Do Mortality Differentials Associated with Body Mass Decline over Age? An Age-Period-Cohort Analysis and Evidence of Cohort Distortions in the US

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Abstract

Excess mortality due to overweight or obesity was found to decline over cross-sectional age groups, which has been interpreted as a declining age effect in the public health literature. This finding is susceptible to potential cohort and period distortions because the age groups belong to different birth cohorts, and their mortality is observed over a considerably long period of time. In addition, prior research used time since baseline as analysis time, making it impossible to evaluate age-specific mortality. This paper conducts an age-period-cohort analysis of mortality differentials by body mass for men and women who were born in 1901-57 and observed in the 1988-94 National Health and Nutrition Examination Survey with mortality through 2006 in the US. The body mass-mortality association strengthens across cohort but changes little over age or the study period. As excess overweight or obese mortality has been increasing from earlier to later cohorts, failing to account for cohort differences leads to a declining age pattern. There is little evidence of period influences. American men and women do not show the same associations of body mass with mortality or with a series of socio-economic, demographic and behavioral factors.

BACKGROUND

Weight gain has led to epidemic proportions of excess body mass in the US and elsewhere. American adult mean weight increased by 11 kilograms between 1960 and 2002 (Ogden et al., 2004). Today, two of every three adults have a Body Mass Index (BMI) greater than 25 and are considered overweight or obese (Ogden et al., 2007). The life-course profile is more dramatic. American women born in 1941-50 gained 16 kilograms of weight on average in adulthood, and 70% of them were overweight before reaching age 65. Excess body mass is associated with a host of fatal and non-fatal diseases such as cardiovascular diseases, cancer, diabetes, gallbladder diseases, osteoarthritis and pulmonary diseases (WHO, 2000). One controversy remains whether excess body mass is detrimental to survival in old age. It has been argued that age is associated with a decline in BMI-related excess mortality (Bender et al., 1999; Calle et al., 1999; Park et al., 2006; Stevens et al., 1998), and an extra amount of fat is protective or at least brings no additional harm to old-age survival (Andres et al., 1985; Bender et al., 1999; Grabowski and Ellis, 2001). Public health guidelines about healthy weight have become a bone of contention. Some researchers proposed an age adjustment to reflect the change over age in the mortality consequences of body mass (Heiat, 2003; Heiat et al., 2001), whereas others argued that weight guidelines should largely ignore analysis of old subjects (Hu, 2008).

Age variations of mortality differentials should reflect the varying importance of the risk factor for biological aging or physiological states. But it is not well-understood why excess body fat should affect survival more or less as people grow older. Lypolysis is believed to be the biochemical process that transforms adipose issues into fatty acids,

an overabundance of which contributes to the development of insulin resistance and related metabolic disorders (Eckel et al., 2005). Lypolytic activities were found to decline over age (Ostman et al., 1969), leading to some speculations that the hazard of body fat may be reduced in old age (Elia, 2001; Seidell and Visscher, 2000).

Measurement error could vary by age. BMI, which is the most commonly used measure of body fat, does not distinguish between lean and fat mass, and assumes that at the same level of height, most of the variability is due to body fat. Although BMI is strongly correlated with fat mass among middle-aged adults, this assumption could be questionable among old adults. For reasons not at all clear, body composition changes over age, and even when weight does not change, lean mass turns into fat mass, and more fat mass is redistributed to abdominal cavity (Willett et al., 1999). Waist circumference might be a better indicator of body fat with advancing age, but empirical evidence is more limited (Seidell and Visscher, 2000).

Mortality selection is another popular explanation. Survivors to old age may be selected for good health, perhaps more so in the heavier groups due to their higher early mortality. Health conditions, however, are far from good for the elderly overweight or obese, as compared with the lean. The former tend to have more illnesses, disabilities or functional limitations in old age (Himes, 2000; Lang et al., 2008; Launer et al., 1994). Moreover, there is evidence of the association between weight gain and the incidence of coronary heart disease and its risk factors such as diabetes and hypertension (Biggs et al., 2010; Willett et al., 1999).

Given the high incidence and prevalence of chronic diseases and disabilities in old age, public health experts pointed out that both the quality and quantity of life should be

valued (Seidell and Visscher, 2000), and excess fat could lead to a prolonged life lived in poor health. It is also recognized that mortality differentials, commonly measured in relative terms (that is, in terms of mortality ratios), may fail to adequately capture the death burden of excess BMI. Adult mortality rates increase by age, so even if relative differences decline, absolute differences may be increasing, leading to a higher number of weight-related excess deaths at older ages (Calle et al., 1999; Stevens et al., 1998).

Despite the controversy and discussion surrounding the age effect, methodological issues are yet to be resolved to obtain variations in the BMI-mortality relationship that can be appropriately related to age. Most prior work compared cross-sectional age groups that belong to a multitude of birth cohorts, and are observed for mortality over a long period of time (Bender et al., 1999; Calle et al., 1999; Park et al., 2006; Stevens et al., 1998). Thus, one cannot discern age patterns that are independent of differences over birth cohort and time period. In addition, as previous studies used time since baseline as analysis time, there is age overlapping among comparison groups, making it impossible to determine the age to which mortality rates or differentials pertain.

These issues can be seen more clearly in Figure 1, which shows a standard research design, using data from the 1988-94 National Health and Nutrition Examination Survey (NHANES) with mortality followed through 2006. Any cross-sectional sample with a mortality follow-up would do for the illustration, but the NHANES is further used for the main analysis and replication of previous studies in this paper. The typical prior approach is to divide the baseline sample into age groups (young, middle-aged and old in Figure 1), and analyze how these groups differ in the relationship between baseline body mass and mortality averaged over the entire follow-up period. A consistent finding is

that the excess mortality of the overweight or obese is higher among the younger than older groups (Bender et al., 1999; Calle et al., 1999; Park et al., 2006; Stevens et al., 1998).

-- Figure 1 about here --

Caution should be used to attribute these differences to age. First, in all previous studies, the time metric is time since baseline, and as shown in Figure 1, the age to which mortality differentials pertain cannot be told. In a time-since-baseline framework, when age groupings are broad, age overlaps both within and across categories during the follow-up period. In Figure 1, a 40-year old at baseline (in the young group) may attain, in 2006, the age of 58, which is within the age range of the middle-aged at baseline. Similarly, within each age group, baseline age is blurred with age in the follow-up time. The issue is negligible when the follow-up is short, perhaps five years or less, which is rare in weight-mortality research. Although time since baseline is the standard approach in medical research, and appropriate, for example, for analyzing differences among treatment groups in a clinical trial, it is confusing and ineffective to study age variations in samples covering a multitude of age groups at baseline.

