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Original Contribution

Body Mass Index in Young Adulthood, Obesity Trajectory, and Premature Mortality

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Although much research has been conducted on the role adult body mass index (BMI) plays in mortality, there have been fewer studies that evaluated the associations of BMI in young adulthood and adult weight trajectory with mortality, and it remains uncertain whether associations differ by race or sex. We prospectively examined the relationships of BMI in young adulthood (21 years of age) and adult obesity trajectory with later-life mortality rates among 75,881 men and women in the Southern Community Cohort Study. Study participants were enrolled between 2002 and 2009 at ages 40–79 years and were followed through December, 2011. Multivariable Cox proportional hazards models were used to estimate hazard ratios and 95% confidence intervals. There were 7,301 deaths in the 474,970 person-years of follow-up. Participants who reported being overweight or obese as young adults had mortality rates that were 19% (95% confidence interval: 12, 27) and 64% (95% confidence interval: 52, 78) higher, respectively, than those of their normal weight counterparts. The results did not significantly differ by race or sex. Participants who reported being obese in young adulthood only or in both young and middle adulthood experienced mortality rates that were 40%–90% higher than those of participants who were nonobese at either time. These results suggest that obesity in young adulthood is associated with higher mortality risk regardless of race, sex, and obesity status in later life.

body mass index; mortality; obesity; young adulthood

Abbreviations: BMI, body mass index; CHC, community health center; CI, confidence interval; CVD, cardiovascular disease; HR, hazard ratio; SCCS, Southern Community Cohort Study.

The prevalence of obesity among children in the United States has more than doubled in the past 30 years, and more than 30% of Americans are considered obese by the time they reach young adulthood (1). The short-term risks associated with childhood obesity include orthopedic, neurological, pulmonary, gastrointestinal, endocrine, and social and behavioral (e.g., low self-esteem and altered body image) problems, any of which could have lasting consequences in adulthood (2). Additionally, obese children are likely to become obese adults (3–7), and midlife obesity has been linked to a host of adverse conditions, including type 2 diabetes mellitus, cardiovascular disease (CVD), and several cancers (8–12). Midlife obesity has also consistently been shown to hasten death (8, 9, 12–21), with stronger associations suggested for whites than for East Asians and blacks (13–18, 22).

In several studies, most of which have involved men of European descent (23–27), adolescent or young-adulthood obesity has been linked to a higher long-term mortality risk (23–31). In 1 large US prospective study, which is the only multiethnic study to date to address this question, Park et al. (31) recently reported a significant positive association between body mass index (BMI; weight (kg)/height $(m)^2$) in young adulthood and higher rates of premature mortality later in life. The magnitude of the association was somewhat stronger among men than among women, and analyses stratified by racial/ethnic group were not presented (31).

Table 1. Characteristics of 75,881[a] Study Participants Reported at the Time of Cohort Entry, Stratified by Body Mass Index at 21 Years of Age, Southern Community Cohort Study, 2002–2011

Characteristic	Overall (*n* = 75,881)		BMI[b] Category at 21 Years of Age							
			Underweight, <18.5 (*n* = 8,728)		Normal, 18.5–24.9 (*n* = 46,855)		Overweight, 25–29.9 (*n* = 14,022)		Obese, ≥30 (*n* = 6,276)	
	No.	%	No.	%	No.	%	No.	%	No.	%
Sex										
Male	30,954	40.8	2,141	24.5	18,909	40.4	7,608	54.3	2,296	36.6
Female	44,927	59.2	6,587	75.5	27,946	59.6	6,414	45.7	3,980	63.4
Race										
White	24,492	32.3	2,942	33.7	15,461	33.0	4,135	29.5	1,954	31.1
Black	51,389	67.7	5,786	66.3	31,394	67.0	9,887	70.5	4,322	68.9
Age, years[c]	52.2 (8.8)		53.3 (9.0)		52.5 (8.9)		51.2 (8.5)		50.0 (7.8)	
BMI at cohort entry[c]	30.3 (7.5)		26.5 (6.0)		29.0 (6.4)		33.1 (7.3)		38.5 (9.4)	
Physical activity level, MET-hours/week[c]	22.8 (19.1)		22.4 (18.4)		22.9 (19.0)		23.4 (19.9)		21.5 (18.6)	
Smoking status										
Never smoker	26,887	35.7	3,262	37.7	16,303	35.1	4,846	34.8	2,476	39.8
Former smoker	17,293	23.0	1,948	22.5	10,779	23.2	3,241	23.3	1,325	21.3
Current smoker, <1 pack/day	20,008	26.6	2,227	25.7	12,551	27.0	3,754	27.0	1,476	23.7
Current smoker, ≥1 pack/day	11,058	14.7	1,214	14.0	6,825	14.7	2,069	14.9	950	15.3
Alcohol intake, drinks/week										
None	34,534	46.3	4,326	50.4	20,757	45.1	6,165	44.7	3,286	53.0
<7	23,767	31.8	2,679	31.2	14,810	32.2	4,373	31.7	1,905	30.7
7–14	12,070	16.2	1,156	13.5	7,858	17.1	2,355	17.1	701	11.3
>14	4,272	5.7	422	4.9	2,641	5.7	895	6.5	314	5.1
Educational level										
<9 years	5,723	7.6	711	8.2	3,403	7.3	1,060	7.6	549	8.8
9–11 years	15,684	20.7	1,868	21.4	9,415	20.1	2,990	21.3	1,411	22.5
High school graduate	29,522	38.9	3,321	38.1	18,233	39.0	5,454	38.9	2,514	40.1
Some college	14,933	19.7	1,709	19.6	9,299	19.9	2,734	19.5	1,191	19.0
College graduate or beyond	9,963	13.1	1,113	12.8	6,466	13.8	1,774	12.7	610	9.7

