Chapter 2
2. Little effect of obesity on life expectancy at middle and old age

Abstract
The evidence of the effect of overweight and obesity on mortality at middle and old age is conflicting. The increased relative risk of cardiovascular disease and diabetes for overweight and obese individuals is well documented, but the absolute risk of cardiovascular death has decreased spectacularly since the 1980s. We estimate the burden of mortality due to obesity among middle and old aged adults in the Health and Retirement Study (HRS), a U.S. prospective longitudinal study. We calculate univariate and multivariate age-specific probabilities and proportional hazard ratios of death in relation to self-reported body mass index (BMI), smoking and education. The life table translates age specific adjusted event rates in survival times, dependent on risk factor distributions (smoking, levels of education and self reported BMI). 95% confidence intervals are calculated by bootstrapping. The highest life expectancy at age 55 was found in overweight (BMI 25-29.9), highly educated non smokers: 30.7 [29.5:31.9] years (men) and 33.2 [32.1:34.3] years (women), slightly higher than a BMI 23-24.9 in both sexes. Smoking decreased the population life expectancy with 3.5 [2.7:4.4] years (men) and 1.8 [1.0:2.5] years (women). Less than optimal education cost men and women respectively 2.8 [2.1:3.6] and 2.6 [1.6:3.6] years. Obesity and low normal weight decreased population life expectancy respectively by 0.8 [0.2:1.3] and 0.8 [0.0:1.5] years for men and women in a contemporary, U.S. population. The burden of mortality of obesity is limited, compared to smoking and low education.

Introduction
In 2004, Mokdad et al. calculated that obesity was overtaking smoking as actual cause of death (Mokdad et al. 2004). Equating the health risks of smoking with those of obesity struck the imagination (Littlejohns 2006; McTigue et al. 2003). Subsequent corrections were major: the original 365,000 attributable deaths came down to 112,000, the ranking of obesity as actual cause of death dropped from the 2nd to 7th place (Flegal et al. 2005; Mokdad et al. 2004). What happened to obesity?

We documented high mortality among obese and overweight persons in the Framingham Heart Study (FHS) before (Peeters et al. 2003a). However, the FHS describes the life history
of a cohort born between 1900 and 1920, alive at 1948-50 and followed up throughout the second half of the twentieth century. The cohort lived throughout the coronary heart disease epidemic, reaching its peak at the end of the 1960s (Kimm et al. 1983; Sempos et al. 1988). Since then, cardiovascular disease death rates have been declining considerably (Gregg et al. 2005). Cardiovascular disease with coronary heart disease is by far the most important cause of excess death due to obesity (McGee 2005). These secular changes in cardiovascular mortality might explain the bewildering range of results linking BMI to mortality, even in the same age groups (McGee 2005).

We studied the mortality experience of a recent cohort, the combined HRS and AHEAD studies which began in 1992 and 1993, respectively, and were merged in 1998. The design is comparable to the more recent Survey of Health, Ageing and Retirement in Europe (SHARE), allowing for later international comparisons (Andreyeva, Michaud and van Soest 2007). We described the burden of mortality of overweight, obesity, smoking and education with life tables. Life tables translate age specific death rates in life expectancies, taking into account competing mortality risks.

**Data and methods**

**Data**

We used the RAND Health and Retirement Study (HRS) data file containing the HRS and the Asset and Health Dynamics Among the Oldest Old (AHEAD) (Willis 2005). More information is available elsewhere (http://hrsonline.isr.umich.edu/). The HRS and AHEAD surveys include a nationally representative sample of initially non-institutionalized persons born in 1931-1941 (HRS, aged 51–61 in 1992) and in 1923 or earlier (AHEAD, aged 70 and older in 1993). Sampled persons were re-interviewed every two years. Response was on average 86% (HRS) and 90% (AHEAD). We selected white non-Hispanic men and women of whom date of birth, gender, level of education, Body Mass Index (BMI), and smoking status was available. Data on vital status and month and year of death are obtained through the mortality register (the National Death Index) and through HRS answers. The sample includes surveyrounds from 1992 to 2002, covering 6 waves.
**BMI, weight loss and self-report of health**

Body Mass Index (BMI in kg/m\(^2\)) is determined by self-reports of height and weight at the first contact. We define the BMI groups according to the classification of the World Health Organization (www.who.int/bmi): underweight, BMI lower than 18.5, normal weight, BMI of 18.5 to 24.9, overweight, BMI of 25 to 29.9, obese, BMI of 30 to 34.9 and severely obese, BMI greater than or equal to 35. Because our analyses showed heterogeneity among the normal weight individuals, we split this group into low normal weight with a BMI of 18.5 to 22.9 and normal weight with BMI of 23 to 24.9. Because weight loss at older ages can be an indication of deteriorating health and increased risk of dying we exclude persons with BMI less than 18.5 and use for every individual the BMI value that was first reported in the survey period. We start counting exposures and events after three years follow up. Respondent's self-reported general health status is used to control for morbidity at baseline, ranging from 1 for excellent to 5 for poor.

