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Healthcare outcomes for patients with type 2 diabetes with and without comorbid obesity☆

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ABSTRACT

Aims: Examine the burden of comorbid obesity associated with type 2 diabetes (T2D).
Methods: The IBM® MarketScan® Explorys Claims Electronic Medical Records Data were used to identify adults with T2D, two recorded body mass index (BMI) values, and continuous insurance coverage from 1 year prior through 1 year post index date. Patients with index BMI ≥18 kg/m^2 and <30 kg/m^2 (normal/overweight) were matched to patients with index BMI ≥ 30 kg/m^2 (obese) using propensity score matching (PSM). Using the PSM cohort, multivariable analyses examined the association between obesity and patient comorbidities, healthcare costs, and resource utilization.
Results: In the matched cohort (16,006 normal/overweight; 16,006 obese), multivariable analyses showed that obesity, compared to normal/overweight, was associated with increased odds of a diabetes-related comorbidity (Odds Ratio [OR] = 1.29; 95% Confidence Interval [CI] 1.21–1.38) and an obesity-related comorbidity (OR = 1.42; 95% CI 1.29–1.56). Obesity was also associated with significantly higher annual diabetes-related and all-cause total costs and resource utilization.
Conclusions: This research increases the knowledge of how patients with T2D and obesity should be of greater concern for healthcare providers compared to T2D patients without comorbid obesity, given their worse comorbidity profile, increased resource utilization, and higher healthcare costs.

1. Introduction

Diabetes and obesity have increased steeply in prevalence since the latter half of the 20th century.[1,2] Sometimes referred to as “the twin epidemic,”[3] the two diseases share some common etiology[4] and pathophysiology.[5] Moreover, both diagnoses are expected to become even more common over the next decade. According to recent estimates, 39.8% of the U.S. population is obese,[6] and the majority of Americans (51%) are expected to be obese by 2030.[2] Meanwhile, the number of people in the U.S. with diabetes (types 1 and 2 combined) is projected to rise to 54.9 million individuals by 2030, a 54% increase from 2015, while the cost of diabetes is projected to increase to $622.3 billion, a 53% increase from 2015.[7] Type 2 diabetes (T2D) currently affects nearly 10% (30.6–32.3 million) of the overall U.S. population and accounts for 90–95% of all U.S. diabetes cases.[8,9]

Obesity is also a common comorbidity of diabetes, as illustrated by a 61.3% obesity rate among U.S. patients diagnosed with diabetes in the years 2013–2016.[10] Beyond co-occurrence, obesity is considered a key risk factor for T2D.[11] For instance, in one study of 65 year old adults, men with class 2 obesity (body mass index [BMI] ≥ 35) were 23.9% more likely to develop diabetes than men who were of normal-weight, while women with class 2 obesity were 26.7% more likely to develop diabetes than their normal-weight peers.[12]

Despite the common co-occurrence of diabetes and obesity, little research has explored the impact of obesity on the health-related outcomes of patients with T2D. The research that does exist in this area has shown that higher BMI is generally associated with worse outcomes. For instance, one study indicated that patients who are overweight or obese have higher odds of above-target (≥7%) HbA1c relative to patients who are normal weight or overweight.[13] Similarly, in a retrospective study that grouped patients with T2D according to BMI, average HbA1c generally increased as average BMI increased.[14] Other research among patients with T2D revealed that those who gained ≥5% of their baseline weight had higher 3-year healthcare costs relative to those who maintained their weight within 5% of baseline.[15]

To further the literature, the present study examined the impact of comorbid obesity on the health-related burden of patients with T2D.

☆ Declaration of competing interest: Boye and Terrell completed this research as employees and shareholders of Eli Lilly and Company. Lage was compensated for her work on this research project by Eli Lilly and Company.

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Focusing on a population of U.S. patients with T2D, these analyses sought to determine associations between a diagnosis of obesity and patient comorbidity profile. In addition, the analyses calculated the additional costs and resource use associated with a comorbid diagnosis of obesity.

2. Methods

The analyses were conducted using patient health information from the U.S.-based IBM® MarketScan® Explorys Claims and Electronic Medical Records (EMR) Data Set. In this data set, medical claims and EMR data are linked at the patient level, and the linked data are fully de-identified and Health Insurance Portability and Accountability Act (HIPAA) compliant. For this study, the data set supplied longitudinal information on patient demographics, coverage eligibility, inpatient and outpatient services, outpatient prescription fills, payments, vital signs, laboratory results, and medical surgical history. Data for this study covered the period from January 1, 2012 through April 30, 2019. Given the use of retrospective and de-identified data, ethics committee approval was not required.

