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Original Contribution

Body Mass and Weight Change in Adults in Relation to Mortality Risk

Kenneth F. Adams*, Michael F. Leitzmann, Rachel Ballard-Barbash, Demetrius Albanes, Tamara B. Harris, Albert Hollenbeck, and Victor Kipnis

* Correspondence to Dr. Kenneth F. Adams, Minnesota Cancer Surveillance System, Minnesota Department of Health, 85 East 7th Place, P.O. Box 64882, St. Paul, MN 55164-0882 (e-mail: kenneth.adams@state.mn.us).

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Using data from the National Institutes of Health-AARP Diet and Health Study, we evaluated the influence of adulthood weight history on mortality risk. The National Institutes of Health-AARP Diet and Health Study is an observational cohort study of US men and women who were aged 50–71 years at entry in 1995–1996. This analysis focused on 109,947 subjects who had never smoked and were younger than age 70 years. We estimated hazard ratios of total and cause-specific mortality for recalled body mass index (BMI; weight (kg)/height (m)^2) at ages 18, 35, and 50 years; weight change across 3 adult age intervals; and the effect of first attaining an elevated BMI at 4 successive ages. During 12.5 years' follow-up through 2009, 12,017 deaths occurred. BMI at all ages was positively related to mortality. Weight gain was positively related to mortality, with stronger associations for gain between ages 18 and 35 years and ages 35 and 50 years than between ages 50 and 69 years. Mortality risks were higher in persons who attained or exceeded a BMI of 25.0 at a younger age than in persons who reached that threshold later in adulthood, and risks were lowest in persons who maintained a BMI below 25.0. Heavier initial BMI and weight gain in early to middle adulthood strongly predicted mortality risk in persons aged 50–69 years.

body mass index; body weight; mortality; obesity; weight gain; weight loss

Abbreviations: BMI, body mass index; CDC, Centers for Disease Control and Prevention; CVD, cardiovascular disease; HR, hazard ratio; ICD-9, *International Classification of Diseases*, *Ninth Revision*; ICD-10, *International Classification of Diseases*, *Tenth Revision*.

Editor's note: *An invited commentary on this article appears on page 145, and the authors' response appears on page 147.*

In the United States, the body mass of adolescents and adults of all ages has been increasing for the past 2 decades (1, 2). Because high body mass tends to persist from adolescence to adulthood (3) and people tend to gain weight over most of the life span (4, 5), a high proportion of the current generation of children and young adults will probably carry excess weight for many decades.

Excess body mass in adolescence (6) and young adulthood (7–9) is associated with increased mortality risk. Moreover, studies comparing relationships between body mass and mortality in 2 (10–15) or more (16, 17) different age periods in adulthood have found that body mass index (BMI; weight (kg)/height (m)^2) at younger ages more strongly predicts mortality than does BMI at older ages. One explanation is that people who attain and maintain a high relative weight in early adulthood carry excess weight longer than those who become heavy only later in life and will consequently experience more of the adverse metabolic effects of excess weight (18).

Given that excess body mass is associated with mortality, particularly excess body mass in early to middle adulthood, it would be expected that weight gain would be associated with risk of death. However, several studies have found that weight gain is unrelated to mortality (12, 19–29) or is only equivocally associated with mortality (27, 30–32). Some of these studies are limited by lack of sufficient statistical power to detect a relationship; few evaluate weight gain over specific periods of the life span; and most consider only a single weight-gain interval, often extending into advanced age. Because weight gain may be less adverse in older persons (18), because body mass in older age may be influenced by preexisting disease, or because body composition may be more important in older persons, these weight-gain results are difficult to interpret. Considering weight change across younger age intervals may have the advantage of reducing the potentially confounding influence of preexisting disease on the association between weight change and risk of death (14).

In this study, we addressed these issues by evaluating body mass and weight change at multiple time points spanning early, middle, and late adulthood. The National Institutes of Health-AARP cohort is sufficiently large to allow us to address biases due to smoking by restricting the analysis to never smokers while retaining sufficient numbers of subjects to examine the joint relationships between body mass and weight change over 3 age intervals. We further extended previous research (33) by examining average BMI over the course of early to middle adulthood as a measure of cumulative exposure and explicitly considered the influence of the age at which a healthy BMI was first exceeded.

MATERIALS AND METHODS

Study population

The National Institutes of Health-AARP Diet and Health Study is composed of men and women living in 6 US states and 2 metropolitan areas. A self-administered baseline questionnaire was mailed to 3.5 million members of AARP (formerly the American Association of Retired Persons) aged 50–71 years in 1995–1996, with an initial cohort size of 566,402. The baseline questionnaire included current height and weight. Six months later, a second questionnaire seeking information on height and weight at earlier ages and on other variables was sent to persons who responded to the baseline questionnaire. From a starting population of 334,908 men and women who completed both questionnaires, we restricted the data set to the 118,823 who reported never smoking. We excluded subjects whose questionnaires were completed by a surrogate respondent ($n = 3,373$) and subjects who reported extremely high values for alcohol consumption (more than 3 standard deviations above the 75th percentile ($n = 766$)) or provided no weight or height data ($n = 509$). Finally, to ensure that no individual had an age interval greater than 20 years for the analysis of weight change between age 50 years and study baseline, we excluded subjects aged 70 years or more ($n = 4,228$). The remaining 109,947 participants (53,126 men and 56,821 women) comprised our analytical cohort.