Table continues

Furthermore, in the majority of previous studies (23–29, 31) of young-adulthood BMI and mortality, investigators did not account for midlife BMI in their analyses, and findings from studies that included adjustment for midlife BMI have been inconsistent (30, 32). Thus, it remains uncertain how BMI in young adulthood might affect later-life mortality differently in terms of sex or race and whether the influence of young-adulthood BMI on premature adult mortality is independent of obesity later in life.

With the rising prevalence of obesity in children and young adults, particularly among racial/ethnic minorities (1, 33, 34), understanding whether and to what extent future mortality risk is "set" early in life is of major public health importance because it could mark early life as a critical time for thwarting premature adult death. Therefore, we examined the risks of all-cause and cause-specific mortality according to both BMI in young adulthood and the obesity trajectory from young to middle adulthood among black and white participants in a large prospective cohort study.

METHODS

Study participants

The Southern Community Cohort Study (SCCS) was established in 2001 to investigate the causes of cancer disparities (35, 36). This prospective study comprised 85,759 individuals who were 40–79 years of age at cohort entry and who were enrolled in 12 southeastern states (Alabama, Arkansas, Florida, Georgia, Kentucky, Louisiana, Mississippi, North Carolina, South Carolina, Tennessee, Virginia, and West Virginia) from 2002 to 2009. Two-thirds of SCCS participants are black. Eighty-six percent of participants were recruited from community health centers (CHCs), which are institutions that provide basic health care in underserved areas; thus, the cohort includes a large number of people with low levels of income and education. The remaining 14% of participants were enrolled using a mailed questionnaire sent to randomly selected residents of the 12-state area; 2.5% of invited participants returned the questionnaire.

Table 1. Continued

Characteristic	Overall ($n = 75,881$)		BMI[b] Category at 21 Years of Age							
			Underweight, <18.5 ($n = 8,728$)		Normal, 18.5–24.9 ($n = 46,855$)		Overweight, 25–29.9 ($n = 14,022$)		Obese, ≥30 ($n = 6,276$)	
	No.	%	No.	%	No.	%	No.	%	No.	%
Enrollment source										
Community health center	65,867	86.8	7,754	88.8	40,280	86.0	12,160	86.7	5,673	90.4
General population	10,014	13.2	974	11.2	6,575	14.0	1,862	13.3	603	9.6
Household income										
<$15,000	41,130	54.9	4,909	56.9	24,850	53.8	7,579	54.6	3,792	60.9
$15,000–$24,999	15,902	21.2	1,752	20.3	9,843	21.3	3,005	21.7	1,302	21.0
$25,000–$49,999	10,626	14.2	1,224	14.2	6,642	14.4	1,976	14.2	784	12.6
≥$50,000	7,275	9.7	738	8.6	4,868	10.5	1,319	9.5	350	5.6
Self-reported medical history[d]										
Cancer	5,916	7.9	822	9.5	3,804	8.2	932	6.7	358	5.8
Diabetes	15,883	20.9	1,502	17.2	8,310	17.8	3,640	26.0	2,431	38.8
Myocardial infarction or coronary artery bypass surgery	5,257	6.9	516	5.9	3,044	6.5	1,130	8.1	567	9.0
Stroke or transient ischemic attack	4,846	6.4	606	7.0	2,796	6.0	951	6.8	493	7.9
High cholesterol	25,343	33.5	2,958	34.0	15,395	33.0	4,740	33.9	2,250	35.9
Hypertension	41,280	54.5	4,371	50.2	24,344	52.0	8,400	60.0	4,165	66.4

Abbreviations: BMI, body mass index; MET, metabolic equivalents.

