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Obesity-mortality link over the life course: the contribution of population compositional changes

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ABSTRACT

A key uncertainty in the obesity-mortality association continues to be how this association changes over the life course. Prior studies tend to rely on cross-sectional design with static weight status taken at the time of the survey. This study tracks a cohort of individuals and employs lifelong body mass index information from the Framingham Heart Study original cohort (1948–2010). We focus on respondents who were younger than age 45 at time of their first survey (n = 2,176) and evaluate how the mortality risk associated with obesity changes over three age groups (below 45, 45–59, and 60 and above) and how population compositions may contribute to this pattern. We find the hazard ratio associated with obesity compared to normal weight decreases over three age groups, but this pattern is influenced by different ages of onset of obesity, inconsistency in the reference group (normal weight) over ages, and mortality selection effects. These factors explain away the decreasing effect of obesity (with onset before age 45) on mortality up to age 60; after age 60, the detrimental effect still declines, but to a much less degree. Later onset of obesity, however, is not significantly associated with excess mortality risks after age 60.

As one of the most urgent epidemics in many societies, obesity has emerged as a key risk factor for many illnesses and morbidities and may even threaten the long-term secular increase in human life expectancy (Olshansky et al. 2005; Solomon and Manson 1997; Stewart, Cutler, and Rosen 2009). The extent of this threat, however, is still being debated (Allison et al. 1999; Flegal et al. 2005; Mokdad et al. 2004; Olshansky et al. 2005; Stewart, Cutler, and Rosen 2009; Stokes and Preston 2016a). Earlier estimates of the percentage of total deaths due to obesity vary widely, from 5% to 13% (Allison et al. 1999; Flegal et al. 2005; Mokdad 2005; Mokdad et al. 2004). While the obesity-mortality association has been extensively studied, a key uncertainty continues to be how this association changes over the life course (Calle et al. 1999; Fontaine et al. 2003; Freedman et al. 2006; Lantz et al. 2010; Reynolds, Saito, and Crimmins 2005; Zheng and Dirlam 2016).

Weight control guidelines and intervention targets require an accurate characterization of the obesity-mortality association in late life. Therefore, resolving the uncertainty over the age patterning of the obesity-mortality relationship is critical to designing clinical and public health strategies to manage an aging population in the wake of the obesity epidemic. Moreover, as most deaths in the United States occur at older ages, the age dependency of the

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obesity-mortality association has important ramifications for estimates of the number of total deaths attributable to obesity. If obesity's effect grows stronger by age, then prominent estimates of the number of obesity-attributable deaths may be seriously underestimated. However, if the actual relationship is a diminishing one, then obesity's national-level impact may be more modest. Similarly, projections of obesity's effect on the future path of U.S. life expectancy will be highly sensitive to the age dependency of the obesity-mortality association. Thus, a clarification of the age dependency of the obesity-mortality association will shed critical light on the damage that obesity is having on population health in the United States and other nations grappling with the obesity epidemic.

Many studies in this topic conclude that the deleterious effect of obesity on mortality weakens with age (e.g., Bender et al. 1999; Fontaine et al. 2003; Freedman et al. 2006; Stevens et al. 1998; Zheng and Yang 2012), with some studies finding no harmful effect (e.g., Kuk and Ardern 2009; Reynolds, Saito, and Crimmins 2005) or even a protective effect of obesity among older adults (Kim et al. 2012; Lantz et al. 2010; McAuley et al. 2010; Stallard 2011; Uretsky et al. 2007). In contrast, some research suggests that obesity may be more harmful for older adults than younger adults (Masters et al. 2013).

The age-dependent nature of the obesity-mortality association, however, may be plagued by biasing factors, e.g., healthy participant effect, mortality selection, and reverse causality. The healthy participant effect refers to the fact that survey respondents have to be healthy enough to participate in the survey. Among older adults, obese individuals may be more likely to be institutionalized due to poor health, which may cause survey data to include substantially higher proportions of healthy older adults in the obese group, as compared to the nonobese group (Masters et al. 2013). Mortality selection refers to the process that eliminates individuals who are frailer or have severe diseases earlier in the life course, and leaves those who are more robust to survive to old age. This selection process may operate more strongly among obese adults than among non-obese adults, as obese adults may be at greater risk of premature death from obesity-related diseases (Zheng and Dirlam 2016). Reverse causality refers to the possibility that illness-induced weight loss can cause normal weight group to be more heterogeneous and less healthy in older ages, which may include individuals who were previously overweight or obese but lose weight due to diseases (Stokes and Preston 2016b). All three processes can reduce the observed hazard ratios of mortality associated with obesity across the life course. But the contributions of healthy participant effect and mortality selection effect have been disputed by several studies (Zheng and Dirlam 2016; Wang and Liu 2014; Wang 2014; Hanley 2017; Mehta and Stokes 2013).

If the selection effects mentioned above are minimal, other possible explanations for the reduced harmful effects of obesity must be explored. One plausible explanation, which we will test, is that of the role of obesity duration. A recent, but growing body of literature indicates that the accumulation of time spent obese contributes to morbidity and mortality risk beyond weight status at a single point in time (e.g., Abdullah et al. 2011a; Abdullah et al. 2011b; Everhart et al. 1992; Greenberg 2006; Greenberg, Fontaine, and Allison 2007; Lee et al. 2012; Mehta et al. 2014; Zhang and Pincus 2016; Zheng, Tumin, and Qian 2013). People who become obese at earlier ages are at significantly higher risk of death compared to those who become obese at older ages because they tend to remain so for most of their life course (Adams et al. 2014). Therefore, the accumulation of time in the obese category among people who were obese in early adulthood could increase their mortality risk above that of people who became obese in later adulthood. Moreover, people who are obese at

older ages are a heterogeneous group, some of whom may have been overweight or normal weight at younger ages. The heterogeneity in population composition with regard to duration of obesity for different age groups may contribute to the age pattern of the obesity-mortality association.

Most prior studies that have documented changes in the association of obesity with mortality over age have relied on cross-sectional survey data with a single measure of weight status taken at the time of the survey. Such a research design is insufficient to understand the role of selection processes in shaping the age dependency of the obesity-mortality association. A more appropriate design would be to track a cohort of individuals and study how selection patterns evolve over the life course. In this study, we employ relatively complete cohort data from the Framingham Heart Study (FHS) original cohort, which collected health and body mass index (BMI) information across all of its 30 waves (Framingham Heart Study 2017), and examine how these selection or population composition patterns may change over the life course and how they may or may not contribute to the weakening obesity-mortality link over ages.

Materials and Methods

Data and Participants

The data used in this study derive from the original cohort of FHS. The original cohort consisted of 5,079 men and women, 28–74 years of age at the onset of the study. Participants were examined every 2–3 years from 1948 to 2010. The study period consisted of 30 exams. We focus on respondents who were younger than age 45 at time of their first survey (n = 2,722, 53%). After removing individuals with missing data on the time constant variables (gender, educational attainment) or without valid data on time varying variables (height, weight, age, smoking behavior, and disease), we obtained a final sample size of 2,176. FHS collected information on deaths through newspapers, personal physician communications, or coroner reports. As of 2011, 1,913 individuals in our analytic sample died, and 263 survived or were censored. FHS supplied the days since exam 1 as the date of death, allowing us to compute the time spent at risk in a very detailed manner. For the 1,913 respondents that have died, exposure to mortality risk was calculated as the duration from age at first survey until the date of death (in years). For the 263 surviving respondents, we computed exposure to mortality risk as the duration from age at first survey until date of last contact or the last exam these individuals participated in. We reshaped the data to a person-year format, which was left truncated at age at first survey and right-censored at the age of death, age of last contact, or age at last exam. The reshaped data were sorted by age of exam. After reshaping the data, the total number of observations was 27,048.

