	—	0.72–1.40	0.9–1.89	1.08–2.24	0.49–1.36	1.01–3.05
Women 55+ years (median age = 61 at baseline)								
No. of women	155	655	903	854	540	463	315	106
No. of deaths	74	210	221	202	130	124	81	38
RR	1.67	1.29	1.0	1.00	1.11	1.28	1.32	2.32
95% CI	1.28–2.17	1.07–1.57	—	0.82–1.21	0.89–1.38	1.02–1.59	1.02–1.71	1.63–3.29
Women 55+ years (never-smokers; excl. 5 years)								
No. of women	39	256	396	396	244	233	151	45
No. of deaths	13	67	74	71	49	48	32	18
RR	1.10	1.25	1.0	1.00	1.30	1.29	1.30	3.34
95% CI	0.60–2.02	0.89–1.75	—	072–1.40	0.90–1.89	0.89–1.87	0.85–1.98	1.96–5.71
Men <55 years (median age = 36 at baseline)								
No. of men	100	907	2732	4108	3999	3147	1459	343
No. of deaths	7	55	119	160	141	140	78	29
RR	1.61	1.47	1.0	0.86	0.71	0.84	1.00	1.61
95% CI	0.75–3.45	1.07–2.03	—	0.68–1.09	0.55–0.90	0.66–1.07	0.75–1.34	1.07–2.41
Men <55 years (never-smokers; excl. 5 years)								
No. of men	36	368	1138	1682	1549	1139	548	145
No. of deaths	0	7	17	33	31	24	18	10
RR	—	1.30	1.0	1.19	1.17	1.17	1.91	4.15
95% CI		0.54–3.14	—	0.66–2.15	0.65–2.12	0.63–2.20	0.98–3.72	1.89–9.13
Men 55+ years (median age = 61 at baseline)								
No. of men	20	122	313	570	553	426	180	32
No. of deaths	9	60	117	214	161	122	68	15
RR	1.20	1.42	1.0	1.12	0.89	0.91	1.47	2.37
95% CI	0.60–2.38	1.03–1.95	—	0.89–1.49	0.70–1.13	0.70–1.17	1.08–1.99	1.36–4.15
Men 55+ years (never-smokers; excl. 5 years)								
No. of men	7	25	82	144	146	118	54	9
No. of deaths	2	9	25	40	26	26	19	4
RR	0.69	0.99	1.0	0.91	0.57	0.68	1.61	3.11
95% CI	0.15–3.09	0.43–2.25	—	0.54–1.55	0.32–1.01	0.38–1.21	0.86–3.02	1.02–9.42

[a]Restricted to subjects who responded to the baseline questionnaire and were cancer free (other than non-melanoma skin cancer) and had no history of myocardial infarction at that time. RR estimated using Cox's proportional-hazards regression with age as the time-scale, stratified at baseline by birth cohort in 5-year intervals. Multivariate risks adjusted for smoking duration, alcohol consumption, race and education. Missing information was coded in a separate category.

1.14 (0.49–2.61), 1.0 (0.42–2.40), 0.87 (0.35–2.16), 1.74 (0.65–4.66) and 1.38 (0.35–5.45). Case numbers were too small to analyze subgroups of men (data not shown).

Although stratifying by age in the total group of men led to small numbers in each stratum, we found that never-smoking men under the age of 55 years (excluding the first 5 years of follow-up), risk was relatively linear, with lowest risks at a BMI of 21.0–22.9 kg/m^2 (Table 3). Risks were roughly 20% higher at larger BMI levels in the normal and overweight range. Mortality risk climbed to twofold among those with a BMI between 30.0 and 34.9 kg/m^2 and fourfold among heavier men.

In never-smoking older men (age $\geqslant$55 years), risk was lowest in those with BMIs in the overweight category. In the obese, risks rose to between 60% and threefold, although numbers were quite small ($n = 4$) among the very obese.

Discussion

In this prospective cohort study, we focused our analysis of the mortality risk of a large cohort of women and men with follow-up beyond 5 years in never-smokers so as to limit potential bias owing to smoking and/or pre-existing illness-related weight loss. In both women and men under the age of 55 years at baseline, we found a direct relationship between BMI and mortality risk, although the small number of men prevented extrapolating below a BMI of 21.0 kg/m^2. Notably, the effect of excluding smokers and early follow-up was to reduce risks substantially among those considered 'underweight', supporting the hypothesis that much of the risks observed among 'underweight' adults under the age of 55 years is related to smoking or illness-related weight loss.

