ORIGINAL RESEARCH

The Association Between Obesity and the 5-Year Prevalence of Morbidity and Mortality Among Adults with Type 2 Diabetes

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ABSTRACT

Introduction: This retrospective claims database study examined the prevalence of mortality and morbidity among adults with type 2 diabetes (T2D) and obesity.

Methods: The study used deidentified data from 2007 to 2021 from the Optum® Market Clarity Dataset. A cohort of adults with T2D and obesity were identified, and age- and sex-adjusted prevalence rates were calculated for mortality, a composite cardiovascular outcome (CCO), a composite microvascular outcome (CMO), and other complications. Results were examined overall and by obesity class (class 1, class 2, and class 3).

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Results: For the 15,970 adults included in the study, the prevalence of CCO and CMO after 5 years was 15.3% and 60.7%, respectively. The 5-year prevalence of mortality was 10.9%. There were statistically significant differences in prevalence rates by obesity class, with obesity class 3 associated with higher rates of morbidity and mortality compared to obesity classes 1 or 2. Specifically, after 5 years, the prevalence of mortality was 9.4%, 10.3% and 13.6% for obese classes 1, 2 and 3, respectively ($P < 0.05$ between class 3 and class 2 or 1). Similarly, For obesity classes 1, 2 and 3, the 5-year prevalence of CCO was 13.0%, 14.5% and 18.4% and the rates for CMO were 58.0%, 57.9% and 64.8%, respectively (both $P < 0.05$ between class 3 and class 2 or 1). Regarding other complications, differences in the prevalence of atherosclerotic cardiovascular disease (ASCVD) and obstructive sleep apnea (OSA) were statistically significantly higher with increasing obesity class.

Conclusions: The results indicate that for a cohort of adults with T2D and obesity, obesity class 3 is associated with significantly higher mortality and morbidity, including CCO, CMO, ASCVD and OSA. These findings suggest that treatment which reduces obesity among individuals with T2D may have significant health benefits, although additional studies are needed to confirm the results.

Keywords: Complications; Morbidity; Mortality; Obesity; Prevalence; Type 2 diabetes

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Key Summary Points

Why Carry out this study?

In the USA, the rates of both obesity and diabetes are high and still growing.

This study examines the prevalence of morbidity and mortality among adults with both type 2 diabetes (T2D) and obesity, both overall and by obesity class.

What was Learned from the Study?

The results indicate that for a cohort of adults with T2D and obesity, obesity class 3 (body mass index [BMI] $\geq$ 40 kg/m^2) is associated with significantly higher mortality as well as significantly higher prevalence of cardiovascular and microvascular complications.

Statistically significant increases in the prevalence of atherosclerotic cardiovascular disease and obstructive sleep apnea were associated with higher obesity classes.

INTRODUCTION

Among the population of all US adults, an estimated 42% have obesity [1], and 13.2–14.0% have type 2 diabetes (T2D) [2, 3]. Furthermore, research has shown that, among individuals with T2D in the USA, the proportion of individuals with obesity is rising [4]. The costs of obesity and diabetes are staggering. In the USA in 2016, the medical costs of obesity among adults totaled $260.6 billion in aggregate, while the mean per-person medical costs among those with obesity were double those of normal-weight adults ($5010 vs. $2504) [5]. In 2017, the costs of diabetes in the USA came to an estimated $327 billion, which included $237 billion in direct medical expenses and $90 billion in reduced productivity [6].

Previous research has shown both obesity and T2D to be associated with disease and premature death. For instance, obesity has been found to be associated with comorbid obstructive sleep apnea (OSA) [7, 8], as well as with T2D, hypertension, hyperlipidemia, osteoarthritis and coronary artery disease [8]. T2D has been correlated with overweight/obesity, as well as with hypertension, hyperlipidemia, chronic kidney disease and cardiovascular disease [9]. Both obesity and T2D have been shown to be major risk factors for cardiovascular disease [10–12]. Together, diabetes and obesity have been shown to increase mortality risk by sevenfold [13, 14]. In addition, research has shown that among individuals with T2D, those with comorbid obesity were significantly more likely to have comorbid nephropathy, neuropathy, cardiovascular disease, peripheral vascular disease and metabolic disease [15].