Patients were required to have a recorded BMI indicating normal weight or above (BMI $\geq$ 18.5 kg/m^2)[16] over the period January 1, 2013 through May 1, 2018 (i.e., the identification window). For each patient, the data of the first such recorded BMI was identified as the index date. In addition, to focus on patients with relatively stable weight, patients were required to have a recorded BMI one year prior to the index date ($\pm$90 days), with the prior BMI and the index date BMI being in the same weight category. The weight categories included: normal weight (18.5 kg/m^2 $\leq$ BMI $<$ 25 kg/m^2); overweight (25 kg/m^2 $\leq$ BMI $<$ 30 kg/m^2); class 1 obesity (30 kg/m^2 $\leq$ BMI $<$ 35 kg/m^2); class 2 obesity (35 kg/m^2 $\leq$ BMI $<$ 40 kg/m^2); and class 3 obesity (BMI $\geq$ 40 kg/m^2).[16]

Patients were also required to have had, during the 12 months prior to the index date (i.e., during the pre-period), 2 or more diagnoses of T2D *or* a filled prescription for an oral glucose-lowering agent (GLA) in addition to 1 diagnosis of T2D and not more than 1 diagnosis of type 1 diabetes (T1D).[17] Patients were excluded from the analyses if they were younger than age 18 years at index date or diagnosed with gestational diabetes or pregnancy at any time from the start of the pre-period through 1 year post index date (e.g., the post-period). Finally, in order to ensure complete records of diagnoses, costs and resource utilization, all patients were required to be continually insured from the start of the pre-period through the end of the post-period.

Propensity score matching (PSM) was used to match a cohort of normal/overweight individuals with T2D to the cohort of obese individuals (obese I, II, or III) with T2D to examine differences in health outcomes over the post-period. This analysis utilized a greedy nearest neighbor match without replacement and a specified caliper distance of 0.20.[18] Covariates included in the propensity score model were patient age, sex, insurance plan type, and general health, as proxied by a pre-period adjusted Charlson Comorbidity Index (CCI)[19] and a pre-period Diabetes Complications Severity Index (DCSI).[20] The CCI creates a composite morbidity score that reflects mortality risk based upon the presence of any of 19 comorbidities, each scored on a scale of 1–6.[19] In this study, the comorbidities of myocardial infarction, peripheral vascular disease and diabetes with or without complications were omitted from the calculation of the adjusted CCI. These conditions were omitted because they applied to all individuals (e.g., diabetes), or were included in the DCSI. The DCSI is a 13-point scale calculated from patient medical records and designed to quantify the severity of diabetes-related complications and to predict the risk of adverse outcomes in people with diabetes.[20] The final sample after PSM consisted of 32,012 patients. Fig. 1 illustrates how each of the study inclusion and exclusion criteria affected sample size.

Outcomes of interest included comorbidities, resource utilization, and costs. All outcomes were measured annually over the 1-year post-period. Diabetes-related comorbidities were based upon the DCSI and were defined based upon receipt of a diagnosis for retinopathy, neuropathy, nephropathy, cerebrovascular disease, cardiovascular disease, peripheral vascular disease, and metabolic disease.[20] Coding for each of these conditions used updated codes incorporating ICD-10 coding.[20] Obesity-related comorbidities were based upon research which summarized the epidemiology and comorbidities associated with obesity and consisted of receipt of diagnoses for hypertension, hyperlipidemia, cardiovascular disease, and ischemic stroke.[21] In addition to examining *specific* diabetes-related and obesity-related comorbidities, the analyses also examined the probability of having *any* diabetes-related or obesity-related comorbidity.

All-cause and diabetes-related resource utilization variables examined included the number of hospitalizations, hospital length of stay (LOS), number of emergency room visits, and number of office visits. The analyses also examined both all-cause and diabetes-related total costs, where diabetes-related costs were defined as any costs with an accompanying diagnosis of diabetes or any cost of filling a prescription for a GLA or diabetic supplies. In addition to examining total costs, both all-cause and diabetes-related total costs were sub-divided into outpatient, drug, and acute care (inpatient and emergency room [ER]) costs. All costs were defined as gross payments to a provider for a service and were converted to 2018 dollars using the medical care component of the consumer price index.

Unadjusted descriptive statistics were examined both before and after matching. Patient characteristics were summarized for the cohort overall as well as across BMI categories (normal/overweight or obese). Differences in continuous variables across groups were examined using t-statistics, while differences in categorical variables were examined using chi-square statistics.

