

# Life Years Lost Associated with Obesity-Related Diseases for U.S. Non-Smoking Adults

Su-Hsin Chang<sup>1\*</sup>, Lisa M. Pollack<sup>2</sup>, Graham A. Colditz<sup>1</sup>

**1** Division of Public Health Sciences, Department of Surgery, Washington University School of Medicine, St. Louis, Missouri, United States of America, **2** George Warren Brown School of Social Work, Washington University in St. Louis, St. Louis, Missouri, United States of America

## Abstract

The objectives of this paper are to predict life years lost associated with obesity-related diseases (ORDs) for U.S. non-smoking adults, and to examine the relationship between those ORDs and mortality. Data from the National Health Interview Survey, 1997–2000, were used. We employed mixed proportional hazard models to estimate the association between those ORDs and mortality and used simulations to project life years lost associated with the ORDs. We found that obesity-attributable comorbidities are associated with large decreases in life years and increases in mortality rates. The life years lost associated with ORDs is more marked for younger adults than older adults, for blacks than whites, for males than females, and for the more obese than the less obese. Using U.S. non-smoking adults aged 40 to 49 years as an example to illustrate percentage of the life years lost associated with ORDs, we found that the mean life years lost associated with ORDs for U.S. non-smoking black males aged 40 to 49 years with a body mass index above 40 kg/m<sup>2</sup> was 5.43 years, which translates to a 7.5% reduction in total life years. White males of the same age range and same degree of obesity lost 5.23 life years on average – a 6.8% reduction in total life years, followed by black females (5.04 years, a 6.5% reduction in life years), and white females (4.7 years, a 5.8% reduction in life years). Overall, ORDs increased chances of dying and lessened life years by 0.2 to 11.7 years depending on gender, race, BMI classification, and age.

**Citation:** Chang S-H, Pollack LM, Colditz GA (2013) Life Years Lost Associated with Obesity-Related Diseases for U.S. Non-Smoking Adults. PLoS ONE 8(6): e66550. doi:10.1371/journal.pone.0066550

**Editor:** Alex R. Cook, National University of Singapore, Singapore

**Received:** August 28, 2012; **Accepted:** May 13, 2013; **Published:** June 18, 2013

**Copyright:** © 2013 Chang et al. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

**Funding:** Funding from the Foundation for Barnes-Jewish Hospital and U54 CA 155496 supported this research. G. Colditz is supported by an American Cancer Society Clinical Research Professorship. The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.

**Competing Interests:** The authors have declared that no competing interests exist.

\* E-mail: changsh@wudosis.wustl.edu

## Introduction

The increasing prevalence of overweight and obesity has caused an increased risk of obesity-related comorbidities. These obesity-related diseases (ORDs) include serious chronic diseases, such as coronary heart disease, hypertension, type 2 diabetes, stroke, dyslipidemia, and some cancers, such as endometrial, breast, colon cancers [1,2], and multiple myeloma [3]. The rising trend of ORDs has not only increased annual medical spending [4,5] but also increased the risks of mortality. The Centers for Disease Control and Prevention (CDC) estimates that approximately 112,000 deaths are associated with obesity each year in the United States [6,7].

A large body of literature has studied the relationship between mortality and obesity [8–27]. However, most of the studies did not take ORDs into consideration, even though obesity-attributable comorbidities have been known to add variation to the simple relationship between mortality risk and body mass index (BMI – the ratio of weight in kilograms to the height in meters squared) [25,26,28–32]. In terms of life years measurement, Stevens et al. [27], Peeters et al. [11], Fontaine et al. [14], and, recently, Finkelstein et al. [33] attempted to calculate life years lost to obesity, but did not estimate the change in the life years associated with ORDs. It is known that not all obese individuals are at a higher health risk. Moreover, obesity per se does not cause death directly; it is those diseases associated with obesity that shorten life

years. To our knowledge, none has focused on the incidence of ORDs or the association of ORDs with mortality and life expectancy.

Furthermore, most of the published literature studying the association between BMI and mortality employed Cox Proportional Hazards (PH) models [34]. The problem with using the Cox PH models is that they do not take into account unobserved individual heterogeneity, e.g., familial risks, which affects the outcome; however those data were unavailable to investigators. Evidence has shown that failing to control for unobserved heterogeneity results in biased estimation and, consequently, biased hazard ratios and leads to erroneous conclusions [35–39]. Our study used the Mixed Proportional Hazard (MPH) model [37], which takes unobserved heterogeneity into account and therefore presumably provides a more precise estimation [35–38] than the Cox PH models. The MPH model was preferred in the duration analysis because individuals with relatively high hazard rates for unobserved reasons (e.g., people who have family history of cancer(s) and genetic abnormalities) die earlier on average. Consequently, samples of survivors are selected [36]. Inferences based on these selected samples are likely to be biased. We further extended the estimation results to simulate life years for the group of individuals with the same characteristics and calculate the life years lost associated with ORDs. The simulation approach we employed provides an alternative to the life table approach to project life years.

