The Body Mass Index-Mortality Link across the Life Course: Two Selection Biases and Their Effects

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Abstract

In this study, we investigated two selection biases that may affect the obesity-mortality link over the life course: mortality selection and healthy participant effects. If these selection mechanisms are stronger among obese adults than among non-obese adults, they may contribute to the weakening obesity-mortality link over the life course. We used data from the National Health and Nutrition Examination Survey 1988-2004 with linked mortality files from 1988-2006. We employed weighted Cox models to test and adjust for these two selection biases. We also used complementary log-log models, adjusted for a normal distribution of frailty, to test for mortality selection effects; accelerated failure-time models to mitigate the mortality selection effect; and ordinary least squares regression to test for healthy participant effects. The link between class II/III obesity and mortality weakens at older ages. We did not find evidence for significant mortality selection or healthy participant effects. Also, even if the healthy participant effects were stronger among obese adults, they are not strong enough to produce a weakening association between obesity and morbidity at higher ages at the time of the survey. Therefore, neither of these selection biases explains the diminishing effect of class II/III obesity on mortality over the life course.

Keywords:

USA; Obesity; Mortality; Life Course; Mortality Selection; Healthy Participant Effects

Obesity has emerged as a potential threat to future increases in life expectancy, but the extent of this threat is still being debated (Allison et al., 1999: Flegal et al., 2005; Mehta & Chang, 2009; Mokdad et al., 2000; Mokdad et al., 2005; Olshansky et al., 2005; Stewart, Cutler, & Rosen, 2009). Recent studies have reported population heterogeneity in obesity's effect on mortality, as well as an age-dependence of this effect (Calle et al., 1999; Fontaine et al., 2003; Freedman et al., 2006; Lantz et al., 2010; Reynolds, Saito, & Crimmins, 2005; Stallard, 2010; Zheng & Yang, 2012). Most studies find that the deleterious effect of obesity on longevity weakens with age (Bender et al., 1999; Fontaine et al., 2003; Freedman et al., 2006; Stevens, 1998; Zheng & Yang, 2012); with some studies finding no harmful effect (Kuk & Arden, 2009; Reynolds, Saito, & Crimmins, 2005) or even a protective effect of obesity among older adults (Lantz et al., 2010; Stallard, 2010). Other recent research suggests obesity may be potentially more harmful for older adults than younger adults (Masters, Powers, & Link, 2013), but this may be due to model misspecification and result misinterpretation (Mehta & Stokes, 2013; Wang 2014).

Prior studies on this topic mostly rely on survey data with linked mortality files to estimate the hazard ratio associated with obesity, making their findings potentially vulnerable to two sources of selection bias: mortality selection and healthy participant effects. Mortality selection refers to survival of the fittest over time. This process eliminates individuals who are frailer or have severe diseases early on in the life course, and leaves those who are more robust to survive to old age (Hernan, 2010). 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 and conditions. Thus, a smaller proportion of frail individuals in the obese group might survive to older ages, compared to the non-obese group. This selection process would then weaken the observed harmful effect of obesity on mortality at older ages

(Zheng & Yang, 2012). Such mortality selection bias is especially salient for survival analysis using time-specific hazard ratios (Hernan, 2010), or age-specific hazard ratios in this case.

The healthy participant effect refers to the fact that survey respondents have to be healthy enough to participate in the survey, and is especially salient in surveys that exclude people who are institutionalized or hospitalized. Among older adults, the healthy participant effect may be stronger for obese as opposed to non-obese people, with the former being more likely to suffer from chronic illnesses or to be institutionalized due to poor health. This disparity may cause survey data to include substantially higher proportions of healthy older adults in the obese group, as compared to the non-obese group. This mechanism would then potentially lead to estimating a diminishing effect of obesity on mortality at older ages (Masters et al., 2013).