Given the foregoing research, we hypothesized that a US population diagnosed with concomitant obesity and T2D would have a large burden of comorbidity and mortality. In addition, we theorized that the rate of illness and death would increase as body mass index (BMI) rose. To test these hypotheses, we constructed a retrospective study using data from US health insurance claims and electronic medical records (EMRs). The aims of the study were to: (1) observe the 5-year prevalence and incidence of cardiovascular, microvascular and other comorbidities and mortality in a population of American adults with concomitant obesity and T2D, and (2) compare the prevalence of death and comorbidity across obesity categories in this same population.
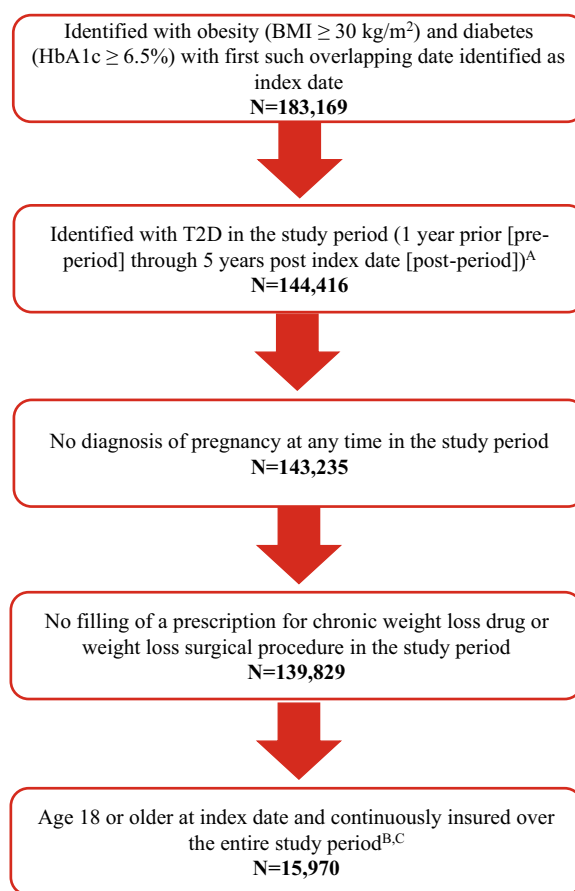
METHODS

The retrospective cohort analyses were conducted using patient health information from the US-based Optum® Market Clarity Dataset, a source of insurance claims, EMRs and outpatient laboratory results. The linked data were fully deidentified and compliant with the Health Insurance Portability and Accountability Act (HIPAA). For this study, the dataset supplied

longitudinal information on patient demographics, coverage eligibility, diagnostic and procedure codes, outpatient prescription fills, laboratory test results, mortality and observational data, such as BMI and blood pressure. Data for this study covered the period from 1 January 2007 through to 30 June 2021. Given the use of retrospective and deidentified data, ethics committee approval was not required. Permission was granted by Optum® for use of the data, and all research was conducted in accordance with the 1964 Declaration of Helsinki [16].

To be included in the study, individuals were required to have both a recorded BMI indicating obesity (BMI $\geq$ 30 kg/m^2) [17] and a recorded hemoglobin A1c (HbA1c) test result indicating diabetes (HbA1c $\geq$ 6.5%) [18]. The date of first overlap between such BMI and HbA1c results was identified as the index date. Individuals were also required to have had T2D, based upon receipt of at least one diagnosis of T2D and no diagnosis of type 1 diabetes at any time from 1 year prior to the index date (the pre-period) through 5 years after the index date (the post-period). Individuals were excluded from the study if at any time from the start of the pre-period through to the end of the post-period their medical claims revealed that they had received: (1) a diagnosis of pregnancy, (2) a prescription fill for a chronic weight loss medication or (3) a weight loss procedure. Individuals were required to have been aged $\geq$ 18 years at the index date and continuously insured from the start of the pre-period to either the end of the post-period or their date of death, whichever came first. Figure 1 illustrates how each of the inclusion and exclusion criteria affected the sample size.

For each 365-day period from 1 year prior to the index date (the baseline) through to 5 years post index date, the study examined the prevalence and incidence of comorbidities and mortality. All rates were adjusted for age and sex based upon the 2019 US Census Bureau data [19]. Consistent with prior research which has utilized claims and EMR data [20], the "lookback period" was defined as a fixed time period of the 1 year prior to the index date, and prevalence was defined as the number of

patients identified with the complication of interest over the year(s) of interest post index date or the lookback period divided by the number of patients included in the study. Similarly, incidence was defined as the number of individuals who did not have the complication of interest in the lookback time who are subsequently observed to develop the disease in the post index year of interest divided by the number of patients included in the study. Outcomes of interest included mortality, a composite cardiovascular outcome (CCO) and a composite microvascular outcome (CMO). The

Identified with obesity (BMI $\geq$ 30 kg/m^2) and diabetes (HbA1c $\geq$ 6.5%) with first such overlapping date identified as index date
N=183,169

Identified with T2D in the study period (1 year prior [pre-period] through 5 years post index date [post-period])[A]
N=144,416

No diagnosis of pregnancy at any time in the study period
N=143,235

No filling of a prescription for chronic weight loss drug or weight loss surgical procedure in the study period
N=139,829

Age 18 or older at index date and continuously insured over the entire study period[B,C]
N=15,970

T2D – type 2 diabetes
[A] Identification of T2D based upon receipt of at least 1 diagnosis of T2D and no receipt of any diagnoses for type 1 diabetes.
[B] 28 Individuals excluded due to the age restriction.
[C] When examining mortality, the continuous insurance coverage condition was relaxed resulting in a total sample of 20,633 individuals.