**Table 1.** Descriptive statistics for U.S. non-smoking adults in the sample and the population, 1997–2000.

Variable	n <sup>a</sup> (%)	N <sup>b</sup> (%)	Variable	n <sup>a</sup> (%)	N <sup>b</sup> (%)	
<b>Total</b>	61,873	93,853,798	<b>Phy. Act<sup>f</sup></b>	31,217 (50.45)	51,464,802 (54.84)	
<b>Gender</b>			<b>Age at survey</b>			
Male	23,518 (38.01)	41,383,588 (44.09)	19–	2,174 (3.51)	5,095,174 (5.43)	
Female	38,355 (61.99)	52,470,210 (55.91)	20–29	12,865 (20.79)	20,715,096 (22.07)	
<b>Race</b>			30–39	15,047 (24.32)	22,390,794 (23.86)	
White	46,598 (75.31)	73,640,855 (78.46)	40–49	11,742 (18.98)	18,765,606 (20.00)	
Black	9,679 (15.64)	12,379,346 (13.19)	50–59	7,078 (11.44)	10,746,130 (11.45)	
<b>Education</b>			60–69	5,152 (8.33)	7,028,974 (7.49)	
High school <sup>c</sup>	49,082 (79.33)	78,561,270 (83.71)	70+	7,815 (12.63)	9,112,022 (9.71)	
Under	12,791 (20.67)	15,292,528 (16.29)	<b>Age at death</b>			
<b>BMI Classification</b>			29–	46 (1.15)	89,986 (1.90)	
Underweight	1,304 (2.11)	2,023,392 (2.16)	30–34	36 (0.90)	54,090 (1.14)	
Normal weight	27,345 (44.20)	40,070,478 (42.69)	35–39	50 (1.24)	73,094 (1.55)	
Overweight	20,492 (33.12)	32,360,352 (34.48)	40–44	85 (2.12)	119,106 (2.52)	
Class I obese	8,406 (13.09)	12,867,565 (13.71)	45–49	120 (2.99)	178,146 (3.77)	
Class II obese	2,773 (4.48)	4,246,025 (4.52)	50–54	118 (2.94)	154,952 (3.28)	
Class III obese	1,553 (2.51)	2,285,986 (2.44)	55–59	112 (2.79)	154,217 (3.26)	
<b>ORDs<sup>d</sup></b>	15,178 (24.53)	20,772,263 (22.13)	60–64	156 (3.88)	194,259 (4.11)	
0	46,695 (75.47)	73,081,535 (77.87)	65–69	209 (5.20)	276,619 (5.85)	
1	12,003 (19.40)	16,680,111 (17.77)	70–74	299 (7.44)	381,127 (8.06)	
2	2,642 (4.27)	3,434,897 (3.66)	75–79	468 (11.65)	556,254 (11.76)	
3	474 (0.77)	578,575 (0.62)	80–84	698 (17.38)	766,960 (16.22)	
4	59 (0.10)	78,679 (0.08)	85–89	1,144 (28.48)	1,231,868 (26.05)	
<b>No alcohol<sup>e</sup></b>	7,173 (11.59)	10,464,992 (11.15)	90+	476 (11.85)	498,720 (10.55)	
	<b>n</b>	<b>N</b>	<b>Minimum</b>	<b>Maximum</b>	<b>Mean</b>	<b>Standard deviation</b>
<b>BMI (kg/m<sup>2</sup>)</b>	61,873	93,853,798	6.6	89.9	29.77	16.10
<b>Age at death (years)</b>	4,017	4,729,398	20.0	94.0	76.57	15.01

Source: Authors' calculations based on data from National Health Interview Survey, 1997–2000.

Notes: a. n: sample size; b. estimated population size; c. high school graduates; d. ORD: obesity-related diseases; e. the individual had had no more than 12 drinks of any type of alcoholic beverage in the individual's entire life; f. the individual engaged in physical activities for 10 minutes at least once per week.

doi:10.1371/journal.pone.0066550.t001

The aims of this study are (i) to examine the relationship between ORDs and mortality by using the MPH models and data from a national probability sample of the U.S. civilian noninstitutionalized population; and (ii) to predict life years lost associated with ORDs using simulated cohorts of the population. The projection of life years lost is based on the observed characteristics of the sample between 1997 and 2000 as a snapshot of their life span, and their characteristics upon survey determines their predicted life years. Our purpose is to investigate how ORDs in general observed at different life stages will impact life years for the target populations, rather than to examine ORDs separately.

## Materials and Methods

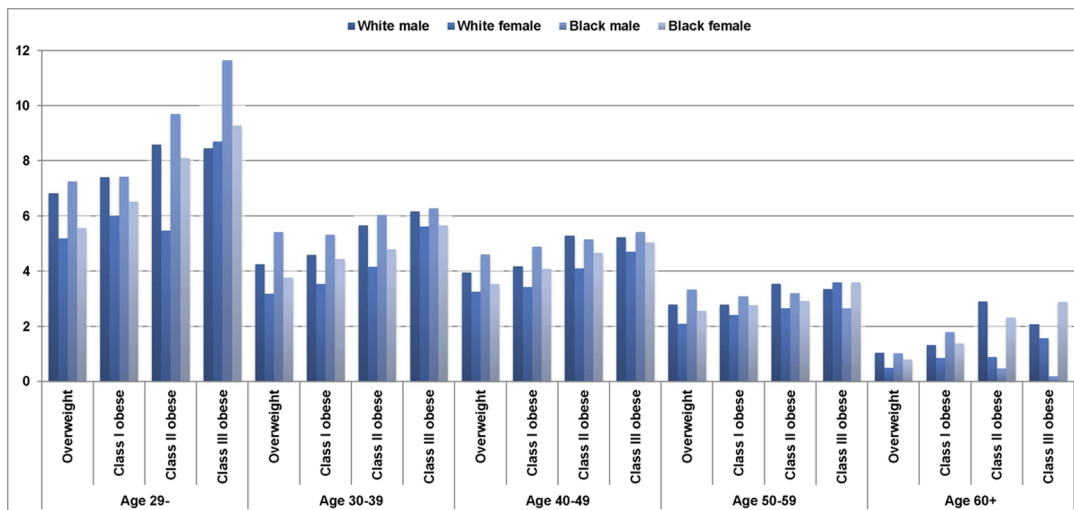
### The Data

Our data were extracted from (i) the National Health Interview Survey (NHIS) [40]; and (ii) the NHIS Linked Mortality Public-use Files [41]. The NHIS is a multi-purpose health survey providing health information on the civilian, noninstitutionalized, household population of the United States. The NHIS consists of three major components: Family, Sample Adult, and Sample Child. From each family in the survey, one sample adult and one

sample child (if any children under age 18 are present) are randomly selected, and information on each is collected from the sample adult core and the sample child core questionnaires [42]. This study used the Sample Adult Data Files, which contain data on adults aged 18 years and older.

