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Association of Body Mass Index With Lifetime Risk of Cardiovascular Disease and Compression of Morbidity

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Supplemental content

IMPORTANCE Prior studies have demonstrated lower all-cause mortality in individuals who are overweight compared with those with normal body mass index (BMI), but whether this may come at the cost of greater burden of cardiovascular disease (CVD) is unknown.

OBJECTIVE To calculate lifetime risk estimates of incident CVD and subtypes of CVD and to estimate years lived with and without CVD by weight status.

DESIGN, SETTING, AND PARTICIPANTS In this population-based study, we used pooled individual-level data from adults (baseline age, 20-39, 40-59, and 60-79 years) across 10 large US prospective cohorts, with 3.2 million person-years of follow-up from 1964 to 2015. All participants were free of clinical CVD at baseline with available BMI index and CVD outcomes data. Data were analyzed from October 2016 to July 2017.

EXPOSURES World Health Organization–standardized BMI categories.

MAIN OUTCOMES AND MEASURES Total CVD and CVD subtype, including fatal and nonfatal coronary heart disease, stroke, congestive heart failure, and other CVD deaths. Heights and weights were measured directly by investigators in each study, and BMI was calculated as weight in kilograms divided by height in meters squared. We performed (1) modified Kaplan-Meier analysis to estimate lifetime risks, (2) adjusted competing Cox models to estimate joint cumulative risks for CVD or noncardiovascular death, and (3) the Irwin restricted mean to estimate years lived free of and with CVD.

RESULTS Of the 190 672 in-person examinations included in this study, the mean (SD) age was 46.0 (15.0) years for men and 58.7 (12.9) years for women, and 140 835 patients (73.9%) were female. Compared with individuals with a normal BMI (defined as a BMI of 18.5 to 24.9), lifetime risks for incident CVD were higher in middle-aged adults in the overweight and obese groups. Compared with normal weight, among middle-aged men and women, competing hazard ratios for incident CVD were 1.21 (95% CI, 1.14-1.28) and 1.32 (95% CI, 1.24-1.40), respectively, for overweight (BMI, 25.0-29.9), 1.67 (95% CI, 1.55-1.79) and 1.85 (95% CI, 1.72-1.99) for obesity (BMI, 30.0-39.9), and 3.14 (95% CI, 2.48-3.97) and 2.53 (95% CI, 2.20-2.91) for morbid obesity (BMI, ≥40.0). Higher BMI had the strongest association with incident heart failure among CVD subtypes. Average years lived with CVD were longer for middle-aged adults in the overweight and obese groups compared with adults in the normal BMI group. Similar patterns were observed in younger and older adults.

CONCLUSIONS AND RELEVANCE In this study, obesity was associated with shorter longevity and significantly increased risk of cardiovascular morbidity and mortality compared with normal BMI. Despite similar longevity compared with normal BMI, overweight was associated with significantly increased risk of developing CVD at an earlier age, resulting in a greater proportion of life lived with CVD morbidity.

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Overweight and obesity are highly prevalent in the United States, have increased dramatically over the past 3 decades, and affect approximately 2.1 billion adults worldwide.[1,2] In recent years, controversy about the health implications of overweight status (ie, body mass index [BMI, calculated as weight in kilograms divided by height in meters squared] of 25.0 to 29.9) has grown, given findings of similar or lower all-cause mortality rates in overweight compared with normal-weight groups.[3,4] However, current studies have not taken into account the age at onset and duration of cardiovascular disease (CVD), limiting the ability to account for proportion of life lived with CVD morbidity in individuals who are overweight and obese compared with normal weight. This is especially important because disease burden associated with development of CVD results in less healthful years of life, poorer quality of life, and increased health care expenditures.[5,6]

Estimates of lifetime risk of CVD offer a more comprehensive assessment of the overall burden of CVD morbidity in the general population, allow adjustment for competing risks (eg, noncardiovascular mortality), and can help guide public health policy regarding weight guidelines by offering projections of the overall burden of CVD by weight status in the population. Such estimates are especially important given competing risks of concomitant non-CVD morbidity seen with excess weight. Upward shifts in the prevalence of obesity in the past several decades, including continued increases among adolescents, raise concern for future population-level burden of cardiovascular morbidity and mortality associated with excess weight.[7-9]

Our objectives were to calculate lifetime risk estimates of incident total CVD and subtypes of CVD and to estimate years lived with and without CVD by weight status in adults (aged 20 to 89 years). We hypothesized that compared with normal BMI, overweight would be associated with greater lifetime CVD risk even after consideration of competing risks from non-CVD death, fewer years lived free of CVD, and greater life-years lived with CVD.