To accurately capture age variation in the obesity-mortality relationship, we need to adjust for these two selection biases. In this study, we used the U.S. National Health and Nutrition Examination Survey 1988-2004 with linked mortality files covering the period 1988-2006, and investigated these two sources of selection bias step by step. Age of death or censoring (i.e., attained age) was used as the time metric to model the baseline hazard function (Korn, Graugard, & Midthune, 1997). We accounted for left truncation by starting respondents' exposure to the risk of death at their age at the time of the baseline survey (Singer & Willett, 2003). We used Cox models with grouped age-dependence of obesity to test whether there are differential mortality selection effects and healthy participant effects across different body mass index (BMI) groups; and to test how these two sources of selection bias may affect estimates of the obesity-mortality link at older ages. We also tackled the issue of mortality selection by fitting a complementary log-log discrete time hazard model, adjusted for a normal distribution of frailty (Flinn & Heckman, 1982); and using accelerated failure-time regression models, which provided

relatively stable estimates under a variety of frailty assumptions (Hougaard, Myglegaard, & Borch-Johnson, 1994; Keiding, Andersen, & Klein, 1997). Next, we considered healthy participant effects, which are a form of sample selection bias. If the healthy participant effect were not random, no adjustment of the model could completely account for it. Therefore, we attempted to indirectly test for differential healthy participant effects by examining variation in the relationship between obesity and morbidity across age at the time of the survey. If differential healthy participant effects were the main reason for a weakening link between obesity and mortality at older ages (Masters et al., 2013), then the obesity-morbidity link would be weaker for people who are older at the time of the survey.

METHODS

Data and participants

We used data from the National Health and Nutrition Examination Survey (NHANES) 1988-2004 with linked mortality files covering the period 1988-2006. The NHANES collected information about health and diet from a nationally representative sample of the noninstitutionalized civilian U.S. population, with an oversample of older adults and racial minorities. Data were collected from household interviews as well as physical examinations and laboratory tests performed in a mobile examination center. Detailed descriptions of the NHANES design, procedures, and methodologies are published elsewhere ("About the National Health and Nutrition Examination Survey," 2013; "NHANES Analytic and Reporting Guidelines," 2013). We combined NHANES III data, collected between 1988 and 1994, with the data collected in three continuous waves of the NHANES, conducted from 1999 to 2004. The follow-up mortality data tracked the mortality status of respondents from the date of the survey

through December 31, 2006. Mortality ascertainment was based on results from a probabilistic match between the NHANES data and the National Death Index (NDI) death certificate records. Ethics approval was not required because the analysis was performed on secondary data, which did not include personal identifiers. All analyses were adjusted for sample weights and the stratification and clustering of the sample design, except when specifically mentioned otherwise. The final sample was composed of 22,177 individuals aged 25 to 84.9 at the time of the survey, with 3,820 deaths occurring between ages 27.2 and 106.3 years (Table 1).

[Table 1 about here]

Predictors of mortality

Body mass index (BMI) categories were defined using the World Health Organization guidelines, and included normal weight (BMI of 18.5-24.9 kg/m^2), overweight (BMI of 25-29.9 kg/m^2), class I obese (BMI of 30-34.9 kg/m^2), and class II/III obese (BMI $\geq$35 kg/m^2). Underweight, or BMI below 18.5, is linked to wasting diseases at old age. Therefore, we have excluded 369 respondents in the underweight category from the sample. Consequently, this study compared survival time between obese adults and adults in the normal weight or overweight categories. Demographic variables in our analysis included age at the time of the survey, sex (male = 1, female = 0), race/ethnicity (non-Hispanic White, non-Hispanic Black, Hispanic, or all others), and country of birth (U.S. = 1, any other country = 0). Ten-year birth cohorts were coded from 1 (1900-1909) to 8 (1970-1979). Socioeconomic factors included inflation-adjusted family income, educational attainment (less than high school, high school diploma, more than high school), marital status (married, cohabiting, separated, widowed, never married, divorced), and health insurance status (has insurance = 1, no insurance = 0). Health and behavioral factors included smoking status (never smoked, former smoker, and current smoker), and the number of self-

reported chronic conditions (angina, arthritis, asthma, bronchitis, diabetes, emphysema, heart attack, heart failure, cancer, stroke, hip fracture, spine fracture, wrist fracture, and osteoporosis).

Statistical analysis

The time metric in all 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. 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 (attained age), and is required to assess the interaction between age and obesity (or the age-dependent association between obesity and mortality.)