The relationships between index BMI category and comorbidities were examined using logistic models, since all complications were identified as dichotomous variables (whether the comorbidity was present or not). Adjusted incidence rate ratios (IRRs) for resource utilization were computed using negative binomial models. The relationships between index BMI category and healthcare costs were examined using generalized linear models (GLM) with gamma distribution and log link.[22] Acute care costs were examined using a two-part model, where the first step examined the probability of having an acute care visit and the second part examined acute care costs for patients who had such a visit.[23] In the GLM models, costs were estimated using the method of recycled predictions with standard errors calculated from 1000 bootstrap iterations.[24] All multivariable analyses controlled for patient age, sex, type of insurance coverage, and adjusted CCI. In addition to the above variables, multivariable analyses that examined the probability of a post-period comorbidity (diabetes- or obesity-related) included the pre-period comorbidity as an additional covariate.

All analyses were conducted using SAS, version 9.4 (Cary, NC), and a p value $<$ 0.05 was considered, a priori, to be statistically significant.

3. Results and discussion

This study compared the medical claims of two cohorts of U.S. patients with T2D: one obese, and the other of normal weight or overweight. The comparisons between these cohorts revealed statistically significant associations between obesity and increased comorbidity, greater medical resource use, and higher medical costs. For instance, relative to a normal or overweight patient, a patient with obesity was, on average, 21% more likely to have had a diabetes-related comorbidity (Odds Ratio [OR] = 1.21; 95% Confidence Interval [CI] 1.14–1.28) and 42% more likely to have had an obesity-related comorbidity (OR = 1.42; 95% CI 1.29–1.56). Moreover, consistent with their greater likelihood of comorbidity, the obese patients in this population had substantially greater use of healthcare resources and significantly higher average annual diabetes-related and all-cause total costs. Sections 3.1–3.5 discuss these results in more detail and compare them with previous research.