Cohort follow-up

Cohort members were followed for vital status from the return date of the second questionnaire in 1996–1997 through December 31, 2009. Vital status was ascertained by annual linkage of the cohort to the Social Security Administration Death Master File, which contains information on all deaths occurring in the United States (34). The design and maintenance of this cohort have been described previously (35, 36). All study participants provided written informed consent, and the National Institutes of Health-AARP Diet and Health Study was approved by the Special Studies Institutional Review Board of the US National Cancer Institute.

Causes of death

Cause of death was obtained through linkage to the National Death Index Plus, using *International Classification of Diseases*, *Ninth Revision* (ICD-9), and *International Classification of Diseases*, *Tenth Revision* (ICD-10), codes for death certificate underlying cause of death. The codes were initially grouped using the National Center for Health Statistics' "113 selected causes of death" (37, 38) and then further consolidated to create broad categories, as follows: cancer (ICD-9 codes 140–239; ICD-10 codes C00–C97 and D00–D48), cardiovascular disease (CVD) (ICD-9 codes 390–398, 401–404, 410–429, and 440–448; ICD-10 codes I00–I13, I20–I51, and I70–I78), and stroke (ICD-9 codes 430–438; ICD-10 codes I60–I69). All other codes were considered together.

Assessment of BMI and weight change

Data on current height and weight, health status, smoking habits, race/ethnicity, physical activity, alcohol consumption, and recalled height at age 18 years and weight at ages 18, 35, and 50 years were collected by questionnaire. We created BMI variables for 3 distinct ages (18, 35, and 50 years) and for the weighted average of BMI at ages 18, 35, and 50 years. BMI categories were nested within broad, generally accepted weight classifications (39), including underweight (<18.5), 2 categories of normal weight (18.5–22.4 (referent) and 22.5–24.9), 2 categories of overweight (25.0–27.4 and 27.5–29.9), and 2 categories of obesity (30.0–32.4 and ≥32.5). The BMI categories were constructed to: 1) reflect the weight distributions of the study population at ages 18, 35, and 50 years; 2) create large, statistically stable groups; and 3) incorporate established BMI cutpoints. For example, at age 18 years, most subjects had a BMI in the normal or underweight category and relatively few (1.4%) had a BMI in the obese range. In contrast, at age 50 years, sufficient numbers of subjects had an obese BMI to allow the creation of 2 obesity categories. The leaner category in the normal BMI range was chosen as the referent BMI category. For an alternative analysis of BMI at age 18 years, we calculated BMI percentiles using the Centers for Disease Control and Prevention (CDC) sex-specific BMI-for-age growth charts for children (40) and categorized these values according to the CDC-recommended cutpoints.

Weight-change categories were created for 3 age intervals spanning adulthood: ages 18–35 years, ages 35–50 years, and ages 50–69 years (i.e., self-reported weight from the baseline questionnaire). In contrast to the 2 younger age intervals, the width of the 50- to 69-year interval differed according to the subject's age at entry (maximum age at baseline questionnaire = 69.9 years; average age = 61.9 years (standard deviation, 5.2)). As described above, we truncated the study population age limit slightly to ensure that the weight-change

Table 1. Distribution of Never Smokers According to Body Mass Index[a] at Various Ages ($n = 109{,}947$), National Institutes of Health-AARP Diet and Health Study, 1996–2009

BMI Category	BMI at Age 18 Years		BMI at Age 35 Years		BMI at Age 50 Years		Average BMI[b]	
	No.	%	No.	%	No.	%	No.	%
<18.5	14,839	13.5	2,526	2.3	1,120	1.0	14,198	1.4
18.5–22.4	57,340	52.2	39,504	35.9	22,050	20.1	37,363	34.0
22.5–24.9	16,967	15.4	29,261	26.6	28,274	25.7	31,121	28.3
25.0–27.4	6,796	6.2	19,148	17.4	26,384	24.0	15,955	14.5
27.5–29.9 (≥27.5[c])	3,218	2.9	6,448	5.9	11,612	10.6	6,183	5.6
30.0–32.4 (≥30.0[d])			5,446	5.0	6,646	6.0	3,630	3.3
≥32.5					7,140	6.5		
Missing data	10,787	9.8	7,614	6.9	6,721	6.1	14,197	12.9

Abbreviation: BMI, body mass index.
[a] Weight (kg)/height (m)^2.
[b] Average BMI was calculated as the weighted average of BMIs at 18, 35, and 50 years of age.
[c] Subjects with a BMI of ≥27.5 were combined into a single category.
[d] Subjects with a BMI of ≥30.0 were combined into a single category.

interval at older ages was no more than 20 years in duration, to provide greater comparability with the younger age intervals. A weight change of 0.2 kg/year or less during an age interval was defined as stable weight, and this category served as the referent group. Health status was evaluated using subjects' responses to the question, "Would you say your health in general is: ___?," with 5 response categories ranging from poor to excellent.