Mortality data were extracted from the NHIS Linked Mortality Public-use Files [41], which provide mortality follow-up data for the NHIS sample from the date of interview through December 31, 2006 [43]. We linked the individual data in the NHIS Sample Adult Data Files to the data in the NHIS Linked Mortality files by personal identification numbers.

The sample in our study was retrieved from NHIS years 1997 to 2000 [44], and the exclusion criteria were as follows: (i) individuals with any missing data on the target variables; (ii) individuals smoking over 100 cigarettes in their entire life, because analyses can be confounded by illnesses associated with smoking [20,21,45]; (iii) women pregnant at the time of survey, because BMI levels are unstable during pregnancy; and (iv) patients who have ever been diagnosed with cancer or a malignancy of any kind, because their BMI levels are less stable due to the cancer treatments and appetite loss.



**Figure 1. Life years lost associated with obesity-related diseases for U.S. white and black, male and female, overweight and obese, non-smoking adults.**

doi:10.1371/journal.pone.0066550.g001

### Outcome Variable, Covariates, and Model Specifications

Age at death or censor was the outcome variable. We included the following covariates in each model: gender, race, educational attainment, alcohol consumption, and physical activities. For race, we used dichotomized variables for whites and blacks. We controlled for educational attainment by using a binary variable to indicate whether the individual is a high school graduate. Alcohol consumption is dichotomized by whether an individual had had no more than 12 drinks of any type of alcoholic beverage in the individual's entire life upon survey. Physical activity was dichotomized by whether the individual was engaged in modest or vigorous physical activities for 10 minutes at least once per week.

We also examined variables containing ORD information and constructed an ordinal variable recording the number of ORDs. The ORDs in our study included coronary heart disease, hypertension, diabetes, and stroke [46]. In addition, we generated age dummies delineating an individual's age at survey. We also considered a binary variable recording whether individuals reported that they had at least one ORD. Age dummies included individuals between ages 20 and 29, 30 and 39, 40 and 49, 50 and 59, 60 and 69, and 70 and above at survey. The reference group was individuals below 20 years of age.

We considered BMI classifications based on the standards established by the World Health Organization [47]: underweight for people whose BMI is less than  $18.5 \text{ kg/m}^2$ ; normal if  $\text{BMI} \in [18.5, 25)$ ; overweight if  $\text{BMI} \in [25, 30)$ ; class I obese if  $\text{BMI} \in [30, 35)$ ; class II obese if  $\text{BMI} \in [35, 40)$ ; and class III obese if BMI is at least  $40 \text{ kg/m}^2$ . We also considered BMI level of linear, quadratic [14,48], and inverted forms [14,19,22].

We tested different model specifications and parametric assumptions. For the parametric specification, we assumed different distributions of unobserved heterogeneity and changed the number of parameters for the baseline hazard. Different combinations of model specifications and parametric assumptions were performed. All model specifications considered in our study are listed in Table S1 in Appendix S1. Our final model was determined by a weighted Akaike information criterion (WAIC) because of the complex sampling design in the NHIS data [49]. The following covariates were included in the final model: male, white, black, high school graduate, the number of ORDs, alcohol

consumption, physical activity, BMI classifications in the form of binary variables (underweight, overweight, class I, II, and III obese, where normal-weight was considered the base group), age dummies, and the interaction terms of age dummies with the number of ORDs. Model estimation is detailed in Appendix S1.

### Prediction of Life Years Lost Associated with ORDs

Life years lost was predicted by simulating life years for populations with at least one ORD and without ORDs based on the estimates in the final model. We divided our sample into groups with different combinations of race, gender, age, and BMI classification. For each group, we simulated their survival densities based on the parameter estimates in the final model and predicted life years. Life years lost was projected by comparing the predicted life years of people with ORDs to that of people without ORDs within the same group. The bootstrap method [50,51] was performed to resample the subpopulations 1,000 times in order to compute the means and standard errors.

All estimations and bootstraps were adjusted for the complex sampling design [50–53] in the NHIS [42]. STATA (11, Stata Corp, College Station, TX) was used to obtain the summary statistics for the sample and population, and MATLAB (7.13, R2011b, MathWorks Inc, Natick, MA) was used to perform estimations and simulations.

### Sensitivity Analyses

A probabilistic sensitivity analysis was conducted to explore the variation in life years lost prediction arising from the parameter uncertainty in the simulations [54]. We first sampled the parameters from the distribution of our estimators [52]. For each set of parameters, we simulated life years and computed the life years lost associated with ORDs for each subgroup. We repeated this process 1,000 times and computed the means and standard errors [55].

### Hazard Ratios for Death

We computed the changes in the risk of death at different life stages associated with an additional ORD. These marginal effects of ORDs on hazard rate enabled us to explore how an additional ORD impacted mortality.

**Table 2.** Predicted life years lost associated with obesity-related diseases for U.S. non-smoking adults, 1997–2000<sup>a</sup>.