**Smoking status and educational attainment**

Smoking status is divided into three groups: never smokers, past smokers and current smokers. We use the oldest available information on smoking status. We distinguish three groups of educational attainment: Less than high-school or General Educational Development (GED), High school graduate and College graduate and above.

**Methods**

We estimated the hazard of mortality by age for males and females and for each determinant of interest. Since individuals may enter and leave observation anytime during the survey, left-truncation is taken into account and we used the Nelson-Aalen estimator to determine the mortality hazard rather than the more common Kaplan-Meier estimator. The Nelson-Aalen estimator determines the cumulative hazard whenever an event (death) occurs (Klein and Moeschberger 2005). Age, education and smoking adjusted mortality rates by BMI were estimated using Poisson (loglinear) regression.

Next we estimated Cox proportional hazard ratios, comparable to relative risks of death by BMI, smoking and education. Single year age is used as the timescale for the baseline hazard instead of time, accounting for left truncation and right censoring. Schoenfeld residuals with significance level set at 5% tested the proportionality assumption (Kleinbaum and Klein
2005). Because the mortality hazard for women was not proportional over age, we divided the data in groups of under age 80 and 80 and over.

Mortality rates are translated in annual probabilities using the Poisson assumption which define stratified life tables calculating life expectancy ($e_x$) at age $x \geq 55$. Confidence intervals for the life expectancies and differences in life expectancies were calculated using bootstrapping with 1000 replicates. To check the confidence intervals we also applied Chiang’s analytical method using the rule of variance of a linear function (Chiang 1984), which gave practically the same results.

Table 1 Sample population by sex, BMI, smoking status, education and age at baseline.

<table>
<thead>
<tr>
<th></th>
<th>Males</th>
<th>Females</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total sample</td>
<td>7281</td>
<td>8911</td>
<td>16192</td>
</tr>
<tr>
<td>Low normal weight</td>
<td>912</td>
<td>2515</td>
<td>3427</td>
</tr>
<tr>
<td>Normal weight</td>
<td>1361</td>
<td>1684</td>
<td>3045</td>
</tr>
<tr>
<td>Overweight</td>
<td>3621</td>
<td>2997</td>
<td>6618</td>
</tr>
<tr>
<td>Obese</td>
<td>1095</td>
<td>1179</td>
<td>2274</td>
</tr>
<tr>
<td>Severely obese</td>
<td>292</td>
<td>536</td>
<td>828</td>
</tr>
<tr>
<td>Never smoked</td>
<td>1881</td>
<td>4608</td>
<td>6489</td>
</tr>
<tr>
<td>Stopped smoking</td>
<td>3893</td>
<td>2686</td>
<td>6579</td>
</tr>
<tr>
<td>Currently smoking</td>
<td>1507</td>
<td>1617</td>
<td>3124</td>
</tr>
<tr>
<td>Low education</td>
<td>2016</td>
<td>2348</td>
<td>4364</td>
</tr>
<tr>
<td>Medium education</td>
<td>3536</td>
<td>5288</td>
<td>8824</td>
</tr>
<tr>
<td>High education</td>
<td>1729</td>
<td>1275</td>
<td>3004</td>
</tr>
<tr>
<td>&lt;65</td>
<td>3931</td>
<td>4559</td>
<td>8490</td>
</tr>
<tr>
<td>65-74</td>
<td>1375</td>
<td>1514</td>
<td>2889</td>
</tr>
<tr>
<td>75-84</td>
<td>1617</td>
<td>2146</td>
<td>3763</td>
</tr>
<tr>
<td>85+</td>
<td>358</td>
<td>692</td>
<td>1050</td>
</tr>
</tbody>
</table>

To assess the effect of a determinant as a cause of loss of life in a population we multiply the age-specific baseline hazard by the relative risk estimated by the Cox model, weighted by the actual or hypothetical proportions of the population (Diekmann 1990). This is a counterfactual thought experiment comparable to the calculation of population attributable risk. However, the life table takes into account age at death and recalculates changes in mortality as changes in life expectancy. Interactions between BMI and smoking are only significant for males aged 80 and over. Since this group contains rather few individuals and
interactions have no effect on other variables and did not improve the model, we did not include interactions in the model.