Second, the youngest and oldest groups were born years apart (1901 vs. 1957 in Figure 1). Rapid socio-economic and technological improvements of the last century have left among surviving cohorts a large amount of variation in life history, which could affect how mortality differs by body mass. In a cross-sectional sample, these cohort differences would show up as differences among age groups because different cohorts

happen to be at different ages.[2] A third problem shared by all prior work is about the follow-up period, which is typically long (19 years in Figure 1). The survival of fat relative to lean individuals could be affected by changes over the study period, for example, in the better diagnosis and treatment of diseases related to excess fat such as diabetes and hypertension.

An age-period-cohort (APC) framework would be needed to distinguish the three temporal dimensions along which mortality differentials could vary. However, it has been long recognized that the three time quantities cannot be identified simultaneously or are over-identified because when measured in the same units they form a mathematical identity (Mason and Smith, 1985). Unless an external substantive argument is available (For example, see Preston and Wang, 2006), to break this identification problem would often require adding higher-order terms (e.g., polynomial terms) or imposing equality constraints (e.g., grouping together certain cohorts). This common approach admittedly lacks theoretical underpinning and can be arbitrary.

While not completely solving the identification problem, a tradition exists in demographic research about how to distinguish period from cohort influences. Contemporaneous or immediate factors are often interpreted from a period perspective, whereas persistent or delayed influences from the past are regarded as embedded in cohorts (Guillot, 2010; Hobcraft et al., 1982; Ryder, 1965). Abundant evidence suggests the persistent and long-term metabolic, cardiovascular and mortality consequences of

[2] Potential cohort effect has been recognized but not tested empirically (Elia, 2001; Seidell and Visscher, 2000). A few analyses followed the same cohort to examine how the BMI-mortality relationship varies over follow-up time (that is, between the baseline and December 2006 in Figure 1), and obtained mixed findings (Lindsted and Singh, 1997; Visscher et al., 2000). These temporal variations, however, could not be properly related to age because the time metric is time since baseline, as explained above.

excess body fat (Kumanyika et al., 2008), and birth cohorts differ in exposure. The adoptions of new drugs and therapies, often regarded as contemporaneous factors, are also well-documented (Gregg et al., 2005), but their effectiveness in providing a permanent cure is less satisfactory (Cannon, 2010; Hu, 2005). Although this contrast has not been pointed out previously, the two perspectives (period vs. cohort) underlie the ongoing debate about the future of population health in the US. It has been suggested that historical advances in medical and health care have reduced or even eliminated the negative health consequences of excess fat (Flegal et al., 2005; Gregg et al., 2005). On the other hand, it is believed that recent birth cohorts' extended exposure to excess weight may incur an even more elevated mortality and health risk (Olshansky et al., 2005; Sturm et al., 2004).

This paper aims to analyze meaningful age patterns of the BMI-mortality relationship that are independent of period and cohort influences for American men and women who were born in 1901-57 and observed in the NHANES sample from 1988 to 2006, using age as analysis time and applying an APC framework that relies on equality constraints for model identification. Given that science is uncertain about an unambiguous way of estimating pure age effects, this paper tackles the problem from a different angle. Instead of attempting to establish the correct age patterns, I ask what age patterns are more or less plausible, given the cohort and period patterns that are observed in the data. In addition, I explore the sources (cohort vs. period) that are more or less likely to have distorted the cross-sectional age patterns discussed in the existent literature. Specifically, I compare age patterns under an APC specification against three other specifications: 1) only age and cohort are specified, 2) only age is specified; and 3) none

of the three time dimensions but baseline age groups are specified, which is to replicate previous studies.

A further issue to consider is heterogeneity. The dying out of selected members of the reference or comparison groups affects within-group compositions, leading to temporal variations in mortality differences across groups (Vaupel and Yashin, 1985). The selection mechanism, already hypothesized to interpret the cross-sectional age patterns in the existent literature as mentioned above, may occur along each and all of the three chronological dimensions. To reduce heterogeneities, the analysis adjusts for a common set of compositional factors including socio-economic background such as educational attainment, race/ethnicity, marital status and income/poverty status, and health behaviors and conditions such as smoking, weight loss and lung diseases. Cardiovascular diseases and diabetes are well-known sequalae of excess fat, and it is controversial whether, in analyzing the health and mortality consequences of excess fat, such conditions should be adjusted for. Results from analysis with their adjustment are discussed in the paper. As heterogeneities and compositional differences may vary by sex, all analysis is done separately for men and women.

DATA AND METHODS

The 1988-94 NHANES was conducted by the US National Center for Health Statistics. At baseline, it interviewed and examined a clustered and stratified probability sample of the US non-institutionalized population. Anthropometric data (including measured body weight and height) were collected at a health examination, and standard social, demographic and behavioral information was self-reported during the interview.

Mortality has been followed up through December 2006 via linkage with the National Death Index.

The analysis sample is selected based on age at baseline. Subjects are excluded if younger than 36 years of age because the covariate for weight loss is coded from a question about body weight ten years ago that was only asked of respondents aged 36 and above. Subjects aged 90 and above are also excluded because of age top-coding at 90.

Year of birth is imputed from age and survey time at baseline. This is because the NHANES data in the public domain do not provide information on either year of birth or year of survey but age at baseline and survey phase (between the October of 1988 and 1991, or between September 1991 and October 1994). I use the mid-point (in century months) of each survey phase to proxy survey time. After the age restrictions, year of birth in the analysis sample ranges from 1901 to 57. Subjects are classified into three birth cohorts: 1901-30 (C1), 1931-40 (C2) and 1941-57 (C3). A more refined cohort classification using ten-year intervals indicates no substantial differences among those born in 1901-30.

The Lexis diagram in Figure 2 describes the age, period and cohort classification of the sample. The lifelines connecting the baseline and study end (December 2006) delineate the cohorts as well as the mortality follow-up period. The age range on study is 59-103 for C1, 49-77 for C2 and 36-67 for C3. Due to the lack of information on year of survey as mentioned above, calendar year is approximated by months since baseline. A slightly different specification that adds up the mid-point of each survey phase and time since baseline is also experimented but produces basically the same results.

-- Figure 2 about here --

The data structure appears similar to that in Figure 1. What differs is the research design. In the old design, time since baseline (the horizontal axis) is analysis time, and the group indicator is baseline age in broad intervals. As there is neither cohort distinction nor specification of age in the follow-up period, it is impossible to pinpoint the age of death. In the new design, analysis time is age (the vertical axis), and combined with a specification for time period and birth cohort, this makes it possible to estimate age-specific mortality rates and full APC models.

As a relative measure of body weight, Body Mass Index (BMI) is calculated as weight in kilograms divided by squared height in meters. Based on the World Health Organization Guidelines (WHO, 2000), the following BMI groups are defined: underweight (BMI less than 18.5), normal-weight (BMI 18.5 or above but less than 25, reference group), overweight (BMI 25 or above but less than 30), moderately obese (BMI 30 or above but less than 35) and severely obese (BMI 35 or above). Two classes of obesity are distinguished to allow for the shift to the right of the BMI distribution. The analysis excludes underweight subjects because the focus is on excess weight, and excess underweight mortality has been largely attributed to manifest or occult diseases that lead to weight loss (Flegal et al., 2007).