Data analysis

Multivariate hazard ratios for mortality were estimated using Cox regression analysis (41), with age at return of the second questionnaire used as the underlying time metric. On average, the time between return of the baseline questionnaire and return of the second questionnaire was 0.57 years (standard deviation, 0.19). Age-adjusted mortality rates were calculated using the Mantel-Haenszel method. We estimated associations for BMI at ages 18, 35, and 50 years, average BMI from early adulthood to middle adulthood (as a measure of cumulative body mass), and weight change over 3 consecutive age intervals of 18–35 years, 35–50 years, and 50 years to study entry (ages 50–69 years). Subjects who died but had no available information on underlying cause of death were excluded from cause-specific analyses ($n = 1{,}706$). Subjects who were missing body weight data were excluded on an analysis-specific basis. To examine the potential influence of illness on body weight, we stratified analyses of weight change from age 50 years to age 69 years according to self-reported health status. All models adjusted for race/ethnicity, education, physical activity, and alcohol consumption at study entry. Analyses combining men and women included adjustment for gender. Weight-change models additionally adjusted for initial BMI (i.e., BMI at the beginning of the weight-change age interval) and recalled height at age 18 years. Our final analysis considered the influence of long-term excess weight by estimating risks based on the youngest age at which participants reported having a BMI of 25.0 or higher, compared with a referent group that maintained a BMI below 25.0 in all 4 age periods (this analysis included BMI at study entry).

RESULTS

During 12.5 years' follow-up, on average, 12,017 deaths occurred: 6,635 in men and 5,382 in women. Subjects tended to be lean at age 18 years (Table 1) but to gain considerable weight over the 18–35 and 35–50 age intervals (Table 2). Weight gain was highest in the youngest age interval and lowest in the oldest age interval. Relatively large proportions of subjects lost weight during the 50–69 age interval, particularly those reporting poor or fair health (16.9%). Subjects with a less optimal health status appeared more likely to lose weight and less likely to maintain stable weight or avoid weight gain than those in better health. Nearly half of the subjects (48.6%) reported regularly engaging in leisure-time physical activity (activity that lasted at least 20 minutes and caused either sweating or increases in breathing or heart rate) 3 or more times per week, whereas only 15.8% reported rarely or never doing so.

BMI at age 18 years was strongly positively related to total mortality in men and women (Table 3). Total mortality risk was elevated in all categories above the lean referent group (BMI 18.5–22.4), including the upper-normal weight category (BMI 22.5–24.9), and further increased in the heavier BMI categories. Similarly, mortality risk was greater in the 2 upper CDC-defined BMI percentile-for-age categories. Weighted average BMI was strongly associated with mortality in both men and women. Comparing hazard ratios for a given BMI category at ages 18, 35, and 50 years, associations were strongest for BMI at age 18 years and then declined somewhat with increasing age, although there was often considerable overlap in confidence intervals. For example, hazard ratios for a BMI of 25.0–27.4 at ages 18, 35, and 50 years

Table 2. Weight Change Among Never Smokers During Various Age Intervals, National Institutes of Health-AARP Diet and Health Study, 1996–2009

Category of Weight Change, kg/year	Age Interval, years								
	18–35		35–50		50–69		50–69 (by Health Status)		
	No. of Subjects	%	No. of Subjects	%	No. of Subjects	%	Very Good to Excellent, %	Good, %	Poor to Fair, %
Loss of >0.2	4,438	4.0	7,127	6.5	13,558	12.3	11.9	13.0	16.9
Stable (±0.2)	21,779	19.8	34,235	31.1	38,303	34.8	37.1	29.9	24.5
Gain of >0.2–0.6	44,257	40.3	34,280	31.2	28,899	26.3	26.7	25.2	20.0
Gain of >0.6–1	18,427	16.8	18,711	17.0	11,842	10.8	10.4	11.9	11.7
Gain of >1	10,453	9.5	8,918	8.1	11,507	10.5	9.4	14.1	18.6
Missing data	10,593	9.6	6,676	6.1	5,838	5.3	4.5	5.8	8.3

were 1.40, 1.14, and 1.11, respectively, in men and 1.52, 1.45, and 1.24, respectively, in women. Age-adjusted mortality rates for a BMI in the 18.5–22.4 referent group were stable across the 3 age periods. Age-adjusted total mortality rates increased with BMI category within each age period and gender. Because the overall relationships appeared similar in men and women, the genders were combined in subsequent analyses. BMI at ages 18, 35, and 50 years was associated with mortality for each of the 4 cause-of-death groupings (see Web Table 1, available at http://aje.oxfordjournals.org/). The strongest associations were observed for CVD-related deaths. The hazard ratio for a mildly overweight BMI (25.0–27.4) at age 18 years was 1.65, and the risk increased to 2.42 for a BMI of 27.5 or more.