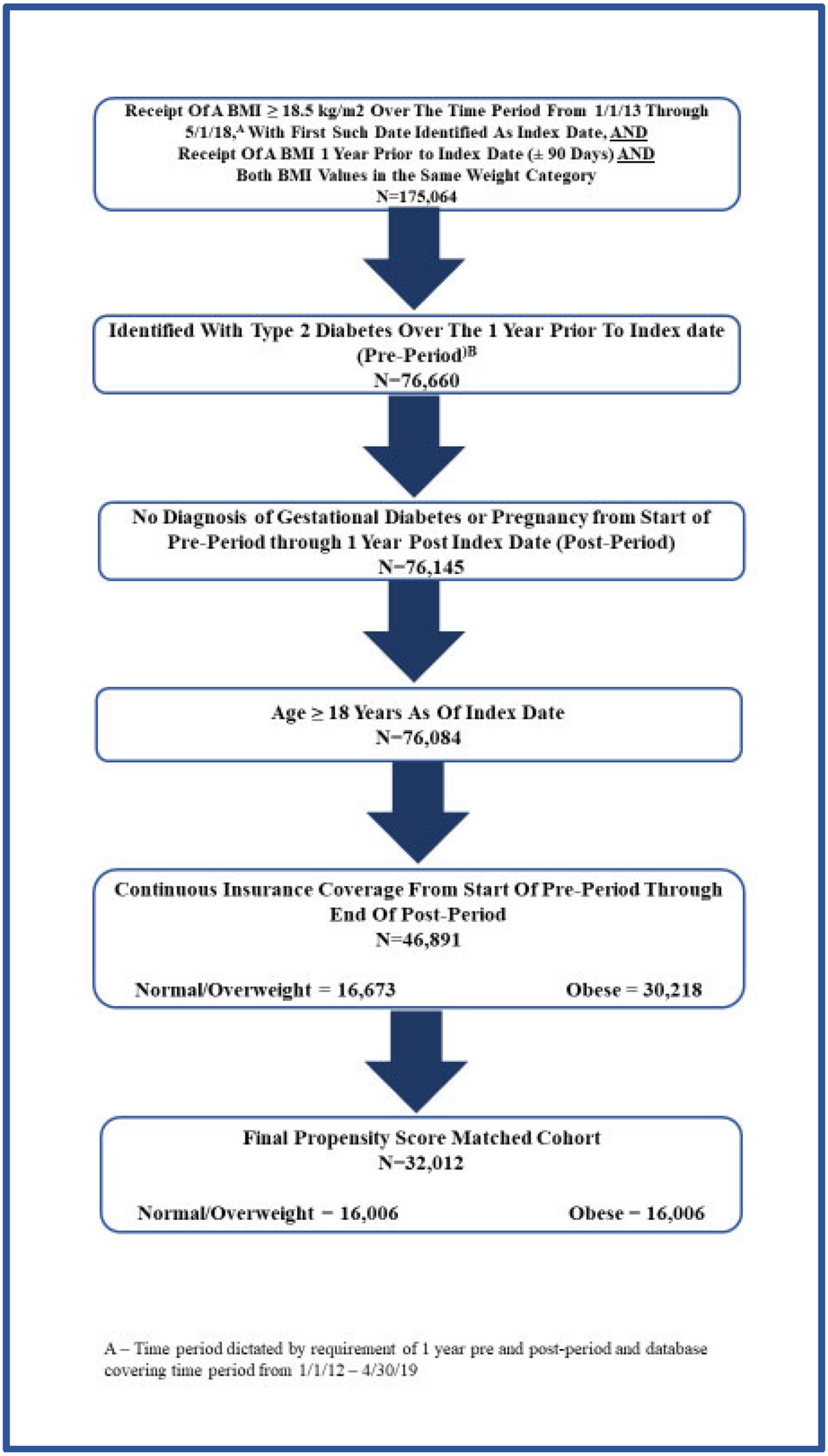

Fig. 1. Inclusion/exclusion criteria and sample size.

3.1. Propensity score matching and descriptive statistics

Tables 1 provides descriptive statistics for the propensity score matched cohort. Results indicate that the average patient was 67.1 years old (SD = 12.5 years) and that the cohort consisted of slightly more females (52%) than males (48%). After matching, significant differences remained between the two cohorts, with patients with obesity being significantly younger, more likely to be female, and in poorer general health, as suggested by the significantly higher adjusted CCI and DCSI scores. However, the absolute value of the standardized difference in means for all covariates included in PSM were <0.25, the absolute value of the standardized difference of the mean propensity score was <0.20, and the ratio of variances between the normal/overweight and obese cohorts of patients with T2D was 1.02. All of these results suggest balance between the two cohorts.[25]

3.2. Comorbidities

In this population, the patients with obesity were 21% more likely to be diagnosed in the post-period with *any* diabetes-related comorbidity (Odds Ratio [OR] = 1.21; 95% CI 1.14–1.28), and they were more likely to be diagnosed with the *specific* diabetes-related comorbidities of nephropathy, neuropathy, cardiovascular disease (excluding ischemic heart disease), peripheral vascular disease, and metabolic disease (see Fig. 2). These findings are in concert with previous literature indicating that obesity is a driver of a number of serious comorbidities, including microvascular disease, metabolic disease, and cardiovascular disease.[26,27] Our findings are also generally consistent with T2D research which revealed that obesity, compared having a BMI indicating normal or overweight status, was associated with higher frequencies of the cardiovascular risk factors of hypertension, hyperlipidemia, and microalbuminuria,[28] as well as long-term increased rates of mortality.[29] As Fig. 2 illustrates, the patients with obesity in our population were also 42% more likely to be diagnosed with *any* obesity-related comorbidity (OR = 1.42; 95% CI 1.29–1.56), and they were more likely to be diagnosed with the *specific* obesity-related comorbidities of hypertension, hyperlipidemia, and cardiovascular disease. These results are in agreement with literature indicating that obesity is a leading risk factor for high blood pressure, dyslipidemia, cardiovascular disorders, and other chronic diseases.[11,27]

Although the patients with obesity in our population were more likely to be diagnosed with the aggregate comorbidities of *any* diabetes-related or obesity-related comorbidity, they were no more likely than the patients without obesity to have the *specific* diabetes-related comorbidities of retinopathy or cerebrovascular disease, or the *specific* obesity-related comorbidity of ischemic heart disease. A number of studies have likewise indicated that obesity by itself is not a risk factor for cerebrovascular disease, although abdominal obesity is a risk factor for stroke.[30,31] However, previous research has shown that obesity is a risk factor for ischemic heart disease,[32] diabetic retinopathy,[33] and metabolic disorders.[5,27] The reason for the contradictory findings is unknown but may be related to the limited (1-year) post-period in the present study.

3.3. Resource utilization

In keeping with previous evidence from the general population both worldwide[34] and in the United States,[35] as well as with the present cost findings (see Section 3.4), the patients with obesity in this study used significantly more medical resources relative to the normal/overweight cohort. As Fig. 3 illustrates, obesity was associated with 1.20 times the number of diabetes-related hospitalizations and 1.17 times the number of all-cause hospitalizations. Obesity was also associated with significantly more diabetes-related and all-cause ER visits, office visits, and increased hospital LOS.