[a] The numbers of subjects with missing data are as follows: for BMI at cohort entry, $n = 299$; for physical activity level, $n = 1,642$; for smoking status, $n = 635$; for alcohol intake, $n = 1,238$; for educational level, $n = 56$; for household income, $n = 948$; for cancer, $n = 1,039$; for diabetes, $n = 158$; for myocardial infarction or bypass, $n = 179$; for stroke or transient ischemic attack, $n = 196$; for high cholesterol, $n = 281$; and for hypertension, $n = 146$.

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

[c] Values are expressed as mean (standard deviation).

[d] Categories are not mutually exclusive.

Compared with participants who were enrolled via mailed questionnaire, those who enrolled at CHCs were more likely to be black (70% vs. 42%) and to have less than 12 years of education (32% vs. 9%). All participants completed a baseline questionnaire at cohort entry that detailed demographic, medical, lifestyle, and other characteristics (questionnaire available at www.southerncommunitystudy.org).

Inclusion criteria

We excluded participants with a self-reported race other than black or white ($n = 4,129$) because we had too few participants to evaluate associations within other racial groups. For our main analysis of young-adulthood BMI and later-life mortality, we excluded participants with missing data on either weight at 21 years of age ($n = 3,162$; 3.9%), height at cohort entry ($n = 455$; 0.6%), or both ($n = 1,108$; 1.4%), leaving a study population of 75,881 participants (51,389 blacks and 24,492 whites). For the analysis of obesity trajectories, we additionally excluded participants who were missing data on BMI at cohort entry ($n = 299$) and those who were underweight (BMI <18.5) at 21 years of age ($n = 8,239$), at cohort entry ($n = 489$), or both ($n = 451$) to avoid the potential mixing of high- and low-risk individuals in our reference category of nonobese participants. Because adult BMI can be affected by frailty (especially among individuals 65 years of age or older (37)) and disease processes close to the date of death (38, 39), we also excluded participants older than 65 years of age at cohort entry ($n = 5,644$) and those with fewer than 3 years of follow-up ($n = 3,911$) from the obesity trajectory analyses, leaving a final sample size of 56,848 participants (39,556 blacks and 17,292 whites). This study was approved by institutional review boards at Vanderbilt University, Meharry Medical College, and the Harvard School of Public Health. All participants provided written informed consent.

BMI assessment

BMI in young adulthood was calculated using self-reported weight at 21 years of age and height at cohort entry, both of which were obtained from the baseline questionnaire. BMI in middle adulthood was calculated using the reported or measured weight and height at cohort entry (when subjects were 40–65 years of age). For analyses of the association between young-adulthood BMI and mortality, BMI was categorized into 4 groups: underweight (<18.5), normal weight (18.5–24.9), overweight (25–29.9), and obese (≥30). After excluding participants who were underweight in either young or middle adulthood, we used eligible participants' obesity status at

these 2 time points to define 4 obesity trajectory categories: nonobese at either time point, obese in young adulthood only, obese at cohort entry only, and obese at both time points. Categories were based on the approach described by Viner and Cole (40).

For SCCS participants who enrolled through September 2007 (85.5% of the cohort), current weight and height at time of enrollment were self-reported on the baseline questionnaire; these data were also abstracted from CHC medical records for a subset of this group (≈14,000 participants). For participants who enrolled after this time, height and weight were measured by trained interviewers using a Seca 703 digital scale and height rod (SECA, Chino, California). In the subset of participants for whom we had both self-reported weight and height data and data abstracted from CHC medical records, the calculated BMI values were highly correlated (Pearson's correlation coefficient >0.95), which indicated that the self-reported values were generally of high quality (14).

Mortality ascertainment

Vital status and cause-of-death information were ascertained using the National Death Index (41). Person-years for the main analysis of young-adulthood BMI and mortality were measured starting at cohort entry. For the obesity trajectory analysis, person-years were measured starting 3 years after cohort entry because of the exclusions described above. For both analyses, measurement of person-years ended at the date of death or on December 31, 2011, whichever came first.

