Effect of Weight Change on Economic Outcomes Among Persons with Type 2 Diabetes Mellitus in the United States: Beyond Glycemic Control

Swapna Karkare, MS; Moshe Fridman, PhD; Tam Dang-Tan, PhD; Jingsong Lu, MS; B. Gabriel Smolarz, MD, MS, FACE; Mitch DeKoven, MHSA; and Neeraj N. Iyer, PhD

ABSTRACT

BACKGROUND: Previous studies report weight loss to be associated with significantly lower total health care costs among patients with type 2 diabetes mellitus (T2DM). The effect of weight change on health care costs, independent of glycemic control and after controlling for time-varying covariates among T2DM patients, remains unknown.

OBJECTIVE: To evaluate the effect of weight change, independent of glycemic control, on all-cause and T2DM-related health care resource utilization (HCRU) and costs among T2DM patients in the United States.

METHODS: A retrospective cohort study was conducted using a linked data extract composed of IQVIA's RWI Data Adjudicated Claims-US and Ambulatory Electronic Medical Record data. Adults (aged ≥ 18 years) with T2DM receiving ≥ 1 oral antidiabetic drug (OAD) medication, glucagon-like peptide-1 receptor agonist (GLP-1RA), and/or short- or long-acting insulin between January 1, 2010, and December 31, 2014 were included (the date of the first observed medical claim with a diagnosis code or medication prescription claim was the index date). Baseline characteristics were evaluated in the 6-month pre-index period. Weight loss (3%, 5%, or 7% from baseline) was evaluated over two 6-month periods (months 1-6 and 7-12) following the index date. Covariates included time-varying weight, hemoglobin A1c (A1c), costs, and HCRU within each 6-month period. Outcomes of interest (all-cause and T2DM-related HCRU and costs) were evaluated in the 6-month (months 13-18) and 12-month (months 13-24) periods following the initial 1- to 6-month and 7- to 12-month post-index periods. Structural nested mean models were used to evaluate the effect of weight change on these outcomes, independent of glycemic control.

RESULTS: 1,407 patients were included (mean age = 55 years; 55% male), with a mean baseline weight of 102.2 kg (median = 99.7 kg) and a mean baseline A1c of 7.4% (median = 6.9%). In adjusted analysis, weight loss was associated with significantly lower all-cause and T2DM-related annual total health care costs. Compared with those showing no weight change, a 3%, 5%, and 7% weight loss resulted in approximately \$500, \$800, and \$1,100 in savings, respectively, in all-cause annual total health care costs per patient in the year following the weight loss. Similarly, compared with those with no weight change, a 3%, 5%, and 7% weight loss resulted in approximately \$200, \$300, and \$400 in savings, respectively, in T2DM-related annual total health care costs per patient in the following year. Even greater savings (up to ~\$2,000 and ~\$800 in all-cause and T2DM-related annual costs per patient, respectively) were experienced by those who lost weight compared with those who gained weight.

CONCLUSIONS: After accounting for glycemic control, this study found that weight loss was associated with additional significant reductions in all-cause and T2DM-related annual total health care costs. Understanding the role of weight loss in T2DM may provide useful evidence for decision makers as they evaluate therapy options for T2DM.

J Manag Care Spec Pharm. 2019;25(6):658-68

Copyright © 2019, Academy of Managed Care Pharmacy. All rights reserved.

What is already known about this subject

- More than 80% of patients with diabetes are either overweight or living with obesity.
- Weight loss is associated with improvements in quality of life and glycemic control and decreases in cardiovascular risk factors among patients with type 2 diabetes mellitus (T2DM).
- Results from the few studies that have evaluated the effect of weight change on health care costs beyond glycemic control among T2DM patients have indicated that weight loss is associated with significantly lower health care costs.

What this study adds

- This study evaluated the effect of weight change, independent of glycemic control, on all-cause and T2DM-related health care resource utilization and costs among patients with T2DM in the United States, after controlling for time-varying confounders.
- A greater magnitude of weight loss resulted in greater cost savings.
- Irrespective of the pattern in which weight loss occurred over the study period, losing weight was associated with significant reductions in all-cause and T2DM-related annual total health care costs.