Key Points

Question What is the association of body mass index with cardiovascular disease (CVD) morbidity and mortality?

Findings In this population-based study, overweight and obesity were associated with significantly increased risk for CVD. Obesity was associated with shorter longevity and a greater proportion of life lived with CVD; overweight was associated with similar longevity as normal weight but at the expense of a greater proportion of life lived with CVD.

Meaning These results provide critical perspective on CVD associated with overweight and obesity and challenge both the obesity paradox as well as the view that overweight is associated with greater longevity.

Methods

The Cardiovascular Disease Lifetime Risk Pooling Project[10] collected and pooled individual-level data from numerous longitudinal population-based cohort studies conducted in the United States over the past 7 decades. This pooling approach offers the opportunity to calculate estimates of lifetime risk of CVD events and estimates of years lived free of CVD according to age and BMI categories, which would not be feasible within 1 data set alone. It includes participants free of clinical CVD across the life course from young adulthood to older adulthood, with nearly 100% complete follow-up for vital status. We included data from participants who were free of clinical CVD at baseline from the following 10 prospective cohort studies in the Cardiovascular Disease Lifetime Risk Pooling Project[10]: the Atherosclerosis Risk in Communities Study,[11] the Coronary Artery Risk Development in Young Adults Study,[12] the Chicago Heart Association Detection Project in Industry Study,[13,14] the Cardiovascular Health Study,[15] the Framingham Heart Study,[16] the Framingham Offspring Study,[17] the Kaiser Permanente Study of the Oldest Old,[18] the Multi-Ethnic Study of Atherosclerosis,[19] the National Health and Nutrition Examination Survey I Epidemiologic Follow-up Study,[20] and the Women's Health Initiative.[21] All included cohorts represented community-based or population-based samples with at least 1 examination that included direct measurement of weight and height, at least 10 years of follow-up, and surveillance and adjudication for all subtypes of cardiovascular events of interest (ie, fatal and nonfatal myocardial infarction, fatal and nonfatal stroke, congestive heart failure [HF], and cardiovascular death) and noncardiovascular death (eMethods in the Supplement). This included 190 672 person-examinations across the life course, with 3.2 million person-years of follow-up until 2015. Individual participants were stratified by index age groups (young, aged 20 to 39 years; middle-aged, aged 40 to 59 years; and older, aged 60 to 79 years), sex, and BMI strata. All data were deidentified, and all study protocols and procedures were approved by the institutional review board at Northwestern University with a waiver for informed consent.

The protocols used to obtain data on demographic characteristics, physical examination results, laboratory results, and follow-up procedures for ascertainment of vital status and events for all cohorts have been previously published (eMethods in the Supplement).[10] Height, weight, blood pressure level, fasting glucose level, and total cholesterol level were measured directly in all participants; smoking status was self-reported. Incident cardiovascular events were ascertained with the use of strategies selected by each cohort's investigator group. Nonfatal CVD events of interest included myocardial infarction, stroke, and HF, and fatal events were stratified as death caused by CVD, coronary heart disease (CHD), or non-CVD events.

All statistical analyses were performed with SAS version 9.2 (SAS Institute) and R version 3.1.2 (The R Foundation). For calculation of lifetime risk, we used a modified Kaplan-Meier analysis, which accounts for competing risks for non-CVD death, as previously described.[22,23] In brief, the modified Kaplan-Meier analysis accounts for fatal events from

Table 1. Baseline Characteristics and Body Mass Index Categories Among Men and Women According to Index Age Group