Predictors of Mortality

Height and weight information was collected through clinical assessment at each survey wave. BMI is defined as the ratio of weight in pounds to the square of height in inches multiplied by 703. We calculated the average BMI for each individual by three age groups: Less than age 45, 45–59, and 60 and above. We created four measures of BMI categories. The first measure consists of five categories: underweight (BMI of less than 18.5), normal

weight (BMI between 18.5 and 24.9), overweight (BMI between 25 and 29.9), class I obesity (BMI between 30 and 34.9), and class II/III obesity (BMI greater than or equal to 35). We combined class I obesity and class II/III obesity into a single category and called it obese in the second BMI variable.

The third BMI variable captures the age of the onset and duration of obesity. Among obese individuals within each age group, we differentiated whether the onset of obesity occurred before age 45, between age 45 and 59, or at age 60 and above. Built on the third BMI variable, the fourth BMI variable further distinguishes stable normal weight from unstable normal weight. Stable normal weight refers to individuals who remained as normal weight in the current and previous age groups. In contrast, unstable normal weight refers to individuals who were normal weight in the current age group but were not normal weight in the previous age groups. By differentiating stable from unstable normal weight and using stable normal weight as the reference group, we use a group of individuals who likely have not suffered from disease-induced weight loss thereby accounting as best as possible for this biasing effect.

Sociodemographic and Behavioral Factors

Birth cohorts are controlled in the analysis because prior studies have reported substantial cohort-based pattern in obesity (Reither, Hauser, and Yang 2009; Yu 2018), obesity-related mortality (Yu 2012), and mortality of all causes (Yang 2008; Zheng, Yang, and Land 2016). They are treated as a continuous variable. Educational attainment consists of four categories: less than high school, high school graduate, some college, and college graduate. Smoking status includes four categories: nonsmoker, low smoking (1–9 cigarettes), moderate smoking (10–19 cigarettes), and heavy smoking (20 or more cigarettes). Smoking is a time varying variable.

Health and Medical History

In each exam, respondents were asked if they took any medication to treat a health condition and if they were diagnosed with or had any disease. They were also examined by teams of doctors and nurses in order to obtain information about their overall health status. We created a dummy variable that measures whether the participant was diagnosed or reported to have degenerative arthritis, gouty arthritis, rheumatoid arthritis, asthma or wheezing, prostate trouble, prostate disease, heart disease, hypertension, rheumatic heart disease, hypertensive cardiovascular disease, arrhythmia, aortic disease, mitral valve disease, vascular brain disease, pulmonary disease, gallbladder disease, urinary tract disease, renal disease, neurological disease, or thyroid disease. We also coded the dummy variable as 1 if the participant took medication to treat cardiovascular/heart diseases, arthritis, thyroid disease, or diabetes or thyroid trouble. We did not create a summary index of diseases because the number of diseases examined changed across exams.

Statistical Analysis

We fitted Cox hazard models adjusted for sociodemographic, smoking behavior, health and medical history to calculate the relative mortality risk associated with BMI categories by three age intervals, <45, 45–59, and 60 and above, separately. We used attained age as the time metric. Smoking behavior, health and medical history variables were assessed multiple

times in the duration of the Framingham Heart study. A Cox-model with time-dependent covariates as it is the case in our models compares the risk of an event at each time. Considering time-varying disease characteristics as both potential confounders and mediators, we proceed by fitting models both with and without adjustment for these factors.

Results

Table 1 shows the descriptive statistics of the sample across three age intervals. Since individuals could die or drop out from the study at any point after age 45, the sample size for older age groups is smaller. Overall, the composition of each sample is fairly similar, indicating that the dropout of individuals due to death or missing to follow-up does not produce dramatic changes in sample characteristics. But the proportion compositions of BMI categories do change across three age groups as shown in Table 2. The percentages of individuals in class I obesity or class II/III obesity increase from 8.73% and 1.56%, to 10.94%

Table 1. Descriptive statistics of individuals in the original cohort across three age groups, FHS, 1948–2011.

Time-invariant variables						
	Less than 45		45–59		Greater than 60	
	N	Mean (or %)	*N*	Mean (or %)	*N*	Mean (or %)
Gender						
Female	1,207	55.47%	1,188	55.77%	1,117	56.79%
Male	969	44.53%	942	44.23%	850	43.21%
Educational attainment						
Less than high school	697	32.03%	677	31.78%	624	31.72%
High school graduate	782	35.94%	769	36.10%	706	35.89%
Some college	379	17.42%	371	17.42%	349	17.74%
College graduate	318	14.61%	313	14.69%	288	14.64%
Birth cohorts (1906–1923)	2176	1913	2130	1913	1967	1913
Time-variant variables						
	Less than 45		45–59		Greater than 60	
	N[a]	Mean (or %)	N[a]	Mean (or %)	N[a]	Mean (or %)
BMI	27,048	26.21	27,000	26.21	26,062	26.22
Smoking behavior						
Nonsmoker	17,706	65.46%	17,700	65.56%	17,409	66.80%
Low smoking (1–9 cigarettes)	1,652	6.11%	1,648	6.10%	1,576	6.05%
Moderate smoking (10–19 cigarettes)	1,974	7.30%	1,966	7.28%	1,871	7.18%
Heavy smoking (20 or more cigarettes)	5,716	21.13%	5,686	21.06%	5,206	19.98%
Disease index	18,341	67.81%	18,330	67.89%	17,839	68.45%

[a]N shows total number of observations in the person-year data.
[b]Weight (pounds)/height(feet)2*703.

Table 2. Distribution of individuals according to average body mass index across three age groups, FHS, 1948–2011.

	Less than 45			45–59			60 and above		
	Deaths	*N*	%	Deaths	*N*	%	Deaths	*N*	%
Underweight	34	36	1.65	23	24	1.13	21	21	1.07
Normal weight	993	1,149	52.80	832	953	44.74	653	750	38.13
Overweight	680	767	35.25	758	864	40.56	736	828	42.09
Class I obesity	176	190	8.73	206	233	10.94	247	296	15.05
Class II/III obesity	30	34	1.56	52	56	2.63	66	72	3.66
Total	1,913	2,176		1,871	2,130		1,723	1,967	

and 2.63%, to 15.05% and 3.66% across three age groups, respectively. The percentage of individuals who are normal weight decreases from 52.8% to 38.13% across age groups. These numbers imply that the changes in weight status over the life course at the individual level have altered the compositions within each BMI category across the three age groups at the aggregate level.

Table 3 more clearly demonstrates this message. All the BMI groups gradually become more heterogeneous across ages. For example, among class II/III obese group in age 45–59, 54% of them were in the lower BMI category before age 45. This number increases to 79% for class II/III obese group in age 60 and above, among whom 51% were class I obese, 24% were overweight, and 4% were normal weight before age 45. For class I obese group in age 45–59, 43%, and 2% were overweight and normal weight before age 45. These numbers increase to 57% and 11% for class I obese group in age 60 and above. The delayed onset of obesity at the individual level has made the obese group in later ages increasingly come from individuals who were normal- or over-weight in the early adulthood. If later onset of obesity is associated with lower mortality rate compared to earlier onset of obesity, this changing composition of obese groups then can lead to weakening link between obesity and mortality over ages.

Moreover, normal weight in later ages increasingly comes from individuals who were in higher weight status in early adulthood. About 6% of them in age 45–59 were overweight before age 45, and 13% of them in age 60 and above were overweight or obese before age 45. If weight loss is associated with higher mortality risk, the changing composition of normal weight group can also lead to the weakening link between obesity and mortality over ages. We test these two hypotheses in the next two tables.

Table 4 shows the age pattern of BMI-mortality link before and after accounting for different ages of onset of obesity. The top three sets of models test how the association

Table 3. Composition of body mass index categories in age groups 45–59, 60, and above by body mass index categories in age group before age 45, FHS, 1948–2011.