In older women, aged 55 years and above, the association was more J-shaped, although risks remained lowest in normal BMIs between 21.0 and 24.9 kg/m^2. In older men, however, risks were J-shaped, with lowest risks in the overweight category. Mortality risks were highest in both women and men in both age groups among the obese, particularly in men aged <55 years.

Although small numbers limited subgroup analysis, we found that black subjects, as in the total study cohort, showed higher mortality risks associated with obesity. A number of other studies that have examined the relationship in black women have found obesity weakly associated with mortality,[7,28,29] but there is some suggestion that education may modify the mortality/obesity relationship in black women[28] with stronger associations among high school graduates, a status characterizing the vast majority of black subjects in this cohort.

Our results for the total cohort are generally consistent with prospective studies that have taken into account smoking, age at baseline and baseline illness or weight loss. Many,[10,14,16,30] but not all, studies[1,31] have found risk was lowest among younger subjects with the lowest BMI. In contrast, many studies have found increased risk in older subjects who were leanest,[6,15,19,32,33] although the American Cancer Society study found J-shaped associations limited to those aged 75 years and older.[10]

There are a number of potential explanations for the increased mortality risk associated with a low BMI among older subjects. It is possible that a low BMI actually contributes to mortality owing to nutritional deficiencies or impaired immune status, as suggested by Kalmijn *et al.*[34] Dietary restriction has been related to immunological impairments in rats.[35] Willett *et al.*[22] argue, however, that evidence is lacking of increased incidence of specific diseases or case fatality rates associated with leanness, as would be expected with a causal relationship. In this study, because of the small numbers of older subjects with a low BMI, we were unable to assess risk by disease category.

The association between low BMI and death in older adults could also reflect insufficient consideration of early or chronic disease leading to both thinness and death. This cohort, however, provides limited evidence for this explanation inasmuch as the risk associated with a low-normal BMI, particularly among women, remained essentially the same whether or not we excluded smokers and the initial 5-year follow-up period.

There are, however, potentially serious limitations in using BMI as a surrogate for body fat or for the relevant pattern of body fat or composition in understanding the relationship between BMI and mortality with increasing age. It does not take into account frame size or musculature. In older adults, where differential loss of lean mass contributes to variation in weight, BMI is likely to be a poor surrogate for general adiposity. The distribution of body fat, particularly abdominal adiposity, rather than the amount of fat, may be a better predictor of mortality. Thus, some studies[36,37] have found that the waist to hip circumference ratio (WHR) or waist circumference is a better marker of mortality risk than BMI in older adults. Folsom *et al.*[36] found that although the association between BMI and mortality in older women was U-shaped, the association with mortality was linear when WHR was used as the indicator of body fat. Several studies have also found that abdominal adiposity, as measured by WHR or waist circumference, is a better marker than BMI in older persons for cardiovascular disease,[30,36,38–40] which contributes substantially to overall mortality. At least one study found that muscle strength may be a better predictor of long-term mortality than BMI in healthy middle-aged men.[41] Other studies, using surrogates for fat mass such as skin-fold thickness[42] and for fat-free mass such as potassium counting,[43] have found that fat mass and fat-free mass have inverse associations with mortality, which could contribute to a J-shaped association between BMI and total mortality. Thus, the J-shaped association between BMI and mortality in older adults may not provide appropriate guidance on optimal weight as people age. Rather, other measures of adiposity or body composition may be more directly related to actual biological risk factors.

We note some other limitations of the study, including our reliance on self-reported values for weight and height. Other studies that have validated self-reported weight or height, however, have found strong correlations with measured values.[5,14,44] Nonetheless, it is likely that heavy participants under-reported their weight, leading to some overestimating of risks at lower BMI categories. Data on BMI was missing on less than 3% of the study population who were excluded from the analysis. Thus, we were able to retain a very large percentage of the study population with actual reported data. Although some participants were also missing covariate information, the covariates had modest confounding effects, thus limiting the need for sophisticated imputation methods to assign values to the missing data.