Fig. 1 Flow chart of inclusion–exclusion criteria and sample size. *BMI* Body mass index, *HbA1c* glycated hemoglobin, *T2D* type 2 diabetes

CCO comprised: (1) acute care visits (hospitalization or emergency room) with an accompanying diagnosis of heart failure, (2) myocardial infarctions and/or (3) strokes. The CMO comprised diagnoses of (1) nephropathy, (2) neuropathy and/or (3) retinopathy. The study also examined the prevalence of diagnoses of atherosclerotic cardiovascular disease (ASCVD), atrial fibrillation, liver cirrhosis, nonalcoholic steatohepatitis/nonalcoholic fatty liver disease (NASH/NAFLD) and OSA.

All outcomes were examined for the population as a whole. Consistent with prior research which has examined obesity using categorical variables [12, 21, 22], the analyses also examined results for subgroups defined by obesity class, where class 1 obesity was defined as 30 kg/m^2 < BMI < 35 kg/m^2; class 2 was defined as 35 kg/m^2 < BMI < 40 kg/m^2; class 3 was defined as BMI $\geq$ 40 kg/m^2 [17]. The analyses were primarily descriptive in nature. For descriptive statistics, means and standard deviations were reported for continuous variables, and frequencies and percentages were reported for categorical variables. Differences in continuous variables were examined using *t*-tests, and differences in categorical variables were reported using Chi-square statistics. Trends over time were examined using generalized estimating equations (GEE) tests, and differences in prevalence rates between obesity classes were examined based upon their 95% confidence intervals (CIs). All analyses were conducted using SAS version 9.4 (SAS Institute, Cary, NC, USA), and a *P* value < 0.05 was considered, a priori, to be statistically significant.

RESULTS

Table 1 presents patient characteristics for the overall cohort and for each obesity class. The average age of individuals included in the study was 62.4 years, with the majority of participants identified as female (51.0%), Caucasian (77.5%) and Non-Hispanic (85.8%), and to be residing in the Midwest (45.1%) or Southern (28.9%) regions of the USA. Examination of characteristics across the obesity classes revealed that the higher obesity class was statistically

significantly associated with younger age and with a higher proportion of individuals identified as African American, and with a lower proportion of males and individuals identified as Hispanic (all *P* < 0.05). Furthermore, the higher obesity class was associated with a statistically significantly lower percentage of individuals who resided in the Northeast or West and with more participants who resided in the Southern or Midwest regions (*P* < 0.05).

Figure 2 illustrates and compares the prevalence of mortality by obesity class, adjusted for age and sex, for each of the 5 years of study. After 5 years, the overall prevalence of mortality was 11.0% (95% CI 10.5–11.3%), and the rates for obesity class 1, 2 and 3 were 9.4%, 10.3% and 13.6%, respectively. As Fig. 2 shows, higher obesity class was associated with higher mortality each year, although the differences between obesity class 1 and 2 were not statistically significant and differences between class 2 and 3 did not reach statistical significance in the first year post index date. The prevalence of mortality rose faster for obese class 3 than for the other classes.

Figures 3 and 4 illustrate the baseline and 5-year prevalence, adjusted for age and sex, of the CCO and CMO, respectively. As expected, both types of composite outcomes were highly prevalent. Specifically, the overall 5-year prevalence of the CCO was 15.3% (95% CI 14.7–15.8%) and 60.7% (59.9–61.4%) for the composite microvascular outcome. In addition, higher obesity class was associated with a higher prevalence of each type of composite outcome. For example, after 5 years, the prevalence of the CCO for obesity class 1, 2 and 3 was 13.0% (95% CI 12.3–13.8%), 14.5% (95% CI 13.5–15.6%) and 18.4% (95% CI 17.1–19.6%), respectively. Similarly, the prevalence after 5 years of the CMO for obesity class 1, 2 and 3 was 58.0% (95% CI 56.9–59.1%), 57.9 (95% CI 56.5–59.3%) and 64.8% (95% CI 63.3–66.3%), respectively. For both the CCO and CMO, no statistically significant difference existed at any time period when the prevalence of outcomes for obesity class 1 was compared to that for obesity class 2. However, the prevalence of both outcomes for individuals with obesity class 3 was statistically significantly higher compared to the prevalence