	BMI categories in age group 45–59					
BMI categories before age 45	Underweight	Normal weight	Overweight	Class I obesity	Class II/III obesity	Total
	N (%[a])	*N* (%[a])	*N* (%[a])	*N* (%[a])	*N* (%[a])	*N* (%[a])
Underweight	14 (58.33)	20 (2.10)	0 (0.00)	0 (0.00)	0 (0.00)	34 (1.60)
Normal weight	10 (41.67)	872 (91.50)	239 (27.66)	4 (1.72)	0 (0.00)	1,125 (52.82)
Overweight	0 (0.00)	61 (6.40)	591 (68.40)	100 (42.92)	1 (1.79)	753 (35.35)
Class I obesity	0 (0.00)	0 (0.00)	34 (3.94)	121 (51.93)	29 (51.79)	184 (8.64)
Class II/III obesity	0 (0.00)	0 (0.00)	0 (0.00)	8 (3.43)	26 (46.43)	34 (1.60)
Total	24	953	864	233	56	2,130
BMI categories before age 45	BMI categories in age group 60 and above					
	Underweight	Normal weight	Overweight	Class I obesity	Class II/III obesity	Total
	N (%[a])	N (%[a])	N (%[a])	N (%[a])	N (%[a])	N (%[a])
Underweight	10 (47.62)	21 (2.80)	3 (0.36)	0 (0.00)	0 (0.00)	34 (1.73)
Normal weight	11 (52.38)	635 (84.67)	369 (44.57)	33 (11.15)	3 (4.17)	1,051 (53.43)
Overweight	0 (0.00)	91 (12.13)	408 (49.28)	169 (57.09)	17 (23.61)	685 (34.82)
Class I obesity	0 (0.00)	3 (0.40)	45 (5.43)	80 (27.03)	37 (51.39)	165 (8.39)
Class II/III obesity	0 (0.00)	0 (0.00)	3 (0.36)	14 (4.73)	15 (20.83)	32 (1.63)
Total	21	750	828	296	72	1,967

[a]Column percentage.

Table 4. Total mortality risk in relation to body mass index across three age groups, FHS, 1948–2011.

	Less than 45 (Obs. = 27,048)				45–59 (Obs. = 27,000)				60 and above (Obs. = 26,062)			
	Deaths	N	HR	SE	Deaths	N	HR	SE	Deaths	N	HR	SE
Total	1,913	2,176			1,871	2,130			1,723	1,967		
BMI variable 1												
Underweight	34	36	1.15	(1.19)	23	24	1.08	(1.24)	21	21	1.87***	(1.25)
Normal weight	993	1149	1.00		832	953	1.00		653	750	1.00	
Overweight	680	767	1.15*	(1.05)	758	864	1.05	(1.05)	736	828	0.93	(1.06)
Class I obesity	176	190	1.56***	(1.09)	206	233	1.42***	(1.08)	247	296	0.99	(1.08)
Class II obesity	30	34	2.31***	(1.21)	52	56	2.21***	(1.16)	66	72	1.60***	(1.14)
BMI variable 2												
Underweight	34	36	1.15	(1.19)	23	24	1.08	(1.24)	21	21	1.86***	(1.25)
Normal weight	993	1149	1.00		832	953	1.00		653	750	1.00	
Overweight	680	767	1.15*	(1.05)	758	864	1.05	(1.05)	736	828	0.92	(1.06)
Obese	206	224	1.64***	(1.08)	258	289	1.53***	(1.08)	313	368	1.07	(1.07)
BMI variable 3												
Underweight	34	36	1.15	(1.19)	23	24	1.08	(1.24)	21	21	1.87***	(1.25)
Normal weight	993	1149	1.00		832	953	1.00		653	750	1.00	
Overweight	680	767	1.15*	(1.05)	758	864	1.05	(1.05)	736	828	0.92	(1.06)
Obese (onset of obesity before age 45)	206	224	1.64***	(1.08)	167	184	1.59***	(1.09)	132	146	1.36**	(1.10)
Obese (onset of obesity during ages 45–59)					91	105	1.43**	(1.12)	63	76	1.23	(1.14)
Obese (onset of obesity after age 59)									118	146	0.82	(1.11)

between five categories of BMI (BMI variable 1) and mortality changes across the three age groups. The hazard ratios associated with class I obesity and class II/III obesity have declined from 1.56 (P <.001) and 2.31 (P < .001) in age group under 45 years to 0.99 and 1.60 (P < .001) in age group above 60 years. The middle three sets of models combine class I obesity and class II/III obesity into one obese group (BMI variable 2). The hazard ratios associated with obesity have declined from 1.64 (P < .001) in age group under 45 years to 1.53 (P < .001) and 1.07 in the two older age groups. These hazard ratios associated with obesity are the basis of comparison to check how population compositional changes may alter them.

The bottom three sets of models distinguish the age of onset of obesity (BMI variable 3). Three important findings can be drawn from these models: (1) later onset of obesity is associated with lower mortality risk compared to earlier onset of obesity. For example, among individuals in age group 45–59, those with onset of obesity during this age group face 43% increase in mortality risk, while those with onset of obesity in the preceding age group face 60% increase in mortality risk; (2) changing composition of obese group explains the weakening obesity-mortality link over ages to some extent. After accounting for different ages of onset of obesity, the hazard associated with obesity declines to a less degree over ages. The hazard ratio associated with obesity with onset before 45 has declined from 1.64 (P < .001), to 1.59 (P < .001), to 1.36 (P < .01) over the three age groups compared to the whole obese group whose hazard ratio declines from 1.64 (P < .001), to 1.53 (P < .001), to 1.07. In other words, without accounting for different ages of onset of obesity, we can overestimate the degree of reduction in obesity related mortality risk over ages; and (3) later

onset of obesity (onset after age 45) is not significantly associated with excess mortality risk after age 60.

Table 5 investigates whether changing composition of reference group (normal weight) may play a role in the weakening obesity-mortality link over ages. We distinguish stable normal weight from unstable normal weight (BMI variable 4) and use stable normal weight as the reference group throughout all the age groups. We find the obesity-mortality link declines to an even less extent over the ages. The hazard ratio associated with obesity with onset before 45 declines from 1.64 ($P < .001$), to 1.61 ($P < .001$), to 1.42 ($P < .01$) over the three age groups. Therefore, the illness induced reverse causality also makes some contribution to the weakening obesity-mortality link over ages, but the contribution is less than different ages of onset of obesity. After accounting for changing composition of reference group, later onset of obesity (onset after age 45) is still not significantly associated with excess mortality risk after age 60.

Now turn to healthy participant effect. Sample size decreases by 46 from 2,176 to 2,130 from the youngest age group to the middle group as shown in Table 5, which includes 42 (1,913–1,871) deaths occurring in the youngest age group. In other words, only four individuals dropped across these two age groups due to reasons other than death. Sample size decreases by 163 from 2,130 to 1,967 from the middle age group to the oldest group, which includes 148 (1,871–1,723) deaths occurring in the middle age group. In other words, only 15 individuals dropped across these two age groups due to reasons other than death. The reasons for this dropout are not clear, some of which might be related to healthy participant effect. But overall, the salience of this effect is inconsequential due to the very small amount of dropout.

Table 6 constrains the sample to those who survived to age 60, so that mortality selection effect is removed in the analyses. After removing mortality selection effect and accounting for changing composition of obese and reference group (BMI variable 4 in the bottom three sets of models), hazard ratio associated with onset of obesity before age 45 increases from 1.63 ($P < .001$) to 1.65 ($P < .001$) across the first two age groups, but then declines to 1.42 ($P < .001$) in the oldest age group (compared to 1.07 without correcting for these population

Table 5. Total mortality risk in relation to onset of obesity and normal weight consistency across three age intervals, FHS, 1948–2011.