In addition, we were unable to adjust for a number of factors that were not collected at baseline, such as physical activity, muscle strength, diet or other measures of adiposity, which may be independent risk factors associated with BMI. The issue of physical activity or fitness in particular is of potential importance. Many studies have found that regular physical activity or fitness has benefits for health at any weight, thus potentially confounding the effects of excess weight or obesity on mortality.[45,46]

We did not have specific data on illness-related weight loss, although we had baseline health information on some key categories of major illness, that is, cancer and heart disease, and excluded 5 years of follow-up to control for potential recent weight loss owing to pre-existing illness. There is some disagreement over the value of excluding initial follow-up (and thus early deaths) to take into account confounding owing to pre-existing disease. Allison *et al*.[47–49] have used a meta-analysis, a mathematical demonstration and a simulation to provide evidence that excluding early follow-up does not necessarily decrease bias and could 'exacerbate [the] confounding' owing to pre-existing illness. On the other hand, using the Atherosclerosis Risk in Communities (ARIC) Study, Stevens *et al*.[50] have suggested the potential usefulness of excluding early deaths with evidence that participants who died during the early years of follow-up were more likely than survivors to have changed from the obese category before a baseline to non-obese at baseline. To deal with bias owing to the effects of disease on weight loss, ideally one would want full information on pre-existing disease or a recent history of weight change,[49] but such information is generally unavailable. In this study, we report both the association in the entire study population and in the group after excluding early deaths and smokers.

Advantages of the study include its large size, the nationwide distribution of participants, the inclusion of both women and men, the available baseline information from a medically knowledgeable population on smoking and alcohol behavior as well as serious medical conditions, and a follow-up period that is sufficiently long to permit excluding early deaths. The predominance of non-college educated members in the cohort offers the opportunity to explore the implications of BMI in a group that appears comparable socioeconomically to the overall US population.

In summary, our findings support a strong, direct relationship between mortality and BMI in adults under the age of 55 years and between mortality and obesity among both younger and older adults. The more complicated relationship between BMI and mortality in older subjects, however, suggests the importance of assessing whether other markers of body size and composition, including adiposity, better explain mortality risk in older adults.

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References

1 Engeland A, Bjorge T, Selmer RM, Tverdal A. Height and body mass index in relation to total mortality. *Epidemiology* 2003; **14**: 293–299.
2 Calle EE, Rodriquez C, Walker-Thurmond K, Thun MJ. Overweight, obesity, and mortality from cancer in a prospectively studied cohort of US adults. *N Engl J Med* 2003; **348**: 1625–1628.
3 Meyer HE, Sogaard J, Tverdal A, Selmer RM. Body mass index and mortality: the influence of physical activity and smoking. *Med Sci Sports Exercise* 2002; **34**: 1065–1070.
4 Song YM, Sung J. Body mass index and mortality: a twelve-year prospective study in Korea. *Epidemiology* 2001; **12**: 173–179.
5 Haapanen-Niemi N, Miilunpalo S, Pasanen M, Vuori I, Oja P, Malmberg J. Body mass index, physical inactivity and low level of physical fitness as determinants of all-cause and cardiovascular disease mortality – 16 y follow-up of middle-aged and elderly men and women. *Int J Obes Relat Metab Disord* 2000; **24**: 1465–1474.
6 Singh PN, Lindsted KD, Fraser GE. Body weight and mortality among adults who never smoked. *Am J Epidemiol* 1999; **150**: 1152–1164.
7 Calle EE, Thun MJ, Petrelli JM, Rodriquez C, Heath Jr CW. Body mass index and mortality in a prospective cohort of US adults. *N Engl J Med* 1999; **341**: 1097–1105.
8 Durazo-Arvizu RA, McGee DL, Cooper RS, Liao Y, Luke A. Mortality and optimal body mass index in a sample of the US population. *Am J Epidemiol* 1998; **147**: 739–749.
9 Yuan JM, Ross RK, Gao YT, Yu MC. Body weight and mortality: a prospective evaluation in a cohort of middle-aged men in Shanghai, China. *Int J Epidemiol* 1998; **27**: 824–832.
10 Stevens J, Cai J, Pamuk ER, Williamson DF, Thun MJ, Wood JL. The effect of age on the association between body-mass index and mortality. *N Engl J Med* 1998; **338**: 1–7.
11 Lindsted KD, Singh PN. Body mass and 26-year risk of mortality among women who never smoked: findings from the Adventist Mortality Study. *Am J Epidemiol* 1997; **146**: 1–11.
12 Dorn JM, Schisterman EF, Winkelstein Jr W, Trevisan M. Body mass index and mortality in a general population sample of men and women: The Buffalo Health Study. *Am J Epidemiol* 1997; **146**: 919–931.
13 Seidell JC, Verschuren M, van Leer EM, Kromhout D. Overweight, underweight, and mortality. *Arch Intern Med* 1996; **156**: 958–963.
14 Manson JE, Willett WC, Stampfer MJ, Colditz GA, Hunter DJ, Hankinson SE *et al*. Body weight and mortality among women. *N Engl J Med* 1995; **333**: 677–685.
15 Folsom AR, Kaye SA, Sellers TA, Hong CP, Cerhan JR, Potter JD *et al*. Body fat distribution and 5-year risk of death in older women. *JAMA* 1993; **269**: 483–487.
16 Lee IM, Manson JE, Hennekens CH, Paffenbarger Jr RS. Body weight and mortality. A 27-year follow-up of middle-aged men. *JAMA* 1993; **270**: 2823–2828.
17 Lindsted K, Tonstad S, Kuzma JW. Body mass index and patterns of mortality among Seventh-day Adventist men. *Int J Obes Relat Metab Disord* 1991; **15**: 397–406.