Model 1 was a Cox model for the whole sample, and included grouped age-dependence of obesity:

$$\log h_i(t) = \log h_0(t) + \gamma_1 obeseI_i + \gamma_2 obeseII_i + \gamma_3 obeseI_i \times Age_i + \gamma_4 obeseII_i \times Age_i + \sum_j \beta_j x_{ij},$$

where $h_i(t)$ is the hazard function for individual *i*; $h_0(t)$ is the baseline hazard function; *t* is attained age; Age_i represents the seven 10-year age groups; $obeseI$ refers to class I obesity and $obeseII$ refers to class II/III obesity (with the reference BMI group being normal or overweight); and x_{ij} are j control variables, including race, gender, country of birth, marital status, education, income, health insurance, smoking status, number of chronic conditions and survey year. The main variables of interest here are $obeseI \times Age$ and $obeseII \times Age$. If the effects of obesity on

mortality were to decline with age, γ_3 and γ_4 would be negative, and the corresponding hazard ratios would be smaller than 1.

Models 2-4 were Cox models for each BMI status (normal weight and overweight; class I obese; and class II/III obese, respectively), as specified below:

$$\log h_i(t) = \log h_0(t) + \sum_j \beta_j x_{ij} + \beta_{cy} birthcohort_i \times surveyyear_i.$$

The main variable of interest here is the interaction between birth cohort and survey year. If there were a selection bias due to the healthy participant effect or mortality selection, individuals in the same cohort who were interviewed in a later period (i.e., at older ages) would have a lower mortality risk than those who were interviewed in an earlier period (i.e., at younger ages). Therefore, if either of the two effects exists, we would observe a negative β_{cy} within each BMI category. If either of the two effects were more pronounced among obese adults, we would observe a stronger negative effect β_{cy} in the obese I and obese II/III groups, as compared to the normal weight and overweight group.

Model 5 was a Cox model for the whole sample, adjusted for both mortality selection and sample selection bias:

$$\log h_i(t) = \log h_0(t) + \gamma_1 obeseI_i + \gamma_2 obeseII_i + \gamma_3 obeseI_i \times Age_i + \gamma_4 obeseII_i \times Age_i + \sum_j \beta_j x_{ij} + \beta_{cy} birthcohort_i \times surveyyear_i$$

If mortality selection or healthy participant effects accounted for the diminishing effect of obesity on mortality, γ_3 and γ_4 would be substantially reduced here, relative to the estimates of these coefficients in Model 1.

Model 6 was a complementary log-log discrete time hazard model, adjusted for a normal distribution of frailty:

$$\log[-\log(1-P_{ik})] = \alpha \log k + \gamma_1 obeseI_{ik} + \gamma_2 obeseII_{ik} + \gamma_3 obeseI_{ik} \times k + \gamma_4 obeseII_{ik} \times k + \sum_j \beta_j x_{ikj} + u_i,$$

where k represents the seven 10-year age groups; P_{ik} is the probability that individual i in age group k dies; and u_i is the unobserved frailty term, assumed to be normally distributed. If there were significant differences in mortality selection among BMI groups, the variance of the frailty distribution would be significant and γ_3 and γ_4 would be substantially reduced, relative to the estimates of these coefficients in Model 1.

Hazard ratios, however, may be sensitive to the choice of the parametric form of the frailty distribution (Heckman & Singer, 1982; Keiding et al., 1997). Therefore, we used a series of accelerated failure-time regression models (AFT) in Models 7-9:

$$\log(T_i) = \propto_0 + \gamma_1 obeseI_i + \gamma_2 obeseII_i + \gamma_3 obeseI_i \times Age_i + \gamma_4 obeseII_i \times Age_i + \sum_j \beta_j x_{ij} + \varepsilon_i,$$

where T_i denotes the survival time for the *i*th individual; ε_i is a measure of residual variability in the survival times and is assumed to have a log-Weibull distribution (Model 7), log-gamma distribution (Model 8), or normal distribution (Model 9), meaning the distribution of *T* would be Weibull, gamma, or log-normal, respectively. One advantage of the AFT over the hazard model is that the AFT is much less affected by different assumptions about the frailty distribution: when a heterogeneity or frailty term is added to AFT models, it only contributes to the dispersion, leaving regression coefficients unchanged (Hougaard et al, 1994; Keiding et al., 1997). If obesity were detrimental to survival, γ_1 and γ_2 would be negative, and the corresponding time ratios would be smaller than 1. If the effects of obesity on mortality were to decline with age, γ_3 and γ_4 would be positive, and the corresponding time ratios would be greater than 1.