Statistical analyses

We used Cox proportional hazards models with age as the underlying time metric to estimate hazard ratios and 95% confidence intervals for the associations of young-adulthood BMI and the obesity trajectory categories with all-cause mortality and cause-specific mortality. We evaluated time-dependent predictors to assess the proportionality assumptions of the Cox models. Potential confounders were included in the model based on prior knowledge of factors associated with BMI and mortality. The multivariable model included sex, race, smoking, alcohol consumption, educational level, annual household income, enrollment source, total physical activity level, and health insurance coverage, all of which were reported at study entry. We included fine categorization of past and current pack-years of smoking in the model to account for the strong influence of smoking on both BMI and mortality. We also examined baseline dietary variables (i.e., total fat, fiber, and energy intake) and marital status as potential confounders, but inclusion of these variables did not alter the hazard ratios and therefore they were not retained. Because conditions such as cancer, diabetes, hypercholesterolemia, hypertension, heart attack, and stroke might be on the causal pathway from young-adulthood BMI to premature death, we did not include these as covariates in the model of young-adulthood BMI and later-life mortality. However, because these conditions could conceivably confound analyses of obesity trajectory and mortality, we did evaluate these conditions as potential covariates in the obesity trajectory models; because their inclusion did not change our results, they were not included in the final model.

Cause-specific mortality was examined in models using the same set of covariates used in the all-cause mortality models. Causes of death were obtained from National Death Index records using the *International Classification of Diseases*, *Tenth Revision* codes. We examined the following cause-specific mortality outcomes: CVD (codes I00–I99), cancer (codes C00–C97), and all "other causes" excluding CVD, cancer, and injury, accidents, and consequences of external causes. We additionally evaluated models for the top 2 causes of "other" nonexternal deaths: diabetes (codes E11–E14) and chronic obstructive pulmonary disease (code J449). Tests for trend were conducted across categories of young-adulthood BMI using the Wald test with BMI category treated as an ordinal variable. We evaluated models stratified by race, sex, and BMI at cohort entry and statistically compared models with and without relevant interaction terms between these factors and young-adulthood BMI using the likelihood ratio test.

We estimated the shape of the continuous relationship between young-adulthood BMI and mortality endpoints using restricted cubic splines (42). Cubic polynomials were fitted and restrictions were placed on the resulting curve to ensure a smooth appearance using 4 knots, which were specified based on the distributions of young-adulthood BMI at 5%, 35%, 65%, and 95% cutoffs. We applied multiple combinations of knot numbers and placement, and the curves were similar.

We assessed the role of later-life BMI in several ways. First, we stratified our analyses of the association between young-adulthood BMI and later-life mortality by categories of BMI at cohort entry. Second, we additionally adjusted for participants' BMIs at cohort entry in the full model. To minimize potential confounding related to smoking status and bias introduced by prevalent disease (which might cause weight loss and increase the risk of death (39)), we also examined associations among never smokers and then further restricted our models to include never smokers who reported no history of major chronic disease at cohort entry (i.e., heart attack, stroke, or any type of cancer). Models stratified by enrollment source were also examined to assess potential heterogeneity. To provide an indication of the extent to which prematurity of death was associated with BMI in young adulthood, we considered the alternate outcomes of deaths occurring before the ages of 60, 65, 70, and 75 years. For the obesity trajectory analysis, in which the first 3 years of follow-up were already excluded, we additionally examined models that excluded the fourth and then fifth year of follow-up to evaluate any potential differences. All analyses were conducted using SAS software, version 9.3 (SAS Institute, Inc., Cary, North Carolina).

RESULTS

Participants who were obese in young adulthood (8.3% of cohort participants) were more likely to be women, black, nonsmokers, nondrinkers, and recruited from CHCs and to have lower household incomes (Table 1). Nearly 40% of those who were obese at 21 years of age reported having diabetes at cohort entry, and 66% reported hypertension. Young-adulthood BMI was positively associated with BMI at cohort

Table 2. Hazard Ratios for All-Cause and Cause-Specific Mortality in Relation to Body Mass Index at 21 Years of Age, Southern Community Cohort Study, 2002–2011