		White male		White female		Black male		Black female		Other male		Other female		Overall	
29–	Underweight	6.88	(8.71)	6.75	(4.70)	–	(–)	7.74	(6.67)	10.12	(11.67)	6.54	(5.52)	7.11	(3.03)
	Normal-weight	6.54	(1.57)	5.92	(1.46)	7.48	(3.95)	6.57	(2.12)	6.53	(4.08)	5.06	(2.87)	6.13	(0.89)
	Overweight	6.83	(1.29)	5.20	(1.45)	7.25	(2.17)	5.57	(1.71)	6.70	(4.72)	4.90	(2.85)	5.85	(0.70)
	Class I obese	7.41	(2.10)	6.00	(1.61)	7.42	(3.63)	6.52	(2.02)	7.60	(4.06)	5.86	(3.30)	6.38	(0.98)
	Class II obese	8.59	(2.97)	5.48	(2.91)	9.69	(4.10)	8.11	(3.20)	9.45	(7.24)	5.91	(4.50)	7.44	(1.49)
	Class III obese	8.45	(3.94)	8.71	(3.22)	11.65	(5.34)	9.29	(2.99)	8.16	(11.40)	6.05	(9.96)	9.10	(1.75)
	Overall	6.94	(0.83)	5.67	(0.79)	7.67	(1.60)	6.81	(0.98)	7.07	(2.20)	5.15	(1.56)	6.24	(0.44)
30–39	Underweight	5.45	(4.29)	4.49	(3.80)	–	(–)	7.07	(7.22)	–	(–)	–	(–)	5.83	(2.60)
	Normal-weight	4.85	(0.93)	3.59	(0.67)	5.18	(2.04)	3.96	(1.29)	4.49	(2.60)	3.55	(1.95)	4.12	(0.49)
	Overweight	4.26	(0.61)	3.19	(0.78)	5.42	(1.51)	3.78	(1.15)	4.39	(2.04)	3.57	(1.81)	3.85	(0.41)
	Class I obese	4.60	(0.85)	3.55	(0.91)	5.32	(1.65)	4.45	(1.32)	4.75	(3.16)	3.49	(2.45)	4.17	(0.50)
	Class II obese	5.66	(1.49)	4.16	(1.31)	6.03	(2.74)	4.80	(1.59)	4.87	(3.69)	3.87	(2.93)	4.83	(0.74)
	Class III obese	6.17	(2.33)	5.63	(1.56)	6.29	(3.86)	5.67	(1.75)	5.63	(4.63)	3.92	(5.37)	5.97	(1.01)
	Overall	4.83	(0.42)	3.84	(0.41)	5.73	(0.88)	4.67	(0.59)	4.88	(1.26)	3.52	(1.00)	4.48	(0.24)
40–49	Underweight	5.75	(5.20)	5.87	(6.28)	–	(–)	3.09	(8.75)	–	(–)	4.72	(9.21)	5.90	(3.29)
	Normal-weight	4.12	(0.88)	3.43	(0.51)	4.74	(1.99)	3.82	(1.08)	4.51	(2.26)	2.89	(1.68)	3.65	(0.40)
	Overweight	3.97	(0.53)	3.27	(0.61)	4.62	(1.24)	3.55	(0.94)	3.96	(1.71)	3.09	(1.62)	3.70	(0.34)
	Class I obese	4.18	(0.78)	3.43	(0.67)	4.90	(1.63)	4.08	(1.08)	4.22	(2.63)	3.43	(1.95)	3.83	(0.43)
	Class II obese	5.29	(1.21)	4.10	(1.04)	5.17	(3.45)	4.68	(1.94)	3.66	(4.11)	4.07	(2.66)	4.62	(0.67)
	Class III obese	5.23	(1.90)	4.70	(1.22)	5.43	(4.89)	5.04	(1.99)	6.34	(5.51)	4.82	(3.27)	5.00	(0.85)
	Overall	4.52	(0.36)	3.82	(0.29)	5.00	(0.85)	4.44	(0.54)	4.49	(1.09)	3.68	(0.87)	4.23	(0.19)
50–59	Underweight	3.84	(6.32)	2.82	(3.11)	4.39	(10.37)	5.27	(9.80)	–	(–)	–	(–)	4.61	(2.55)
	Normal-weight	2.81	(0.86)	2.30	(0.46)	3.92	(1.72)	2.89	(1.15)	3.21	(2.18)	1.96	(1.43)	2.54	(0.35)
	Overweight	2.80	(0.55)	2.10	(0.48)	3.34	(1.33)	2.57	(0.98)	2.89	(1.66)	2.12	(1.45)	2.44	(0.32)
	Class I obese	2.80	(0.79)	2.41	(0.64)	3.10	(1.97)	2.78	(1.16)	2.83	(3.07)	2.24	(2.19)	2.70	(0.43)
	Class II obese	3.55	(1.69)	2.66	(1.10)	3.22	(4.44)	2.94	(2.04)	1.70	(8.51)	2.43	(4.33)	2.97	(0.77)
	Class III obese	3.36	(2.66)	3.59	(1.60)	2.66	(8.02)	3.60	(2.51)	2.91	(11.35)	3.88	(3.57)	3.49	(1.12)
	Overall	3.11	(0.36)	2.54	(0.27)	3.59	(0.91)	3.19	(0.60)	2.87	(1.14)	2.40	(0.87)	2.86	(0.18)
60+	Underweight	0.84	(2.27)	0.32	(0.62)	–	(–)	1.07	(2.59)	7.43	(8.42)	0.30	(2.60)	0.33	(0.56)
	Normal-weight	0.88	(0.37)	0.27	(0.18)	1.48	(0.99)	0.99	(0.60)	1.15	(1.28)	1.15	(0.79)	0.47	(0.16)
	Overweight	1.05	(0.35)	0.51	(0.23)	1.03	(0.93)	0.80	(0.65)	1.40	(1.51)	0.75	(1.18)	0.67	(0.19)
	Class I obese	1.33	(0.74)	0.85	(0.39)	1.79	(1.83)	1.38	(0.92)	2.09	(3.27)	1.88	(2.19)	1.05	(0.31)
	Class II obese	2.92	(1.69)	0.90	(0.88)	0.50	(5.22)	2.32	(1.71)	1.74	(4.48)	1.82	(7.38)	1.44	(0.72)
	Class III obese	2.08	(2.99)	1.58	(1.31)	0.20	(5.35)	2.89	(3.26)	–	(–)	–	(–)	1.86	(1.04)
	Overall	1.31	(0.23)	0.62	(0.14)	1.38	(0.62)	1.45	(0.38)	1.29	(0.88)	1.33	(0.61)	0.89	(0.10)
Overall	2.67	(0.16)	0.79	(0.11)	3.45	(0.35)	2.25	(0.22)	3.39	(0.55)	2.11	(0.35)	1.58	(0.08)	

Notes: a. Bootstrapping means and standard errors in parentheses are presented; –: no observations in the sample.  
doi:10.1371/journal.pone.0066550.t002

We also computed hazard ratios for BMI classifications by dividing the death rates for the underweight, overweight, class I, II, and III obese by the death rates for the normal-weight. These hazard ratios allowed us to compare and contrast our findings with those in previous studies that used other approaches and models.