After further deleting 56 cases pregnant at time of survey or missing for BMI measurement, the sample has a total of 5218 men and 5790 women, leading to 749434 and 879622 person-months, and 2187 and 1885 deaths, respectively. Table 1 presents sample descriptive statistics for each birth cohort and BMI group. Notable is the small number of deaths in the two later cohorts. This is due to low overall mortality at the younger ages. Death exposure is also limited for some cohort-weight groups. The

NHANES is nationally representative, but the sample size is smaller than the convenience samples used in previous studies (Bender et al., 1999; Calle et al., 1999; Park et al., 2006; Stevens et al., 1998).

-- Table 1 about here --

I first examine for each BMI group, distributions of educational achievement, race/ethnicity, poverty income ratio, marital status, smoking, weight loss, lung diseases, heart problems, diabetes and hypertension. Distributions within birth cohort are analyzed but not shown due to space limitation.

I then model person-months mortality data, using the parametric Gompertz function. The model is characterized by an exponential increase of mortality over age *a*:

$$h(a) = \exp(\beta + \gamma \cdot a),$$

where *h(a)* denotes age-specific mortality rates in the NHANES sample, and β and γ, the scale and shape parameter of the mortality curve.

To examine age (*a*) variations in how mortality differs by BMI (*W*), and whether period (*T*) and cohort (*C*) differences in the BMI-mortality association distort the age patterns, I consider and compare three models of interest. The first model allows mortality differentials to differ over period and cohort (by specifying two-way *W*-*T* and *W*-*C* interactions) but imposes a constant age pattern:

$$h(a) = \exp(\beta_0 + \beta_1 \cdot W + \beta_2 \cdot C + \beta_3 \cdot T + \beta_4 \cdot W \times C + \beta_5 \cdot W \times T + \gamma_0 \cdot a), \quad (1)$$

where the "×" sign indicates interaction, and the coefficients denote vectors when the variables are of more than two levels. Under Equation 1, the coefficients β_4 and β_5 capture cohort and period differences, respectively, whereas the lack of interaction between age and BMI constrains mortality differentials to be constant over age.

The second model allows mortality differentials to vary over age but stay constant over cohort and time period:

$$h(a) = \exp(\beta_0 + \beta_1 \cdot W + \gamma_0 \cdot a + \gamma_1 \cdot W \times a), \quad (2)$$

where the coefficient γ_1 captures age variations in how mortality differs by BMI. Equation 1 and 2 provides a contrast of a constant against a varying age pattern, depending on whether cohort and period differences are taken into account or not.

Should that be warranted, the third model attempts to adjudicate between cohort and period influences on the distortion of age patterns. This is accomplished by deleting the *T* terms in Equation 1:

$$h(a) = \exp(\beta_0 + \beta_1 \cdot W + \beta_2 \cdot C + \beta_3 \cdot W \times C + \gamma_0 \cdot a). \quad (3)$$

Covariates are included in a standard fashion as in a regression framework. Model comparison is based on the *AIC* criteria, with a smaller *AIC* indicating a better model. These three models are not the only ones that can be fitted to the data. In preliminary analysis, I explored a more complete set (e.g., a model where mortality differentials are allowed to vary over all three time dimensions), and found that the above three are the most relevant ones.

To replicate previous studies and analyze differences between cross-sectional age groups, I fit a Cox model with time since baseline as analysis time and baseline age as strata. Whether BMI differences in mortality vary among baseline age groups is captured by interaction terms between BMI and the age strata. The replication includes the same covariates as in the Gompertz models. The semi-parametric Cox model, with age as analysis time, can be used for the age-specific analysis. However, as the NHANES mortality rates on the logarithmic scale appear to be linear over age in preliminary

explorations (not shown), and thus satisfy the parametric assumption rather well, the Gompertz model would be more efficient as well as robust for the analysis of age-specific mortality.

The statistical software STATA (version 11.1) is used to implement both the parametric and semi-parametric survival analysis. Unless otherwise noted, sample weights are used to represent the target population. Standard error estimates are similar in additional analysis adjusting for survey design effects (that is, clustering and stratification).

RESULTS

Compositions

Compositions within BMI groups are shown in Table 2 (for socio-economic and demographic background) and Table 3 (for health behaviors and conditions). Among women, BMI is inversely associated with educational achievement, income and being non-Hispanic whites. Percentage married is similar for the normal-weight and overweight, and lower for the obese. The association with weight loss, smoking, and lung disease appear to be weak. Patterns are similar across the three birth cohorts (not shown).

-- Table 2 about here --

-- Table 3 about here --

Unlike women, the male SES-BMI association is weak or even reversed. Normal-weight and overweight men are similar in their tendency to have dropped out of high school, and the latter are only slightly less likely to graduate from college. Of all four BMI groups, normal-weight men are the least likely to be non-Hispanic whites or

currently married, whereas the overweight are the most likely to have an income that more than triples the poverty threshold. In addition, normal-weight men are substantially more likely to be current smokers, have lung diseases and have lost 10kg or more of their body weight in the past ten years. While male cohorts are in general similar in terms of the social, behavioral and health disadvantages associated with leanness, this may have increased for the latest cohort. For those born in 1941-57, overweight men surpass the normal-weight to have the highest percentage of college graduates, and lowest percentage of high-school dropouts (not shown).

As shown in the three bottom rows of Table 3, diabetes, hypertension and heart diseases, which are likely the physiological effects of excess fat, are consistently more prevalent among heavier men and women, except for heart problems among men. I also examined stroke and cancers of sites other than the lung, but their associations with BMI are weak. Among men, congestive heart failures and heart attacks are similarly prevalent across BMI groups. This lack of difference could be due to smoking, which is an established risk factor for cardiovascular diseases, and is positively related to leanness.

Replication: Comparing Baseline Age Groups

Figure 3 shows overweight or obese mortalities relative to the normal-weight in three baseline age groups (aged 36-54, 55-69 or 70-89 at baseline), as estimated in a Cox model with time since baseline as analysis time. Among women, excess mortality declines consistently from the younger to the older ages. For those aged under 55 at baseline, obese or overweight mortality more than doubles that of the normal-weight. This excess declines to nil or insignificance for those aged 70 and above. Among men,

there is no overweight or obese excess mortality, except for the severely obese. The elevation of mortality among severely obese men is moderately statistically significant for the young group and declines for the older groups.

-- Figure 3 about here --

As a whole, the exercise reproduces the pattern of declining excess mortality across baseline age groups as found in previous studies (Bender et al., 1999; Calle et al., 1999; Park et al., 2006; Stevens et al., 1998). Given the methodological issues identified earlier (that is, the age groups belong to various birth cohorts, and overlap in age during the long mortality follow-up), the declining pattern could be distorted by cohort or period differences, and have no bearing on whether the survival disadvantage of excess body mass varies over age. The overweight survival advantage, which has been widely reported in previous research, is limited to men.