Demographic Characteristics	No. (%)					
	Young (20-39 y)		Middle-aged (40-59 y)		Older (60-79 y)	
	Men (n = 14 790)	Women (n = 12 072)	Men (n = 21 390)	Women (n = 51 100)	Men (n = 13 657)	Women (n = 77 663)
Follow-up, person-years	461 648	382 792	472 519	856 523	179 397	893 702
African American	1998 (13.5)	3113 (25.8)	2762 (12.9)	6700 (13.1)	1807 (13.2)	6951 (9.0)
Risk factors						
Diabetes	141 (1.0)	104 (0.9)	1175 (5.5)	2122 (4.2)	1544 (11.5)	4386 (5.7)
Current smoking	7089 (48.0)	5387 (44.6)	8536 (39.9)	9500 (26.2)	2882 (21.9)	6344 (14.5)
Systolic blood pressure, mean (SD), mm Hg	130 (16)	118 (15)	131 (21)	123 (19)	136 (22)	131 (19)
Hypertension treatment	176 (1.3)	137 (1.2)	2373 (11.9)	8249 (16.7)	3803 (28.1)	23 400 (30.1)
Total cholesterol, mean (SD), mg/dL	190 (37)	182 (34)	210 (40)	212 (42)	208 (41)	227 (45)
10-y ASCVD risk, mean (SD), %	1.2 (1.8)	1.5 (5.0)	7.1 (6.1)	3.1 (5.0)	18.2 (10.8)	11.0 (9.8)
Body mass index categories[a]						
Underweight (<18.5)	123 (0.8)	792 (6.6)	76 (0.4)	592 (1.2)	90 (0.7)	814 (1.0)
Normal weight (18.5-24.9)	6430 (43.5)	8197 (67.9)	5861 (27.4)	21 807 (42.7)	3863 (28.3)	30 340 (39.1)
Overweight (25.0-29.9)	6471 (43.8)	2094 (17.3)	10 831 (50.6)	15 946 (31.2)	6769 (49.6)	27 266 (35.1)
Obesity (30.0-39.9)	1711 (11.6)	850 (7.0)	4400 (20.6)	10 630 (20.8)	2836 (20.8)	16 920 (21.8)
Morbid obesity (≥40.0)	55 (0.3)	139 (1.2)	222 (1.0)	2125 (4.2)	99 (0.7)	2323 (3.0)

Abbreviation: ASCVD, atherosclerotic cardiovascular disease.

[a] Body mass index calculated as weight in kilograms divided by height in meters squared.

non-CVD causes as a separate end point rather than a censoring event. Rates of CVD death, CHD, HF, and stroke were calculated for each index age group to age 95 years, or the oldest age with robust person-time, to estimate lifetime risk of total CVD.

We calculated cumulative risk for CVD events and non-CVD death by BMI strata in age-stratified and sex-stratified analyses. We determined the proportion of incident first events (CVD event or non-CVD death) that occurred during the follow-up time. In these analyses, the occurrence of one type of event precluded consideration of another CVD event or non-CVD death event in that participant. We used the data augmentation method as described by Lunn and McNeil[24] to fit Cox proportional hazard models to estimate hazard ratios for all CVD events combined compared with non-CVD death as the first event within BMI strata. In separate analyses, we used the method described by Fine and Gray[25] to estimate the competing hazards for each CVD event (ie, CHD, HF, stroke, and other CVD death) and non-CVD death by BMI strata and adjusted for age, race/ethnicity, and smoking status. In addition, we performed sensitivity analyses for estimating hazards in nonsmokers. The mean survival time or years lived free of CVD, with CVD, and overall were estimated using the Irwin restricted mean to assess differences in compression of morbidity by BMI strata.[26]