We evaluated the relationships between weight change and total mortality over 3 successive age intervals, combining men and women (Table 4). Weight gain was strongly associated with mortality in the 18–35 and 35–50 age intervals, with risk increasing at each increment of weight gain. In contrast, in the 50–69 age interval, mild weight gain of >0.2–0.6 kg/year was associated with slightly lower risk (hazard ratio (HR) = 0.91) and higher weight gain of >1 kg/year was associated with only modestly increased risk (HR = 1.17). Observed associations between weight change in the 50–69 age interval and mortality appeared to differ according to health status at entry. For subjects reporting very good to excellent health, a weight gain greater than 0.6 kg/year was associated with modestly increased mortality risk. In contrast, among subjects who reported good or poor-to-fair health, no linear trend was observed between weight gain and total mortality, and intermediate categories of weight gain were associated with statistically significant or borderline-significant lower risk. Age-adjusted mortality rates in the stable-weight reference categories in the 50–69 age interval were comparable to those in the 18–35 and 35–50 age groups. However, age-adjusted mortality rates in the 50–69 age interval for stable-weight (referent group) subjects in poor to fair health were sharply higher than corresponding rates for those in very good to excellent health. Weight loss in the 50–69 age interval was associated with greater risk regardless of health status.

Similar patterns were observed in cause-specific analyses, although the magnitudes of association differed by underlying cause of death (Web Table 2). Weight gain was most strongly associated with CVD mortality. In the 18–35 and 35–50 age intervals, weight gain greater than 1 kg/year was associated with a doubling of CVD mortality (HR = 2.10 and HR = 2.08, respectively). However, in the 50–69 age interval, weight gain greater than 1 kg/year was associated with only a 20% increase in CVD mortality (HR = 1.21). Weight gain in the 18–35 and 35–50 age intervals was associated with cancer mortality, but weight gain in the 50–69 age interval was not.

We then examined the combined influence of BMI and weight change on total mortality risk for each of the 3 age intervals (Table 5). The referent group for these analyses was BMI less than 25.0 at the beginning of the interval (e.g., 18 years) with stable weight over the subsequent interval. In the 18–35 and 35–50 age intervals, mortality risk generally increased progressively with both higher initial body mass (i.e., body mass at ages 18 and 35 years) and subsequent weight gain. In the 18–35 age interval, for example, mortality risk was greatest among subjects who had an initial BMI of 25.0 or more (at age 18 years) and also gained more than 1 kg/year by age 35 (HR = 2.69). Mortality risk was intermediate in subjects who either had an initially normal BMI but gained weight over the interval (HR = 1.63 for weight gain of more than 1 kg/year) or who had an initially high BMI (≥25.0) but did not gain weight (HR = 1.44). In the 50–69 age interval, positive associations of combined initial BMI and weight change with mortality were observed, but the associations were weaker than in younger age intervals, at least among subjects with an initially normal BMI. In this group, weight gain of 1 kg/year or less was not associated with increased mortality risk. Among subjects reporting very good or excellent health, both initial BMI and weight gain in the 50–69 age interval were positively associated with mortality. However, these associations appeared to be attenuated in subjects with less optimal health. Among subjects in poor to fair health and normal BMI at age 50 years, mortality risk was lower in those who gained weight (*P*-trend = 0.008) than in subjects with a stable weight.

CVD mortality risk increased sharply with both initial BMI and weight gain in the 18–35 and 35–50 age intervals (Web Table 3). In the 50–69 age interval, we did not observe statistically significant associations between weight gain and CVD mortality risk in subjects who were initially normal-weight or

Table 3. Total Mortality Risk Among Never Smokers in Relation to Body Mass Index[a] at Ages 18, 35, and 50 Years, by Gender, National Institutes of Health-AARP Diet and Health Study, 1996–2009