Age Patterns and Cohort Distortions

Table 4 shows results for selected Gompertz models fitted to the female sample. Compared with normal-weight women, (log) mortality is higher for the overweight and obese. Under Equation 1, the excess is constant over age and declines insignificantly across time, but increases substantially from earlier to later cohorts. Under Equation 2 where both period and cohort differences are deleted, excess mortality declines over age, as indicated by the statistically significant and negative estimates of interactions between age and excess weight. According to the *AIC* (shown at the bottom of Table 4), Equation 1 fits the data better than Equation 2. Equation 3 deletes the period variations but retains the cohort differences and constant age pattern, and appears to fit the data the best,

according to the *AIC*. This indicates significant cohort but not period differences that should not be ignored. Failing to account for cohort influences distorts the constant age pattern into a declining one.

-- Table 4 about here --

-- Figure 4 about here --

Figure 4 shows ratios of female age-specific mortality rates estimated under Equation 2 (all cohorts combined) and Equation 3 (by cohort). 95% confidence intervals are calculated from the corresponding variance-covariance matrix (not shown) by using the delta method. These intervals are shown in Figure 4 for the cohort-specific estimates only to avoid cluttering. Among women born in 1930 or earlier, mortality differentials are trivial except for a 50% higher mortality among the severely obese. For the two later cohorts, excess mortality reaches 100% or more for all three excess BMI groups. All estimates are not statistically significant at α=0.05, but this is due to the small number of deaths (Table 1). Statistical uncertainties could be reduced by combining the two later cohorts (not shown). Relative mortality takes on a declining age pattern when the cohort pattern is ignored, as indicated by the darkened lines in Figure 4.

Corresponding male results are shown in Table 5 and Figure 5. Similar to females, the male BMI-mortality relationship differs substantially across cohort but insignificantly over time (Equation 1 vs. Equation 3), and ignoring the increasing cohort differences in mortality differentials leads to distorted age patterns (Equation 2 vs. Equation 3). Based on the *AIC*, the cohort model with a constant age pattern (Equation 3) is the best of all three.

-- Table 5 about here --

-- Figure 5 about here --

However, unlike women, overweight or moderately obese men suffer no excess mortality. Instead, the overweight are subject to the lowest mortality of all BMI groups, and this advantage has increased substantially for the latest cohort. Severely obese men suffer elevated mortality, and the elevation increases by cohort. The more than 100% excess among those born after 1940 is significant at α=0.1. In the male sample, how cohort differences distort age patterns depends on BMI status (Figure 5). Overweight relative mortality has become increasingly lower across cohorts, so it rises over age when all cohorts are combined. The opposite holds true for the relative mortality of severe obesity: Cohort increments, when ignored, leads to a declining age pattern. Relative mortality for moderate obesity varies little by cohort, and the corresponding age distortions are trivial.

DISCUSSION

For three cohorts of American men and women born in 1901-57, the long-term mortality consequences of body mass strengthen across cohorts but change little over age or the study period between 1988 and 2006. When cohort differences are ignored, mortality differentials vary over age. As excess mortality due to overweight or obesity has been increasing from earlier to later cohorts, and earlier cohorts tend to be older in the study sample, failing to account for cohort increments leads to a declining age pattern. A model that accommodates cohort differences but imposes a constant age pattern is more consistent with the data than one that ignores the former but allows for age variations.

These results are not directly comparable to prior research. In previous studies (Bender et al., 1999; Calle et al., 1999; Park et al., 2006; Stevens et al., 1998), overweight or obese mortality relative to the normal-weight declines over baseline age groups. This is also replicated with the NHANES data. Such results have been interpreted as a declining effect of age on the survival disadvantages of excess body mass, leading to the widespread notion that a moderate amount of weight gain over the life course should incur no additional mortality risk, and that weight guidelines should be adjusted for age. One study, for example, recommended a gain of 2.25 BMI units per decade to optimize survival (Bender et al., 1999). This would translate to a weight gain of over 6kg every ten years for a woman 1.65m tall, an amount which is greater than that observed for recent US cohorts.

Baseline age groups, however, belong to a multitude of birth cohorts, and their mortality is typically observed over a long period of time. Their comparison would therefore confound age with potential cohort and period differences in the BMI-mortality relationship. In the APC analysis, mortality differentials appear to be constant over age but expanding across cohort, with or without adjustment for period differences. When all cohorts are lumped together, relative mortality takes on a declining (or rising for overweight or moderately obese men only) age pattern, accompanied by a significant deterioration of model fit. These results suggest cohort (but not period) influences on the cross-sectional age patterns discussed in the existent literature.

Although purely statistical efforts are not sufficient to adjudicate between period and cohort, the predominance of the latter is supported by a large body of epidemiological evidence. Body mass has been increasing steadily in the last century,

slowly first, but more dramatically in the last thirty or so years. The BMI trend is found primarily to be a period effect that affects the population of all ages (Keyes et al., 2010). Its health imprint, however, could be cohort-specific, because 1) cohorts differ in their life-course profile of exposure, and 2) excess fat has long-term implications for metabolic, cardiovascular and mortality risks that persist and probably accumulate over the life course (e.g., Franks et al., 2010; Must et al., 1992). Among women where excess mortality is consistently observed across excess BMI groups, marked cohort increments occur with the overweight or moderately obese, rather than the severely obese; among women born after 1940, excess mortality is comparable across overweight and obese categories. It is with the moderately fat groups that an early exposure appears to have taken a more aggravated death toll. Period influences include contemporaneous factors such as the adoption of new drugs and therapies to treat chronic diseases related to excess fat. After accounting for significant cohort trends in the BMI-mortality association, estimates of period trends are all insignificant, in the negative direction for females but positive for males. Thus, evidence of a period trend from 1988 to 2006 is weak. Such influences, however, cannot be ruled out, as biomedical breakthroughs may occur in the future.

In addition to debunking the cross-sectional age patterns and investigating the sources of distortions, this paper advocates an age-specific framework that has been much neglected in epidemiology. Time since baseline is the standard time scale in medical research, appropriately so because the predominant interest has been in comparing the on-study time of treatments that are administered at baseline. Despite a growing body of methodological and empirical work in favor of using age as time scale

to analyze epidemiological survey data, the considerations are primarily of estimation bias rather than substantive interpretation (e.g., Flegal et al., 2005; Korn et al., 1997; Thiébaut and Bénichou, 2004). In one exception, the difficulty of estimating age-related quantities such as mean age at death under the time-on-study framework was mentioned (Lamarca et al., 1998). Extending this line of thinking, this study shows that when the research interest is age variations in the association between the risk factor and time to event, it is imperative to use age as analysis time because otherwise, when multiple birth cohorts and long-term follow-ups are involved, it is impossible to pinpoint the age of event. Because of well-documented empirical regularities in the age curve of human mortality (Preston et al., 2001), the additional advantage of an age-specific analysis is to allow for estimating parametric models (e.g., the Gompertz model) rather than semi-parametric ones, which improves statistical efficiency.