BMI Category at 21 Years of Age	No. of Deaths	Mortality Rate[a]	Minimally Adjusted HR[b]	95% CI	Fully Adjusted HR[c]	95% CI
			All-Cause Mortality			
Underweight	748	1,361.3	1.02	0.94, 1.10	1.00	0.92, 1.08
Normal	4,266	1,448.5	1.00	Referent	1.00	Referent
Overweight	1,494	1,745.1	1.17	1.11, 1.24	1.19	1.12, 1.27
Obese	793	2,164.6	1.72	1.59, 1.85	1.64	1.52, 1.78
P for trend			<0.001		<0.001	
			Cause-Specific Mortality			
Cardiovascular disease						
Underweight	206	369.2	0.99	0.85, 1.14	0.98	0.84, 1.14
Normal	1,212	409.8	1.00	Referent	1.00	Referent
Overweight	483	571.2	1.34	1.20, 1.49	1.33	1.19, 1.49
Obese	258	716.6	2.02	1.77, 2.31	1.87	1.63, 2.15
P for trend			<0.001		<0.001	
Cancer						
Underweight	210	371.6	1.10	0.94, 1.27	1.08	0.92, 1.26
Normal	1,076	360.9	1.00	Referent	1.00	Referent
Overweight	315	377.3	1.02	0.90, 1.15	1.06	0.93, 1.21
Obese	120	341.3	1.09	0.90, 1.32	1.12	0.92, 1.36
P for trend			0.96		0.53	
Other diseases[d]						
Underweight	279	516.1	0.98	0.86, 1.12	0.96	0.84, 1.09
Normal	1,630	554.5	1.00	Referent	1.00	Referent
Overweight	581	672.9	1.20	1.09, 1.32	1.21	1.10, 1.34
Obese	358	972.6	2.00	1.78, 2.24	1.85	1.64, 2.08
P for trend			<0.001		<0.001	

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

[a] Mortality rates per 100,000 person-years, directly standardized to the age distribution of the entire study population.

[b] Adjusted for age, race (black or white), and sex.

[c] Adjusted for age (continuous), race (black or white), sex, educational level (<9 years, 9–11 years, high school graduate, some college or junior college, or college graduate or beyond), annual household income (<$15,000, $15,000–$24,999, $25,000–49,999, or ≥$50,000), enrollment source (community health center or general population), smoking status (never smokers, former smokers by tertiles of pack-years of smoking, or current smokers by tertiles of pack-years of smoking), alcohol consumption (never drinkers, current nondrinkers with past consumption <1 drink/day, current nondrinkers with past consumption >1 drink/day, current drinkers of <1 drink/day, or current drinkers of >1 drinks/day), total physical activity level in metabolic equivalent-hours/day (continuous), and any type of public or private health insurance coverage (yes or no).

[d] Other diseases include those coded with the *International Classification of Diseases, Tenth Revision,* codes other nonexternal causes of death (excluding deaths due to cardiovascular disease, cancer, and injury, accidents, and consequences of external causes).

entry (Pearson correlation coefficient = 0.44, $P < 0.001$). Those who were obese only as young adults were more likely to be male and current smokers and to have low educational levels and low household incomes compared with persons in the other trajectory categories (Web Table 1, available at http://aje.oxfordjournals.org/).

During a median follow-up period of 6.3 years, 7,301 deaths occurred among the 75,881 study participants who were included in our primary analysis. We observed a significant trend of increasing risk of all-cause mortality (P for trend < 0.001), CVD mortality (P for trend < 0.001), and death from other causes (P for trend < 0.001) but not cancer mortality ($P = 0.43$) with increasing young-adulthood BMI (Table 2). Participants who reported being overweight or obese in young adulthood had mortality risks that were 19% (95% confidence interval (CI): 12, 27) or 64% (95% CI: 52, 78) higher, respectively, than their normal-weight counterparts. For later-life CVD deaths specifically, young-adult

overweight and obesity were associated with even larger risk elevations of 31% (95% CI: 18, 46) for overweight young adults and 89% (95% CI: 64, 117) for obese young adults. Overall results for deaths from other noncancer diseases were similar to those for CVD deaths. Included in the category of other disease were diabetes and chronic obstructive pulmonary disease, for which hazard ratios for participants who were obese in young adulthood were 3.31 (95% CI: 2.51, 4.36) and 2.01 (95% CI: 1.31, 3.07), respectively. Being underweight in young adulthood did not appear to influence future mortality risk.

Figure 1 shows plots of the estimated continuous associations of young-adulthood BMI with all-cause and cause-specific mortality in later life. For all-cause mortality, CVD mortality, and other disease mortality, the risk of death was slightly higher in participants with young-adulthood BMIs in the underweight and above normal ranges, whereas the risk of cancer death was elevated only among those with BMIs in the obese range. The spline model with 4 knots predicted that a young-adulthood BMI between 19.2 and 19.7 was associated with the lowest risk of later-life all-cause mortality. For CVD mortality, a BMI between 18.4 and 19.2 was associated with the lowest risk; for cancer mortality, it was a BMI between 24.4 and 25.1; and for other disease mortality, it was a BMI between 15.0 and 15.1.