	Men					Women				
	No. of Deaths[b]	MV HR[c]	95% CI	Adjusted Death Rate[d]	*P*-trend[e]	No. of Deaths[b]	MV HR[c]	95% CI	Adjusted Death Rate[d]	*P*-trend[e]
BMI at age 18 years	6,221				<0.0005	4,548				<0.0005
<18.5		1.09	1.01, 1.18	10.0			1.00	0.92, 1.08	6.9	
18.5–22.4		1.0	Referent	8.9			1.0	Referent	6.8	
22.5–24.9		1.15	1.08, 1.23	10.2			1.27	1.16, 1.38	9.0	
25.0–27.4		1.40	1.29, 1.52	12.5			1.52	1.33, 1.74	10.9	
≥27.5		1.92	1.73, 2.14	17.2			2.21	1.92, 2.55	15.6	
BMI percentile at age 18 years	6,217				<0.0005	4,543				<0.0005
<5th		1.07	0.98, 1.16	10.3			1.06	0.95, 1.19	7.6	
5th–<85th		1.0	Referent	9.4			1.0	Referent	7.1	
85th–<95th		1.40	1.29, 1.53	13.3			1.77	1.57, 1.99	13.1	
≥95th		2.01	1.76, 2.30	18.8			2.06	1.66, 2.57	15.1	
BMI at age 35 years	6,172				<0.0005	4,762				<0.0005
<18.5		1.13	0.88, 1.45	9.6			1.04	0.89, 1.21	6.6	
18.5–22.4		1.0	Referent	8.5			1.0	Referent	6.2	
22.5–24.9		1.00	0.93, 1.07	8.4			1.11	1.04, 1.19	7.1	
25.0–27.4		1.14	1.06, 1.23	9.7			1.45	1.32, 1.58	9.6	
27.5–29.9		1.58	1.44, 1.73	13.7			1.88	1.64, 2.16	12.5	
≥30.0		2.10	1.92, 2.31	18.4			2.34	2.08, 2.63	16.2	
BMI at age 50 years	6,185				<0.0005	4,877				<0.0005
<18.5		1.43	1.00, 2.02	11.7			1.36	1.10, 1.68	7.9	
18.5–22.4		1.0	Referent	8.0			1.0	Referent	5.7	
22.5–24.9		1.02	0.93, 1.12	8.1			1.06	0.98, 1.15	6.2	
25.0–27.4		1.11	1.01, 1.22	8.9			1.24	1.14, 1.36	7.4	
27.5–29.9		1.38	1.24, 1.52	11.3			1.47	1.32, 1.64	9.0	
30.0–32.4		1.74	1.56, 1.95	14.8			1.86	1.66, 2.10	11.7	
≥32.5		2.44	2.19, 2.73	21.1			2.57	2.32, 2.84	16.0	
Average BMI[f]	6,033				<0.0005	4,231				<0.0005
<18.5		1.28	0.98, 1.67	10.6			1.20	0.99, 1.46	7.3	
18.5–22.4		1.0	Referent	8.4			1.0	Referent	6.0	
22.5–24.9		1.02	0.96, 1.10	8.5			1.15	1.07, 1.24	7.1	
25.0–27.4		1.25	1.17, 1.35	10.6			1.46	1.33, 1.61	9.3	
27.5–29.9		1.70	1.55, 1.86	14.5			2.13	1.88, 2.41	13.9	
≥30.0		2.43	2.18, 2.70	21.2			2.59	2.27, 2.97	17.0	

Abbreviations: BMI, body mass index; CI, confidence interval; MV HR, multivariate hazard ratio.

[a] Weight (kg)/height (m)^2.

[b] Numbers of deaths differed by age because of missing values for height and weight. The total number of deaths was 12,017.

[c] All regression analyses adjusted for age (in the baseline hazard of the Cox regression) and the following covariates: race/ethnicity (Caucasian; African-American; Hispanic; or Asian, Pacific Islander, and Native American combined); education (<8 years; 8–11 years; high school; vocational school or some college; or ≥4 years of college), leisure-time physical activity (never, rarely, 1–3 times/month, 1 or 2 times/week, 3 or 4 times/week, ≥5 times/week, or missing information); and alcohol consumption (0, 0.01–4.9, 5.0–14.9, or ≥15 g/day).

[d] Total number of deaths per 1,000 person-years, adjusted for age using the Mantel-Haenszel method.

[e] Statistical significance of the linear trend in BMI categories, evaluated using BMI category medians.

[f] Average BMI was calculated as the weighted average of BMIs at 18, 35, and 50 years of age.

Table 4. Total Mortality Risk Among Never Smokers in Relation to Weight Change During 3 Age Intervals, National Institutes of Health-AARP Diet and Health Study, 1996–2009