	Less than 45[a] (Obs.[b] = 27,048)				45–59[a] (Obs.[b] = 27,000)				60 and above[a] (Obs.[b] = 26,062)			
	Deaths	*N*[c]	HR	SE	Deaths	*N*[c]	HR	SE	Deaths	*N*[c]	HR	SE
Total	1,913	2,176			1,871	2,130			1,723	1,967		
BMI variable 4												
Underweight	34	36	1.15	(1.19)	23	24	1.09	(1.24)	21	21	1.94***	(1.25)
Stable normal weight	993	1,149	1.00		762	872	1.00		510	588	1.00	
Unstable normal weight	([d])				70	81	1.15	(1.13)	143	162	1.21	(1.10)
Overweight	680	767	1.15*	(1.05)	758	864	1.06	(1.05)	736	828	0.96	(1.06)
Obese (onset of obesity before age 45)	206	224	1.64***	(1.08)	167	184	1.61***	(1.09)	132	146	1.42***	(1.11)
Obese (onset of obesity during ages 45–59)					91	105	1.45**	(1.12)	63	76	1.28	(1.14)
Obese (onset of obesity after age 59)									118	146	0.86	(1.11)

Table 6. Total mortality risk among individuals that survived to age 60 in relation to body mass index across three age groups, FHS, 1948–2011.

	Less than 45[a] (Obs.[b] = 26,062)				45–59[a] (Obs.[b] = 26,062)				60 and above[a] (Obs.[b] = 26,062)			
	Deaths	*N*[c]	HR	SE	Deaths	*N*[c]	HR	SE	Deaths	*N*[c]	HR	SE
Total	1,723	1,967			1,723	1,967			1,723	1,967		
BMI variable 2												
Underweight	32	34	1.20	(1.20)	23	24	1.17	(1.24)	21	21	1.86***	(1.25)
Normal weight	906	1051	1.00		770	887	1.00		653	750	1.00	
Overweight	605	685	1.13*	(1.06)	697	792	1.05	(1.06)	736	828	0.92	(1.06)
Obese	180	197	1.63***	(1.09)	233	264	1.59***	(1.08)	313	368	1.07	(1.07)
BMI variable 3												
Underweight	32	34	1.20	(1.20)	23	24	1.18	(1.24)	21	21	1.87***	(1.25)
Normal weight	906	1051	1.00		770	887	1.00		653	750	1.00	
Overweight	605	685	1.13*	(1.06)	697	792	1.05	(1.06)	736	828	0.92	(1.06)
Obese (onset of obesity before age 45)	180	197	1.63***	(1.09)	153	170	1.64***	(1.10)	132	146	1.36**	(1.10)
Obese (onset of obesity during ages 45–59)					80	94	1.49**	(1.13)	63	76	1.23	(1.14)
Obese (onset of obesity after age 59)									118	146	0.82	(1.11)
BMI variable 4												
Underweight	32	34	1.20	(1.20)	23	24	1.18	(1.24)	21	21	1.94***	(1.25)
Stable normal weight	906	1,051	1.00		707	813	1.00		510	588	1.00	
Unstable normal weight	([d])				63	74	1.11	(1.14)	143	162	1.21	(1.10)
Overweight	605	685	1.13*	(1.06)	697	792	1.05	(1.06)	736	828	0.96	(1.06)
Obese (onset of obesity before age 45)	180	197	1.63***	(1.09)	153	170	1.65***	(1.10)	132	146	1.42***	(1.11)
Obese (onset of obesity during ages 45–59)					80	94	1.50**	(1.13)	63	76	1.28	(1.14)
Obese (onset of obesity after age 59)									118	146	0.86	(1.11)

compositional changes). In other words, these three factors explain away the decreasing hazard associated with obesity (with onset before age 45) up to age 60; after age 60, the hazard still declines, but to a much less degree after accounting for these three factors. However, later onset of obesity (onset after age 45) is still not significantly associated with excess mortality risk after age 60. Since mortality selection effect still exists in the oldest age group, we further split it into two age groups (60–64, 65+) (see Appendix 1 and 2). We find (1) hazard ratio associated with obesity with onset before age 45 still declines after age 60; and (2) obesity with onset after age 45 is still not significantly associated with excess mortality risk after age 60.

Discussion

A key uncertainty in estimate of the extent of threat of obesity on human life expectancy is how the obesity-mortality association changes over the life course. Improving upon prior studies that rely on cross-sectional design with static weight status taken at the time of the survey, this study takes advantage of lifelong body mass index information from the almost

extinct original cohort of FHS and evaluates the mortality risk associated with obesity over three age periods (below 45, 45–59, and 60 and above). Using these longitudinal cohort data, we are able to track the changes in weight status, detect the onset and duration of obesity, and examine their mortality consequences. Our analyses reveal the complexity in the obesity-mortality link over the life course.

We find the excess mortality risk of obesity compared to normal weight as measured by hazard ratios decreases over three age groups, but this pattern is influenced by three population compositional changes. First, it is influenced by the different ages of onset of obesity. Obese group in later ages is composed of individuals with early and later onset of obesity. For obese group (including class I and II/III obese) in age 60 and above, 51% and 10% were overweight and normal weight before age 45. Since later onset of obesity is associated with lower mortality risk compared to earlier onset of obesity (Adams et al. 2014), inflow into obesity as a cohort ages can reduce the aggregate observed effect of obesity on mortality over ages.

Second, the putative decline in the hazard ratio associated with obesity over age is influenced by inconsistency in the reference group (normal weight) over ages. Some normal weight individuals in later ages may be in higher weight categories in earlier life (Stokes and Preston 2016b). For example, about 13% of normal weight group in age 60 and above were overweight or obese before age 45. Illness-induced weight loss can reduce the estimate of the detrimental impact of obesity on mortality compared to normal weight over ages because normal weight group in later ages increasingly includes individuals who were previously overweight or obese but lose weight. Third, it is influenced by more pronounced selective survival among obese group compared to normal weight group. Due to higher mortality rate in earlier ages, a relatively larger proportion of weak obese individuals die in early adulthood and leaves robust individuals surviving to older ages that then reduces hazard ratio associated with obesity in later ages.

The joint impacts of changing population compositions of obese and normal weight groups and mortality selection mechanism over the life course explain away the decreasing impact of obesity (with onset before age 45) on mortality up to age 60; after age 60, the detrimental effect of obesity on survival still declines, but to a much less degree after accounting for these factors. We do not find sufficient evidence for healthy participant effect, which supports some prior studies that dispute the contribution of healthy participant effect in the age – dependence of the obesity-mortality association (Hanley 2017; Mehta and Stokes 2013; Wang 2014; Wang and Liu 2014; Zheng and Dirlam 2016).

But there exists another layer of complexity that is mortality hazard associated with obesity still declines after age 60. This pattern applies to obesity with different timings of onset. For obesity with onset before age 45, as explained above, its impact on mortality decreases after age 60, but to a much less degree after accounting for the three population compositional changes mentioned above. For obesity with onset after age 45, it is not significantly associated with excess mortality risk after age 60. Therefore, even though population compositional changes substantially explain the reduction in mortality risk in mid and late life associated with early onset of obesity, they do not change the fact that obesity related mortality risk decreases in older populations.