In order to further test the healthy participant effect, we investigated whether the effect of obesity on morbidity (measured by the number of chronic illnesses) is different across age at the time of the baseline survey. Here, we used the original individual-level data and fitted an ordinary least squares regression model. If the old-age decline in mortality risk associated with obesity were a result of a more pronounced healthy participant effect in obese groups (Masters et al., 2013), then the correlation between obesity and morbidity at the time of the survey would be weaker among older respondents.

RESULTS

Table 2 presents adjusted hazard ratios of obesity from weighted Cox models. Model 1, which uses "normal weight and overweight" as the reference BMI category, shows that every ten year increase in age decreases class II/III obesity-related hazard by 15%. The effect of class I obesity, however, is not significant and does not change over the life course.

[Table 2 about here]

The next three models present adjusted hazard ratios of interactions between birth cohort and survey year, obtained from weighted Cox models fitted separately for each BMI group. These results suggest that, in the same cohort, subjects who were interviewed in later periods (i.e., at older ages) were not significantly less likely to die than those who were interviewed in earlier periods (i.e., at younger ages). This finding is consistent across the three BMI groups (normal weight and overweight; class I obese; and class II/III obese), and suggests no existence of *significant* healthy participant or mortality selection effects.

Model 5, presented in Table 3, adjusts for both healthy participant and mortality selection effects by adding interactions between birth cohort and survey year to the covariates from Model

1. The results remain almost the same when compared to Model 1: the positive association between class II/III obesity and mortality risk is significantly smaller at older ages. Model 6 replicates this finding with an adjustment for a normal distribution of frailty. A likelihood ratio test of the frailty distribution's variance suggests that there is no significant unobserved frailty. AFT Models 7-9, presented in Table 4, suggest that class II/III obesity significantly reduces survival time by about 16-18%, but this detrimental effect weakens over the life course. These findings further refute the hypothesis that differential mortality selection across BMI groups leads to weaker class II/III obesity effects on mortality risk later in the life course.

[Tables 3 and 4 about here]

Figure 1 illustrates the predicted number of chronic illnesses across age at the time of the survey, stratified by BMI category. Figure 1 is derived from a weighted OLS regression of the number of chronic illnesses on BMI category, age at survey, age at survey squared, the interaction between BMI category and age at survey, and additional individual covariates (full results from this model are presented in Appendix I). The gap in the number of chronic illnesses between class II/III obese adults and adults in the normal or overweight category widens significantly at older ages (gaps in this outcome among normal or overweight, class I obese, and class II/III obese respondents are summarized in Appendix II). This finding suggests that even if the healthy participant effect were stronger among the obese group (an argument not supported by Table 2), this effect would not be strong enough to weaken the link between obesity and morbidity at older ages. Therefore, differential healthy participant effects across BMI categories probably do not explain the declining mortality effect of class II/III obesity over the life course.

[Figure 1 about here]

DISCUSSION

Although several studies have reported that the adverse effect of obesity on mortality risk decreases over the life course (Bender et al., 1999; Fontaine et al., 2003; Freedman et al., 2006; Stevens, 1998; Zheng & Yang, 2012), this phenomenon may be caused by more pronounced mortality selection and healthy participant effects among obese adults. Using NHANES data and a series of hazard models, we found no evidence that mortality selection or healthy participant effects were significantly more pronounced among obese adults, as compared to normal- and overweight adults. As estimates of the hazard ratios suffer from bias induced by the mortality selection (or unobserved frailty) problem (Cole & Hernan, 2004; Hernan, 2010), we also used a series of accelerated failure-time regression models, which are much less affected by different assumptions about the frailty distribution (Hougaard et al., 1994; Keiding et al., 1997), and achieved similar results. We replicated all the analyses using National Health Interview Survey data from the years 1986-2004, with linked mortality files covering the period 1986-2006, and obtained results consistent with our main findings (Appendices III-IV). Therefore, neither source of selection bias can explain why the effect of class II/III obesity on mortality declines with age. It deserves clarification that while the associations are of smaller magnitude among older people on the relative scale, they are greater on the absolute scale (Stevens et al. 1998). Because mortality is so much greater in older people than younger people, the absolute number of deaths associated with obesity is greater in older people even though the hazard ratio is lower.