Table 1 Patient characteristics

Patient characteristics	All patients	By obesity class[a]		
		Obese class 1	Obese class 2	Obese class 3
Sample size	15,970	7513	4635	3822
Age (years), mean $\pm$ SD	62.4 $\pm$ 11.7	64.7 $\pm$ 11.3	61.8 $\pm$ 11.6	58.7 $\pm$ 11.4
Sex, n (%)				
Female	8138 (51.0)	3397 (45.2)	2415 (52.1)	2326 (60.9)
Male	7829 (49.0)	4113 (54.7)	2220 (47.9)	1496 (39.1)
Unknown	3 (0.0)	3 (0.0)	0 (0.0)	0 (0.0)
Race, n (%)				
African American	2303 (14.4)	1048 (13.9)	649 (14.0)	606 (15.9)
Asian	207 (1.3)	149 (2.0)	43 (0.9)	15 (0.4)
Caucasian	12,378 (77.5)	5761 (76.7)	3639 (78.5)	2978 (77.9)
Other/unknown	1082 (6.8)	555 (7.4)	304 (6.6)	223 (5.8)
Ethnicity, n (%)				
Hispanic	1141 (7.1)	606 (8.1)	309 (6.7)	226 (5.9)
Non-Hispanic	13,710 (85.8)	6349 (84.5)	3998 (86.3)	3363 (88.0)
Unknown	1119 (7.0)	558 (7.4)	328 (7.1)	233 (6.1)
Region, n (%)				
Midwest	7202 (45.1)	3258 (43.4)	2100 (45.3)	1844 (48.2)
Northeast	1874 (11.7)	991 (13.2)	525 (11.3)	358 (9.4)
South	4610 (28.9)	2088 (27.8)	1365 (29.4)	1157 (30.3)
West	1814 (11.4)	941 (12.5)	525 (11.3)	348 (9.1)
Other/unknown	470 (2.9)	235 (3.1)	120 (2.6)	115 (3.0)

All differences in patient characteristics by obesity class are statistically significant ($P < 0.0001$)
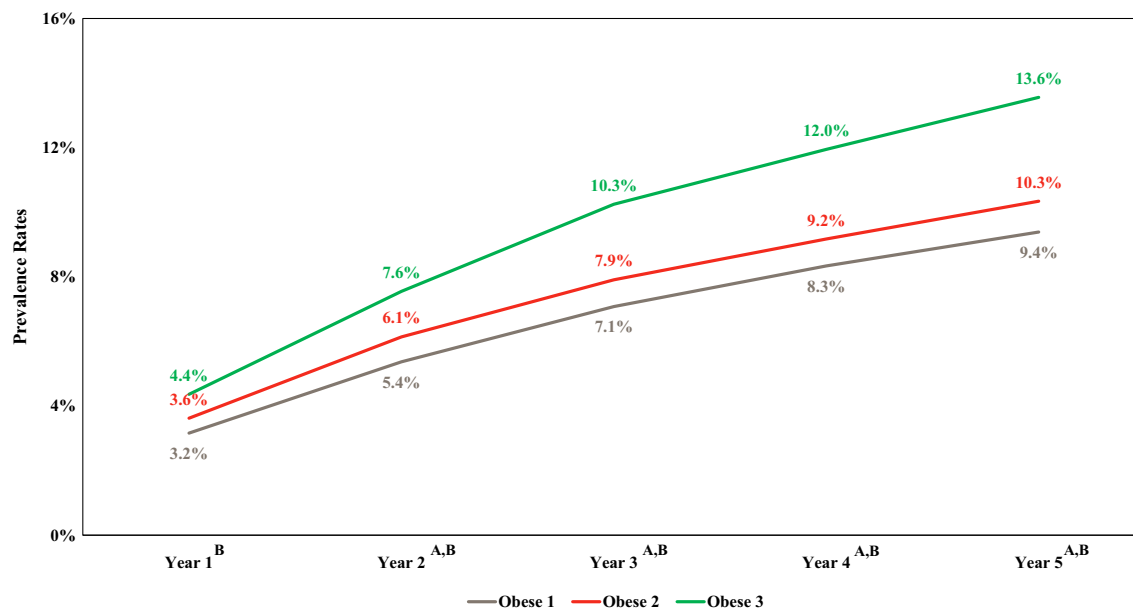
SD Standard deviation

[a]Class 1 obesity: 30 kg/m^2 < body mass index (BMI) < 35 kg/m^2. Class 2 obesity: 35 kg/m^2 < BMI < 40 kg/m^2. Class 3 obesity: BMI $\geq$ 40 kg/m^2

for individuals with obesity class 1 or obesity class 2 for the CMO for years 1 through 5 and for the CMO for all years.