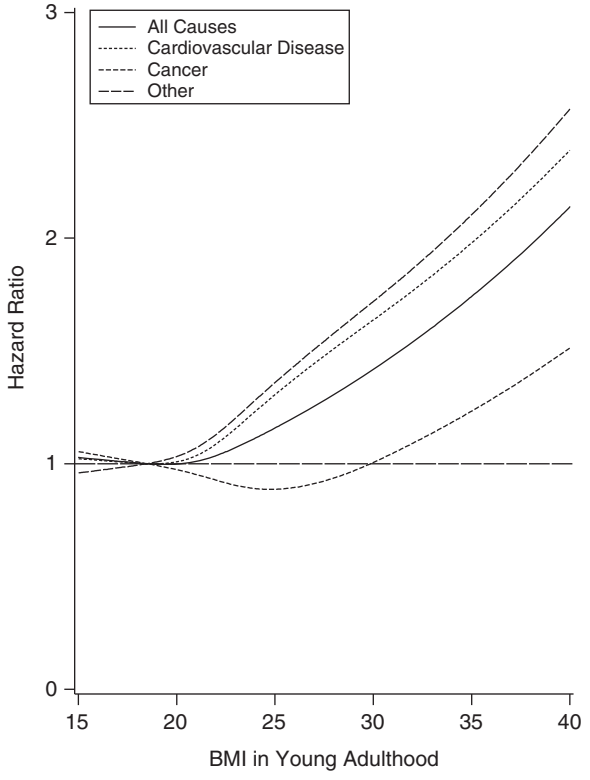

Figure 1. Restricted cubic spline plot of the association between body mass index (BMI) in young adulthood (age 21 years) and later-life all-cause and cause-specific mortality, Southern Community Cohort Study, 2002–2011. The restricted cubic spline reflects the fully adjusted hazard ratios, with knots at young-adulthood BMI measurements (weight (kg)/height (m^2)) of 17.4, 21.0, 23.7, and 31.4.

The association between young-adulthood BMI and later-life risk of all-cause mortality was not significantly modified by race (P for interaction = 0.42) or sex (P for interaction = 0.18), and we did not detect effect modification by race or sex for the cause-specific mortality endpoints. Furthermore, tests for the interaction between BMI in young adulthood and BMI at cohort entry were not significant for all-cause mortality (P for interaction = 0.08), CVD mortality (P for interaction = 0.42), and other disease mortality (P for interaction = 0.36). Young-adulthood overweight and obesity also remained significant predictors of later-life mortality risk after adjustment for BMI at cohort entry (for participants who were overweight as young adults, hazard ratio (HR) = 1.29, 95% CI: 1.21, 1.38; for participants who were obese as young adults, HR = 1.91, 95% CI: 1.76, 2.08), which suggests that the observed associations with young-adulthood BMI were independent of later-life BMI.

People who reported being obese in young adulthood only or in both young and middle adulthood had premature later-life mortality rates during follow-up that were 40%–90% higher than those of people who were nonobese at either time point (Table 3). For CVD mortality, young-adulthood obesity was associated with a 2-fold higher risk regardless of obesity status in middle adulthood. In addition, compared with those who were nonobese at both time points, the risk of death from CVD was significantly higher (by approximately 20%) for persons who were nonobese in young adulthood but became obese by the time of cohort entry. Hazard ratios for death from diabetes were higher for those who were obese only in young adulthood (HR = 7.08, 95% CI: 3.90, 12.84), those who were obese in both young and middle adulthood (HR = 3.13, 95% CI: 1.88, 5.23), and those who became obese in middle adulthood (HR = 1.70, 95% CI: 1.15, 2.49) relative to those who were nonobese at both time points (data not shown). Participants who reported being obese in both young and middle adulthood had a higher risk of death from chronic obstructive pulmonary disease (HR = 2.17, 95% CI: 1.07, 4.39) than did those who were nonobese at both time points (not shown).

We did not find significant evidence of a differential association between obesity trajectory and later-life all-cause mortality risk by race (P for interaction = 0.10), although we detected a significant interaction by sex (P for interaction = 0.02). In additional analyses, we determined that this was driven by apparent effect modification for the cancer mortality outcome (Web Table 2); thus, these results only are shown stratified by sex (Table 3). Women who were obese only in young adulthood had a 3-fold higher risk of dying from cancer (95% CI: 1.90, 5.76), but no association with cancer mortality was apparent for women or men in other trajectory groups.