Reverse causation and confounding are long recognized issues in BMI research (Willett et al., 1999). Smoking, for example, could cause emaciating illnesses (e.g., lung diseases and cancer) that lead both to higher mortality and weight loss. This paper adjusts for a common set of compositional factors, and results are similar when heart diseases, diabetes and hypertension are further adjusted for. However, there remains telltale evidence of heterogeneities within weight groups. The overweight survival advantage, which has been extensively documented in the literature, e.g., in the NHANES study by Flegal et al. (2005) that combined men and women in the same analysis and adjusted for sex, is limited to men only, whereas overweight women suffer substantial long-term excess mortality. Both the overweight survival advantage (for men) and disadvantage (for women) have strengthened for those born after 1940.

While biological explanations such as sex differences in body composition (Gallagher et al., 1996) are plausible, this paper finds substantial sex and cohort differences in the association between BMI and a series of socio-economic, demographic and behavioral factors. A higher BMI is associated with less education and more poverty among women, but among men, lower socio-economic status and risky behaviors are more prevalent among the lean. The overweight advantage relative to the normal-weight either strengthens (in being non-Hispanic whites) or emerges (in graduating from college) with the most recent male cohort in the data. Despite the statistical adjustment and cohort distinction, residual confounding and reverse causation could be substantial in the male sample. The determinants of body mass may also be changing for more recent cohorts of women, due to the uptake of smoking by women in low socio-economic strata (Escobedo and Peddicord, 1996). Further research is needed to trace the dynamic social and behavioral mechanisms that select individuals into various weight statuses.

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Table 1 Sample size, person-months and deaths, un-weighted

Birth Cohort and BMI Status	Females N	Females Person-Months	Females Deaths	Males N	Males Person-Months	Males Deaths
Born in 1901-30 (C1)						
Normal weight	904	112824	564	895	93052	684
Overweight	973	126311	392	1105	130720	750
Moderate Obesity	480	65464	265	395	51458	244
Severe Obesity	272	35502	154	92	11732	64
Total	2629	340101	1564	2487	286962	1742
Born in 1931-40 (C2)						
Normal weight	282	47746	38	266	41512	87
Overweight	330	55514	58	389	64835	82
Moderate Obesity	212	34405	43	194	31647	44
Severe Obesity	176	27595	42	58	8898	17
Total	1000	165260	181	907	146892	230
Born in 1941-57 (C3)						
Normal weight	697	122775	33	596	101092	93
Overweight	653	113017	45	770	135292	65
Moderate Obesity	441	75637	32	321	55880	31
Severe Obesity	370	62832	30	137	23316	26
Total	2161	374261	140	1824	315580	215
Total	5790	879622	1885	5218	749434	2187

Source: 1988-94 National Health and Nutrition Examination Survey, mortality through December 2006

Notes: Body Mass Index (BMI), calculated from weight and height measured at baseline, is classified into four groups: normal weight (BMI 18.5-25), overweight (BMI 25-30), moderate obesity (BMI 30-35) and severe obesity (BMI >=35). The analysis deletes underweight subjects (BMI less than 18.5).

Table 2 Distributions (%) for social, demographic and economic conditions, by BMI status

	Females: BMI				Males: BMI			
	[18.5, 25)	[25, 30)	[30, 35)	>=35	[18.5, 25)	[25, 30)	[30, 35)	>=35
Education								
< High school	19	30	33	31	26	27	30	35
High school	33	36	38	41	25	16	30	30
Some college	21	17	16	15	18	31	18	19
4-year college	25	15	12	11	30	25	21	16
Missing	2	1	1	2	1	1	1	1
Total	100	100	100	100	100	100	100	100
Race								
Non-Hispanic whites	84	77	72	72	78	82	80	84
Non-Hispanic blacks	6	11	14	18	10	8	9	10
Mexican Americans	2	4	5	5	3	4	5	4
Other	7	7	9	5	8	5	6	3
Total	100	100	100	100	100	100	100	100
Poverty income ratio								
< 1	8	11	14	16	9	8	8	6
[1, 3)	35	40	41	40	36	33	38	52
>=3	49	41	35	35	49	53	49	39
Missing	7	8	10	9	6	6	4	3
Total	100	100	100	100	100	100	100	100
Marital status								
Married	62	63	55	58	74	79	81	79
Widowed	15	19	19	15	5	4	4	3
Never married	7	4	5	8	8	7	5	5
Separated/divorced	14	12	18	16	12	9	7	11
Cohabiting	2	1	3	3	2	2	3	3
Missing	0	0	0	1	0	0	0	0
Total	100	100	100	100	100	100	100	100

Source: Same as Table 1.

Notes: The four BMI groups are respectively defined as: normal-weight, overweight, moderately obese and severely obese; The analysis deletes underweight subjects (BMI less than 18.5).

Table 3 Distributions (%) for health behaviors and conditions, by BMI status

	Females: BMI				Males: BMI			
	[18.5, 25)	[25, 30)	[30, 35)	>=35	[18.5, 25)	[25, 30)	[30, 35)	>=35
Smoking								
Current	23	18	20	17	36	26	21	21
Former	24	24	23	26	34	41	50	48
Never	53	58	58	57	30	32	28	31
Total	100	100	100	100	100	100	100	100
Weight loss last 10 years								
>=10 kg	5	5	4	4	11	7	7	7
<10 kg	92	91	90	92	87	90	91	91
Missing	3	4	6	4	3	3	2	2
Total	100	100	100	100	100	100	100	100
Bronchitis, emphysemia or lung cancer	10	9	12	13	10	6	8	8
Congestive heart failure or heart attack	4	7	7	8	8	8	10	9
Diabetes	5	12	13	26	6	10	19	24
Hypertension	21	35	46	56	20	29	42	61

Source: Same as Table 1.

Notes: The four BMI groups are respectively defined as: normal-weight, overweight, moderately obese and severely obese; The analysis deletes underweight subjects (BMI less than 18.5).