Results

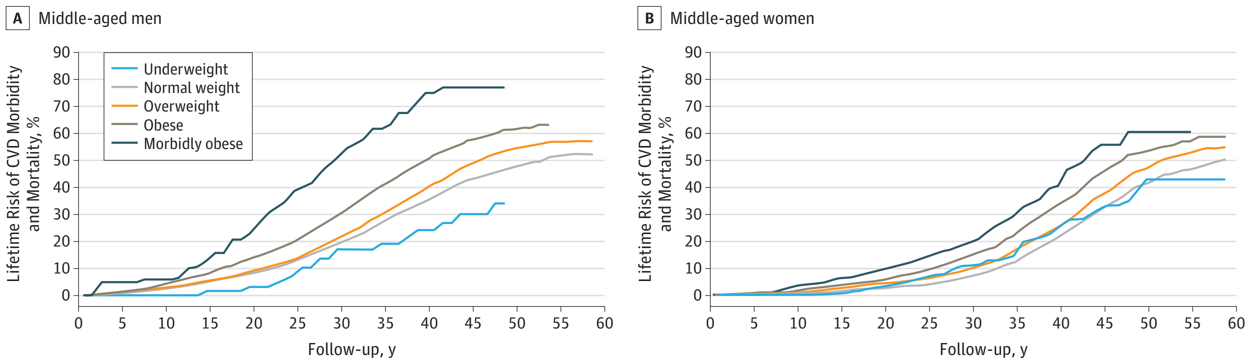
A total of 190 672 person-examinations were included in the pooled cohort, of whom 23 331 (12.2%) were African American. As expected, older adults had a higher prevalence of diabetes and hypertension treatment and higher mean total cholesterol levels, whereas younger adults had a higher rate of smoking (**Table 1**). The proportion of adults in the underweight and morbidly obese groups was relatively small, ranging from 0.3% to 6.6%. Approximately two-thirds of adults were in the normal or overweight BMI categories. Baseline characteristics by BMI strata for young, middle-aged, and older adults are in eTables 1, 2, and 3, respectively, in the Supplement, with a higher prevalence of diabetes in the overweight and obese categories in all age groups. Only 233 participants (0.1%) died within the first 6 months of follow-up.

Lifetime Risks for Cardiovascular Events and Noncardiovascular Death by BMI Strata

During 856 523 person-years of follow-up in middle-aged adults (index age, 40-59 years), there were 7136 incident fatal or nonfatal myocardial infarctions, 3733 incident fatal or nonfatal strokes, 4614 diagnoses of incident congestive HF, and a total of 13 457 incident CVD events. Among middle-aged men, unadjusted rates of incident CVD events per thousand person-years were 13.72, 15.53, 20.21, and 30.15 in normal BMI, overweight, obese, and morbidly obese categories, respectively. In general, unadjusted rates of CVD were higher in men and women who are overweight and obese in all 3 age groups (eTables 1, 2, and 3 in the Supplement).

Among middle-aged men and women, adults who are overweight and obese had a higher cumulative lifetime risk of incident CVD events and CVD death compared with adults with normal BMI (**Figure 1**; eFigure 1 in the Supplement). The findings were similar in older adults (eFigure 2 in the Supplement). In young men and women, the findings were similar, with increased lifetime risk of incident CVD events in adults in the obese and morbidly obese groups but not in adults in the overweight group (eFigure 3 in the Supplement). There

Figure 1. Lifetime Risk of Cardiovascular Disease (CVD) Morbidity and Mortality Among Middle-aged Individuals



Remaining cumulative lifetime risk estimates for total CVD events (adjusted for competing risk of noncardiovascular death) in middle-aged (index age, 40-59 years) men (A) and women (B) stratified by body mass index groups: underweight, normal, overweight, obese, and morbidly obese. Lifetime risks for total cardiovascular disease exceeded 30% for men and women in all body mass index groups. Participants in higher body mass index strata had higher lifetime risks for total cardiovascular disease through age 95 years.

Table 2. Hazard Ratio and Cumulative Incidences for First Event Among Middle-aged Men and Women According to Body Mass Index Strata[a]

	Body Mass Index, %[b]				
Category	Underweight (<18.5)	Normal (18.5-24.9)	Overweight (25.0-29.9)	Obesity (30.0-39.9)	Morbid Obesity (≥40)
Male					
CVD event vs non-CVD death, adjusted hazard ratio (95% CI)[c]	0.55 (0.30-0.99)	1.33 (1.24-1.43)	1.79 (1.69-1.89)	2.26 (2.07-2.47)	4.35 (2.67-7.07)
Non-CVD death	43.9	22.2	19.3	20.1	19.1
CVD event	25.3	32.1	37.0	47.0	65.4
Fatal and nonfatal MI	12.6	17.2	20.0	23.5	27.0
Fatal and nonfatal stroke	1.7	6.4	6.6	7.6	4.3
CHF	9.3	5.9	7.0	11.3	29.0
CVD death	1.7	2.5	3.3	4.6	5.1
Female					
CVD event vs non-CVD death, adjusted hazard ratio (95% CI)[c]	0.91 (0.68-1.21)	1.17 (1.10-1.24)	1.48 (1.38-1.59)	1.96 (1.79-2.15)	2.18 (1.75-2.72)
Non-CVD death	24.2	16.3	16.9	17.4	22.4
CVD event	23.0	21.5	27.9	38.8	47.6
Fatal and nonfatal MI	10.2	8.2	11.1	14.5	15.3
Fatal and nonfatal stroke	5.7	6.5	7.3	9.0	8.2
CHF	4.9	4.6	6.9	11.7	21.6
CVD death	2.3	2.2	2.5	3.5	2.4

Abbreviations: CHF, congestive heart failure; CVD, cardiovascular disease; MI, myocardial infarction.