There are two other possible explanations for the weakening relative link between obesity and mortality over the life course. First, the accumulation of time spent obese, or the cumulative amount of body mass, may contribute to mortality risk beyond weight status at a single point in time. People who become obese at earlier ages are at significantly higher risk of death compared

to those who become obese at older ages (Adams et al., 2014). Moreover, modest weight gain after age 50 does not confer excess mortality risk (Adams et al., 2014; Myrskyla & Chang, 2009; Zheng, Tumin, & Qian, 2013). People who are obese at older ages are a heterogeneous group, some of whom may have been overweight or normal weight at younger ages. By contrast, people who are obese at younger ages tend to remain so for most of their life course. Therefore, the accumulation of time in the obese category among people who were obese in early adulthood could increase their mortality hazard above that of people who became obese in later adulthood (Adams et al., 2014).

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 (Curtis et al., 2005). The combination of these two patterns may then produce a declining effect of obesity on mortality later in the life course. One study that followed 34,132 patients who experienced an acute ischemic stroke found obese patients had lower long-term mortality rates (Kim et al., 2012). Patients whose BMI classified them as obese (30-32.5 and >32.5 kg/m^2) had lower hazard ratios (HR) (0.77 (95% CI: 0.63, 0.93) and 0.85 (95% CI: 0.64, 1.12), respectively) compared to the normal weight reference group (BMI in the 20-23 kg/m^2 range) (Kim et al., 2012). Another clinical study investigated the risks of death, nonfatal myocardial infarction, and nonfatal stroke among patients with hypertension and coronary artery disease, finding that these risks were lower among class I obese patients (adjusted HR = 0.68 (95% CI: 0.59, 0.78)) and class II/III obese patients (adjusted HR = 0.76 (95% CI: 0.65, 0.88)), compared to normal weight patients (Uretsky et al., 2007).

Differential healthy participant effects imply older adults who are obese are more likely to be hospitalized and be excluded from surveys than their non-obese peers, leading analyses of

survey data to suggest a lower obesity effect on mortality at older ages. This hypothesis presumes that obese people who are hospitalized are weaker and more likely to die than non-obese people who are hospitalized; and that if we could include the hospitalized population in the sampling frame, the effect of obesity on mortality risk would not decline with age. But studies have found that obesity predicts lower in-hospital mortality (Hutagalung et al., 2011). One study that monitored 16,812 Intensive Care Unit (ICU) patients at a Boston hospital found that obese patients had 26% (95% CI: 0.14, 0.36) lower mortality risk 30 days after ICU admission and 43% (95% CI: 0.33, 0.51) lower mortality risk one year after ICU admission, compared to normal weight patients (Abhyankar et al., 2012). Another study that analyzed 108,927 hospitalizations for acute decompensated heart failure found that patients in higher BMI categories had lower in-hospital mortality after heart failure (Fonarow et al., 2007). This risk decreased with higher BMI in a nearly linear fashion. Using BMI as a continuous variable, every 5 unit increase in BMI was associated with 10% (95% CI: 0.07, 0.12) lower odds of risk-adjusted mortality (Fonarow et al., 2007). These studies further dispute the plausibility of a differential healthy participant effect causing the effect of obesity on mortality to diminish at older ages.