Age Interval and Weight Change, kg/year	No. of Deaths	Multivariate Hazard Ratio[a]	95% Confidence Interval	*P*-trend[b]	Adjusted Death Rate[c]
18–35 years	10,449			<0.0005	
Loss of >0.2		0.88	0.79, 0.98		9.3
Stable (±0.2)		1.0	Referent		7.7
Gain of >0.2–0.6		1.10	1.04, 1.16		8.0
Gain of >0.6–1		1.26	1.18, 1.34		9.5
Gain of >1		1.66	1.55, 1.78		13.4
35–50 years	10,734			<0.0005	
Loss of >0.2		1.06	0.98, 1.14		9.9
Stable (±0.2)		1.0	Referent		7.4
Gain of >0.2–0.6		1.04	0.99, 1.09		7.8
Gain of >0.6–1		1.19	1.13, 1.26		9.7
Gain of >1		1.61	1.51, 1.73		14.3
50–69 years	10,843			<0.0005	
Loss of >0.2		1.40	1.33, 1.49		13.1
Stable (±0.2)		1.0	Referent		7.7
Gain of >0.2–0.6		0.91	0.86, 0.95		7.2
Gain of >0.6–1		1.05	0.98, 1.12		9.0
Gain of >1		1.17	1.09, 1.25		11.5
50–69 years (by health status)					
Very good to excellent	4,525			0.003	
Loss of >0.2		1.37	1.25, 1.50		8.4
Stable (±0.2)		1.0	Referent		5.5
Gain of >0.2–0.6		0.94	0.87, 1.01		5.2
Gain of >0.6–1		1.21	1.09, 1.33		7.0
Gain of >1		1.14	1.01, 1.30		6.5
Good	4,019			0.16	
Loss of >0.2		1.30	1.18, 1.42		14.8
Stable (±0.2)		1.0	Referent		9.8
Gain of >0.2–0.6		0.85	0.79, 0.93		8.5
Gain of >0.6–1		0.91	0.81, 1.01		9.4
Gain of >1		1.08	0.97, 1.21		12.7
Poor to fair	2,157			0.45	
Loss of >0.2		1.35	1.19, 1.52		30.0
Stable (±0.2)		1.0	Referent		20.5
Gain of >0.2–0.6		0.91	0.81, 1.03		18.4
Gain of >0.6–1		0.88	0.76, 1.03		18.7
Gain of >1		0.94	0.82, 1.08		23.8

[a] All regression analyses adjusted for age (in the baseline hazard of the Cox regression) and the following covariates: gender, race/ethnicity, education, leisure-time physical activity, body mass index at the beginning of the age interval (weight (kg)/height (m)^2; categorical), and height (inches, in quintiles). (For additional definitions, see Table 3.)

[b] Statistical significance of the linear trend in weight-gain categories, evaluated using weight-gain category medians.

[c] Total number of deaths per 1,000 person-years; adjusted for age and gender using the Mantel-Haenszel method.

Table 5. Total Mortality Risk Among Never Smokers in Relation to Combined Initial Body Mass Index[a] and Weight Change During 3 Age Intervals, National Institutes of Health Diet and Health Study, 1996–2009

Age Interval and Weight Change, kg/year	No. of Deaths	Initial BMI <25.0				Initial BMI ≥25.0			
		MV HR[b]	95% CI	P-trend[c]	Adjusted Death Rate[d]	MV HR[b]	95% CI	P-trend[c]	Adjusted Death Rate[d]
18–35 years	8,959			<0.0005				<0.0005	
Loss of >0.2		1.04	0.89, 1.21		9.0	1.39	1.21, 1.59		10.1
Stable (±0.2)		1.0	Referent		7.2	1.44	1.27, 1.64		11.2
Gain of >0.2–0.6		1.06	1.00, 1.13		7.7	1.80	1.63, 2.00		14.0
Gain of >0.6–1		1.22	1.13, 1.31		9.3	1.85	1.61, 2.13		13.5
Gain of >1		1.63	1.50, 1.77		13.4	2.69	2.32, 3.12		21.3
35–50 years	10,511			<0.0005				<0.0005	
Loss of >0.2		1.21	1.05, 1.39		8.2	1.58	1.44, 1.73		11.2
Stable (±0.2)		1.0	Reference		6.7	1.31	1.22, 1.41		9.6
Gain of >0.2–0.6		1.02	0.96, 1.08		7.0	1.47	1.36, 1.58		10.4
Gain of >0.6–1		1.17	1.09, 1.26		8.4	1.74	1.60, 1.89		12.8
Gain of >1		1.60	1.45, 1.75		12.2	2.41	2.19, 2.64		18.3
50–69 years	10,727			0.03				<0.0005	
Loss of >0.2		1.52	1.37, 1.69		10.3	2.01	1.87, 2.15		14.5
Stable (±0.2)		1.0	Reference		6.8	1.28	1.20, 1.36		9.2
Gain of >0.2–0.6		0.87	0.81, 0.94		6.1	1.19	1.11, 1.28		8.5
Gain of >0.6–1		0.99	0.89, 1.10		7.1	1.42	1.30, 1.54		10.4
Gain of >1		1.14	1.01, 1.28		9.4	1.61	1.48, 1.75		12.4
50–69 years (by health status)									
Very good to excellent	4,476			0.03				0.03	
Loss of >0.2		1.48	1.28, 1.72		7.5	1.77	1.59, 1.98		9.0
Stable (±0.2)		1.0	Reference		5.1	1.22	1.11, 1.34		6.4
Gain of >0.2–0.6		0.95	0.86, 1.04		4.9	1.12	1.01, 1.25		5.6
Gain of >0.6–1		1.16	1.00, 1.35		5.9	1.53	1.34, 1.74		8.0
Gain of >1		1.16	0.96, 1.40		5.7	1.42	1.21, 1.66		6.6
Good	3,979			0.65				0.04	
Loss of >0.2		1.40	1.18, 1.66		12.6	1.68	1.50, 1.89		15.6
Stable (±0.2)		1.0	Reference		9.0	1.17	1.05, 1.30		10.6
Gain of >0.2–0.6		0.77	0.68, 0.87		6.8	1.09	0.97, 1.22		9.8
Gain of >0.6–1		0.82	0.68, 0.98		7.9	1.16	1.01, 1.33		10.5
Gain of >1		1.11	0.92, 1.34		12.7	1.34	1.17, 1.54		12.7
Poor to fair	2,132			0.008				0.21	
Loss of >0.2		1.26	0.99, 1.61		25.0	1.50	1.28, 1.76		32.0
Stable (±0.2)		1.0	Reference		20.6	0.99	0.84, 1.16		20.6
Gain of >0.2–0.6		0.84	0.69, 1.03		17.3	0.93	0.78, 1.10		19.1
Gain of >0.6–1		0.70	0.53, 0.93		14.0	0.95	0.79, 1.16		20.5
Gain of >1		0.74	0.56, 0.97		18.3	1.06	0.89, 1.26		26.3