Table 2 illustrates the 5-year prevalence rates, adjusted for age and sex, of the components of both types of composite comorbidities as well as the additional complications for the cohort overall and for each obesity class. The prevalence rates for every year in the study are included in Electronic Supplementary Material

(ESM) Table 1. Taken together, these results show that statistically significant differences in the CCO were driven by statistically significant differences in acute care visits for heart failure. These tables also illustrate that differences in the CMO were consistent with statistically significant differences in nephropathy and neuropathy. Generally, patients identified with obesity class 3 had significantly higher rates of neuropathy compared to individuals identified

All trends over time statistically significant (P<0.05).
[A] Statistically significant difference between obese class 2 and obese class 3 (P<0.05).
[B] Statistically significant difference between obese class 1 and obese class 3 (P<0.05).

Fig. 2 The 5-year age- and sex-adjusted prevalence of morality by obesity class. *Obes1* Class 1 obesity: 30 kg/m^2 < body mass index (BMI) < 35 kg/m^2, *Obes2* class 2 obesity: 35 kg/m^2 < BMI < 40 kg/m^2. *Obes3* class 3 obesity: BMI $\geq$ 40 kg/m^2
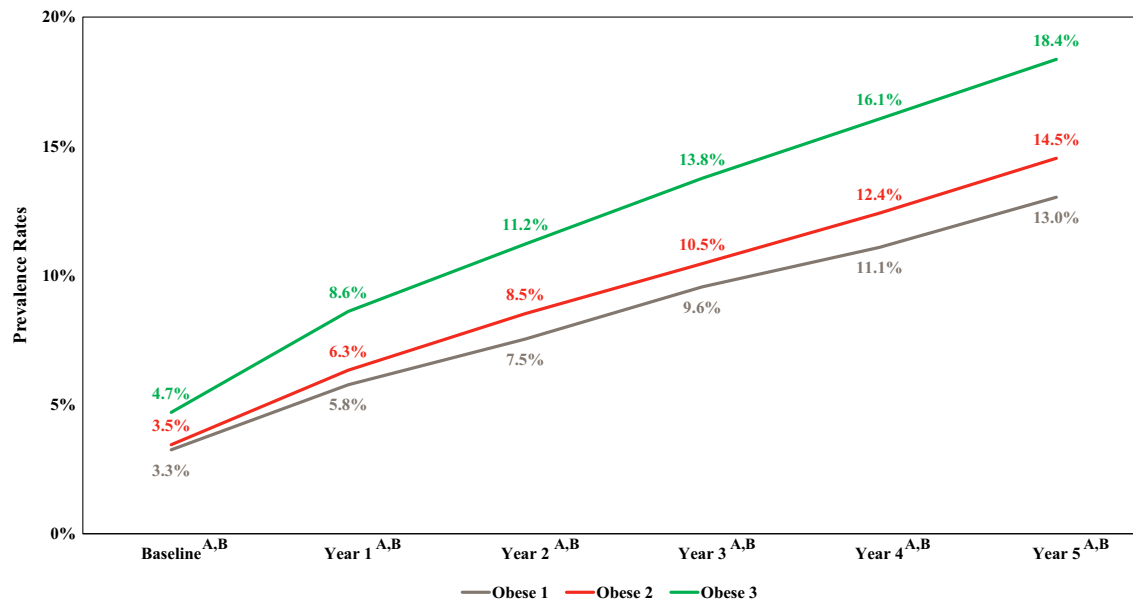
All trends over time statistically significant (P<0.05).
[A] Statistically significant difference between obese class 2 and obese class 3 (P<0.05).
[B] Statistically significant difference between obese class 1 and obese class 3 (P<0.05).
Composite cardiovascular outcome defined as acute care visit with accompanying diagnosis of heart failure, myocardial infarction, or stroke.

Fig. 3 The 5-year age- and sex-adjusted prevalence of composite cardiovascular outcome by obesity class