As of 2015, the prevalence of diabetes in the United States was an estimated 30.3 million (9.4% of the total U.S. population).¹ Diabetes-related health care expenditures in the United States were \$327 billion in 2017 (U.S. dollars), with 73% (\$237 billion) attributed to diabetes-related direct health care expenditures and 27% (\$90 billion) attributed to decreases in productivity.² It is reported that, after controlling for age and gender, patients with diabetes incur 2.3 times greater annual health care expenditures compared with those without diabetes.³ The majority of these medical expenditures can be attributed to hospital inpatient visits and medication utilization (other than insulin and other antidiabetic agents).^{2,4}

Weight reduction is important for prevention and management of type 2 diabetes mellitus (T2DM).⁵ Excess adiposity leading to insulin resistance is the major risk factor for T2DM.^{1,6} The Centers for Disease Control and Prevention reported that between 2011 and 2014, 87.5% of adults (aged ≥ 18 years)

with diabetes in the United States were overweight or living with obesity, with 26.1% being overweight (body mass index [BMI] >25.0 and <30.0 kg/m²), 43.5% being obese (BMI ≥ 30 to <40.0 kg/m²), and 17.8% being severely obese (BMI ≥ 40 kg/m²).¹ Since obesity deteriorates the control of hemoglobin A1c, blood pressure, and cholesterol among patients with diabetes, patients having both obesity and diabetes are at an increased risk for developing microvascular and macrovascular morbidity and mortality.⁷⁻⁹ Thus, having excess weight significantly increases the clinical and economic burden of diabetes.

Diabetes treatment guidelines emphasize the paramount importance of weight loss among overweight and obese T2DM patients and highlight that even a relatively modest 5%-10% (but consistent) weight loss helps manage glycemic control among these patients.^{6,10-12} It is reported that patients with moderate weight loss (5% to $<10\%$) are more likely to achieve reductions in A1c, blood pressure, C-reactive protein, low-density lipoprotein cholesterol, and triglyceride levels (cardiovascular disease risk factors) compared with patients with stable weight, and greater weight loss results in greater clinical improvements.^{12,13} The effect of weight change on clinical outcomes among patients with T2DM is well established in the literature. Weight loss is associated with improvements in quality of life; glycemic control and blood pressure; and reductions in cardiovascular risk factors, mortality, and diabetes complications.¹⁴⁻²⁰

A few studies have evaluated the association between weight changes and health care costs among patients with T2DM.²¹⁻²⁸ Results from these studies have generally indicated that weight loss is associated with significantly lower costs. However, these studies have several limitations. Most of these studies measure weight change in the initial 6-month period and then evaluate the effect of this weight change on costs in the subsequent 1-year period. Studies either assume weight change patterns or the timing of weight change to be consistent for all patients during the follow-up period or that weight changes during the follow-up period do not significantly affect health care costs in the follow-up period. These assumptions make it difficult to evaluate the true long-term effect of weight changes on costs. Although several weight change patterns over time in a real-world setting have been reported in the literature, studies on the associations between weight change and costs have used static designs using single measurements of weight and outcomes.^{21,22,24-26,28,29} Few studies have accounted for weight change patterns that are commonly observed in a real-world setting, including the ubiquitously observed weight gain over time.²⁷ Previous studies also inadequately account for time-varying covariates (e.g., glycemic control and age) and do not focus on the effect of weight change patterns incremental to glycemic control.

The goal of this study was to evaluate the effect of weight change, independent of glycemic control, on all-cause and

T2DM-related health care resource utilization (HCRU) and costs among patients with T2DM in the United States. A secondary objective was to evaluate whether patterns or timing of weight change had any effect on all-cause and T2DM-related HCRU and costs. This study will help link weight change to outcomes that matter to health care decision makers and may provide additional evidence to evaluate therapy options for T2DM.

Methods

Data Source

This retrospective cohort study was conducted using a linked data extract developed by using IQVIA's RWI Data Adjudicated Claims-US and Ambulatory Electronic Medical Record (EMR) database from January 1, 2010, through December 31, 2014. A deterministic matching algorithm was used to link patient data across the 2 databases. All data were compliant with the Health Insurance Portability and Accountability Act to protect patients' privacy. Most of the patients in the database have commercial insurance through preferred provider organization (PPO) plans.