The reasons why obese people are less likely to die from some chronic illnesses than non-obese people remain unclear. Extra body weight, including both fat mass and lean tissue mass, may serve as a nutrition reservoir to help fight against chronic illness. For example, studies on patients with heart failure suggest normal weight patients may not have enough metabolic reserves to overcome the catabolic stress associated with heart failure (Fonarow 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). In addition, patients with heart failure have been shown to have low levels of insulinlike growth factor 1 and elevated

levels of several factors that are associated with anorexia and muscle wasting, indicating cardiac cachexia and an increased risk of adverse outcomes (Curtis et al., 2005). The "normal weight" category may include a higher proportion of cachectic patients than higher BMI categories, as these patients are more susceptible to weight loss and muscle wasting.

Another explanation for why sick people may experience a protective effect from obesity in old age 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). In addition, the elderly obese may have better nutritional intake (Casas-Vera et al., 2012), greater fitness levels (McAuley et al., 2010), or less sedentary lifestyles (Flicker, McCaul, & Hankey, 2010) than the normal weight elderly; as well as greater bone density, predicting a lower risk of hip fracture (Chapman, 2010). Finally, animal studies show that increases in adipocyte size in obese organisms lead to an accumulation of M1 macrophages in adipose tissue that produce pro-inflammatory cytokines (Abhyankar et al., 2012). But when patients get critically ill, they may develop M2 macrophages that produce anti-inflammatory agents (Abhyankar et al., 2012). Obese patients may experience a protective effect during critical illness that entails a switch from M1 pro-inflammatory activation to M2 anti-inflammatory activation in the larger pool of macrophages their adipose tissue stores, compared to normal weight patients (Abhyankar et al., 2012).

In conclusion, this study finds that the mortality hazard associated with class II/III obesity declines over the life course, and that this decline is not a result of more pronounced mortality selection or healthy participant effects among obese adults as compared to non-obese adults. Instead, this pattern may be related to the duration of exposure to obesity and a possible

protective effect of extra body weight against death from chronic illness in old age. Public health efforts aimed at controlling obesity should focus on earlier stages of the life course, rather than obesity among the elderly.

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Figure 1. Estimated number of chronic illnesses in two body mass index groups across age at survey from weighted OLS (ordinary least squares) regression model. Data are from the U.S. National Health and Nutrition Examination Survey 1988-2004. Model was adjusted for race, gender, country of birth, marital status, education, income, health insurance, smoking status, and survey year. The body mass index groups are as follows: solid line, normal weight and overweight; ×, class II/III obese; and I, 95% confidence bands.