## Results

### Descriptive Statistics

Table 1 presents the summary statistics of our sample and the estimated population. The sample contained 61,873 individuals, representing a population of 93,853,798 U.S. non-smoking adults. Among the sample, 38% were male, 75% were white, and 16%

were black. Almost 80% of the sample had a high school degree. 4,017 deaths were identified. The mean age at death was 77 years. The maximum age in our sample was 94 years. The largest percentage of people (28%) died between 85 and 89 years of age; 476 people died at age 90 or older.

The average BMI of the sample was 29.77 kg/m<sup>2</sup>; 2% of the sample were underweight; 44% of the sample had a BMI within the normal-weight range; 33% were overweight; 13%, 5%, and 3% of the sample belonged to class I, II, and III obese, respectively. Approximately 75% of the sample reported no ORDs before the survey; 19% of the sample reported that they had one ORD; 4% had two ORDs; and less than 1% of the sample had at least three ORDs. About 12% of the sample

reported that they had no more than 12 drinks of any type of alcoholic beverage in their entire life, and more than half of the sample engaged in vigorous or moderate physical activity for 10 minutes at least once per week.

### Life Years Lost Associated with ORDs

Figure 1 presents the patterns of life years lost associated with ORDs for U.S. white and black, male and female, non-smoking adults who were at least overweight. Table 2 shows life years lost associated with ORDs for all race-gender-age-BMI classification cohorts of U.S. non-smoking adults. In general, the younger an adult developed ORDs, the more life years were lost associated with the comorbidities. For blacks and whites who were overweight or obese, ORDs were expected to decrease life years from 5.20 (overweight white female) to 11.65 (class III obese black male) for people under 29 years of age, while ORDs were expected to decrease life years from 0.20 (class III obese black male) to 2.92 (class II obese white male) for people over 60 years of age (Table 2), depending on degree of obesity, gender, and race.

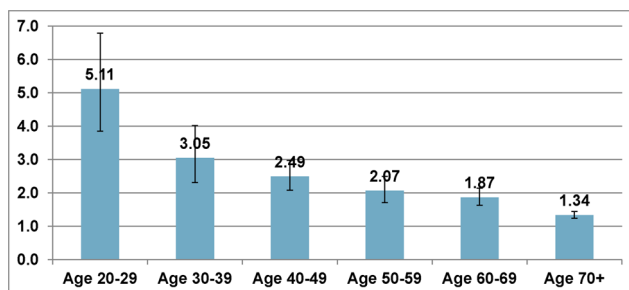
ORDs appeared to decrease life years with increasing degree of obesity. Overall, the class III obese lost 4.32 life years (from 0.20 to 11.65 life years across race-gender-age groups as shown in Table 2); the class II obese lost 3.17 life years (from 0.5 to 9.69 life years); the class I obese lost about 2.17 life years (from 0.85 to 7.42 years); and the overweight lost 1.31 life years (from 0.51 to 7.25 life years, depending on their age, gender, and race).

In terms of gender and race, black males lost the most life years to ORDs (3.45 years) across all ages and all degrees of obesity, followed by males other than blacks and whites (3.39 years), white males (2.67 years), black females (2.25 years), females other than blacks and whites (2.11 years), and, lastly, white females (0.79 years). ORDs appeared to lessen the most life years of class III obese black males aged 40 years and under (11.65 years for ages 29 and below and 6.29 years for ages 30 to 39).

The pattern of the predicted life years lost associated with ORDs in the sensitivity analysis was only marginally different from the main analysis (Table 2), though most of the standard errors in sensitivity analysis were larger. We present the sensitivity results in Table S3 in Appendix S1.

### Hazard Ratios for Death

Figure 2 shows the marginal effects of ORDs on hazard rate. An additional ORD was associated with an increase in risk of death for every age group, though mortality risk was more severe for younger individuals: 5.11 [95% CI: 3.85–6.79] for ages 20 to 29; 3.05 [95% CI: 2.31–4.02] for ages 30 to 39; 2.49 [95% CI: 2.09–2.98] for ages 40 to 49; 2.07 [95% CI: 1.71–2.50] for ages 50 to



**Figure 2. Marginal effect of obesity-related diseases on mortality rate for each age group.**  
doi:10.1371/journal.pone.0066550.g002

59; 1.87 [95% CI: 1.63–2.14] for ages 60 to 69; and 1.34 [95% CI: 1.24–1.44] for ages 70 and above.

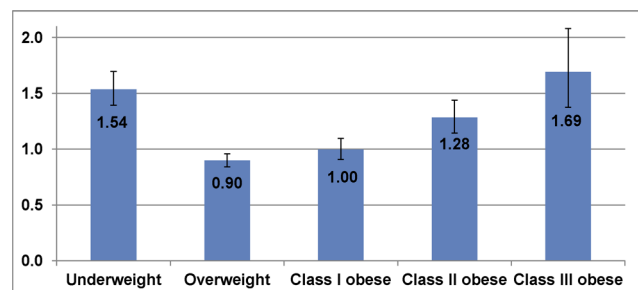
To compare with those in previous studies, the hazard ratios for death for each BMI classification were computed (see the parameter estimates for each BMI classification in the final model in Table S2 in Appendix S1). We found that the underweight, class II, and class III obese had higher mortality rates than the normal-weight (Figure 3). The class III obese had the highest hazard ratio (1.69 [95% CI: 1.37–2.08]) compared to normal-weight people, followed by the underweight (1.54 [95% CI: 1.39–1.70]), and the class II obese (1.28 [95% CI: 1.14–1.44]). The overweight (0.90 [95% CI: 0.84–0.96]) and class I obese (0.997 [95% CI: 0.91–1.09]) had lower death rates than the normal-weight, but the latter was not statistically significant.

### Discussion

We investigated the relationship between ORDs and mortality by using the MPH model controlling for both observed and unobserved individual heterogeneity. Using data from NHIS 1997 to 2000 and NHIS Linked Mortality Files to estimate the parameters in the MPH model, we predicted life years lost associated with ORDs based on the estimates in the model, using simulated race-gender-age-BMI classification-ORD status cohorts of U.S. non-smoking adults.