Claims-Based Inclusion/Exclusion Criteria

Patients were initially included in the study if they had evidence of ≥ 2 medical visit encounter diagnosis codes for T2DM or evidence of ≥ 1 diagnosis code for T2DM and use of oral antidiabetic drugs (OADs) or glucagon-like peptide-1 receptor agonists (GLP-1RAs), with at most one type 1 diabetes mellitus (T1DM) code that could appear only once per day between January 1, 2010, and December 31, 2014. The date of the first observed medical claim with a diagnosis code or medication prescription claim was defined as the index date. Subsequently, among patients excluded using the above criteria, an additional inclusion criterion was applied: evidence of insulin use only plus greater number of T2DM codes than T1DM codes in the 6-month pre-index period. For inclusion, patients needed to be aged ≥ 18 years at the index date, with continuous health plan enrollment for ≥ 180 days immediately preceding the index date (6-month pre-index period) and ≥ 720 days immediately following the index date (24-month post-index period).

Patients were excluded from the study if they had evidence of ≥ 1 diagnosis/procedure code for gestational diabetes, bariatric surgery, pregnancy, total pancreatic failure, acute or chronic pancreatitis, stage 5 end-stage renal disease, dialysis/renal replacement therapy, feeding difficulty, liver cirrhosis, cancer, or malignancy at any time during the study period; had data quality issues (aged ≥ 65 years at the index date and not covered by Medicare Risk due to incomplete Medicare fee-for-service data; Medicare Risk or Medicare Advantage is offered by private commercial health plans as an alternative to traditional Medicare); or had Medicare cost coverage or State Children's Health Insurance Program coverage; or had invalid year of birth, gender, or health plan enrollment dates.

Linkage to EMR and Inclusion/Exclusion Criteria

Patients linkable to the EMR database were then identified. A deterministic matching algorithm was used to link patients between both the databases that used patient information including first name, last name, gender, date of birth, and ZIP code to ensure continuity of patient records across datasets. Patients were additionally required to have ≥ 1 weight measurement or ≥ 1 BMI and height value (to calculate weight) in the 6-month period before the index date (baseline weight) and at any point in time during the 1- to 6-month and 7- to 12-month periods after the index date. Patients were also required to have ≥ 1 A1c measurement in the 6-month pre-index period (baseline A1c) and at any point during the 1- to 6-month and 7- to 12-month periods after the index date. To remove outliers, patients with $> 15\%$ weight loss for any 6-month period or with $> 25\%$ weight loss for the 12-month cumulative period or with $> 20\%$ weight gain for any 6-month period or with $> 30\%$ weight gain for the 12-month cumulative period were excluded from the study sample.

Among patients with > 1 baseline weight measurement available, the weight measurement closest to the index date was considered as the baseline weight. Among patients with > 1 weight measurement available in months 1-6 and 7-12 after the index date, the weight measurement closest to the end of each of the 6-month intervals was considered as the post-index weight. Similar rules were applied among patients with > 1 baseline A1c measurement available.

Patterns of Weight Change

For this study, weight loss (3%, 5%, or 7%) was evaluated over two 6-month periods (1-6, 7-12) following the index date.^{20,23-25} For example, among patients with 3% weight loss in the initial 12-month period, 3 different patterns of weight loss representing different timing of weight loss were evaluated: (1) lose the entire 3% weight in the 1- to 6-month post-index period, or (2) lose the entire 3% weight in the 7- to 12-month post-index period, or (3) lose 1.5% weight in the 1- to 6-month post-index period and the remaining 1.5% weight in the 7- to 12-month post-index period (i.e., cumulative weight loss of 3% over 12 months). Similar patterns were assessed for patients with 5% and 7% weight loss.