All trends over time statistically significant (P<0.05).
A Statistically significant difference between obese class 2 and obese class 3 (P<0.05).
B Statistically significant difference between obese class 1 and obese class 3 (P<0.05).
Composite microvascular outcome defined as neuropathy, nephropathy, or retinopathy.
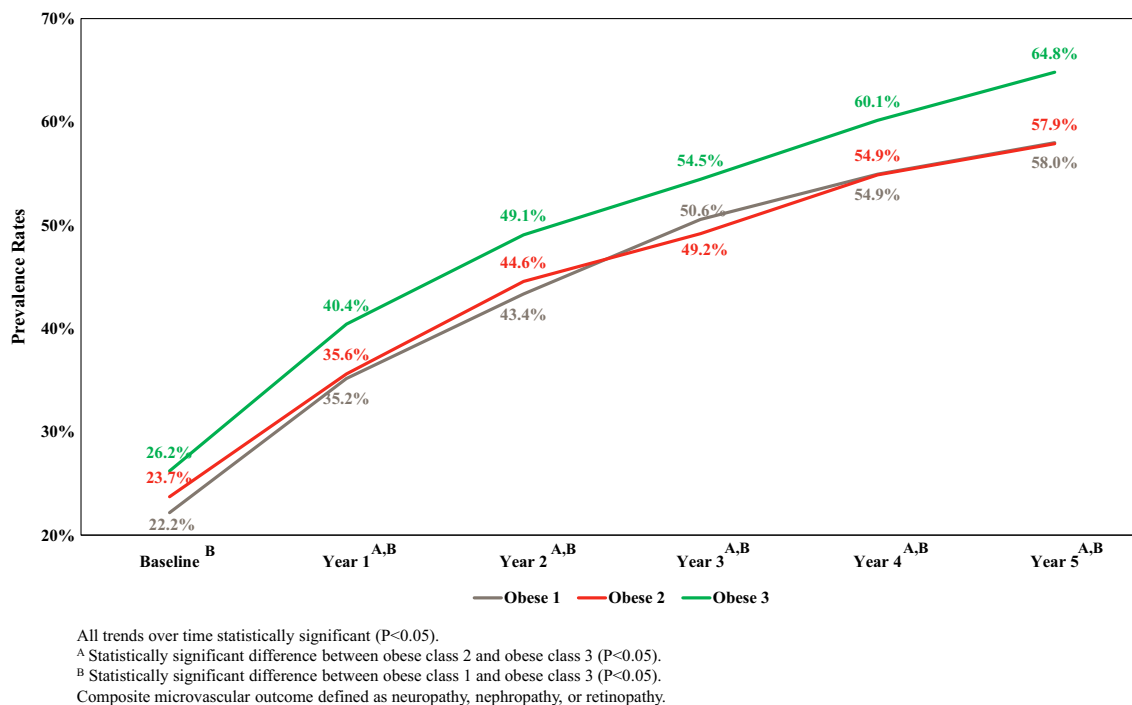
Fig. 4 The 5-year age- and sex-adjusted prevalence of composite microvascular outcome by obesity class

with obesity class 1 or 2 and had a significantly higher prevalence of nephropathy compared to those in class 1.

Results from Table 2 and ESM Table 1 showed that, in general, higher obesity class was associated with higher prevalence of comorbidities. In addition, these results illustrate some statistically significant differences in prevalence when comparison was based upon obesity class. Specifically, for all years, OSA was found to be statistically significantly higher as obesity class increased, and the same result was found for ASCVD in years 1–5 post index date. The results for atrial fibrillation, liver cirrhosis and NASH/NAFLD showed that in years 1–5 post index date, individuals with obesity class 3 had statistically significantly higher prevalences of these comorbidities relative to individuals with obesity class 1 or 2. Incidence rates for all outcomes for years 1–5 for all patients and by obesity class are provided in ESM Table 2.

DISCUSSION

This retrospective, observational study measured the 5-year prevalence of mortality and morbidity in a population of US adults with concomitant obesity and T2D. Consistent with our original hypothesis, this population had a large burden of death and disease, with all comorbidities and mortality increasing significantly over the 5-year post index period. The 5-year prevalence of mortality (10.9%) for individuals with T2D and obesity was more than 11-fold higher than the 0.9% rate previously estimated over the time period from 2010 to 2017 for the average US adult age 55 to 64 years [23]. Regarding the degree of change in prevalences over the study period, mortality almost tripled, cardiovascular events quadrupled and microvascular events more than doubled. Consistent with previous research [21], those in the heaviest BMI category (class 3) in our study had the worst outcomes, with statistically significantly higher prevalences of mortality, cardiovascular events and microvascular