We confirmed that non-smoking adults with ORDs had higher mortality. Depending on the age group, an additional ORD increased risk of death by a range of 34% to 411%. This finding is consistent with Kuk et al. [28], who used the Edmonton Obesity Staging System (EOSS) to measure ORDs and found that the hazard rate for people at stage 2 of EOSS was 119% higher than the hazard rate for people at stage 1, and the hazard rate for people at stage 3 of EOSS was 35% higher than the hazard rate for people at stage 2. However, a direct comparison is difficult because the data, models, and measurements of ORDs are different.

Comparing and contrasting our study with previous studies that explored the relationship between BMI/obesity and mortality and took ORDs into account, we found that adults who belonged to overweight and class I obese classifications had lower mortality rates, while adults who belonged to underweight, class II and III obese classifications had higher mortality rates than normal-weight people, other things being equal. Consistent with previous findings in the literature [20,21,23,26,56], our findings showed that higher degrees of obesity and underweight were associated with higher mortality. But deviating from Berrington de Gonzalez et al. [20] and others [19,21], our BMI-mortality association approximated a U-shaped relationship with the lowest mortality rate in the overweight classification [23,24,26,56], while theirs approximated



**Figure 3. Hazard ratios for death for each BMI classification (reference: the normal-weight).**  
doi:10.1371/journal.pone.0066550.g003



a J-shaped relationship with the lowest mortality rate in the normal-weight classification. This deviation can be explained by at least three reasons: (i) our study adjusted for ORDs, and hence, the nadir for death rates shifted slightly to the right in the range of overweight; (ii) only whites were included in the sample of Berrington de Gonzalez et al. [20], eliminating ethnic variation, which is known to be a key determinant of obesity-mortality relationships; (iii) unobserved heterogeneity was not controlled for in their analyses; thus, the sample was selected toward survivors.

The predicted life years lost associated with ORDs decreased with age. ORDs were expected to shorten the lifespan of people in their 20 s by more than 5 years, while people in their 60 s were predicted to lose just under 1 year of life. Fontaine et al. [14] also found a similar trend in the context of life years lost to obesity. Using U.S. non-smoking adults aged 40 to 49 years as an example to illustrate percentage of the life years lost associated with ORDs, we found that on average a 45-year-old U.S. non-smoking class III obese black male with ORDs (compared with his counterpart without ORDs) was expected to lose 5.43 years of life, which translates to a 7.5% reduction in the total life years (72.78 years). Of the same age and same degree of obesity, white males lost 5.23 life years (a 6.8% reduction in total life years), followed by black females (5.04 years, a 6.5% reduction in life years), and white females (4.70 years, a 5.8% reduction in life years). The total life years were obtained by averaging 4-year life expectancy for the target populations from the U.S. Life Tables [57–60]. Based on these average life years lost estimates, total life years lost associated with ORDs for U.S. non-smoking adults aged 40 to 49 years was estimated to be 914,573 for white males ( $n = 174,821$ ); 1,324,105 for white females ( $n = 281,679$ ); 189,847 for black males ( $n = 34,967$ ); and 501,745 for black females ( $n = 99,556$ ).

The predicted life years lost associated with ORDs also increased with degree of obesity. Although our final model did not directly support the finding that the death rates associated with ORDs were increasing with the degree of obesity, this increase was possibly driven by the fact that ORDs were more prevalent in people with higher degrees of obesity, and an increased risk of mortality was associated with an additional ORD (Figure 2).

Our analysis has several strengths. First, our analysis focused on ORDs and examined their association with mortality and life years, an association that has not been well studied. Second, unlike most studies, our study controlled for unobserved heterogeneity, which captures the effects of unavailable variables in the data; as a result, our estimations are more precise, and our prediction of life years lost associated with ORDs is more reliable. Third, we incorporated the degree of obesity confounding the analysis when exploring the relationship between ORDs and mortality. Overall, this study not only advances in methodology, but provides a different perspective on the relationship between ORDs and mortality, which will inform the future analyses of any weight-loss intervention, ranging from physical activity programs to bariatric surgery, including, but not limited to, cost-effectiveness analyses.

## References

1. Must A, Spadano J, Coakley EH, Field AE, Colditz G, et al. (1999) The disease burden associated with overweight and obesity. *JAMA* 282: 1523–1529.
2. (1998) Clinical Guidelines on the Identification, Evaluation, and Treatment of Overweight and Obesity in Adults—The Evidence Report. National Institutes of Health. *Obes Res* 6 Suppl 2: 51S–209S.
3. Beason TS, Colditz GA (2012) Obesity and Multiple Myeloma. In: Mittelman SD, Berger NA, editors. *Energy Balance and Hematologic Malignancies*. New York: Springer. 71–95.
4. Finkelstein EA, Trogdon JG, Cohen JW, Dietz W (2009) Annual medical spending attributable to obesity: payer- and service-specific estimates. *Health Aff (Millwood)* 28: w822–831.
5. Cawley J, Meyerhoefer C (2011) The medical care costs of obesity: An instrumental variables approach. *J Health Econ*.
6. Centers for Disease Control and Prevention. [http://www.cdc.gov/PDF/Frequently\\_Asked\\_Questions\\_About\\_Calculating\\_Obesity-Related\\_Risk.pdf](http://www.cdc.gov/PDF/Frequently_Asked_Questions_About_Calculating_Obesity-Related_Risk.pdf).
7. Mokdad AH, Marks JS, Stroup DF, Gerberding JL (2005) Correction: actual causes of death in the United States, 2000. *JAMA* 293: 293–294.
8. Cai L, Lubitz J, Flegal KM, Pamuk ER (2010) The predicted effects of chronic obesity in middle age on medicare costs and mortality. *Med Care* 48: 510–517.
9. Flegal KM, Graubard BI, Williamson DF, Gail MH (2005) Excess deaths associated with underweight, overweight, and obesity. *JAMA* 293: 1861–1867.