Table 4 Results for selected Gompertz models, females

	Equation 1		Equation 2		Equation 3	
Parameters	Estimate	S.E.	Estimate	S.E.	Estimate	S.E
Intercept	-15.1386	0.4425	-15.9463	0.4567	-15.3423	0.4223
BMI status						
Normal-weight	ref.	--	ref.	--	ref.	--
Overweight	0.0610	0.1488	1.7765	0.6077	0.0086	0.0783
Moderately obese	0.0058	0.1825	2.4481	0.7344	0.0024	0.1040
Severely obese	0.5591	0.2132	2.3640	0.7172	0.3969	0.1233
Age in months	0.0091	0.0004	0.0101	0.0004	0.0095	0.0004
Birth Cohort						
Born in 1901-30 (C1)	ref.	--			ref.	--
Born in 1931-40 (C2)	-0.1657	0.2452			-0.2732	0.2210
Born in 1941-57 (C3)	0.0470	0.3195			-0.1386	0.2827
Time period						
Months since baseline	0.0018	0.0010				
Interaction (X) terms						
AgeXoverweight			-0.0017	0.0006		
AgeXmoderately obese			-0.0024	0.0008		
AgeXseverely obese			-0.0020	0.0008		
C2 overweight	0.6690	0.2730			0.6535	0.2700
C2 moderately obese	0.6778	0.3225			0.6553	0.3158
C2 severely obese	0.6726	0.3195			0.6244	0.3172
C3 overweight	0.7609	0.3552			0.7430	0.3515
C3 moderately obese	1.1526	0.3808			1.1269	0.3792
C3 severely obese	0.4682	0.4132			0.4066	0.4122
PeriodXoverweight	-0.0006	0.0014				
PeriodXmoderately obese	-0.0002	0.0017				
PeriodXseverely obese	-0.0019	0.0019				
Goodness of fit (AIC)	**331.7403**		**335.1968**		**330.3612**	

Source: Same as Table 1

Notes: Covariates include those listed in Table 2 and Table 3, excluding heart diseases, diabetes and hypertension; See text for details about Equation 1, 2 and 3; Body Mass Index (BMI), calculated from weight and height measured at baseline, is classified into four groups: normal weight (BMI 18.5-25), overweight (BMI 25-30), moderate obesity (BMI 30-35) and severe obesity (BMI >=35); The analysis deletes underweight subjects (BMI less than 18.5).

Table 5 Results for selected Gompertz models, males

	Equation 1		Equation 2		Equation 3	
Parameters	Estimate	S.E.	Estimate	S.E.	Estimate	S.E
Intercept	-14.2403	0.4413	-13.7236	0.4452	-14.3073	0.4393
BMI status						
Normal-weight	ref.	--	ref.	--	ref.	--
Overweight	-0.1359	0.1374	-1.0422	0.5158	-0.1408	0.0778
Moderately obese	-0.4311	0.2056	-0.6036	0.8067	-0.1257	0.1089
Severely obese	-0.0374	0.3188	1.8942	0.9758	0.1305	0.1626
Age in months	0.0087	0.0004	0.0081	0.0004	0.0088	0.0004
Birth Cohort						
Born in 1901-30 (C1)	ref.	--			ref.	--
Born in 1931-40 (C2)	-0.1084	0.1860			-0.1236	0.1823
Born in 1941-57 (C3)	0.3730	0.2464			0.3549	0.2289
Time period						
Months since baseline	-0.0007	0.0010				
Interaction (X) terms						
AgeXoverweight			0.0009	0.0005		
AgeXmoderately obese			0.0006	0.0009		
AgeXseverely obese			-0.0018	0.0011		
C2 overweight	-0.0243	0.2407			-0.0208	0.2392
C2 moderately obese	0.1466	0.2978			0.1960	0.2910
C2 severely obese	0.3385	0.4541			0.3746	0.4337
C3 overweight	-0.6838	0.2840			-0.6773	0.2783
C3 moderately obese	0.0065	0.3418			0.0674	0.3341
C3 severely obese	0.6498	0.3721			0.6865	0.3600
PeriodXoverweight	0.0000	0.0014				
PeriodXmoderately obese	0.0032	0.0019				
PeriodXseverely obese	0.0018	0.0031				
Goodness of fit (AIC)	**854.7946**		**865.5389**		**852.6591**	

Source: Same as Table 1

Notes: Covariates include those listed in Table 2 and Table 3, excluding heart diseases, diabetes and hypertension; See text for details about Equation 1, 2 and 3; Body Mass Index (BMI), calculated from weight and height measured at baseline, is classified into four groups: normal weight (BMI 18.5-25), overweight (BMI 25-30), moderate obesity (BMI 30-35) and severe obesity (BMI >=35); The analysis deletes underweight subjects (BMI less than 18.5).

Figure 1 A Comparison of cross-sectional age groups in the 1988-94 NHANES, mortality through 2006