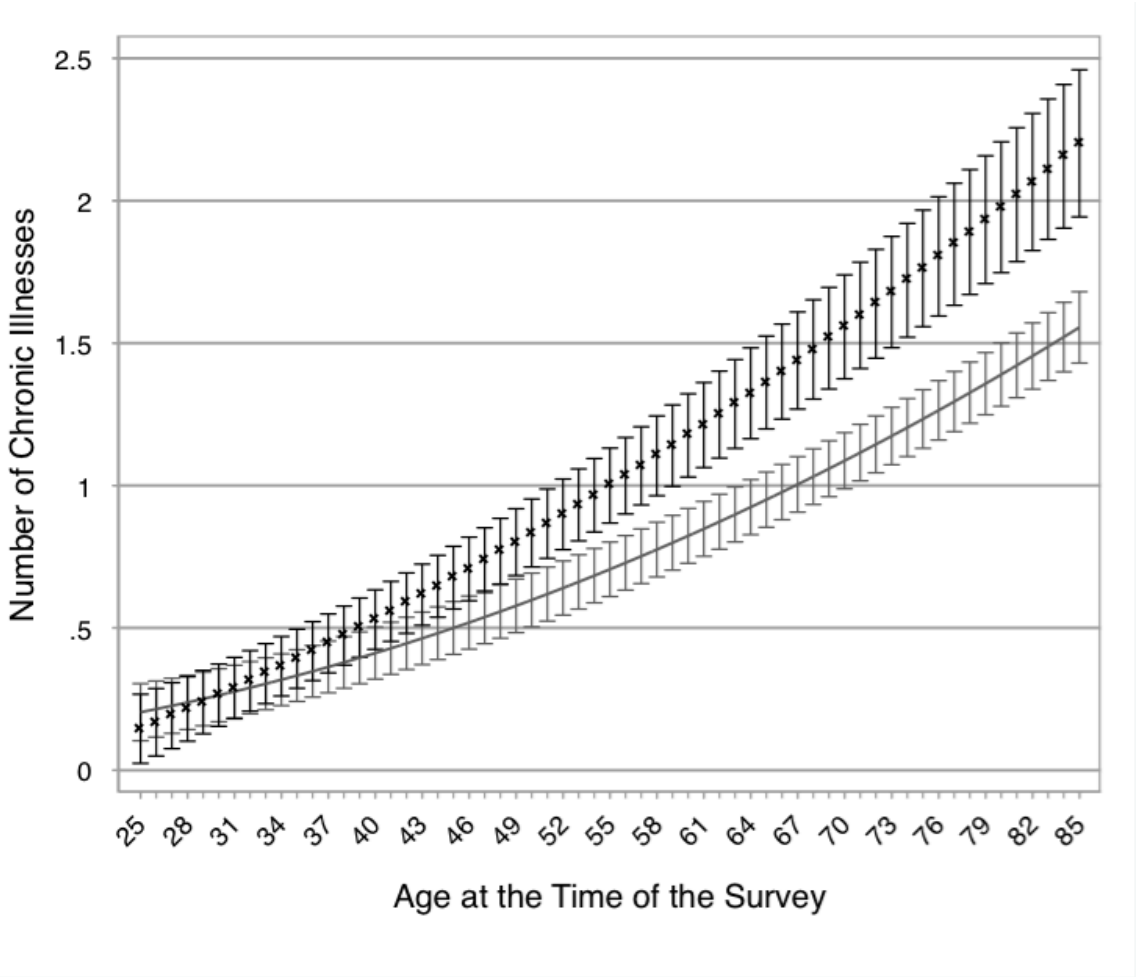

Table 1. Weighted Descriptive Statistics of Participants in the National Health and Nutrition Examination Survey, United States, 1988-2004

	NHANES III, 1988-1991		NHANES III, 1991-1994		NHANES 1999-2000		NHANES 2001-2002		NHANES 2003-2004	
	Mean (SD)	**No.**	**Mean (SD)**	**No.**	**Mean (SD)**	**No.**	**Mean (SD)**	**No.**	**Mean (SD)**	**No.**
Sample size		5487		6514		2844		3668		3664
No. of deaths		1698		1543		263		175		141
Normal weight		2469		2540		910		1174		1136
Overweight		1866		2345		995		1357		1319
Class I obese		768		1042		540		697		769
Class II/III obese		384		586		398		440		476
Demographics										
Age at survey, years	52 (18)		50 (18)		51 (17)		50 (16)		52 (17)	
Birth year	1937.7 (18)		1942.4 (18)		1948.7 (17)		1952.1 (16)		1952.3 (17)	
Male		2634		3192		1365		1797		1795
Non-Hispanic White		4444		5016		2048		2751		2711
Non-Hispanic Black		549		651		284		367		403
Hispanic		219		326		398		440		403
Other race/ethnicity		329		521		85		110		147
U.S. born		4883		5602		2361		3191		3114
Socioeconomic factors										
Income	25991 (15539)		23260 (14233)		27019 (18083)		29690 (17634)		26273 (16577)	
Less than high school		1317		1498		683		624		660
High school		1866		2215		739		917		953
More than high school		2305		2801		1422		2091		2052
Married		3786		4364		1820		2384		2308
Partner		110		195		142		183		220
Separated		110		130		114		110		73
Widowed		439		456		171		183		220
Never married		549		651		341		403		440
Divorced		494		586		313		367		403
Health insurance		5048		5667		2361		3118		3078
Health and behavioral										

factors												
Current smoker		1536		1629		683		880		879		
Former smoker		1591		1824		768		990		989		
Never smoked		2305		3062		1422		1797		1795		
Number of chronic illnesses	1 (0-2)*		1 (0-2)*		1 (0-1)*		1 (0-1)*		(0-2)*			

* Denotes median (Interquartile Range)

Table 2. Adjusted Hazard Ratios from Weighted Cox Model, NHANES III-NHANES 2003-2004, United States