**Results**

The final sample describes 16,192 non-Hispanic white persons aged 55 and over. Table 1 gives the characteristics of the sample population. Persons were observed between May 1995 and December 2002. During the period under survey 2,354 individuals died. The mean follow-up was 7.8 years (range 0 to 10.8 years), including the three first years to avoid weight loss caused by fatal disease. Figure 1 shows the age, smoking and education adjusted mortality by BMI. Variation in all cause mortality was small between BMI 23 and 36 among men and between BMI 20 and 33 among women.

Figure 1 Age, smoking and education standardized proportional mortality hazard ratios for males (M) and females (F) by rounded BMI for ages 55 to 80 (lines are discrete splines weighted by standard errors).
The life expectancy at age 55 based on observed age specific death rates for males and females is respectively 23.7 [95% confidence interval 23.2:24.1] and 28.1 [27.6:28.6] (see table 2, univariate analysis). The actual life expectancy of the white American population in 1997 was 23.6 for men and 27.7 for women. After adjusting for smoking and education (see table 2, multivariate analysis), overweight men lived 0.6 years longer [0.0:1.2] than normal weight men (BMI 23 to 24.9). There were no statistically or clinically significant differences in survival of overweight women or obese men and women, relative to a high normal weight (BMI 23-24.9). However, severe obesity did shorten life of men with 3.0 years [2.2:3.8] and of women with 5.2 years [4.4:6.1] compared to normal weight. Low normal weight (BMI 18.5:22.9) cost 2.4 years for males compared to normal weight [1.8:3.0]. Stratifying for smoking status shows that the increased hazard of death of low normal weight is related to current or former smoking, but not to non-smoking.

Table 2 Life expectancy at age 55 by life style determinants using stratified univariate analysis and multivariate model (95% confidence limits between parentheses). Differences are caused by confounding and interaction.

<table>
<thead>
<tr>
<th>Univariate stratified</th>
<th>Multivariate modeled</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>males</td>
</tr>
<tr>
<td>Total population</td>
<td>23.7 (23.2 to 24.1)</td>
</tr>
<tr>
<td>Low normal weight</td>
<td>20.9 (19.5 to 22.4)*</td>
</tr>
<tr>
<td>Normal BMI †</td>
<td>23.7 (22.5 to 24.9)</td>
</tr>
<tr>
<td>Overweight</td>
<td>24.6 (23.8 to 25.4)</td>
</tr>
<tr>
<td>Obese</td>
<td>24.0 (22.2 to 25.8)</td>
</tr>
<tr>
<td>Severely obese</td>
<td>21.0 (18.9 to 23.1)*</td>
</tr>
<tr>
<td>Never smoking †</td>
<td>28.2 (27.1 to 29.2)</td>
</tr>
<tr>
<td>Stopped smoking</td>
<td>24.2 (23.4 to 25.0)*</td>
</tr>
<tr>
<td>Current smoker</td>
<td>18.7 (17.6 to 19.8)*</td>
</tr>
<tr>
<td>Low education</td>
<td>21.2 (20.2 to 22.2)*</td>
</tr>
<tr>
<td>Medium education</td>
<td>23.5 (22.7 to 24.3)*</td>
</tr>
<tr>
<td>High education †</td>
<td>27.5 (26.2 to 28.8)</td>
</tr>
<tr>
<td>Overweight, highly</td>
<td>29.5 (26.4 to 32.7)</td>
</tr>
<tr>
<td>educated non-smoker</td>
<td></td>
</tr>
</tbody>
</table>

† Reference category
* P < 0.05 compared to reference category.
After adjusting for BMI and education, male and female smokers lived on average 8.2 years [7.3:9.0] and 7.5 years [6.8:8.2] shorter, while quitters lived respectively 3.8 years [2.9:4.6] and 2.3 years [1.6:3.1] years shorter. Highly educated men lived 3.3 years [2.5:4.0] (moderate education) and 4.5 years [3.8:5.3] (low education) longer, highly educated women lived respectively 2.4 [1.4:3.5] and 4.6 [3.6:5.6] years longer. The optimal lifestyle in terms of life expectancy is lived by overweight, highly educated persons who never smoked. Figure 2 shows the fit of our model in the case of this optimal lifestyle, showing a median survival at age 55 of 32.1 and 34.3 years, which is a total life expectancy of 87.1 and 89.3 for men and women. The multivariate Cox proportional hazards model (table 3), adjusting for smoking and levels of education confirms the univariate life table findings.