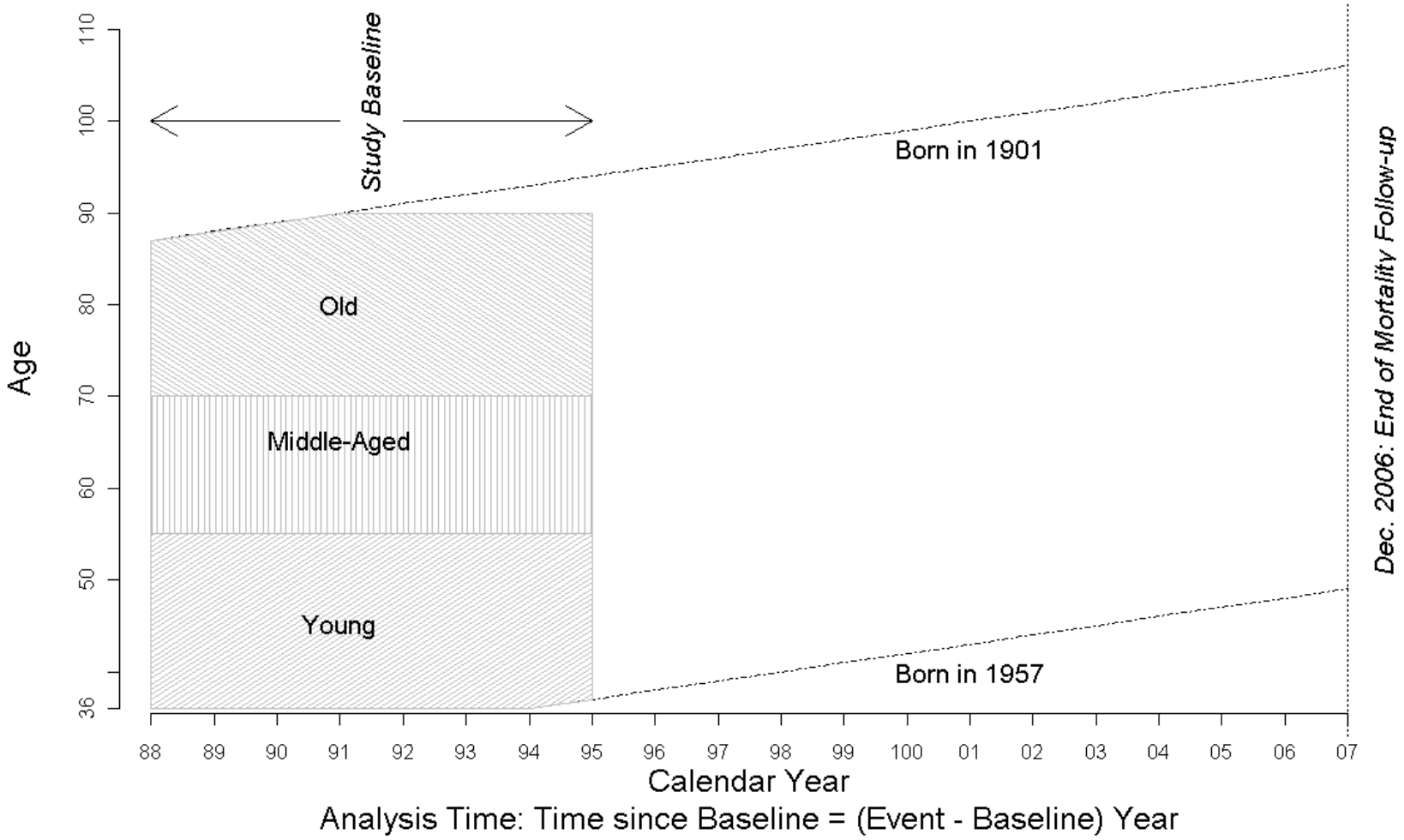

Figure 2 Age and cohort classification in the 1988-94 NHANES, mortality through 2006

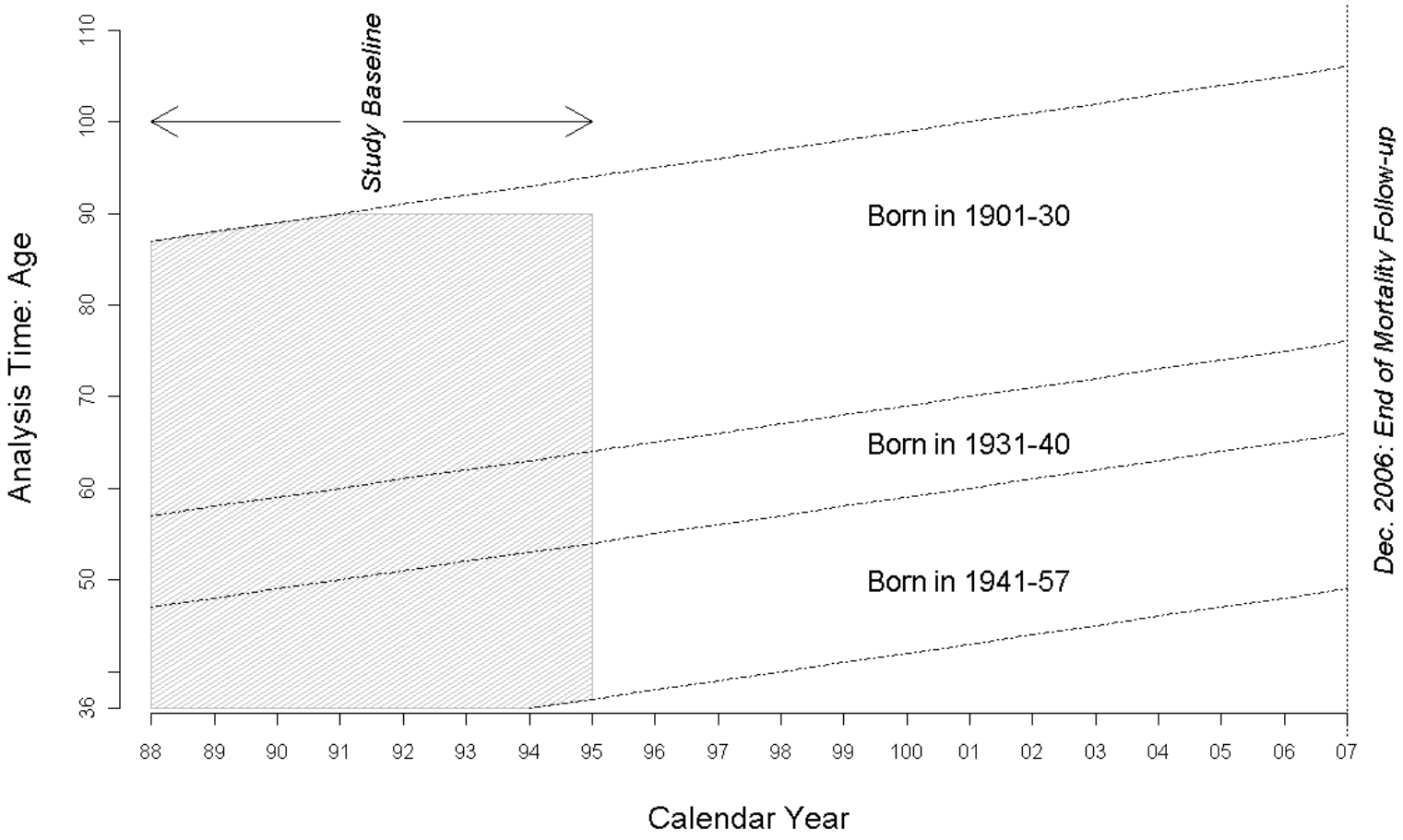

Figure 3 Replication results, mortality ratios by cross-sectional age groups, estimates and 95% CI, normal weight (BMI 18.5-25) as reference, 1988-94 NHANES, mortality through 2006