It is beyond the scope of this paper to further investigate other mechanisms besides population compositional changes that may lead to the weakening impact of obesity on

mortality in old ages. But some prior studies have proposed several possible explanations. First, the hazard ratios of death for many behavioral factors and bio-indicators including obesity likely diminish with increasing age perhaps due to the fact that multiple body systems are failing and the excess risks of any single risk factor (even if it affects more than one body system) will likely fall due to the competing risks (Zheng and Dirlam 2016). Second, although obesity is associated with the onset of many chronic diseases that increase the mortality hazard in old age, being obese may actually improve survival after the onset of certain diseases (e.g., acute ischemic stroke, coronary artery disease). This is because extra body weight, including both fat mass and lean tissue mass, may serve as a nutrition and metabolic reservoir to overcome catabolic stress and muscle wasting associated with chronic illness (Curtis et al. 2005; Fonarow et al. 2007; Kim et al. 2012; Uretsky et al. 2007). These nutritional reserves may also shield obese elderly people from weight loss, as people tend to eat less when they get older, regardless of health status (Chapman 2010). The third possible reason is that obese patients seek or receive treatment at an earlier stage of many diseases. Obese people have a readily identifiable phenotype that is believed to reflect a number of diseases, and therefore may be subjected to earlier and more regular monitoring compared to normal weight patients (Uretsky et al. 2007).

Several caveats merit emphasizing. First, diseases may be on the causal pathways linking obesity with mortality. In the main text, diseases index is controlled to further mitigate the bias caused by illness-induced weight loss. We replicate the analysis without controlling for disease index as shown in Appendixes 3 and 4. Even though the size of the hazard ratio changes slightly, the overall conclusion is not substantially altered by excluding disease index in the model. Second, there may be other potential confounders that cannot be controlled for, so that the hazard ratios associated with obesity may be overestimated. But this bias may not vary significantly across ages. Hence, our analysis that focuses on change over age may be robust to unobserved confounding and other biasing factors. Third, it deserves clarification that while the associations are of smaller magnitude in age 60 and above on the relative scale, they may be greater on the absolute scale (Zheng and Dirlam 2016). Because mortality is so much greater in older people than younger people, the excess deaths associated with obesity as measured on the absolute scale is greater in older, compared to younger, individuals even though the hazard ratio declines by age (Mehta, Zheng, and Myrskylä 2019). Mehta, Zheng, and Myrskylä (2019) find that the excess deaths associated with obesity increase until about age 60 years after which it plateaus and then declines after ages 70–9 years. Therefore, even on the absolute scale, the excess deaths risks associated with obesity decline in older ages.

Fourth, our sample is rather homogeneous (i.e., in the one town and mostly Whites). The advantage of the homogeneity of the samples is that it allows us to better mitigate confounding factors that may be influencing the obesity-mortality association over ages. If we did the same thing with national samples, then we would have to give more consideration about the changing composition of the national population over time. The disadvantage concerns the representativeness of our sample and application of the findings to other racial groups. Blacks and Hispanics report substantially higher rates of obesity at all ages than Whites (Flegal et al. 2002; Krueger and Reither 2015; Wang and Beydoun 2007) and experience differential mortality consequences of obesity (Fontaine et al. 2003; Reynolds, Saito, and Crimmins 2005; Zheng and Yang 2012). Therefore, the life course patterns of obesity-mortality association and the mechanisms shaping these patterns may be potentially different for Blacks and

Hispanics than for Whites. But FHS is the only U.S. data that have a long prospective follow-up on BMI and mortality. Therefore, replicating the analyses for other racial groups is not feasible at this point. Nonetheless, we did a preliminary analysis on whether the degree of changing association between obesity and mortality over ages may be different by racial groups using National Health and Nutrition Examination Surveys 1988–2010 with linked mortality files up to 2011. Although this analysis does not reveal the underlying mechanisms shaping the life-course pattern, it shows that Whites, Blacks, and Hispanics have different magnitudes of changing obesity-mortality association over ages. This association declines at a larger degree among Whites than Blacks and Hispanics, but this racial difference is not statistically significant (see Appendix 5).

Notwithstanding these limitations, this study reveals the complexity in the life course pattern of obesity-mortality relationship, which is not uncovered in existent literature. The decreasing hazard ratio associated with obesity is partially a result of changing population compositions, up to age 60. After correcting for these population compositional changes, hazard ratio associated with obesity (with onset before age 45) still declines after age 60, but to a much less degree. However, obesity with onset after age 45 is not significantly associated with excess mortality risks after age 60 even after accounting for the population compositional changes. These findings have very important clinical practice and public health implications. From the life-course perspective, people who are obese in early adulthood tend to stay obese throughout the life course and early onset of obesity has a greater detrimental impact on survival than later onset of obesity. From this perspective, public health intervention should be placed in early ages. But at the population level, there are many more obese individuals at older, compared to younger, ages. Given that the hazard ratio associated with early onset of obesity increases up to age 60 and decreases to a much less degree after age 60 once the bias due to the population compositional changes is controlled, substantial attention should still be paid to those with early onset of obesity in their older ages. For people with later onset of obesity, even though they do not face excess mortality risks after age 60 compared to normal weight, obesity may still cause them to be at risk of excess diseases and morbidities.

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References

Abdullah, A., J. Stoelwinder, S. Shortreed, R. Wolfe, C. Stevenson, H. Walls, M. de Courten, and A. Peeters. 2011a. The duration of obesity and the risk of type 2 diabetes. *Public Health Nutrition* 14 (1):119–26. doi:10.1017/S1368980010001813.

Abdullah, A., R. Wolfe, J. U. Stoelwinder, M. de Courten, C. Stevenson, H. L. Walls, and A. Peeters. 2011b. The number of years lived with obesity and the risk of all-cause and cause-specific mortality. *International Journal of Epidemiology* 40 (4):985–96. doi:10.1093/ije/dyr018.

Adams, K. F., M. F. Leitzmann, R. Ballard-Barbash, D. Albanes, T. B. Harris, A. Hollenbeck, and V. Kipnis. 2014. Body mass and weight change in adults in relation to mortality risk. *American Journal of Epidemiology* 179 (2):135–44. doi:10.1093/aje/kwt254.

Allison, D. B., K. R. Fontaine, J. E. Manson, J. Stevens, and T. B. VanItallie. 1999. Annual deaths attributable to obesity in the United States. *JAMA* 282 (16):1530. doi:10.1001/jama.282.16.1530.

Bender, R., K. Jöckel, C. Trautner, M. Spraul, and M. Berger. 1999. Effect of age on excess mortality in obesity. *JAMA* 281 (16):1498. doi:10.1001/jama.281.16.1498.

Calle, E. E., M. J. Thun, J. M. Petrelli, C. Rodriguez, and C. W. Heath. 1999. Body-mass index and mortality in a prospective cohort of U.S. adults. *New England Journal of Medicine* 341 (15):1097–105. doi:10.1056/NEJM199910073411501.

Chapman, I. M. 2010. Obesity paradox during aging. *Interdisciplinary Topics in Gerontology* 37:20–36. doi:10.1159/000319992.

Curtis, J. P., J. G. Selter, Y. Wang, S. S. Rathore, I. S. Jovin, F. Jadbabaie, M. Kosiborod, E. L. Portnay, S. I. Sokol, F. Bader, et al. 2005. The obesity paradox: Body mass index and outcomes in patients with heart failure. *Archives of Internal Medicine* 165 (1):55–61. doi:10.1001/archinte.165.1.55.

Everhart, J. E., D. J. Pettitt, P. H. Bennett, and W. C. Knowler. 1992. Duration of obesity increases the incidence of NIDDM. *Diabetes* 41 (2):235–40. doi:10.2337/DIAB.41.2.235.

Flegal, K. M., M. D. Carroll, C. L. Ogden, and C. L. Johnson. 2002. Prevalence and trends in obesity among US adults, 1999-2000. *Journal of the American Medical Association* 288 (14):1723–27. doi:10.1001/jama.288.14.1723.

Flegal, K. M., B. I. Graubard, D. F. Williamson, and M. H. Gail. 2005. Excess deaths associated with underweight, overweight, and obesity. *Journal of the American Medical Association* 293 (15):1861. doi:10.1001/jama.293.15.1861.