Abbreviations: BMI, body mass index; CI, confidence interval; MV HR, multivariate hazard ratio.

[a] Weight (kg)/height (m)^2.

[b] All regression analyses adjusted for age (in the baseline hazard of the Cox regression) and the following covariates: gender, race/ethnicity, education, leisure-time physical activity, BMI at the beginning of the age interval (weight (kg)/height (m)^2; categorical), and height (inches, in quintiles). (For additional definitions, see Table 3.)

[c] Statistical significance of the linear trend in weight-gain categories, evaluated using weight-gain category medians.

[d] Total number of deaths per 1,000 person-years; adjusted for age and gender using the Mantel-Haenszel method.

Table 6. Total Mortality Risk Among Never Smokers in Relation to Age at Which Body Mass Index[a] First Reached or Exceeded 25.0 (for 4 Age Points) as Compared With Maintenance of a Body Mass Index Under 25.0 at All 4 Ages, by Gender, National Institutes of Health-AARP Diet and Health Study, 1996–2009

Time at Which BMI First Exceeded Threshold (BMI ≥25.0)	No. of Deaths	Multivariate Hazard Ratio[b]	95% Confidence Interval	Adjusted Death Rate[c]	Average BMI[d] (SD)
Men	6,068				
BMI <25.0 at all 4 ages		1.0	Reference	7.9	21.7 (1.4)
Baseline		0.98	0.88, 1.08	8.0	22.0 (1.4)
Age 50 years		1.12	1.04, 1.22	9.4	23.4 (1.0)
Age 35 years		1.32	1.23, 1.42	10.9	25.9 (1.6)
Age 18 years		1.68	1.55, 1.82	13.8	28.6 (2.8)
Women	4,265				
BMI <25.0 at all 4 ages		1.0	Reference	5.8	20.7 (1.4)
Baseline		0.96	0.88, 1.06	5.8	21.6 (1.3)
Age 50 years		1.26	1.16, 1.37	7.8	23.4 (1.2)
Age 35 years		1.68	1.54, 1.84	10.8	26.8 (2.1)
Age 18 years		2.04	1.83, 2.28	12.7	28.7 (3.8)

Abbreviations: BMI, body mass index; SD, standard deviation.

[a] Weight (kg)/height (m)^2.

[b] All analyses adjusted for age (in the baseline hazard of the Cox regression) and the following covariates: race/ethnicity, education, physical activity, and alcohol consumption (see Table 3 for definitions).

[c] Total number of deaths per 1,000 person-years; adjusted for age and gender using the Mantel-Haenszel method.

[d] Average BMI was calculated as the weighted average of BMIs at 18, 35, and 50 years of age.

who had elevated initial BMI but gained 1 kg or less in body weight per year.

Finally, we considered the age at which excess weight (BMI ≥25.0) was first attained, based on the 4 age periods for which data were available (Table 6). The referent group in these analyses (in contrast with Table 3) consisted of subjects who maintained a BMI less than 25.0 over all 4 age periods (BMI at entry was included in this analysis). Entering adulthood with a BMI of 25.0 or higher at age 18 years was strongly associated with mortality (HR = 1.68 in men, HR = 2.04 in women) as compared with maintaining normal weight throughout adulthood. The hazard ratio for first attaining a BMI greater than or equal to 25.0 at age 50 years appeared weaker (HR = 1.12 in men, HR = 1.26 in women) but retained statistical significance. All analyses were repeated using the subjects with no missing height and weight data (i.e., BMI available at all 3 time points); results were essentially unchanged.