	Model 1 [a] (age as time metric)		Model 2[b] (normal weight + overweight)		Model 3[b] (class I obese)		Model 4[b] (class II/III obese)	
	HR	**95% CI**	**HR**	**95% CI**	**HR**	**95% CI**	**HR**	**95% CI**
Reference BMI (18.5-29.9)								
Class I obese (30.0-34.9)	1.36	0.69, 2.69						
Class II/III obese (35.0+)	3.25	1.65, 6.40						
Class I obese * Age	0.96	0.85, 1.08						
Class II/III obese * Age	0.85	0.75, 0.95						
Birth cohort * Survey year			0.99	0.98, 1.00	1.00	0.98, 1.02	0.99	0.97, 1.01

Abbreviations: BMI, body mass index; CI, confidence interval; HR, hazard ratio; NHANES, National Health and Nutrition Examination Survey.

[a] Adjusted for race, gender, country of birth, marital status, education, income, health insurance, smoking status, chronic conditions and survey year.
[b] Adjusted for race, gender, country of birth, marital status, education, income, health insurance, smoking status, and chronic conditions.

Table 3. Adjusted Hazard Ratios of Obesity Relative to Normal Weight and Overweight Across the Life Course, NHANES III-NHANES 2003-2004, United States

	Model 5 [a] (adjusted for selection effects)		Model 6 [b] (adjusted for normal distribution of frailty)	
	HR	**95% CI**	**HR**	**95% CI**
Reference BMI (18.5-29.9)				
Class I obese (30.0-34.9)	1.35	0.68, 2.66	1.01	0.65, 1.55
Class II/III obese (35.0+)	3.22	1.64, 6.33	2.23	1.35, 3.69
Class I obese * Age	0.96	0.85, 1.09	0.99	0.92, 1.07
Class II/III obese * Age	0.85	0.75, 0.96	0.87	0.79, 0.96
Birth cohort * Survey year	0.99	0.99, 1.00		
Likelihood ratio test of the frailty distribution variance			*P = .484*	

Abbreviations: BMI, body mass index; CI, confidence interval; HR, hazard ratio; NHANES, National Health and Nutrition Examination Survey.

[a] from Weighted Cox Model, adjusted for race, gender, country of birth, marital status, education, income, health insurance, smoking status, and chronic conditions.

[b] from Weighted Complementary Log-log Discrete Time Hazard Model, adjusted for logarithm of age, race, gender, country of birth, marital status, education, income, health insurance, smoking status, chronic conditions and survey year. This model is not weighted because complementary log-log models (xtcloglog) are not supported by the survey weights command (svy) in Stata.

Table 4. Adjusted Time Ratios of Obesity Relative to Normal Weight and Overweight Across the Life Course from Weighted Accelerated Failure-Time Regression Model, NHANES III-NHANES 2003-2004, United States

	Model 7 [a]		Model 8 [b]		Model 9 [c]	
	TR	**95% CI**	**TR**	**95% CI**	**TR**	**95% CI**
Reference BMI (18.5-29.9)						
Class I obese (30.0-34.9)	0.98	0.87, 1.11	0.98	0.88, 1.10	0.98	0.87, 1.11
Class II/III obese (35.0+)	0.82	0.72, 0.93	0.83	0.74, 0.93	0.84	0.72, 0.98
Class I obese * Age	1.00	0.98, 1.03	1.00	0.98, 1.02	1.00	0.98, 1.03
Class II/III obese * Age	1.03	1.01, 1.06	1.03	1.01, 1.05	1.03	1.00, 1.07

Abbreviations: BMI, body mass index; CI, confidence interval; TR, time ratio; NHANES, National Health and Nutrition Examination Survey.

[a] Assuming Weibull distribution of T, adjusted for race, gender, country of birth, marital status, education, income, health insurance, smoking status, chronic conditions and survey year.

[b] Assuming gamma distribution of T, adjusted for race, gender, country of birth, marital status, education, income, health insurance, smoking status, chronic conditions and survey year.

[c] Assuming log-normal distribution of T, adjusted for race, gender, country of birth, marital status, education, income, health insurance, smoking status, chronic conditions and survey year.