Table 2 The 5-year age- and sex-adjusted prevalence rates

Outcome	All individuals 5-Year prevalence rate (95% CI)	Obese class 1	Obese class 2	Obese class 3
Individual components of the cardiovascular outcome				
Acute care visit with accompanying diagnosis of heart failure	8.4 (7.9–8.8)	6.1[a,c] (5.6–6.7)	7.7[a,b] (6.9–8.5)	12.4[b,c] (11.4–13.5)
Myocardial infarction	4.4 (4.0–4.7)	3.9 (3.5–4.4)	4.7 (4.1–5.3)	4.4 (3.7–5.0)
Stroke	7.5 (7.1–7.9)	7.0 (6.4–7.6)	6.7 (6.0–7.4)	7.6 (6.7–8.4)
Individual components of the microvascular outcome				
Neuropathy	39.5 (38.8–40.3)	34.7[c] (33.7–35.8)	36.3[b] (34.9–37.7)	45.2[b,c] (43.6–46.8)
Nephropathy	30.0 (29.3–30.7)	29.2[c] (28.2–30.2)	29.7 (28.4–31.1)	32.3[c] (30.8–33.8)
Retinopathy	23.5 (22.9–24.2)	23.5 (22.5–24.4)	23.5 (22.3–24.7)	24.0 (22.7–25.4)
Secondary outcomes				
ASCVD	81.9 (81.3–82.5)	77.1[a,c] (76.1–78.0)	81.5[a,b] (80.4–82.6)	85.5[b,c] (84.3–86.6)
Atrial fibrillation	9.2 (8.8–9.7)	7.7[c] (7.1–8.3)	8.7[b] (7.9–9.5)	12.7[b,c] (11.7–13.8)
Liver cirrhosis	24.3 (23.6–24.9)	20.2[c] (19.3–21.1)	21.9[b] (20.7–23.1)	28.7[b,c] (27.3–30.2)
NASH/NAFLD	20.9 (20.2–21.5)	17.0[a,c] (16.2–17.9)	20.5[a,b] (19.3–21.6)	23.2[b,c] (21.8–24.5)
Obstructive sleep apnea	32.1 (31.4–32.9)	19.4[a,c] (18.5–20.3)	31.2[a,b] (29.9–32.5)	47.2[b,c] (45.7–48.8)

ASCVD Atherosclerotic cardiovascular disease, *CI* confidence interval, *eGFR* estimated glomerular filtration rate, *NAFLD* non-alcoholic fatty liver disease, *NASH* non-alcoholic steatohepatitis
[a]Statistically significant difference between obese class 1 and obese class 2 ($P < 0.05$)
[b]Statistically significant difference between obese class 2 and obese class 3 ($P < 0.05$)
[c]Statistically significant difference between obese class 1 and obese class 3 ($P < 0.05$)

events relative to those in the lower BMI categories.

Mortality

Previous studies on the association between BMI and mortality have also examined the relationship between obesity and mortality.

Consistent with the current findings, the ACCORD trial revealed that individuals with T2D and class 3 obesity had the highest risk, relative to those with T2D and lower BMI categories, of all-cause mortality, cardiac death and non-cardiac death [21]. Similarly, a retrospective study of Iranian individuals with T2D found no statistically significant difference in the all-cause mortality rate when comparing

individuals with obesity class 1 and obesity class 2, while individuals with obesity class 3 had statistically significantly higher mortality compared to individuals in either of the lower obesity classes [24]. In contrast, data from the ORIGIN trial revealed that for individuals with obesity class 1, 2 or 3, the unadjusted all-cause mortality rate declined as obesity class increased, although there was no statistically significant difference in the adjusted mortality rate between the three classes [25].

Cardiovascular Composite Outcome

Given that cardiovascular disease is the most common cause of death and illness among individuals with diabetes [26], our finding that obesity class 3 is associated with a statistically significantly higher prevalence of the CCO highlights the fact that individuals in this weight category constitute a unique treatment group. This finding is consistent with research showing that, even relative to other obesity classes, extreme ("morbid") obesity is associated with worse myocardial outcomes, including a higher prevalence of eccentric left ventricular hypertrophy, an increased risk of arrhythmia leading to sudden death and decreased parasympathetic tone leading to an increased mean heart rate [27]. Likewise, other research has shown that the lifetime risk of cardiovascular events rises as BMI increases from obesity class 1 to 3 [12]. Obesity has been shown to increase the risk of cardiovascular disease directly by altering the structure and function of heart tissues and possibly indirectly by increasing the risk of related comorbidities, such as dyslipidemia and hypertension [27, 28].

Microvascular Composite Outcome

Generally consistent with the high prevalence of microvascular complications in our population with obesity and T2D, a recent observational study by Callaghan et al. of 138 individuals with obesity and 46 "lean controls" found a prevalence of neuropathy of 2.2% for the controls versus 7.1% for those with obesity and normoglycemia and 40.8% for those with

obesity and diabetes [29]. Callaghan et al.'s findings suggest that neuropathy is independently associated with obesity and far more likely to be present when obesity co-occurs with diabetes. Given that Callaghan et al. [29] focused on individuals with BMI ≥ 35 kg/m^2, the association between neuropathy and obesity may have been even stronger if they had used the standard BMI ≥ 30 kg/m^2 threshold.

Our finding that individuals with obesity class 3 had a statistically significantly higher prevalence of nephropathy relative to those in class 1 is notable given that renal disease is a major cause of morbidity and mortality among those with either T2D or obesity. For instance, diabetes has been established as the most common cause of end-stage renal disease worldwide, and kidney dysfunction has been shown to be associated with obesity independent of diabetes [30]. In addition, research has shown that diabetic nephropathy is becoming an increasingly important cause of morbidity and mortality worldwide as the prevalence of T2D increases, largely due to the increase in the prevalence of obesity [30].