[a] Lunn and McNeil method.[24]

[b] Body mass index calculated as weight in kilograms divided by height in meters squared.

[c] Adjusted for age, race/ethnicity, and smoking status.

were marked differences across age and BMI strata in the patterns of lifetime risk of non-CVD death. Overall, 10 136 non-CVD deaths (40.8%) were related to cancer (eFigures 1, 2, and 3 in the Supplement).

Competing Risks of CVD Morbidity and Non-CVD Mortality by BMI Strata

The proportions of middle-aged adults who experienced incident CVD or non-CVD death stratified by sex and BMI groups are shown in **Table 2**. Incident CVD events occurred in more middle-aged men and women in overweight (37% and 28%, respectively), obese (47% and 39%), and morbidly obese (65% and 48%) strata compared with adults in the normal BMI group (32% and 22%). Adjusted competing hazard ratios (by the Lunn and McNeil method[24]) for experiencing a CVD event compared with non-CVD death were greater in higher BMI categories and were greatest in the morbidly obese category in middle-aged men and women, predominantly because of a greater proportion of CHD and HF events. In addition, greater all-cause mortality in higher BMI categories occurred at the expense of a greater proportion of deaths from cardiovascular causes in middle-aged men and women who are overweight and obese (eTable 4 in the Supplement). Similar patterns were seen in younger and older adults (eTables 5 and 6 in the Supplement).

Table 3. Adjusted Competing Hazard Ratios[a] for First Event Among Middle-aged Men and Women According to Body Mass Index Strata[b]

Category	Body Mass Index, Hazard Ratio (95% CI)[c] Underweight (<18.5)	Normal (18.5-24.9)	Overweight (25.0-29.9)	Obesity (30.0-39.9)	Morbid Obesity (≥40)
Male					
Non-CVD death	2.01 (1.38-2.92)	1 [Reference]	0.87 (0.81-0.93)	0.85 (0.78-0.94)	0.61 (0.39-0.97)
CVD event	0.68 (0.42-1.10)	1 [Reference]	1.21 (1.14-1.28)	1.67 (1.55-1.79)	3.14 (2.48-3.97)
Fatal and nonfatal MI	0.69 (0.36-1.32)	1 [Reference]	1.18 (1.09-1.28)	1.42 (1.29-1.56)	1.98 (1.42-2.78)
Fatal and nonfatal stroke	0.20 (0.02-1.44)	1 [Reference]	1.08 (0.94-1.23)	1.20 (1.02-1.41)	0.75 (0.35-1.60)
CHF	1.48 (0.64-3.40)	1 [Reference]	1.22 (1.07-1.40)	1.95 (1.68-2.27)	5.26 (3.65-7.57)
CVD death	0.54 (0.07-3.87)	1 [Reference]	1.23 (1.01-1.51)	1.55 (1.22-1.96)	1.52 (0.62-3.73)
Female					
Non-CVD death	1.53 (1.25-1.87)	1 [Reference]	1.02 (0.95-1.09)	1.01 (0.92-1.10)	1.15 (0.95-1.40)
CVD event	1.15 (0.92-1.43)	1 [Reference]	1.32 (1.24-1.40)	1.85 (1.72-1.99)	2.53 (2.20-2.91)
Fatal and nonfatal MI	1.35 (0.99-1.88)	1 [Reference]	1.42 (1.29-1.57)	1.75 (1.56-1.96)	1.80 (1.41-2.30)
Fatal and nonfatal stroke	1.01 (0.67-1.51)	1 [Reference]	1.11 (0.99-1.25)	1.28 (1.12-1.46)	1.01 (0.73-1.39)
CHF	1.09 (0.70-1.69)	1 [Reference]	1.37 (1.21-1.55)	2.28 (2.00-2.60)	4.32 (3.39-5.19)
CVD death	0.87 (0.41-1.86)	1 [Reference]	1.04 (0.84-1.27)	1.09 (0.85-1.40)	1.75 (1.10-2.78)

Abbreviations: CHF, congestive heart failure; CVD, cardiovascular disease; MI, myocardial infarction.