These increased use of hospitals and emergency rooms are internally consistent with the larger burden of comorbidity, principally, diabetes-related comorbidity (see Section 3.2), observed in the obese cohort. In combination, these findings suggest that obesity may be associated with added suffering among patients with T2D. The finding of increased office visits may be additional evidence of poorer outcomes among patients with comorbid obesity. However, in contrast to acute care resource utilization which generally indicate poor patient outcomes, increased office visits may also be a marker of improved adherence to treatment guidelines and/or increased access to care. Prior evidence has suggested that adherence to primary care and increased access to such care is associated with reduced ER visits and hospitalizations.[36,37]

3.4. Diabetes-related and all-cause costs

Fig. 4 shows estimated all-cause and diabetes-related costs for patients with T2D and comorbid obesity compared to these costs for patients with T2D without comorbid obesity. In keeping with this study's findings of increased comorbidities among patients with T2D and obesity,

Table 1
Descriptive statistics for matched cohort.

	All	Normal/overweight	Obese	p value[a]	Standardized difference in means[b]
	Mean ± SD or N (%)	Mean ± SD or N (%)	Mean ± SD or N (%)		
Sample size	32,012	16,006	16,006		
Demographics					
Age - Mean ± SD	67.1 ± 12.5	68.0 ± 12.6	66.2 ± 12.4	<0.0001	−0.1447
Sex – N (%)				<0.0001	
Male	15,369 (48.0)	8661 (54.1)	6708 (41.9)		−0.2447
Female	16,643 (52.0)	7345 (45.9)	9298 (58.1)		
Insurance type – N (%)				<0.0001	
Comprehensive	9456 (29.5)	4833 (30.2)	4623 (28.9)		
Consumer directed health plan	1107 (3.5)	537 (3.4)	570 (3.6)		0.0110
Health maintenance organization[a and b]	8578 (26.8)	4482 (28.0)	4096 (25.6)		−0.0544
Point of service	1962 (6.1)	888 (5.6)	1074 (6.7)		0.0636
Preferred provider organization	9265 (28.9)	4660 (29.1)	4605 (28.8)		−0.0074
Other/unknown	1644 (5.1)	606 (3.8)	1038 (6.5)		0.1342
Pre-period general health – Mean ± SD					
Adjusted Charlson Comorbidity Index	1.3 ± 2.1	1.1 ± 2.0	1.4 ± 2.1	<0.0001	0.1752
Diabetes Complications Severity Index	2.0 ± 2.2	1.8 ± 2.1	2.1 ± 2.2	<0.0001	0.1254
Standard difference of mean propensity score					0.1875
Ratio of variances					1.0193

Abbreviations: SD – standard deviation.
[a] Differences in continuous variables examined using *t*-tests and differences in categorical variables examined using chi-square tests.
[b] Standardized difference in means for the matched cohort of patients who were normal/overweight compared to the matched cohort of patients with obesity.