DISCUSSION

We evaluated the mortality risk associated with excess body mass during 3 adulthood age periods and weight change over 3 consecutive age intervals in nonsmoking men and women. The lowest mortality was observed among persons who entered adulthood with a low BMI, experienced minimal weight gain over young and middle adulthood, and maintained a BMI within the healthy range throughout adulthood. We observed the strongest relationships between body mass and mortality in young adulthood, with associations being successively attenuated in each successive age period. Higher BMI at age 18 years was related to elevated risk in both men and women, even within the normal weight range, similarly to results reported for female nurses (13). Although associations with BMI in middle adulthood (represented by ages 35 and 50 years) were not as strong as those observed at age 18 years, they nevertheless robustly predicted mortality, in contrast with other reports finding weak or null associations over this period (14, 15). The weighted average of body mass over the course of early to middle adulthood, our measure of cumulative exposure, was also strongly associated with mortality risk. In addition, we observed that the earlier in adulthood the threshold for overweight (BMI ≥25.0) was exceeded, the greater was the mortality risk. These results, taken together with previous studies that found stronger BMI and mortality relationships at younger ages (9–11, 13–17), suggest that both the duration of excess body mass and the cumulative amount of mass contribute to mortality risk. Persons who are overweight or obese in middle age or later in life are a heterogeneous group with differing weight histories; that is, many were lean earlier in adulthood. In contrast, persons who enter adulthood overweight tend to remain so for decades. The combination of greater excess body mass in young adulthood and longer duration of excess mass results in increased cumulative exposure relative to persons who are lean when young and become overweight only later.

Weight gain in young (i.e., ages 18–35 years) and middle (ages 35–50 years) adulthood was strongly related to elevated mortality. These findings contrast with the majority of studies, which have found either no increased risk with weight gain (11, 12, 14, 19–29) or an equivocal relationship (27, 30–32), but are consistent with the few that have observed positive associations (42–45). However, moderate weight gain after age 50 years was not associated with mortality even among subjects reporting good to excellent health. Examination of the joint relationship of body mass and weight change over the 3 successive age intervals suggests the importance of having a lean, normal body weight during younger age periods and maintaining stable weight or gaining minimal weight through midlife. In the oldest age interval (50–69 years, study entry), body mass attained at midlife appeared to more strongly influence risk than did subsequent weight gain. One explanation for this is that cumulative body mass is largely determined by middle age, and gaining weight later in life results in little additional increase beyond what has already accumulated. Alternatively, the lack of association between weight gain and mortality at older ages could be influenced by preexisting disease, our attempts to remove the influence of disease on body weight notwithstanding. If so, actual risks of weight gain could be higher. The association between disease and weight gain is complex and is probably dependent on the type of disease and the point in the disease process at which weight is assessed. For example, type 2 diabetes mellitus is often associated with weight gain, particularly early in the course of the disease, while late-stage cancer is often associated with weight loss. Unfortunately, data on repeated measures of body weight in individuals throughout the course of disease are extremely limited, so this issue is not well studied. Change in body composition with age is another potential explanation. As lean mass is replaced with fat, additional body weight may be necessary to maintain the same lean mass.

In all analyses except those evaluating risk in the 50–69 age interval, age-adjusted mortality rates in referent groups (low BMI, stable weight) were low. In the 50–69 age interval, age-adjusted mortality rates in the referent group were progressively higher in subjects with lower health status. This suggests that by restricting the analysis to nonsmokers, considering distinct age groups, and stratifying the results in the older age interval by health status, we may have removed some of the association that is commonly referred to as "reverse causation"—that is, the influence of disease on body weight. The elevated risks that we observed in men and women who lost weight after age 50 years may suggest the influence of chronic disease on weight loss in this age group.

We evaluated the associations of weight and weight change with mortality. Similar assessments in relation to other outcomes, including incident disease and disability, could complement these analyses and provide a more complete picture of the contributions of weight and weight change to potential health-care consequences and costs. Such analysis was beyond the scope of the current study. We do not consider these findings to have been substantially biased by use of self-reported weight data. Information on the validity of self-reported past weight suggests that recalled and measured weights are highly correlated, even for weight in young adulthood (10, 46, 47). Any bias would be expected to operate more strongly at the more distantly recalled age, yet we observed the strongest relationships for body mass at age 18 years, with declining risks at more recent ages.

In conclusion, these results suggest that excess weight-related mortality may be reduced among persons who enter adulthood with a low BMI, avoid gaining weight with age, and maintain a body mass within the healthy range over the course of adulthood. Public health efforts should encourage weight control in early and middle adulthood.

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Author affiliations: HealthPartners Institute for Education and Research, Minneapolis, Minnesota (Kenneth F. Adams); Department of Epidemiology and Preventive Medicine, Regensburg University Medical Center, Regensburg, Germany (Michael F. Leitzmann); Division of Cancer Prevention and Division of Cancer Control and Population Sciences, National Cancer Institute, Bethesda, Maryland (Rachel Ballard-Barbash); Division of Cancer Epidemiology and Genetics, National Cancer Institute, Bethesda, Maryland (Demetrius Albanes); Genetics and Biometry Research Group, Division of Cancer Prevention, National Cancer Institute, Bethesda, Maryland (Victor Kipnis); Laboratory of Epidemiology, Demography, and Biometry, National Institute on Aging, Bethesda, Maryland (Tamara B. Harris); and AARP, Washington, DC (Albert Hollenbeck).

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