[a] Adjusted for age, race/ethnicity, and smoking status.

[b] Fine and Gray method.[25]

[c] Body mass index calculated as weight in kilograms divided by height in meters squared.

Adjusted competing hazard ratios (by the Fine and Gray method[25]) for incident events in middle-aged men and women by BMI strata are shown in **Table 3**. Middle-aged men and women who are overweight, obese, and morbidly obese had significantly higher hazard ratios for incident CVD events compared with normal BMI, ranging from 1.21 to 3.14 across BMI categories. Among CVD subtypes, higher BMI was associated with greatest hazard ratios for incident HF. The adjusted competing hazard ratios of incident CVD events per unit of BMI in middle-aged men and women were 1.05 (95% CI, 1.05-1.06) and 1.05 (95% CI, 1.04-1.05), respectively. In addition, when examining only fatal events, risk of CVD death was significantly higher in excess BMI categories compared with normal BMI (eTable 7 in the Supplement). Similar increased hazard ratios of incident CVD events are seen in young and older men and women in excess weight BMI categories compared with normal BMI (eTables 8 and 9 in the Supplement). Sensitivity analysis in nonsmokers demonstrated similar patterns, with increased risk of CVD in excess weight BMI categories in all age groups (data not shown).

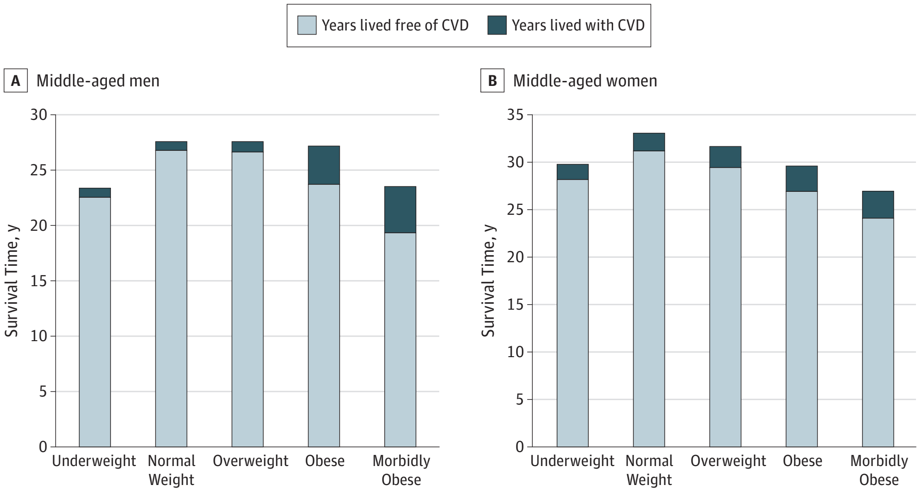
Years Lived Free of and With CVD

In middle-aged men, overall survival time was similar in the normal BMI (29.1 years) and overweight (29.3 years) groups and was significantly shorter in the obese (27.2 years) and morbidly obese (23.4 years) groups (eTable 10 in the Supplement). In middle-aged women, overall survival was longest in the normal BMI category (33.2 years) compared with women in higher BMI categories (overweight, 31.8 years; obese, 29.8 years; and morbidly obese, 27.2). Cardiovascular disease-free years were similar in middle-aged men in the normal BMI and overweight groups and were longer than men who were obese (**Figure 2**). Years lived free of CVD were greater in middle-aged women with normal BMI compared with women who were overweight or obese. Average years lived with CVD in middle-aged men and women were shortest in the normal BMI group compared with adults in higher BMI groups, resulting in relative compression of morbidity. Normal BMI significantly delayed the incidence of CVD in middle-aged men and women by an average of 7.5 and 7.1 years, respectively, compared with men and women with morbid obesity. In addition, on average, men and women with normal BMI lived 5.6 and 2.0 years, respectively, longer compared with men and women with morbid obesity, resulting in a significant relative and absolute compression of morbidity. Overall similar patterns were seen in younger and older men and women (eTable 4 and eFigures 4 and 5 in the Supplement).