Other Complications

In addition to the outcomes discussed above, this study also examined the prevalence of ASCVD, atrial fibrillation, cirrhosis of the liver, NASH/NAFLD and OSA. The findings revealed that the frequency of all of these diagnoses generally increased as the BMI rose. Moreover, for each of these complications of interest, statistically significant differences among obesity classes existed after 5 years.

ASCVD and Atrial Fibrillation
Prior research has found that having overweight or obese is associated with a higher risk of cardiovascular events among individuals with T2D [31]. Consistent with that research and with the composite cardiovascular findings from our study, the prevalence of ASCVD rose with each higher strata of BMI, and the prevalence of atrial fibrillation remained consistently higher for those with class 3 obesity. Previous literature has identified ASCVD as the primary physical

cost related to obesity, making the case that obesity leads to ASCVD by increasing key risk factors, including high cholesterol, high blood pressure and hyperglycemia, as well as "emerging" risk factors, including atherogenic lipid levels, insulin resistance, chronic inflammation and a tendency toward blood clotting [32]. Likewise, obesity has been shown to be a major, independent risk factor for the cause and progression of atrial fibrillation due to the associations between obesity and inflammation, fat deposition around the heart, fibrosis of the atrial myocardium, dysfunction of the nervous system concomitant with sleep apnea and excess visceral fat with its impact on the body's electrical signaling [33].

NASH/NAFLD and Liver Cirrhosis

In our study, each higher BMI strata was associated with a greater prevalence of NASH/NAFLD, consistent with previous literature indicating a strong association between obesity and NAFLD [34], as well as with research which has shown that weight loss of $\geq 7\%$ can mitigate or resolve NASH [35]. Our analyses also looked at liver cirrhosis and found that it was more prevalent among those with obesity class 3, in agreement with research which has shown that liver cirrhosis may progress from NAFLD and NASH [34, 36, 37]. In particular, up to 10% of NASH cases are estimated to progress to cirrhosis [34]. Given that liver cirrhosis is the 12th leading cause of death in the USA and is often asymptomatic at onset [38], our findings suggest that liver function should be monitored closely among individuals with T2D and obesity in general and with class 3 obesity in particular.

Obstructive Sleep Apnea

Nearly one-third (32.1%) of the present study population had OSA after 5 years, consistent with the previously well-documented link between obesity and OSA [39]. In addition, the prevalence of OSA increased as obesity class rose, in alignment with the findings of a study of a UK population of 276,600 individuals who had obesity but not necessarily T2D [22]. The prevalence of OSA was more than fivefold higher in this US population relative to the 5.45% prevalence found in a study in that UK study [22]. This difference in results may be because OSA may be underdiagnosed in the UK [22], and there is a lower prevalence of obesity in the UK relative to the USA [40]. Furthermore, the difference in results may be because our population had concomitant T2D, given the previously established association between glucose intolerance, insulin resistance and OSA [41].

Strengths and Limitations

The strengths of the present study include the large sample size, the use of standard BMI categories, the recent source data and the 5-year observation period. However, as with any research, this study also had limitations. One limitation was a risk of selection bias due to the requirement that patients have at least one recorded HbA1c measurement and one recorded BMI measurement, a requirement which excluded a fairly large proportion of individuals with claims in the database. Second, diabetes type and comorbid conditions were identified based solely on diagnostic codes, a method which is less rigorous than more formal assessments to identify comorbid conditions. Third, the focus on individuals who were relatively well insured may limit applicability to other populations. Fourth, while the study period extended through the beginning of the Covid-19 pandemic, the analyses did not formally examine possible effects of the pandemic. Fifth, while the analyses presented age- and sex-adjusted prevalence rates, it did not attempt to adjust for other factors, such as race, socioeconomic status, medication use or duration of diabetes, all of which also may affect outcomes. Furthermore, the analyses focused on annual prevalence rates and, as such, paid less attention to incidence rates and did not examine less aggregated time periods. In addition, the study focused on the relationship between obesity classes and outcomes but did not examine the development and severity of obesity over time for the patient population. Finally, the study examined prevalence rates only and did not attempt to examine causality.

CONCLUSION

In this US population of adults with concomitant T2D and obesity, higher categories of obesity in general and obesity class 3 in particular were associated with higher prevalence of mortality, cardiovascular events, microvascular diagnoses, ASCVD, atrial fibrillation, cirrhosis of the liver, NASH/NAFLD and OSA. Given the rapid increase in the prevalence of mortality and morbidity over 5 years among a population with consistent health insurance, the results of this study indicate an urgent need to aggressively treat people with obesity and T2D. While additional research is needed to confirm the results, the findings of this study suggest that treatments which help to reduce weight for adults with T2D, especially those who are obese class 3, may have significant health benefits.

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