Yet, our study has several limitations. First, using ORD counts prevented us from differentiating the effects of different diseases. Second, due to data constraints, the ORDs this paper targeted were a subset of obesity-related comorbidities. Third, the data that we used are cross-sectional, and our model is not time-varying and does not capture the dynamics of disease evolution, which limits its projection capability on life years lost [46]. For example, smoking status might change over time for the younger cohorts in particular, which could add variation to the relationships. Fourth, some studies [61–63] suggest that different weight predictors of mortality, e.g., waist-hip ratio, waist circumference, or fitness, might be better measures than BMI. Even if they are not, incorporating them would have made the analysis more comprehensive. However, these data were not available in the NHIS datasets.

## Conclusion

Our results confirm that being obese or underweight increased risk of mortality. Furthermore, our study suggests that the ORDs included in our study – coronary heart disease, hypertension, diabetes, and stroke – increased chances of dying and decreased life years by 0.2 to 11.7 years depending on gender, race, BMI classification, and age. The life years lost associated with ORDs was more pronounced for younger, black, male, and more obese adults than for older, white, female, and less obese adults.

This conclusion not only conveys a message that these populations are more vulnerable to ORDs, but it also informs policy makers that public health initiatives should put more emphasis on the prevention of obesity and obesity-related comorbidities for these populations. More importantly, future studies should investigate how different ORDs separately observed at different life stages impact life years lost.

## Supporting Information

**Appendix S1** Table S1–S3: Considered model specifications and parametric assumptions; Estimation results: final model; Predicted life years lost associated with obesity-related diseases for U.S. non-smoking adults, 1997–2000: sensitivity analysis. (DOCX)

## Acknowledgments

We acknowledge Dr. I-Tang Yu in the Department of Statistics, Tunghai University, for helpful conversations. We also thank the participants in the 33rd Annual Meeting of the Society for Medical Decision Making for their comments and suggestions to make our work better.

## Author Contributions

Conceived and designed the experiments: SHC GAC. Analyzed the data: SHC LMP GAC. Wrote the paper: SHC LMP. Study supervision: SHC GAC. Critical review of manuscript: SHC GAC. Obtained funding: GAC.