Discussion

In this large study of US adults free of clinical CVD at baseline, lifetime risk for incident CVD was high for all adults and was greater in adults who were overweight and obese. Adults who were obese had an earlier onset of incident CVD, a greater proportion of life lived with CVD morbidity (unhealthy life years), and shorter overall survival compared with adults with normal BMI. In addition, the proportion of adults with incident CVD events (compared with non-CVD death) was significantly higher in adults who were overweight or obese compared with adults in the normal BMI group. Overweight and obesity were associated with increased hazards of incident CVD event after adjustment for competing risks of non-CVD death across all index age ranges. The results of this study build on prior research from the Cardiovascular Disease Lifetime Risk Pooling Project[10] highlighting marked differences in lifetime risks of CVD and further highlight the importance of consideration of BMI as a risk factor for diminished healthy longevity and greater overall CVD morbidity and mortality.[22,27]

Figure 2. Years Lived Free of and With Cardiovascular Disease (CVD) Among Middle-aged Individuals



Years lived free of and with CVD in middle-aged (index age, 40-59 years) men (A) and women (B). Participants with normal body mass index experienced greater years lived free of CVD compared with participants who were underweight, overweight, obese, or morbidly obese. Years lived with CVD was greater in participants in higher body mass index groups, accounting for a greater degree of life lived with morbidity in the context of similar or shorter overall survival. Compared with men and women with normal body mass index, men and women with morbid obesity had an accelerated onset of CVD by 7.5 and 7.1 years, respectively, and had reduced overall survival by 5.6 and 2.0 years.

Overweight status and obesity were associated with higher risk of incident CVD overall and subtypes of CVD (ie, CHD and HF), which is a finding of considerable public health importance. Our findings are consistent with prior work from the Framingham Heart Study[28,29] and the Atherosclerosis Risk in Communities study,[30] which demonstrated increased risk of CVD in participants who were overweight and obese. Importantly, we noted the strongest association between BMI categories and HF compared with other subtypes of CVD, with a 5-fold increase in incident HF in middle-aged men with morbid obesity, which has particularly important implications for focusing on weight management strategies for HF prevention. In addition, our findings suggest that earlier occurrence of CVD in those with obesity is most strongly associated with a greater proportion of life lived with CVD and shorter overall survival in adults aged 20 to 59 years at baseline. However, the association of obesity with mortality may change at older ages, which may explain why earlier studies comprising participants from the Rotterdam Study[31] and the US Health and Retirement Survey Study[32] showed no difference in total life expectancy in older men and women with obesity. However, studies from the Framingham Heart Study reported greater differences in years lived free of CVD and total life expectancy in men and women with obesity.[33] The difference between our findings and findings from prior analyses include the ability to stratify by age across the life course (young, middle-age, and older adulthood) and by severity of obesity (obese and morbidly obese) because of the inclusion of 10 large US cohorts with long-term follow-up.

While health hazards of obesity have long been recognized, recent studies[3,4,34-36] have spurred controversy about the specific relationship between overweight status and mortality. In a 2013 meta-analysis,[3] the summary hazard ratio (0.94; 95% CI, 0.91-0.96) for total mortality was significantly lower for overweight relative to normal BMI using data from 97 studies and 2.88 million adults. However, several large cohorts and studies[37-42] were excluded from this meta-analysis, among which a separate analysis demonstrated the lowest mortality in adults with a BMI of 22.5 to 25.0. Further, overweight status was associated with lower number of absolute deaths (−86 094; 95% CI, −151 223 to −10 966) compared with normal BMI in an analysis from the National Health and Nutrition Examination Survey.[4] Among these prior analyses, measurement bias may be present owing to inclusion of self-reported height and weight data. Further, inclusion of participants with comorbidities at baseline, specifically prevalent CVD, may contribute to selection and survival bias because of protopathic bias (reverse causation) related to unintentional weight loss.[34-36] Finally, follow-up times varied significantly in prior studies. In our study, we were able to leverage long-term follow-up in a large group of adults free of CVD at baseline to estimate risk of incident CVD and associated CVD morbidity (unhealthy years lived with CVD). In addition, we performed stratified analyses of competing event risk adjustment accounting for differing risk for non-CVD death by age, sex, and BMI strata.