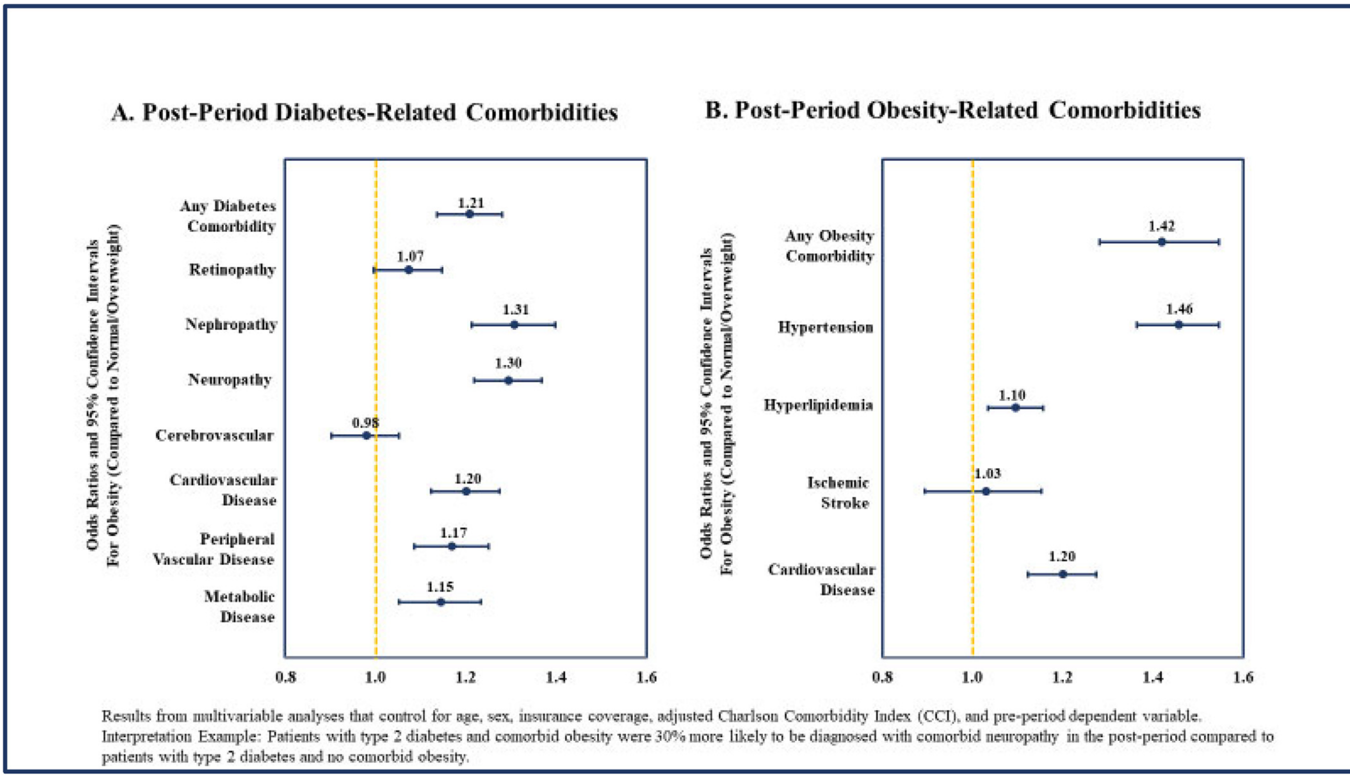

Fig. 2. Diabetes-related and obesity-related comorbidities.

the cohort with obesity in the present study had significantly higher annual diabetes-related total costs ($8987 v $8057; $p < 0.0001$) and higher all-cause total costs ($26,624 v $24,838; $p < 0.0001$) relative to the normal weight/overweight cohort. Furthermore, the patients with obesity had higher costs in the categories of all-cause and diabetes-related drugs, outpatient care, and diabetes-related acute care. These results are