10. Olshansky SJ, Passaro DJ, Hershow RC, Layden J, Carnes BA, et al. (2005) A potential decline in life expectancy in the United States in the 21st century. *N Engl J Med* 352: 1138–1145.
11. Peeters A, Barendregt JJ, Willekens F, Mackenbach JP, Al Mamun A, et al. (2003) Obesity in adulthood and its consequences for life expectancy: a life-table analysis. *Ann Intern Med* 138: 24–32.
12. Rosner F (2010) Obesity shortens life in children and adults. *Isr Med Assoc J* 12: 47–48.
13. Paolini JB, Mancini J, Genestal M, Gonzalez H, McKay RE, et al. (2010) Predictive value of abdominal obesity vs. body mass index for determining risk of intensive care unit mortality. *Crit Care Med* 38: 1308–1314.
14. Fontaine KR, Redden DT, Wang C, Westfall AO, Allison DB (2003) Years of life lost due to obesity. *JAMA* 289: 187–193.
15. Hotchkiss JW, Leyland AH (2010) The relationship between body size and mortality in the linked Scottish Health Surveys: cross-sectional surveys with follow-up. *Int J Obes (Lond)*.
16. Adams KF, Schatzkin A, Harris TB, Kipnis V, Mouw T, et al. (2006) Overweight, obesity, and mortality in a large prospective cohort of persons 50 to 71 years old. *N Engl J Med* 355: 763–778.
17. Katzmarzyk PT, Craig CL, Bouchard C (2001) Original article underweight, overweight and obesity: relationships with mortality in the 13-year follow-up of the Canada Fitness Survey. *J Clin Epidemiol* 54: 916–920.
18. McGee DL (2005) Body mass index and mortality: a meta-analysis based on person-level data from twenty-six observational studies. *Ann Epidemiol* 15: 87–97.
19. Allison DB, Faith MS, Heo M, Kotler DP (1997) Hypothesis concerning the U-shaped relation between body mass index and mortality. *Am J Epidemiol* 146: 339–349.
20. Berrington de Gonzalez A, Hartge P, Cerhan JR, Flint AJ, Hannan L, et al. (2010) Body-mass index and mortality among 1.46 million white adults. *N Engl J Med* 363: 2211–2219.
21. Calle EE, Thun MJ, Petrelli JM, Rodriguez C, Heath CW, Jr. (1999) Body-mass index and mortality in a prospective cohort of U.S. adults. *N Engl J Med* 341: 1097–1105.
22. Durazo-arvizu R, McGee D, Li Z, Cooper R (1997) Establishing the nadir of the body mass index-mortality relationship: a case study. *J Am Stat Assoc* 92: 1,312–319.
23. Flegal KM, Graubard BI, Williamson DF, Gail MH (2007) Cause-specific excess deaths associated with underweight, overweight, and obesity. *JAMA* 298: 2028–2037.
24. Hanson RL, McCance DR, Jacobsson LT, Narayan KM, Nelson RG, et al. (1995) The U-shaped association between body mass index and mortality: relationship with weight gain in a Native American population. *J Clin Epidemiol* 48: 903–916.
25. Manson JE, Willett WC, Stampfer MJ, Colditz GA, Hunter DJ, et al. (1995) Body weight and mortality among women. *N Engl J Med* 333: 677–685.
26. Mehta NK, Chang VW (2009) Mortality attributable to obesity among middle-aged adults in the United States. *Demography* 46: 851–872.
27. Stevens J, Cai J, Juhaeri, Thun MJ, Williamson DF, et al. (1999) Consequences of the use of different measures of effect to determine the impact of age on the association between obesity and mortality. *Am J Epidemiol* 150: 399–407.
28. Kuk JL, Ardern CI, Church TS, Sharma AM, Padwal R, et al. (2011) Edmonton Obesity Staging System: association with weight history and mortality risk. *Appl Physiol Nutr Metab*.
29. Brochu M, Tchernof A, Dionne IJ, Sites CK, Eltabbakh GH, et al. (2001) What are the physical characteristics associated with a normal metabolic profile despite a high level of obesity in postmenopausal women? *J Clin Endocrinol Metab* 86: 1020–1025.
30. Dvorak RV, DeNino WF, Ades PA, Poehlman ET (1999) Phenotypic characteristics associated with insulin resistance in metabolically obese but normal-weight young women. *Diabetes* 48: 2210–2214.
31. Sims EA (2001) Are there persons who are obese, but metabolically healthy? *Metabolism* 50: 1499–1504.
32. Willett WC, Hu FB, Colditz GA, Manson JE (2005) Underweight, overweight, obesity, and excess deaths. *JAMA* 294: 551; author reply 552–553.
33. Finkelstein EA, Brown DS, Wraga LA, Allaire BT, Hoerger TJ (2010) Individual and aggregate years-of-life-lost associated with overweight and obesity. *Obesity (Silver Spring)* 18: 333–339.
34. Cox DR (1972) Regression Models and Life-Tables. *Journal of the Royal Statistical Society Series B-Statistical Methodology* 34: 187–&.
35. Heckman JJ, Singer B (1984) Econometric Duration Analysis. *Journal of Econometrics* 24: 63–132.
36. Abbring JH, Van den Berg GJ (2007) The unobserved heterogeneity distribution in duration analysis. *Biometrika* 94: 87–99.
37. Lancaster T (1997) The econometric analysis of transition data. Cambridge u.a.: Cambridge Univ. Press. XII, 352 S p.
38. Vaupel JW, Manton KG, Stallard E (1979) Impact of Heterogeneity in Individual Frailty on the Dynamics of Mortality. *Demography* 16: 439–454.
39. Gerard J VdB (2001) Chapter 55 Duration models: specification, identification and multiple durations. In: Heckman JJ, Leamer E, editors. *Handbook of Econometrics*: Elsevier. 3381–3460.
40. Centers for Disease Control and Prevention National Health Interview Survey: The Principal Source of Information on the Health of the U.S. Population.
41. Centers for Disease Control and Prevention (2010) National Health Interview Survey (NHIS) Public-use Linked Mortality Files: Survey Years 1986–2004.
42. (2000) Design and estimation for the National Health Interview Survey, 1995–2004. *Vital Health Stat* 2: 1–31.
43. Centers for Disease Control and Prevention. [http://www.cdc.gov/nchs/data\\_access/data\\_linkage/mortality/nhis\\_linkage\\_public\\_use.htm](http://www.cdc.gov/nchs/data_access/data_linkage/mortality/nhis_linkage_public_use.htm).
44. Botman SL, Jack SS (1995) Combining National Health Interview Survey Datasets: issues and approaches. *Stat Med* 14: 669–677.
45. Manson JE, Stampfer MJ, Hennekens CH, Willett WC (1987) Body weight and longevity. A reassessment. *JAMA* 257: 353–358.
46. Chang SH, Stoll CR, Colditz GA (2011) Cost-effectiveness of bariatric surgery: should it be universally available? *Maturitas* 69: 230–238.
47. World Health Organization (2000) Obesity: preventing and managing the global epidemic. Report of a WHO consultation. *World Health Organ Tech Rep Ser* 894: i-xii, 1–253.
48. Heo M, Faith MS, Mott JW, Gorman BS, Redden DT, et al. (2003) Hierarchical linear models for the development of growth curves: an example with body mass index in overweight/obese adults. *Stat Med* 22: 1911–1942.
49. Hens N, Aerts M, Molenberghs G (2006) Model selection for incomplete and design-based samples. *Stat Med* 25: 2502–2520.
50. Rao JNK, Wu CFJ (1988) Resampling inference with complex survey data. *Journal of the American Statistical Association* 83: 231–241.
51. Rao JNK, Wu CFJ, Yue K (1992) Some recent work on resampling methods for complex surveys. *Survey Methodology* 18: 209–217.
52. Sakata S (2002) Quasi-maximum likelihood estimation with complex survey data. *Mimeo*.
53. Efron B, Tibshirani R (1993) An introduction to the bootstrap. New York: Chapman & Hall. xvi, 436 p.
54. Roberts M, Russell LB, Paltiel AD, Chambers M, McEwan P, et al. (2012) Conceptualizing a Model: A Report of the ISPOR-SMDM Modeling Good Research Practices Task Force-2. *Value Health* 15: 804–811.
55. Baio G, Dawid AP (2011) Probabilistic sensitivity analysis in health economics. *Stat Methods Med Res*.
56. Orpana HM, Berthelot JM, Kaplan MS, Feeny DH, McFarland B, et al. (2010) BMI and mortality: results from a national longitudinal study of Canadian adults. *Obesity (Silver Spring)* 18: 214–218.
57. Anderson RN (1999) United States life tables, 1997. *Natl Vital Stat Rep* 47: 1–37.
58. Anderson RN (2001) United States life tables, 1998. *Natl Vital Stat Rep* 48: 1–40.
59. Arias E, Curtin LR, Wei R, Anderson RN (2008) U.S. decennial life tables for 1999–2001, United States life tables. *Natl Vital Stat Rep* 57: 1–36.
60. Arias E (2002) United States life tables, 2000. *Natl Vital Stat Rep* 51: 1–38.
61. Visscher TL, Seidell JC, Molarius A, van der Kuip D, Hofman A, et al. (2001) A comparison of body mass index, waist-hip ratio and waist circumference as predictors of all-cause mortality among the elderly: the Rotterdam study. *Int J Obes Relat Metab Disord* 25: 1730–1735.
62. Beasley JW (2003) Obesity and years of life lost. *JAMA* 289: 1777; author reply 1777–1778.
63. Price GM, Uauy R, Breeze E, Bulpitt CJ, Fletcher AE (2006) Weight, shape, and mortality risk in older persons: elevated waist-hip ratio, not high body mass index, is associated with a greater risk of death. *Am J Clin Nutr* 84: 449–460.