Figure 2 Survival function and median age at death (for 55+) of the multivariate model and the actual life table for the overweight, non-smoking, highly educated population.
To limit the possibility of reverse causation (people with low weight because of existing disease), we studied weight loss. There were 1,284 people who lost 10% or more of their weight in less than three waves (or on average in less than 6 years), which conferred a hazard ratio of death equal for both sexes, 2.6 [2.1:3.2] (between 2 waves or 4 years) and 1.9 [1.6:2.2] (between 3 waves or 6 years). However, 2,554 people, men and women losing weight over 3 waves or more (>6 years) saw their hazard of death lowered: a PHR of 0.6 [0.5:0.7]. We modelled the proportional hazards after excluding those who lost weight, but the changes in hazard ratios were minor. Waiting five years instead of three before counting events did not change the results, except for lowering the statistical power. Waiting three years does not exclude reverse causation entirely but limits it sufficiently.

Table 3 Cox proportional hazard ratios (age under and over 80) with 95% confidence intervals. Model 1 describes the association of BMI with mortality, model 2 adjusts for smoking and education.
Loss or gain in life expectancy

The multivariate model of table 2 can also be interpreted as a counterfactual experiment measuring the life expectancy if the whole imaginary cohort was obese, highly educated, etc. This can be compared to the modelled average population life expectancy. If everybody would be overweight, non-smoker and highly educated, the population life expectancy would be 6.5 [5.2:7.7] years (men) and 4.6 [3.4:5.8] years (women) higher. If nobody would have ever smoked, population life expectancy would be 3.5 [2.7:4.4] years (men) and 1.8 [1.0:2.5] years (women) higher. Less than optimal education cost men and women respectively 2.8 [2.1:3.6] and 2.6 [1.6:3.6] years (considering low education causal and ignoring selection that might lead to lower levels of education). If everybody had been overweight instead of (morbid) obese or had (low) normal weight, population life expectancy would increase with 0.8 [0.2:1.3] for males and 0.8 [0.0:1.5] year for females. Figure 3 is comparable to calculations of attributable risks but shows losses or gains in life expectancy, attributable to the selected risk factors. Losses or gains in life expectancy by each risk factor are weighted by the prevalence of that risk factor in the population illustrating the importance of the contributions of risk factors to the total population life expectancy. Obesity costs severely obese men 2.8 years of life, but because of low prevalence (4%), severe obesity contributes only -0.1 years to life expectancy at the population level.

Discussion

The HRS confirms findings from other studies: being overweight at middle and older ages does not increase, and perhaps even decreases the risk of dying (Al Snih et al. 2007; Flegal et al. 2005; McGee 2005). Only higher levels of BMI increase mortality, which implies that the burden of mortality of obesity is limited even in present day United States. In the HRS study, the burden of mortality of overweight was not higher than of a BMI between 23 and 24.9 and even mild obesity did not show excess mortality. Low normal weight on the other hand did increase the hazard rate significantly for men. The burden of past and current smoking is far higher, decreasing total life expectancy with 3.5 (men) and 1.7 years (women) in the total population. Poor education also has a larger impact on mortality than body weight. Only severe obesity knows a high mortality. These results, indicating lower mortality at high normal BMI and overweight and higher mortality at low normal weights are in line with many other studies (Gu et al. 2006).
Limitations

The HRS is a general purpose study of health and retirement. We have no data on the effect of increased BMI's at younger ages, but people die rarely at younger ages. On the other hand, increasing prevalence of obesity in the future might be successfully tackled by innovative technology. The strength and weakness of our study is the recent but short period of time, namely 10 years in the 1990s. The short period makes it difficult to make statements about the future life course. On the other hand, the recent observation window gives a reliable picture of recent mortality, not of mortality in the past fifty years.

Figure 3 Losses or gains in average population life expectancy attributed to risk factors, adjusted for each other (95% confidence limits).

The HRS contains self-reported BMI. Measured BMI tends to be underreported by self report, especially for women with a higher body weight (Visscher et al. 2006). For overweight and obese women the mean difference was -1.14 BMI (Nawaz et al. 2001). This
would only strengthen our findings as the critical BMI point where mortality hazards start to increase (see Figure 1) would move up even higher. However, underreporting of BMI’s does lead to underestimation of prevalence of obesity and hence to slightly underestimated loss of life expectancy on population level. Metha and Chang show that the prevalence underestimation is small (Metha and Chang 2008). BMI, although widely used in health promotion, is no more than a fair measure of adiposity (Bray, Bouchard and James 1997; Visscher et al. 2001; Visscher et al. 2006);(Wannamethee et al. 2007). Weight is the sum of fat-free mass and body fat, with opposite effects on health (Wannamethee et al. 2007). At a BMI of 26-27, the mean percentage of body fat is 26 but may vary between 16% and 40%.(Bray et al. 1997) Wasting associated with loss of muscle mass sharply increases the risk of death, while high levels of body fat maintain BMI at normal levels. Waist circumference (as proxy of adiposity) and midarm muscle circumference (as proxy of muscle mass) are far better predictors of mortality risks than BMI (Visscher et al. 2001; Wannamethee et al. 2007).