The hazard ratios for the association of young-adulthood BMI with later-life all-cause mortality risk were slightly stronger when we limited our population to never smokers and to healthy never smokers. Among the healthy never smokers, participants who were overweight or obese as young adults had a 27% (95% CI: 8, 48) or 80% (95% CI: 50, 117) higher mortality risk, respectively, than did participants with a young-adult BMI in the normal range (not shown). For the obesity trajectory analyses, these restrictions also resulted in a slightly stronger all-cause mortality risk for young-adulthood obesity, but the association remained null for those who

Table 3. Hazard Ratios for All-Cause and Cause-Specific Mortality in Relation to Obesity Trajectory, Southern Community Cohort Study, 2002–2011

Cause of Death and Subgroup	BMI Trajectory Category[a]															
	Nonobese to Nonobese (n = 28,553)				Nonobese to Obese (n = 22,800)				Obese to Nonobese (n = 1,021)				Obese to Obese (n = 4,474)			
	No. of Deaths	Mortality Rate[b]	Adjusted HR[c]	95% CI	No. of Deaths	Mortality Rate[b]	Adjusted HR[c]	95% CI	No. of Deaths	Mortality Rate[b]	Adjusted HR[c]	95% CI	No. of Deaths	Mortality Rate[b]	Adjusted HR[c]	95% CI
All causes																
All participants	1,836	979.2	1.00	Referent	1,062	692.9	0.92	0.85, 1.00	140	2191.8	1.91	1.60, 2.28	284	986.2	1.45	1.27, 1.65
Men	1,296	1236.6	1.00	Referent	435	1027.5	0.91	0.81, 1.02	89	2373.2	1.64	1.31, 2.05	130	1524.3	1.56	1.29, 1.87
Women	540	650.6	1.00	Referent	627	567.4	0.93	0.82, 1.05	51	1957.1	2.63	1.93, 3.54	154	745.2	1.35	1.11, 1.63
Never smokers	248	465.8	1.00	Referent	324	171.2	1.02	0.85, 1.22	18	502.4	2.19	1.35, 3.56	94	258.9	1.66	1.30, 2.13
Healthy never smokers	188	405.7	1.00	Referent	235	405.5	1.05	0.86, 1.30	12	1107.0	2.39	1.33, 4.30	67	599.7	1.77	1.33, 2.37
CVD																
All participants	480	234.5	1.00	Referent	354	232.5	1.21	1.04, 1.40	38	578.0	1.94	1.38, 2.73	104	366.0	2.08	1.67, 2.60
Cancer																
All participants	445	238.3	1.00	Referent	234	150.6	0.88	0.74, 1.05	25	434.4	1.53	1.01, 2.32	42	153.5	1.06	0.77, 1.48
Other[d]																
All participants	729	389.3	1.00	Referent	411	266.7	0.82	0.71, 0.93	68	1041.4	2.27	1.75, 2.94	118	408.4	1.32	1.07, 1.63

Abbreviations: BMI, body mass index; CI, confidence interval; CVD, cardiovascular disease; HR, hazard ratio.

[a] BMI trajectory from 21 years of age to cohort entry.

[b] Mortality rates per 100,000 person-years, directly standardized to the age distribution of the entire study population.

[c] Adjusted for age, race, sex, educational level, household income, enrollment source, smoking status, alcohol consumption, total physical activity level, and insurance status.

[d] Other diseases include those coded with the *International Classification of Diseases, Tenth Revision,* codes for other nonexternal causes of death (excluding deaths due to CVD, cancer, and injury, accidents, and consequences of external causes).

moved from a nonobese category in young adulthood to an obese category in middle adulthood (Table 3). Small numbers precluded us from restricting the cause-specific mortality analyses to never smokers or healthy never smokers.

The risk of death associated with young-adulthood BMI and with the adult obesity trajectory did not vary according to enrollment source (data not shown). Furthermore, the hazard ratios for the obesity trajectory models in which the first 5 years of follow-up were excluded were negligibly different from those from the original model in which the first 3 years of follow-up were excluded. Finally, the magnitude of the associations between young-adulthood BMI and adult obesity trajectory with later-life all-cause mortality were maintained regardless of age at observation, including for subjects who died very prematurely (before the age of 60 years) (Web Table 3).

DISCUSSION

In the present large prospective study, a higher BMI in young adulthood was associated with a higher risk of premature death later in life that was driven largely by a higher risk of death from CVD and other noncancer diseases; these findings did not significantly vary by race or sex. Furthermore, obesity in young adulthood was associated with a higher later-life mortality risk regardless of obesity status in middle adulthood, which suggests that young-adulthood obesity is a strong predictor of premature mortality and might be responsible for a substantial number of unnecessary years of life lost.