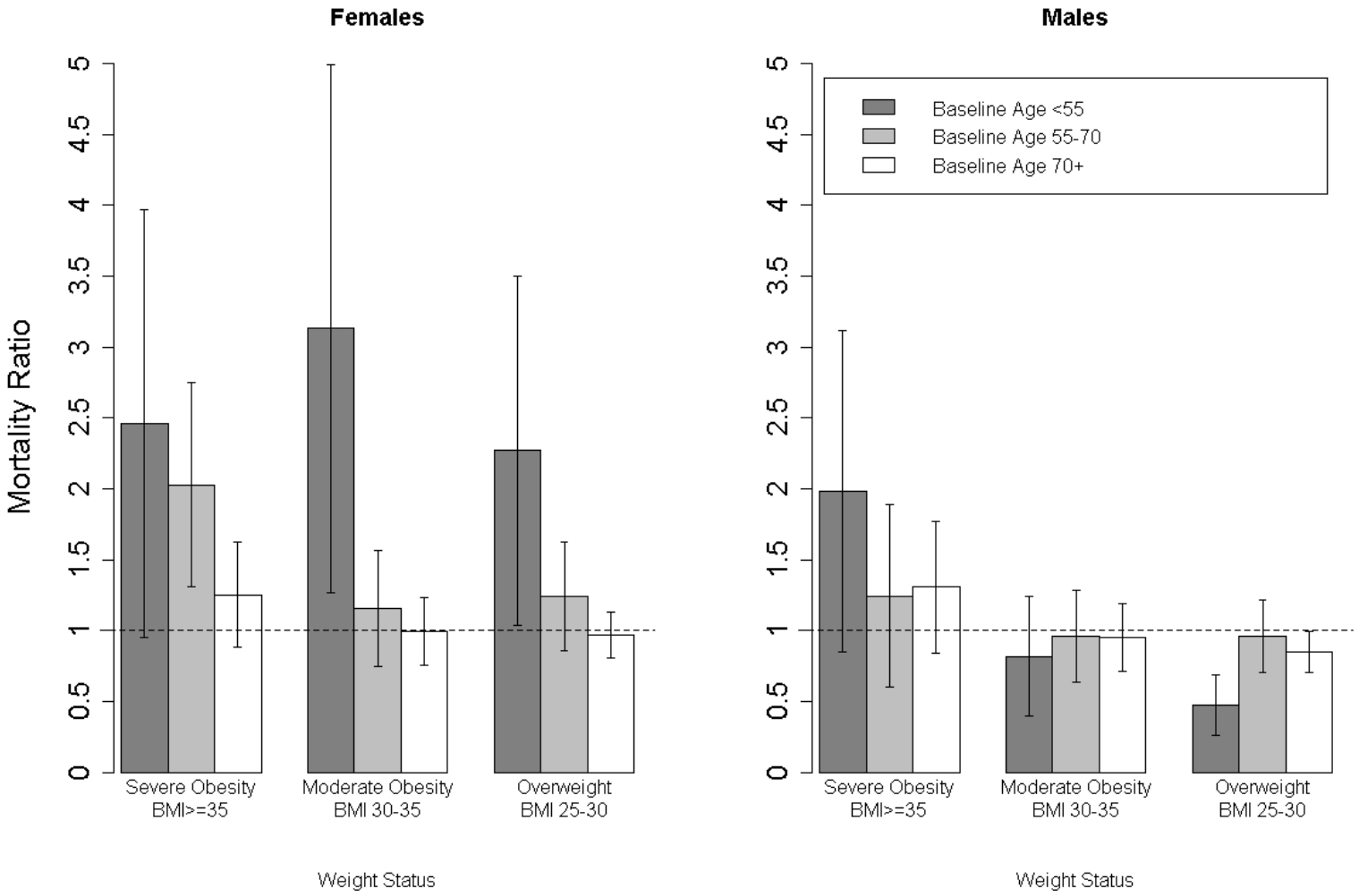

Figure 4 Age-specific mortality ratios, estimates and 95% CI (dashed line), by three birth cohorts vs. all cohorts combined, normal weight (BMI 18.5-25) as reference, females, 1988-94 NHANES, mortality through 2006

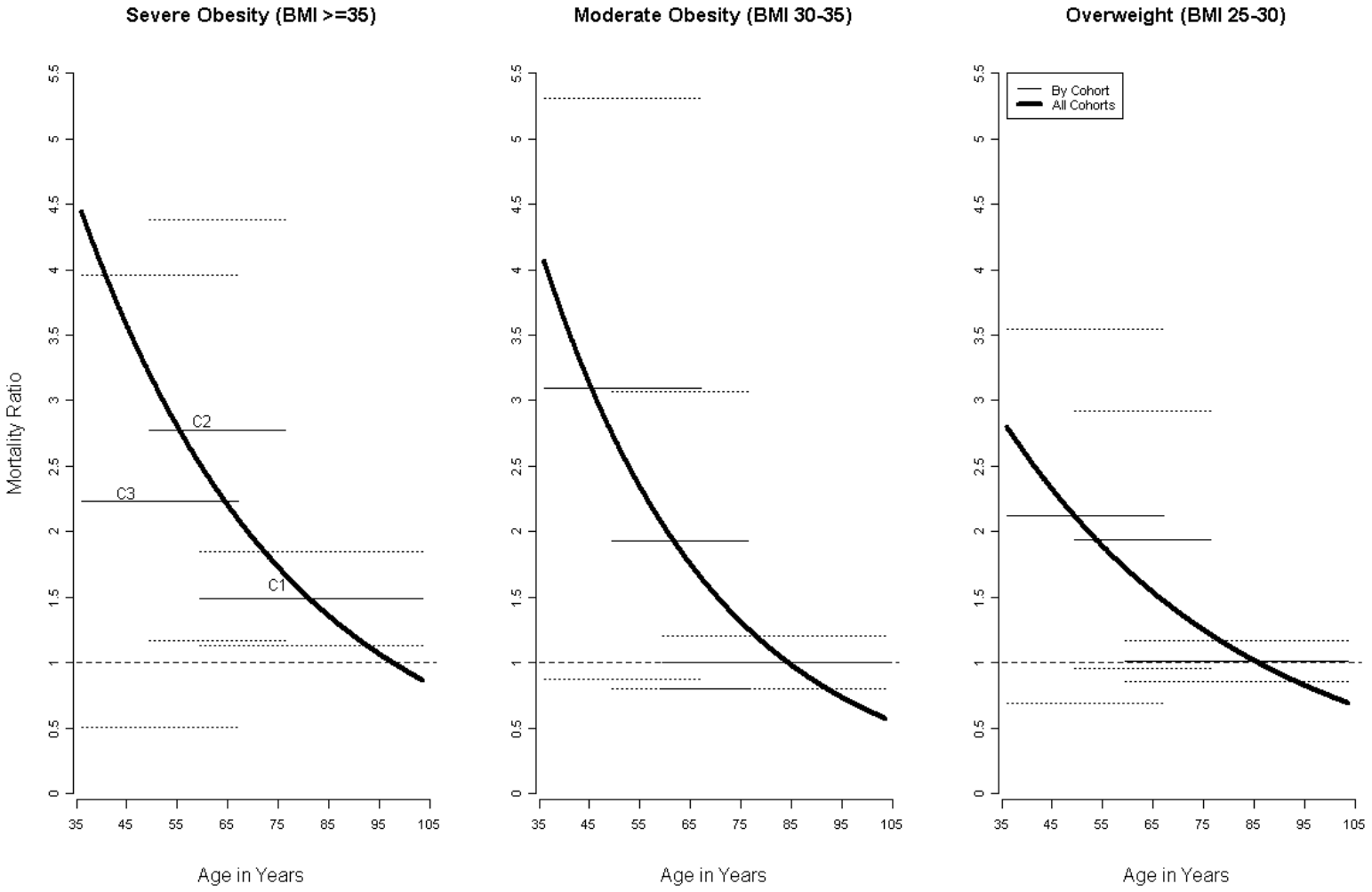

Figure 5 Age-specific mortality ratios, estimates and 95% CI (dashed line), by three birth cohorts vs. all cohorts combined, normal weight (BMI 18.5-25) as reference, males, 1988-94 NHANES, mortality through 2006