18 Wannamethee G, Shaper AG. Body weight and mortality in middle aged British men: impact of smoking. *BMJ* 1989; **299**: 1497–1502.
19 Harris T, Cook EF, Garrison R, Higgins M, Kannel W, Goldman L. Body mass index and mortality among nonsmoking older persons: the Framingham Heart Study. *JAMA* 1988; **259**: 1520–1524.
20 Tuomilehto J, Salonen JT, Marti B, Jalkanen L, Puska P, Nissinen A *et al*. Body weight and risk of myocardial infarction and death in the adult population of eastern Finland. *BMJ (Clin Res Ed)* 1987; **12**: 623–627.
21 Manson JE, Stampfer MJ, Hennekens CH, Willett WC. Body weight and longevity: a reassessment. *JAMA* 1987; **267**: 353–358.
22 Willett WC, Dietz WH, Colditz GA. Guidelines for healthy weight. *N Engl J Med* 1999; **341**: 427–434.
23 Doody MM, Mandel JS, Lubin JH, Boice Jr JD. Mortality among Unites States radiologic technologists, 1926–1990. *Cancer Causes Control* 1998; **9**: 67–75.
24 Boice JD, Mandel JS, Doody MM, Yoder RC, McGowan R. A health survey of radiologic technologists. *Cancer* 1992; **69**: 586–598.
25 National Heart, Lung and Blood Institute. Clinical guidelines on the identification, evaluation, and treatment of overweight and obesity in adults, NIH Publication No. 98-4083, September 1998, National Institutes of Health: Bethesda, MD.
26 Hiza HA, Pratt C, Mardis AL, Anand R. *Body Mass Index and Health. Insight 16*. USDA, Center for Nutrition Policy and Promotion: Washington, DC, 2000.
27 Korn EL, Graubard BI, Midthune D. Time-to-event analysis of longitudinal follow-up of a survey: choice of the time-scale. *Am J Epidemiol* 1997; **145**: 72–80.
28 Stevens J, Plankey MW, Williamson DF, Thun MJ, Rust PF, Palesch Y *et al*. The body mass index – mortality relationship in white and Africa American women. *Obes Res* 1998; **6**: 268–277.
29 Wienpahl J, Ragland DR, Sidney S. Body mass index and 15-year mortality in a cohort of black men and women. *J Clin Epidemiol* 1990; **43**: 949–960.
30 Baik I, Ascherio A, Rimm EB, Giovannucci E, Spiegelman D, Stampfer MJ *et al*. Adiposity and mortality in men. *Am J Epidemiol* 2000; **152**: 264–271.
31 Rissanen A, Knekt P, Heliovaara M, Aromaa A, Reunanen A, Maatela J. Weight and mortality in Finnish women. *J Clin Epidemiol* 1991; **44**: 787–795.
32 Cornoni-Huntley JC, Harris TB, Everett DF, Albanes D, Micozzi MS, Miles TP *et al*. An overview of body weight of older persons, including the impact on mortality. The National Health and Nutrition Examination Survey I – Epidemiologic Follow-up Study. *J Clin Epidemiol* 1991; **44**: 743–753.
33 Heiat A, Vaccarino V, Krumholz HM. An evidence-based assessment of federal guidelines for overweight and obesity as they apply to elderly persons. *Arch Intern Med* 2001; **161**: 1194–1203.
34 Kalmijn S, Curb JD, Rodriguez BL, Yano K, Abbott RD. The association of body weight and anthropometry with mortality in elderly men: the Honolulu Heart Program. *Int J Obes Relat Metab Disord* 1999; **23**: 395–402.
35 Konno A, Utsuyama M, Kurashima C, Kasai M, Kumura S, Hirokawa K. Effects of protein-free diet or food restriction on the immune system of Wistar and Buffalo rats at different ages. *Mech Ageing Dev* 1993; **72**: 183–197.