The association of young-adulthood obesity with premature death was even stronger after we accounted for later-life BMI in our study. Our findings imply that becoming obese in middle adulthood carries few consequences in relation to all-cause mortality in this population, which suggests that the most serious detrimental outcomes of obesity might be triggered in early adulthood. Although it has been shown that adult obesity increases the risk of premature mortality in many studies (8, 9, 12–21), adult obesity has not been found to be a strong predictor of premature death among blacks in the SCCS. The overall risk of death associated with obesity in the SCCS tended to be lower among those with lower incomes, perhaps because other detriments to health are more prominent among low-income participants (14). For example, a greater percentage of deaths due to chronic obstructive pulmonary disease and a lower percentage of deaths from coronary heart disease, breast cancer, and colon cancer were evident among SCCS participants in the lowest income brackets compared with those in the highest income brackets.

Participants who were obese at 21 years of age but nonobese at cohort entry (approximately 20–45 years later) were found to have the highest relative mortality risk. It is possible that some of these participants initiated intentional weight loss in response to adverse obesity-related health concerns, although their comorbidity profiles did not appear worse than those of participants who remained obese (Web Table 1). Alternatively, these results might reflect weight loss due to underlying illness despite our efforts to exclude persons with less than 3–5 years of follow-up. It is also possible that these results reflect residual confounding by cigarette smoking status (the percentage of deaths among smokers was highest in this group) or that this finding might simply reflect the role of chance. Indeed, the potential role of chance looms large given the small number of events in this group and the multiple comparisons made without statistical adjustment. We therefore do not infer that weight control in middle adulthood is harmful, because healthy intentional weight loss has been associated with substantial reductions in all-cause mortality (43, 44).

In the present study, CVD and diabetes were the causes of death that were most strongly related to young-adulthood overweight and obesity, and they were also among the only major causes of death associated with a "nonobese to obese" trajectory. Thus, although our study emphasizes that young-adulthood obesity has considerable long-term health implications, becoming obese in middle adulthood is associated with serious adverse health outcomes such as diabetes and CVD (45), the latter being the single largest killer of men and women in the United States (46). Previous studies of the association between young-adulthood obesity and cancer mortality have been inconsistent (47–49), and we found a small, nonsignificant increase in cancer mortality among participants who were obese in young adulthood. Discrepancies in findings might be partially explained by differing distributions of cancer types between studies, because obesity has been associated with some but not all cancers (50). Our finding that women who were obese in young adulthood but not in middle adulthood might be particularly susceptible to dying from cancer is likely an artifact arising from the small number of cancer deaths among these women ($n = 14$) and men ($n = 12$), and a review of the cancer types (for women, there were 4 cases of lung cancer, 2 of uterine cancer, 2 of pancreatic cancer, and 1 each of liver, skin, breast, kidney, and myeloid cancer, as well as of cancer of unknown origin; for men, there were 7 cases of lung cancer, 2 of liver cancer, and 1 each of stomach, prostate, and bladder cancer) provided no further insights into a potential causal explanation.

The strengths of this study include the use of a well-described, large, population-based, biracial prospective cohort to characterize the contribution of young-adulthood BMI to later-life mortality risk against a public health backdrop of steeply rising childhood obesity rates. We incorporated data on potential covariates that were not considered in many previous studies, such as detailed smoking history, alcohol intake, and physical activity level (23–29). We also evaluated potential differential associations of young-adulthood BMI across sex, race, and later-life BMI categories within the same study. A potential limitation of this study is misclassification of BMI due to the use of self-reported height and weight for a large proportion of participants. However, the extent of this misclassification is likely to be low given the high correlation (>0.95) between self-reported and measured BMI overall and within strata of race, income, and educational level in the SCCS (14). Additionally, some bias in the recall of weight at 21 years of age is expected; however, we observed a striking dose-response signal for young-adulthood BMI and later-life mortality that is unlikely to be entirely explained by bias. Because of our study design, deaths that occurred between the age of 21 years and cohort entry are not represented, and we cannot comment on the influence of young-adulthood

BMI on deaths that occurred before baseline. However, given the relatively low mortality rates in young adulthood and the suggestion that excess mortality due to adolescent overweight might not manifest before participants reach their thirties (29), we consider this a minor limitation. Although we did not have the power to evaluate cause-specific endpoints among healthy never smokers or to evaluate risks for individual cancer types, these unresolved questions could be targeted in future pooled studies.

In the present large prospective cohort study of both black and white participants, young-adulthood overweight and obesity were associated with a higher risk of premature mortality regardless of race, sex, and obesity status in later adult life. These findings emphasize the importance of maintaining a healthy weight into young adulthood and highlight the need for public health efforts to curb the rising prevalence of obesity among children and adolescents.

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