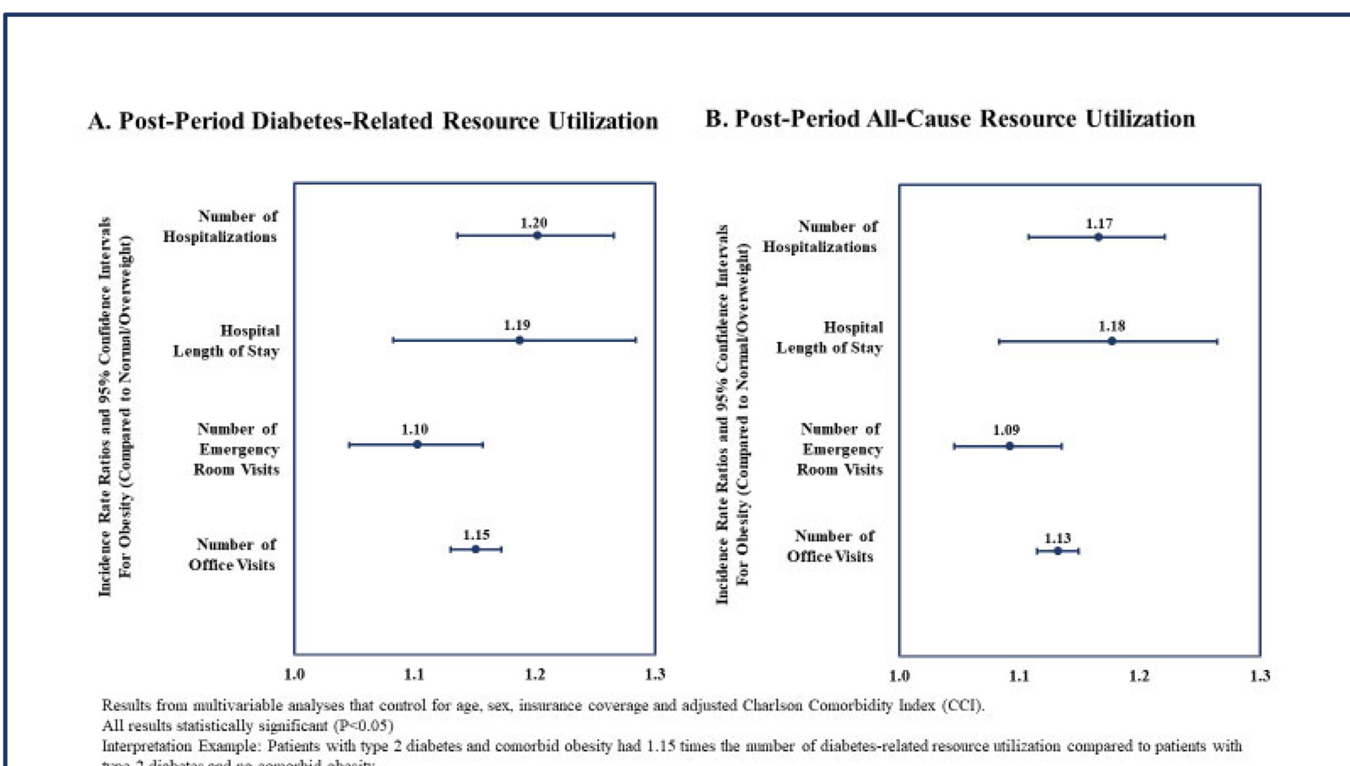

Fig. 3. Diabetes-related and all-cause resource utilization.

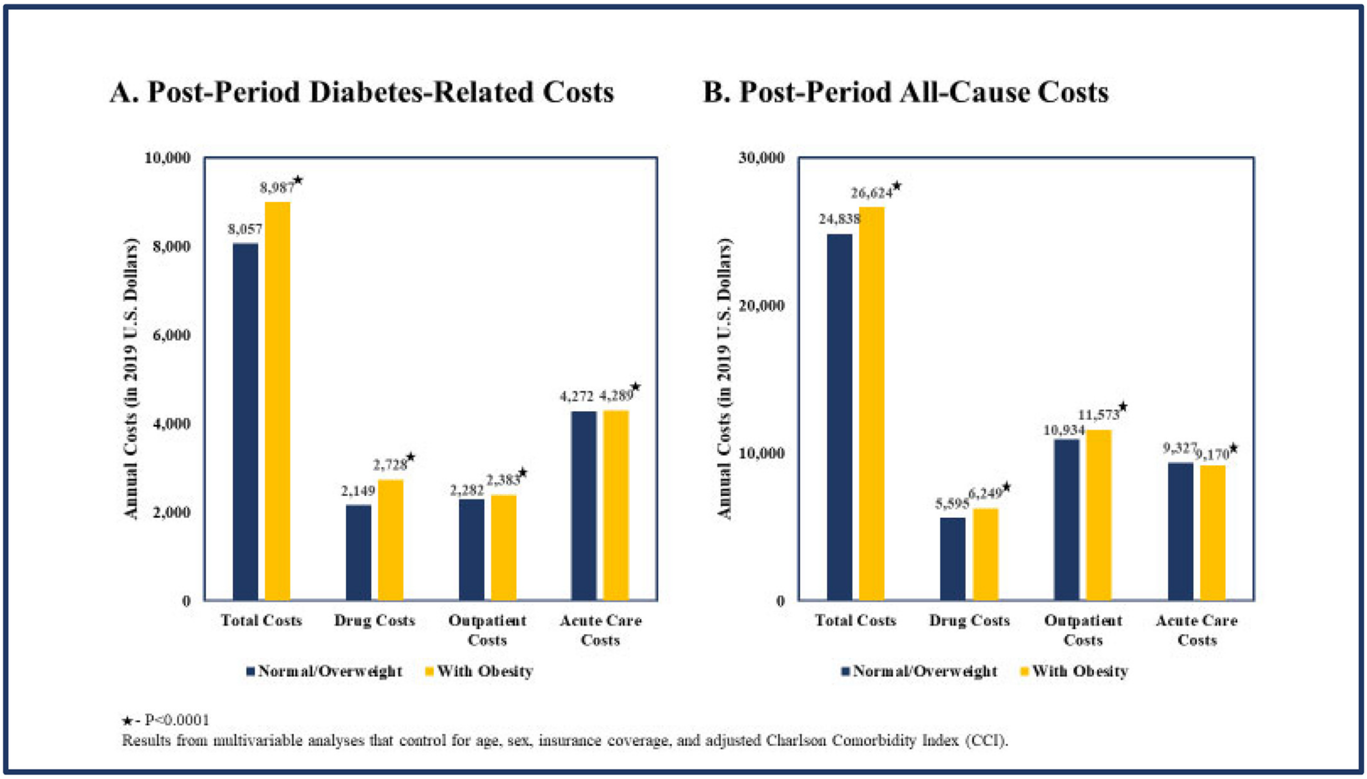

Fig. 4. Diabetes-related and all-cause costs.