Fonarow, G. C., P. Srikanthan, M. R. Costanzo, G. B. Cintron, and M. Lopatin. 2007. An obesity paradox in acute heart failure: Analysis of body mass index and in hospital mortality for 108,927 patients in the acute decompensated heart failure national registry. *American Heart Journal* 153 (1):74–81. doi:10.1016/j.ahj.2006.09.007.

Fontaine, K. R., D. T. Redden, C. Wang, A. O. Westfall, and D. B. Allison. 2003. Years of life lost due to obesity. *JAMA* 289 (2):187. doi:10.1001/jama.289.2.187.

Framingham Heart Study. 2017. FHS original cohort. Location: Biologic Specimen and Data Repository Information Coordinating Center. https://biolincc.nhlbi.nih.gov/.

Freedman, D. M., E. Ron, R. Ballard-Barbash, M. M. Doody, and M. S. Linet. 2006. Body mass index and all-cause mortality in a nationwide US cohort. *International Journal of Obesity* 30 (5):822–29. doi:10.1038/sj.ijo.0803193.

Greenberg, J. A. 2006. Correcting biases in estimates of mortality attributable to obesity. *Obesity* 14 (11):2071–79. doi:10.1038/oby.2006.242.

Greenberg, J. A., K. Fontaine, and D. B. Allison. 2007. Putative biases in estimating mortality attributable to obesity in the US population. *International Journal of Obesity* 31 (9):1449–55. doi:10.1038/sj.ijo.0803615.

Hanley, J. A. 2017. Correction of selection bias in survey data: Is the statistical cure worse than the bias? *American Journal of Epidemiology* 185 (6):1–3. doi:10.1093/aje/kww175.

Kim, B. J., S. Lee, K. Jung, K. Yu, B. Lee, and J. Roh, For Korean Stroke Registry investigators. 2012. Dynamics of obesity paradox after stroke, related to time from onset, age, and causes of death. *Neurology*. 79 (9):856–63. doi:10.1212/WNL.0b013e318266fad1.

Krueger, P. M., and E. N. Reither. 2015. Mind the Gap: Race/Ethnic and Socioeconomic Disparities in Obesity. *Current Diabetes Reports* 15 (11):95. doi:10.1007/s11892-015-0666-6.

Kuk, J. L., and C. I. Ardern. 2009. Influence of age on the ssociation between various measures of obesity and all-cause mortality. *Journal of the American Geriatrics Society* 57 (11):2077–84. doi:10.1111/j.1532-5415.2009.02486.x.

Lantz, P. M., E. Golberstein, J. S. House, and J. Morenoff. 2010. Socioeconomic and behavioral risk factors for mortality in a national 19-year prospective study of U.S. adults. *Social Science & Medicine* 70 (10):1558–66. doi:10.1016/J.SOCSCIMED.2010.02.003.

Lee, J. M., A. Gebremariam, S. Vijan, and J. G. Gurney. 2012. Excess body mass index-years, a measure of degree and duration of excess weight, and risk for incident diabetes. *Archives of Pediatrics & Adolescent Medicine* 166 (1):42–48. doi:10.1001/archpedi.166.1.42.

Masters, R. K., E. N. Reither, D. A. Powers, Y. C. Yang, A. E. Burger, and B. G. Link. 2013. The impact of obesity on US mortality levels: The importance of age and cohort factors in population estimates. *American Journal of Public Health* 103 (10):1895–901. doi:10.2105/AJPH.2013.301379.

McAuley, P. A., P. F. Kokkinos, R. B. Oliveira, B. T. Emerson, and J. N. Myers. 2010. Obesity paradox and cardiorespiratory fitness in 12,417 male veterans aged 40 to 70 years. *Mayo Clinic Proceedings* 85 (2):115–21. doi:10.4065/MCP.2009.0562.

Mehta, N. K., S. Stenholm, I. T. Elo, A. Aromaa, M. Heliövaara, and S. Koskinen. 2014. Weight histories and mortality among finnish adults: The role of duration and peak body mass index. *Epidemiology (Cambridge, Mass.)* 25 (5):707–10. doi:10.1097/EDE.0000000000000147.

Mehta, N. K., and A. Stokes. 2013. Re: "Obesity and US mortality risk over the adult life course". *American Journal of Epidemiology* 178 (2):320–320. doi:10.1093/aje/kwt117.

Mehta, N. K., H. Zheng, and M. Myrskylä. 2019. How do age and major risk factors for mortality interact over the life-course? Implications for health disparities research and public health policy. *SSM - Population Health* 8 (August):100438. doi:10.1016/j.ssmph.2019.100438.

Mokdad, A. H. 2005. Correction: "Actual causes of death in the United States, 2000". *JAMA* 293 (3):293. doi:10.1001/jama.293.3.293.

Mokdad, A. H., J. S. Marks, D. F. Stroup, and J. L. Gerberding. 2004. Actual causes of death in the United States, 2000. *JAMA* 291 (10):1238. doi:10.1001/jama.291.10.1238.

Olshansky, S. J., D. J. Passaro, R. C. Hershow, J. Layden, B. A. Carnes, J. Brody, L. Hayflick, R. N. Butler, D. B. Allison, and D. S. Ludwig. 2005. A potential decline in life expectancy in the United States in the 21st Century. *New England Journal of Medicine* 352 (11):1138–45. doi:10.1056/NEJMsr043743.

Reither, E. N., R. M. Hauser, and Y. Yang. 2009. Do birth cohorts matter? Age-period-cohort analyses of the obesity epidemic in the United States. *Social Science & Medicine* 69(10):1439–48. with commentary. doi:10.1016/j.socscimed.2009.08.040.

Reynolds, S. L., Y. Saito, and E. M. Crimmins. 2005. The impact of obesity on active life expectancy in older American men and women. *The Gerontologist* 45 (4):438–44. doi:10.1093/geront/45.4.438.

Solomon, C. G., and J. E. Manson. 1997. Obesity and mortality: A review of the epidemiologic data. *The American Journal of Clinical Nutrition* 66 (4):1044S–1050S. doi:10.1093/ajcn/66.4.1044S.

Stallard, E. 2011. The Impact of obesity and diabetes on LTC disability and mortality: Population estimates from the national long term care survey. Presented at the Living to 100 Symposium, Orlando, Florida. https://www.soa.org/globalassets/assets/files/resources/essays-monographs/2011-living-to-100/mono-li11-2a-stallard.pdf.

Stevens, J., J. Cai, E. R. Pamuk, D. F. Williamson, M. J. Thun, and J. L. Wood. 1998. The effect of age on the association between body-mass index and mortality. *New England Journal of Medicine* 338 (1):1–7. doi:10.1056/NEJM199801013380101.

Stewart, S. T., D. M. Cutler, and A. B. Rosen. 2009. Forecasting the effects of obesity and smoking on U.S. life expectancy. *New England Journal of Medicine* 361 (23):2252–60. doi:10.1056/NEJMsa0900459.

Stokes, A., and S. H. Preston. 2016a. How dangerous is obesity? Issues in measurement and interpretation. *Population and Development Review* 42 (4):595. doi:10.1111/PADR.12015.

Stokes, A., and S. H. Preston. 2016b. Revealing the burden of obesity using weight histories. *Proceedings of the National Academy of Sciences of the United States of America* 113 (3):572–77. doi:10.1073/pnas.1515472113.

Uretsky, S., F. H. Messerli, S. Bangalore, A. Champion, R. M. Cooper-DeHoff, Q. Zhou, and C. J. Pepine. 2007. Obesity paradox in patients with hypertension and coronary artery disease. *The American Journal of Medicine* 120 (10):863–70. doi:10.1016/J.AMJMED.2007.05.011.