36 Folsom AR, Kushi LH, Anderson KE, Mink PJ, Olson JE, Hong CP *et al*. Associations of general and abdominal obesity with multiple health outcomes in older women. *Arch Intern Med* 2000; **160**: 2117–2128.
37 Visscher TLS, Seidell JC, Molarius A, van der Kuip D, Hofman A, Witteman JCM. A comparison of body mass index, waist-hip ratio and waist circumference as predictors of all-cause mortality among the elderly: the Rotterdam study. *Int J Obes Relat Metab Disord* 2001; **25**: 1730–1735.
38 Rimm EB, Stampfer MJ, Giovannucci E, Ascherio A, Spiegelman D, Colditz GA *et al*. Body size and fat distribution as predictors of coronary heart disease among middle-aged and older US men. *Am J Epidemiol* 1995; **141**: 1117–1127.
39 Larsson B, Svardsudd K, Welin L, Wilhelmsen L, Bjorntorp P, Tibblin G. Abdominal adipose tissue distribution, obesity, and risk of cardiovascular disease and death: 13 year follow-up of participants in the study of men born in 1913. *BMJ* 1984; **288**: 1401–1404.
40 Prineas RJ, Folsom AR, Kaye SA. Central adiposity and increased risk of coronary artery disease mortality in older women. *Ann Epidemiol* 1993; **3**: 35–41.
41 Rantanen T, Harris T, Leveille SG, Visser M, Foley D, Masaki K *et al*. Muscle strength and body mass index as long-term predictors of mortality in initially healthy men. *J Gerontol A* 2000; **55**: M168–M173.
42 Allison DB, Zhu SK, Plankey M, Faith MS, Heo M. Differential associations of body mass index and adiposity with all-cause mortality among men in the first and second National Health and Nutrition Examination Surveys (NHANES I and NHANES II) follow-up studies. *Int J Obes Relat Metab Disord* 2002; **26**: 410–416.
43 Heitmann BL, Erikson H, Ellsinger B-M, Mikkelsen KL, Larsson B. Mortality associated with body fat, fat-free mass and body mass index among 60-year-old Swedish men – a 22-year follow-up. The study of men born in 1913. *Int J Obes Relat Metab Disord* 2000; **24**: 33–37.
44 Stevens J, Keil JE, Waid LR, Gazes PC. Accuracy of current, 4-year, and 28-year self-reported body weight in an elderly population. *Am J Epidemiol* 1990; **132**: 1156–1163.
45 Blair SN, Church TS. The fitness, obesity, and health equation. Is physical activity the common denominator? *JAMA* 2004; **292**: 1232–1234.
46 Blair SN, Brodney S. Effects of physical inactivity and obesity on morbidity and mortality: current evidence and research issues. *Med Sci Sports Exerc* 1999; **31**: S646–S662.
47 Allison DB, Faith MS, Heo M, Townsend-Butterworth D, Williamson DF. Meta-analysis of the effect of excluding early deaths on the estimated relationship between body mass index and mortality. *Obes Res* 1999; **7**: 342–354.
48 Allison DB, Faith MS, Heo M, Kotler DP. Hypothesis concerning the U-shaped relation between body mass index and mortality. *Am J Epidemiol* 1997; **146**: 339–349.
49 Allison DB, Heo M, Flanders DW, Faith MS, Carpenter KM, Williamson DF. Simulation study of the effects of excluding early deaths on risk factor-mortality analyses in the presence of confounding due to occult disease: the example of body mass index. *Ann Epidemiol* 1999; **9**: 132–142.
50 Stevens J, Juhaeri, Cai J. Changes in body mass index prior to baseline among participants who are ill or who die during the early years of follow-up. *Am J Epidemiol* 2001; **153**: 946–953.