Outcomes of Interest

All-cause and T2DM-related (defined as claims for antihyperglycemic agent pharmacy, blood glucose test strips, and medical claims with a diagnosis for T2DM at any position for outpatient claims/primary diagnosis on discharge claim for hospitalizations) HCRU and costs were evaluated in the 6-month (months 13-18 post-index) and 12-month periods (months 13-24 post-index) following the 7- to 12-month post-index period. HCRU was reported for mutually exclusive pharmacy services, outpatient visits, emergency department (ED) visits,

and inpatient visits. Direct health care costs for services covered by the patient's insurance benefit were reported, using the allowed amount on the claim, which represents the contracted reimbursable amount for covered medical services or supplies that the health plan agrees to pay to service providers. Costs were converted to 2016 U.S. dollars using the medical care component of the Consumer Price Index. Study time periods are shown in the Appendix (available in online article).

Patient demographic and clinical characteristics were obtained as of the 6-month pre-index period from the integrated dataset. These included age at index date, gender, region, health plan type, payer type, index year, physician specialty at index, Charlson Comorbidity Index (CCI) score (excluding diabetes [both T1DM and T2DM] as it was the exposure of interest), Adapted Diabetes Complications Severity Index score, comorbidities of interest, pre-index use of antidiabetic classes, concomitant medications, number of pre-index antidiabetic classes used, BMI, weight, and A1c.^{30,31} All-cause and T2DM-related HCRU and costs incurred in the 6-month pre-index period were also reported.

Statistical Analysis

For categorical measures, data were reported as the frequency (number of cases) and percentage of total patients observed in each category. For continuous variables, data were reported as the mean, standard deviation (SD), and median. Differences in the distribution of these variables were tested for statistical significance using the chi-squared test for categorical variables and the nonparametric Wilcoxon rank-sum test for continuous variables. A P value of ≤ 0.05 was considered statistically significant. SAS version 9.3 (SAS Institute, Cary, NC) was used for all statistical analyses.

Structural nested mean models (SNMMs) were used to evaluate the effect of time-varying covariates (weight and A1c) affected by patient baseline characteristics on outcomes of interest (all-cause and T2DM-related HCRU and costs).³² SNMM enables estimation of the effect of weight change at each time point ("j") on end-of-study costs and HCRU outcomes as a function of the history of A1c and cost values through time j-1. The model allows for the potential time-varying causal effect of weight change on end-of-study cost to be moderated by A1c, as may be expected from the temporal effect of glycemic control on weight changes. By conditioning on the history of time-varying covariates, the average effect of weight changes over time on outcomes can be estimated while taking into account changing patterns in the time-varying covariates.

A 6-month pre-index period was used to gather baseline information. Two 6-month periods (1-6, 7-12) after the index date were used to measure time-varying weight and A1c, as well as costs and HCRU within each 6-month period. This allowed measuring the patterns of change for weight and A1c. This 1-year period was defined as the evaluation period.

Six-month (13-18 months post-index) and 12-month periods (13-24 months post-index) after the first one-and-a-half years of baseline and evaluation periods were used to assess all-cause and T2DM-related HCRU and costs. The 2 outcome periods (6 months and 12 months) were necessary to allow for (a) a closer, more immediate effect of the time-varying covariates on HCRU and cost (6 months), and (b) a longer-term effect of 12 months that is more likely to capture ED visits or hospitalizations.

SNMMs estimated all-cause and T2DM-related HCRU and costs for those showing weight loss (3%, 5%, or 7% weight loss in 1-6 months and/or 7-12 months post-index period) compared with those who gained weight (3.5% weight gain in the 1- to 6-month period and another 3.5% weight gain in the 7- to 12-month post-index period). Similarly, costs and resource use differences were also estimated for those who lost weight compared with those showing no weight change.

Results

Study Sample

A total of 3,921,667 patients with T2DM were initially identified in the IQVIA RWI Data Adjudicated Claims–US database. After applying the inclusion and exclusion criteria, a total of 1,407 patients (0.04%) were available for analyses (Figure 1). Patients were excluded primarily due to the following criteria: lack of continuous enrollment in the database to obtain required data points (67.4%), not linkable to EMR database (22.3%), evidence of exclusionary diagnoses/procedures of interest (6.7%), no BMI and A1c measurements in the 6-month pre-index period and in 1- to 6-month and 7- to 12-month post-index periods (2.5%), data quality issues (0.7%), aged <18 years at index (0.4%), and extreme weight loss or weight gain (0.001%).