consistent with previous research among patients with diabetes which found that higher BMI was associated with higher annual healthcare expenditures,[38] as well as with research in a broad population of older adults with T2D which showed that patients with obesity had significantly higher annual healthcare costs.[35]

However, patients with obesity had significantly lower all-cause acute care costs relative to patients without obesity, despite the finding that patients with obesity used more healthcare resources (see Section 3.3 above). However, when comparing costs for patients who used acute care services, the mean costs per patient were lower for obese patients ($19,430) compared to non-obese patients ($20,262). The multivariable analyses utilized a two-part model which is based upon both the probability of using acute care services and costs among patients who utilized such a service to estimate acute care costs. The finding that there are significantly lower all-cause acute care costs despite more utilization, suggests that the lower costs for obese patients compared to non-obese patients who utilized acute care had a larger impact than the result that obese patients utilized more acute care services compared to non-obese patients.

3.5. Sensitivity analyses

As a test of the sensitivity of results, all analyses were conducted a second time where the patients who were normal/overweight with T2D were matched to patients with T2D who were obese using 1:1 exact matching based upon the patient characteristics of age, sex, insurance plan type and adjusted CCI. In addition, consistent with research of patients with T2D which has defined overweight as BMI ≥ 27 kg/m^2,[39] results were examined using a threshold of 27 kg/m^2 rather than 30 kg/m^2. Results were generally consistent when using the alternative matching method or alternative BMI threshold. For example, total diabetes-related costs were found to be $8021 and $8659 for lower weight category individuals and $8664 and $9672 for higher weight category individuals when using exact matching or an alternative BMI threshold, respectively (both $p < 0.0001$), and $8057 for normal/overweight patients compared to $8987 for obese patients in the main analyses ($p < 0.0001$). However, in both sensitivity analyses no statistically significant association was found between higher weight category and metabolic disease or hospital LOS (diabetes-related or all-cause). In contrast, in the main analyses, obesity was associated with a significant increase in all of these outcomes.

4. Conclusions

4.1. Limitations

As a retrospective, claims-based investigation, the present study had inherent limitations. For instance, the generalizability of the results may have been limited by the fact that only commercially insured patients were included. Moreover, the reliance on claims data necessitated the use of diagnostic codes rather than formal assessments to identify patients, while it precluded the capture of lifestyle factors (e.g., diet and physical activity) that may have influenced outcomes. In addition, the use of claims data precludes the inclusion of made it impossible to study or control for duration of diabetes or obesity, race, socioeconomic status, or other unrecorded information which may have influenced outcomes. Furthermore, the study focused on outcomes over a 1 year post-period and hence, is unable to discuss any long-term associations between comorbid obesity and patient outcomes. Lastly, these retrospective analyses revealed associations, not causation and examined statistical rather than clinical differences in outcomes.

5. Conclusions

By comparing the outcomes of patients with T2D with and without a comorbid diagnosis of obesity, this study quantified the excess burden associated with a diagnosis of comorbid obesity among U.S. patients with T2D. The results indicated that comorbid obesity is associated with a greater burden of illness, more resource use, and higher all-cause and diabetes-related costs. However, this study found no relationship between a diagnosis of obesity and diagnoses of retinopathy, cerebrovascular disease, or ischemic stroke in the 1 year post-period and found significantly lower all-cause acute care costs for patients with obesity in the 1 year post-period. Overall, however, the findings illustrate the significant burden of comorbid obesity for patients and payers. Future work will examine the sensitivity of results to an extended duration of study as well as quantifying the potential short-term and long-term benefits of weight management.

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CRediT authorship contribution statement

Boye – Conceptualization; Methodology; Formal analysis; Resources; Investigation; Writing – review & editing; Visualization; Supervision; Project administration; Funding acquisition

Lage – Software; Validation; Formal analysis; Data curation; Writing – original draft

Terrell – Conceptualization; Methodology; Formal analysis; Resources; Investigation; Writing – review & editing; Visualization; Supervision; Project administration; Funding acquisition.

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