Assessment solely of all-cause mortality as an outcome measure indicating the presence of an overweight or obesity paradox does not incorporate morbidity and overall disease burden associated with excess weight, which has significant relevance for overall health, fitness, and health-related disability. While we do observe evidence of the well-described overweight and obesity paradox, in which heavier individuals appear to live longer on average after diagnosis of CVD compared with individuals with normal BMI, our data when following up individuals prior to the onset of CVD indicate that this occurs because of a trend toward earlier onset of disease in individuals who are overweight and obese. This false reassurance is akin to the phenomenon of lead-time bias observed in other situations, such as with cancer screening.[35] This is especially important because overweight status has been associated with poorer quality of life, functional impairment, and greater work-related disability.[43,44] In addition, prior studies[45] have demonstrated that this excess weight-associated morbidity and disability translates into greater health care costs with higher average annual and cumulative Medicare charges (both CVD related and total). Importantly, our study specifically included nonfatal cardiovascular events to incorporate assessment of cardiovascular morbidity and highlight the broad effect of excess weight.

Population-based prevalence of obesity among adults in the United States has increased dramatically from the 1980s and 1990s and has subsequently plateaued in the last decade, with current estimates of 35% among men and 41% among women.[7,46] Trends in overweight, obesity, and extreme obesity through childhood and adolescence have also increased at alarming rates over the past 5 decades.[9] Preliminary data from the US Centers for Disease Control and Prevention demonstrate increases in age-adjusted death rates for the first 9 months of 2015, with relative increases in mortality rates for obesity-related causes of death, including heart disease (1%), stroke (4%), and diabetes (1%).[47] In addition, data published in 2007 also suggest a slowing of reductions in coronary death rates and a growing number of hospitalizations for acute and chronic manifestations of CVD, such as HF.[48,49] These trends are concerning for very likely future increases in the population-level burden of CVD among adults, including a trend for CVD events to occur at younger ages. The economic implications of direct and indirect medical costs of the overweight and obesity epidemic are enormous, and total health care costs attributable to overweight and obesity are estimated to exceed $800 billion by 2030 if current trends persist.[5,6]

Strengths and Limitations

Strengths of our study include the large sample size of adults free of CVD at baseline, direct measurement of height and weight with standardized BMI categories, and extended follow-up with adjudicated CVD events by type and non-CVD death across the life course, which makes the findings robust and generalizable. Additionally, our cohorts included a representative sample of women and African American patients without significant cohort effects on our findings.

Limitations of our study include the use of baseline BMI at index ages without accounting for change in BMI across follow-up. However, recent analyses using latent class model trajectories in population-based cohorts highlight that there is significant tracking of BMI from young adulthood to middle-age with weight gain in all strata regardless of baseline BMI.[50,51] In addition, use of BMI does not account for fat distribution or degree of visceral adiposity, but measures of central adiposity were not universally available across our component studies[40,52]; however, BMI is the most clinically relevant measure and allows broader generalizability of findings. Additional important outcomes of obesity-related morbidity, such as atrial fibrillation, sleep-disordered breathing, and chronic liver disease, were not ascertained routinely in our cohort studies, and we likely underestimated the overall comorbidity burden of excess weight.

Conclusions

In summary, we present an analysis of data from 190 672 in-person examinations derived from 10 population-based cohorts during a period of more than 50 years. We found that overweight status, in addition to obesity, is associated with significantly increased long-term risk for CVD morbidity in the context of similar or shorter total longevity and a greater proportion of life lived with morbidity compared with normal BMI. These findings were consistent across all index age groups ranging from young to older adulthood (20 to 89 years). Our results provide critical perspective on the cardiovascular disease burden associated with overweight, highlight unhealthy years lived with increased cardiovascular morbidity, and challenge the prevalent view that overweight is associated with greater longevity compared with normal BMI. Overweight does not appear to be associated with significantly greater longevity, and there is greater burden of CVD during that lifespan. Taking a life course perspective, we observe that the obesity paradox (ie, greater longevity after diagnosis of CVD for those who are overweight and obese) appears largely to be caused by earlier diagnosis of CVD. Study of inception cohorts of people at the time of CVD diagnosis would not detect this finding, leading to unclear messaging about the true risks of being overweight.

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Study concept and design: Khan, Wilkins, Carnethon, Sweis, Lloyd-Jones.
Acquisition, analysis, or interpretation of data: Khan, Ning, Wilkins, Allen, Berry, Sweis, Lloyd-Jones.
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