Wang, Y., and M. A. Beydoun. 2007. The obesity epidemic in the United States - Gender, age, socioeconomic, racial/ ethnic,and geographic characteristics: A systematic review and meta-regression analysis. *Epidemiologic Reviews* 29 (1):6–28. doi:10.1093/epirev/mxm007.

Wang, Z. 2014. Obesity and US mortality risk over the adult life course. *American Journal of Epidemiology* 179 (4):529–30. doi:10.1093/aje/kwt329.

Wang, Z., and M. Liu. 2014. Obesity-mortality association with age: Wrong conclusion based on calculation error. *American Journal of Public Health* 104 (7):e3–4. doi:10.2105/AJPH.2014.302016.

Yang, Y. 2008. Trends in U.S. adult chronic disease mortality, 1960-1999: Age, period, and cohort variations. *Demography* 45 (2):387–416. doi:10.1353/dem.0.0000.

Yu, Y. 2012. Reexamining the declining effect of age on mortality differentials associated with excess body mass: Evidence of cohort distortions in the United States. *American Journal of Public Health* 102 (5):915–22. doi:10.2105/AJPH.2011.300237.

Yu, Y. 2018. Cohort trends in duration of obesity in the United States, 1925–89: Estimates from cross-sectional data. *Population Studies* 72 (3):399–410. doi:10.1080/00324728.2018.1467032.

Zhang, W. B., and Z. Pincus. 2016. Predicting all-cause mortality from basic physiology in the framingham heart study. *Aging Cell* 15 (1):39–48. doi:10.1111/acel.12408.

Zheng, H., and J. Dirlam. 2016. The body mass index-mortality link across the life course: Two selection biases and their effects. Edited by Shengxu Li. *Plos One* 11 (2):e0148178. doi:10.1371/journal.pone.0148178.

Zheng, H., D. Tumin, and Z. Qian. 2013. Obesity and mortality risk: New findings from body mass index trajectories. *American Journal of Epidemiology* 178 (11):1591–99. doi:10.1093/aje/kwt179.

Zheng, H., and Y. Yang. 2012. Population heterogeneity in the impact of body weight on mortality. *Social Science & Medicine (1982)* 75 (6):990–96. doi:10.1016/J.SOCSCIMED.2012.05.013.

Zheng, H., Y. C. Yang, and K. C. Land. 2016. Age-specific variation in adult mortality rates in developed countries. *Population Research and Policy Review* 35 (1):49–71. doi:10.1007/s11113-015-9379-4.

Appendix 1. Total Mortality Risk in Relation to Body Mass Index across Four Age Groups, FHS, 1948-2011

	Less than 45[a] (Obs.[b] = 26,635)				45–59[a] (Obs.[b] = 25,587)				60–64[a] (Obs.[b] = 24,649)				65 and above[a] (Obs.[b] = 23,202)			
	D[c]	N[d]	HR	SE	D[c]	N[d]	HR	SE	D[c]	N[d]	HR	SE	D[c]	N[d]	HR	SE
Total	1,764	2,016			1,722	1,970			1,574	1,807			1,414	1,616		
BMI variable 2																
Underweight	33	35	1.15	(1.20)	21	21	1.10	(1.25)	17	17	2.29***	(1.28)	21	22	1.80***	(1.25)
Normal weight	899	1,049	1.00		751	867	1.00		602	704	1.00		507	580	1.00	
Overweight	633	718	1.17**	(1.06)	704	808	1.07	(1.06)	661	750	0.97	(1.06)	615	699	0.94	(1.06)
Obese	199	214	1.71***	(1.08)	246	274	1.58***	(1.08)	294	336	1.32***	(1.08)	271	315	1.08	(1.08)
BMI variable 3																
Underweight	33	35	1.15	(1.20)	21	21	1.10	(1.25)	17	17	2.29***	(1.28)	21	22	1.80***	(1.25)
Normal weight	899	1,049	1.00		751	867	1.00		602	704	1.00		507	580	1.00	
Overweight	633	718	1.17**	(1.06)	704	808	1.07	(1.06)	661	750	0.97	(1.06)	615	699	0.94	(1.06)
Obese (onset of obesity before age 45)	199	214	1.71***	(1.08)	162	176	1.67***	(1.09)	135	146	1.51***	(1.10)	111	119	1.40**	(1.11)
Obese (onset of obesity during ages 45–59)					84	98	1.45**	(1.12)	62	75	1.39*	(1.14)	52	62	1.25	(1.16)
Obese (onset of obesity during ages 60–64)									97	115	1.11	(1.12)	56	70	1.01	(1.15)
Obese (onset of obesity after age 64)													52	64	0.69*	(1.16)
BMI variable 4																
Underweight	33	35	1.15	(1.20)	21	21	1.11	(1.25)	17	17	2.37***	(1.28)	21	22	1.91***	(1.26)
Stable normal weight	899	1,049	1.00		686	791	1.00		498	582	1.00		353	410	1.00	
Unstable normal weight	([e])				65	76	1.15	(1.14)	104	122	1.22	(1.11)	154	170	1.22	(1.10)
Overweight	633	718	1.17**	(1.06)	704	808	1.08	(1.06)	661	750	1.00	(1.06)	615	699	0.99	(1.07)
Obese (onset of obesity before age 45)	199	214	1.71***	(1.08)	162	176	1.69***	(1.09)	135	146	1.55***	(1.10)	111	119	1.48***	(1.12)
Obese (onset of obesity during ages 45–59)					84	98	1.46**	(1.12)	62	75	1.43*	(1.15)	52	62	1.33	(1.16)
Obese (onset of obesity during ages 60–64)									97	115	1.14	(1.12)	56	70	1.07	(1.16)
Obese (onset of obesity at or after age 64)													52	64	0.73	(1.16)

Appendix 2. Total Mortality Risk among Individuals that Survived to Age 65 in Relation to Body Mass Index across Four Age Groups, FHS, 1948-2011

	Less than 45[a] (Obs.[b] = 23,202)				45–59[a] (Obs.[b] = 23,202)				60–64[a] (Obs.[b] = 23,202)				65 and above[a] (Obs.[b] = 23,202)			
	D[c]	N[d]	HR	SE	D[c]	N[d]	HR	SE	D[c]	N[d]	HR	SE	D[c]	N[d]	HR	SE
Total	1,414	1,616			1,414	1,616			1,414	1,616			1,414	1,616		
BMI variable 2																
Underweight	28	30	1.24	(1.21)	18	18	1.14	(1.27)	14	14	2.24***	(1.32)	21	22	1.80***	(1.25)
Normal weight	736	860	1.00		619	717	1.00		526	612	1.00		507	580	1.00	
Overweight	497	563	1.13	(1.06)	578	661	1.05	(1.06)	605	685	0.99	(1.06)	615	699	0.94	(1.06)
Obese	153	163	1.70***	(1.10)	199	220	1.67***	(1.09)	269	305	1.36***	(1.08)	271	315	1.08	(1.08)
BMI variable 3																
Underweight	28	30	1.24	(1.21)	18	18	1.14	(1.27)	14	14	2.24***	(1.32)	21	22	1.80***	(1.25)
Normal weight	736	860	1.00		619	717	1.00		526	612	1.00		507	580	1.00	
Overweight	497	563	1.13	(1.06)	578	661	1.05	(1.06)	605	685	0.99	(1.06)	615	699	0.94	(1.06)
Obese (onset of obesity before age 45)	153	163	1.70***	(1.10)	133	143	1.76***	(1.10)	124	133	1.55***	(1.11)	111	119	1.40**	(1.11)
Obese (onset of obesity during ages 45–59)					66	77	1.52**	(1.14)	57	68	1.45*	(1.15)	52	62	1.25	(1.16)
Obese (onset of obesity during ages 60–64)									88	104	1.14	(1.12)	56	70	1.01	(1.15)
Obese (onset of obesity after age 64)													52	64	0.69*	(1.16)
BMI variable 4																
Underweight	28	30	1.24	(1.21)	18	18	1.15	(1.27)	14	14	2.27***	(1.32)	21	22	1.91***	(1.26)
Stable normal weight	736	860	1.00		571	660	1.00		445	517	1.00		353	410	1.00	
Unstable normal weight	([e])				48	57	1.08	(1.16)	81	95	1.11	(1.13)	154	170	1.22	(1.10)
Overweight	497	563	1.13	(1.06)	578	661	1.06	(1.06)	605	685	1.00	(1.07)	615	699	0.99	(1.07)
Obese (onset of obesity before age 45)	153	163	1.70***	(1.10)	133	143	1.77***	(1.10)	124	133	1.57***	(1.11)	111	119	1.48***	(1.12)
Obese (onset of obesity during ages 45–59)					66	77	1.53**	(1.14)	57	68	1.48*	(1.15)	52	62	1.33	(1.16)
Obese (onset of obesity during ages 60–64)									88	104	1.15	(1.12)	56	70	1.07	(1.16)
Obese (onset of obesity at or after age 64)													52	64	0.73	(1.16)