We limited the analysis to all cause mortality, lacking cause specific data. Both overweight and obesity are associated with higher rates of diabetes and cardiovascular mortality (McGee 2005). Older studies like the Framingham Heart Study and to a lesser extent the Cancer Prevention Study II did detect a high excess risk of death in obesity (Calle et al. 1999; Peeters et al. 2003a). However, cardiovascular mortality rates have halved since the 1970’s, particularly after 1980. Smoking, high blood pressure and increased cholesterol levels came down sharply, partly as a consequence of successful cardiovascular risk management (Gregg et al. 2005). This may well explain the disappearing excess mortality in more recent studies. Our analysis is comparable to the NHANES data, a recent meta-analysis of 26 prospective studies and many more (Adams et al. 2006; Flegal et al. 2005; Gu et al. 2006; McGee 2005). Increased morbidity and mortality from cardiovascular diseases and diabetes is a common observation, but mortality of all causes is lower at high normal weight and overweight. Even the Framingham Heart Study shows conflicting results, likely depending on choices made in age bands and calendar periods used (Wilson et al. 2002).

Several studies show that healthier people at baseline show lowest mortality risks at lower BMI than less healthy people: among women, non-smokers, or those free from disease, BMI related to lowest mortality are lower (Adams et al. 2006; Calle et al. 1999; Kuriyama et al.
2004; Manson et al. 1995). Among men, former and current smokers or those with disease, BMI related to lowest mortality are higher. In current populations of middle aged and elderly persons, the former categories are far smaller. The striking differences between the large populations of former smokers and never smokers might suggest other than causal explanations for lowered mortality at lower BMI in these groups. Risk avoidance of people living a prudent life can cause both lowered mortality and lower weight.

Fatal disease causing weight loss can never be fully excluded in observational studies. We assessed potential reverse causation by various sensitivity analyses. We waited five years instead of three, excluded persons who lost weight as well as individuals who reported their health status as poor at baseline. None of these altered the results materially. Longer term weight loss, was associated with an increased, not a decreased life expectancy.

As senescence and degenerative diseases cause loss of weight, a higher weight may extend life by offering increased reserves. Lowered mortality of obesity should not lead to complacency (Basham and Luik 2008; Jeffery and Sherwood 2008). Firstly, while mortality is increased at very high levels of BMI, wasting together with adiposity may increase the mortality risks of ‘normal’ BMI at middle and old age (Visscher et al. 2001; Wannamethee et al. 2007). Weight circumference as a marker of adiposity and midarm muscle circumference are not so difficult to obtain and explain better mortality risks at increasing ages than does BMI. Insertion tapes seem to give more valuable information than balances. Secondly, obesity may be the exact opposite of smoking: while smoking is still fairly fatal, obesity became largely non-fatal (Flegal et al. 2005; Gregg et al. 2005). Smoking prevents morbidity by premature death (Barendregt et al. 1997; Mamun et al. 2004). Older HRS results on obesity showed little change in total life expectancy but shortened active life expectancy (active life expectancy is the ability to perform the activities of daily living) (Andreyeva et al. 2004; Reynolds et al. 2005). The price to pay for the lowered mortality of obesity may well be increased morbidity and health-care costs in the extended life.

While some researchers predict that obesity may cause life expectancy to decline (Olshansky et al. 2005), we conclude that the burden of mortality of obesity among white Americans aged 55 and over is limited to a still small fraction of severely obese people. Highly educated
overweight never smokers may anticipate at age 55 a total life expectancy of 85.7 years and 88.2 years.

Further studies should identify the causes why overweight protects against all cause mortality, while cardiovascular mortality is still increased (McGee 2005). The interaction between overweight, increased cardiovascular risk and successful cardiovascular risk management may cause interesting dilemmas for future health policy. While the burden of mortality of obesity is fairly small, the burden of morbidity and obesity associated health-care costs may increase, partly as a consequence of successful health-care interventions promoting survival of the obese. Future research should focus more on morbidity and disability than on the rather limited excess mortality.

References