Appendix 3. Total Mortality Risk in Relation to Body Mass Index across Three Age Groups without Controlling for Disease Index, FHS, 1948-2011

	Less than 45[a] (Obs.[b] = 27,048)				45–59[a] (Obs.[b] = 27,000)				60 and above[a] (Obs.[b] = 26,062)			
	D[c]	N[d]	HR	SE	D[c]	N[d]	HR	SE	D[c]	N[d]	HR	SE
Total	1,913	2,176			1,871	2,130			1,723	1,967		
BMI variable 2												
Underweight	34	36	1.15	(1.19)	23	24	1.07	(1.24)	21	21	1.91***	(1.25)
Normal weight	993	1149	1.00		832	953	1.00		653	750	1.00	
Overweight	680	767	1.16**	(1.05)	758	864	1.06	(1.05)	736	828	0.94	(1.06)
Obese	206	224	1.68***	(1.08)	258	289	1.58***	(1.08)	313	368	1.11	(1.07)
BMI variable 3												
Underweight	34	36	1.15	(1.19)	23	24	1.07	(1.24)	21	21	1.91***	(1.25)
Normal weight	993	1149	1.00		832	953	1.00		653	750	1.00	
Overweight	680	767	1.16**	(1.05)	758	864	1.06	(1.05)	736	828	0.94	(1.06)
Obese (onset of obesity before age 45)	206	224	1.68***	(1.08)	167	184	1.65***	(1.09)	132	146	1.40**	(1.10)
Obese (onset of obesity during ages 45–59)					91	105	1.46**	(1.12)	63	76	1.28	(1.14)
Obese (onset of obesity after age 59)									118	146	0.85	(1.11)
BMI variable 4												
Underweight	34	36	1.15	(1.19)	23	24	1.09	(1.24)	21	21	1.99***	(1.25)
Stable normal weight	993	1,149	1.00		762	872	1.00		510	588	1.00	
Unstable normal weight	([e])				70	81	1.16	(1.13)	143	162	1.23	(1.10)
Overweight	680	767	1.16**	(1.05)	758	864	1.07	(1.05)	736	828	0.98	(1.06)
Obese (onset of obesity before age 45)	206	224	1.68***	(1.08)	167	184	1.67***	(1.09)	132	146	1.46***	(1.10)
Obese (nset of obesity during ages 45–59)					91	105	1.48***	(1.12)	63	76	1.33*	(1.14)
Obese (onset of obesity after age 59)									118	146	0.89	(1.11)

Appendix 4. Total Mortality Risk among Individuals that Survived to Age 60 in Relation to Body Mass Index across Three Age Groups without Controlling for Disease Index, FHS, 1948-2011

	Less than 45[a] (Obs.[b] = 26,062)				45–59[a] (Obs.[b] = 26,062)				60 and above[a] (Obs.[b] = 26,062)			
	D[c]	N[d]	HR	SE	D[c]	N[d]	HR	SE	D[c]	N[d]	HR	SE
Total	1,723	1,967			1,723	1,967			1,723	1,967		
BMI variable 2												
Underweight	32	34	1.20	(1.20)	23	24	1.17	(1.24)	21	21	1.91***	(1.25)
Normal weight	906	1051	1.00		770	887	1.00		653	750	1.00	
Overweight	605	685	1.14*	(1.06)	697	792	1.06	(1.06)	736	828	0.94	(1.06)
Obese	180	197	1.67***	(1.09)	233	264	1.63***	(1.08)	313	368	1.11	(1.07)
BMI variable 3												
Underweight	32	34	1.20	(1.20)	23	24	1.17	(1.24)	21	21	1.91***	(1.25)
Normal weight	906	1051	1.00		770	887	1.00		653	750	1.00	
Overweight	605	685	1.14*	(1.06)	697	792	1.06	(1.06)	736	828	0.94	(1.06)
Obese (onset of obesity before age 45)	180	197	1.67***	(1.09)	153	170	1.69***	(1.10)	132	146	1.40**	(1.10)
Obese (onset of obesity during ages 45–59)					80	94	1.53***	(1.13)	63	76	1.28	(1.14)
Obese (onset of obesity after age 59)									118	146	0.85	(1.11)
BMI variable 4												
Underweight	32	34	1.20	(1.20)	23	24	1.18	(1.24)	21	21	1.99***	(1.25)
Stable normal weight	906	1,051	1.00		707	813	1.00		510	588	1.00	
Unstable normal weight	([e])				63	74	1.13	(1.14)	143	162	1.23	(1.10)
Overweight	605	685	1.14*	(1.06)	697	792	1.07	(1.06)	736	828	0.98	(1.06)
Obese (onset of obesity before age 45)	180	197	1.67***	(1.09)	153	170	1.70***	(1.10)	132	146	1.46***	(1.10)
Obese (onset of obesity during ages 45–59)					80	94	1.54***	(1.13)	63	76	1.33*	(1.14)
Obese (onset of obesity after age 59)									118	146	0.89	(1.11)

Appendix 5. Adjusted Hazard Ratios from Weighted Cox Model, NHANES III – NHANES 2009-2010, with Linked Mortality Data 1988-2011

	Non-Hispanic Whites		Non-Hispanic Blacks		Hispanics	
	HR	95% CI	HR	95% CI	HR	95% CI
Normal weight (reference)						
Overweight	0.93	0.60, 1.43	0.67	0.41, 1.10	0.86	0.47, 1.56
Obesity	1.83	1.17, 2.85	1.20	0.75, 1.92	1.28	0.68, 2.40
Overweight*Age	1.01	0.94, 1.08	1.04	0.94, 1.14	1.04	0.93, 1.16
Obesity*Age	0.93	0.86, 1.00	0.96	0.87, 1.05	0.97	0.86, 1.09
Death	3,140		1,352		1,043	
Individuals	16,386		7,752		8,762	
Observations	31,489		15,802		17,353	

The time metric in all the survival models was attained age: that is, the age of death or censoring. To account for left truncation, the individual-level data were reshaped into a person-year file describing respondents' cumulative survival time from their age at the baseline survey until the age at which they died or were censored. In these person-year data, attained age was categorized into 10-year groups (25–34, 35–44, 45–54, 55–64, 65–74, 75–84, and 85+), and these categories were coded 1 through 7. This age variable is different from the time-scale variable (i.e., attained age which is a continuous variable), and is required to assess the interaction between age and obesity (or the age-dependent association between obesity and mortality). All the models are adjusted for gender, country of birth, marital status, education, income, health insurance, smoking status, survey year, and birth cohort.