Baseline Characteristics of the Study Sample (6-Month Pre-Index Period)

Mean age of all patients was 55.2 years (median=56.0 years) and approximately half were male (55.2%). The majority of these patients were covered under the PPO health plan type (72.6%), and half of them resided in the Northeast U.S. census region (52.4%). Mean CCI score (excluding T1DM and T2DM) of all patients was 0.3 (median=0.0) and two thirds of these patients had comorbid dyslipidemia/hypertriglyceridemia (62.3%) and hypertension (60.6%). The majority of these patients used all-cause prescription services (91.6%) and had ≥ 1 all-cause outpatient visit (98.4%) in the baseline period. Mean baseline all-cause and T2DM-related total health care costs were \$4,228 and \$550, respectively. Refer to Tables 1, 2, and 3 for additional details.

Effect of Weight Loss on All-Cause and T2DM-Related Costs and HCRU in the Short Term (6-Month Follow-up)

During the 6-month follow-up period (i.e., 13-18 months post-index), mean all-cause and T2DM-related total health

care costs of the study sample were \$5,043 (prescription services=\$1,578; ED costs=\$125; inpatient costs=\$1,011; outpatient costs=\$2,329) and \$1,211 (prescription services=\$471; ED costs=\$62; inpatient costs=\$3; outpatient costs=\$675), respectively (Table 3). After controlling for changes in time-varying covariates using SNMMs, weight loss was associated with significantly 6%-13% lower T2DM-related total health care costs (cost ratio [CR]=0.87-0.94; $P=0.0015$) among patients with 1.5%, 2.5%, and 3.5% weight loss in each of the 1- to 6-month and 7- to 12-month post-index periods, resulting in ~\$72, \$118, and \$162 in savings, respectively, versus no weight change. As expected, greater magnitude of weight loss resulted in greater savings. T2DM-related total health care costs were 18%-26% lower (CR=0.74-0.82; $P=0.0015$) among patients with weight loss versus weight gain (3%, 5%, and 7% weight loss resulted in ~\$224, \$264, and \$302 in savings, respectively vs. those who gained weight). Weight loss did not affect all-cause total health care costs or prescription, inpatient, ED, and outpatient costs in the short term (Table 4).

During the 6-month follow-up period, the majority of T2DM patients used prescription services (all-cause=95.7%; T2DM-related=74.1%) and had ≥ 1 outpatient visit (all-cause=97.2%; T2DM-related=84.5%; refer to Table 2 for additional details). After controlling for changes in time-varying confounders including A1c using SNMM, weight loss was associated with a significant effect on all-cause ED and outpatient visits in the short term. ED visits were 6%-14% higher among patients with 3%, 5%, and 7% weight loss (visit ratio [VR]=1.06-1.14; $P<0.05$) versus no weight change and 23% higher among patients with 7% weight loss (VR=1.23; $P=0.04$) versus weight gain in the 1- to 6-month post-index period. Outpatient visits in the short term were 5%-12% lower among patients with 3%, 5%, and 7% weight loss or a cumulative weight loss of 3%, 5%, and 7% at the end of the 7- to 12-month post-index period (VR=0.88-0.95; $P<0.05$) versus no weight change and 16%-23% lower among patients with weight loss (VR=0.77-0.84; $P<0.05$) versus weight gain. Weight loss did not affect all-cause inpatient visits in the short term (data not shown).

Effect of Weight Loss on Annual All-Cause and T2DM-Related Costs and HCRU in the Long Term

Mean all-cause and T2DM-related annual total health care costs of the study sample were \$10,589 (prescription services=\$3,277; ED costs=\$234; inpatient costs=\$2,439; outpatient costs=\$4,639) and \$2,450 (prescription services=\$998; ED costs=\$127; inpatient costs=\$23; outpatient costs=\$1,303), respectively (Table 3). After controlling for changes in time-varying confounders including A1c using SNMM, weight loss was associated with significantly lower all-cause and T2DM-related annual total health care costs. All-cause annual total health care costs were 5%-10% lower (CR=0.90-0.95; $P<0.05$) among patients with weight loss (resulting in ~\$500,

Effect of Weight Change on Economic Outcomes Among Persons with
Type 2 Diabetes Mellitus in the United States: Beyond Glycemic Control

FIGURE 1 Sample Selection and Resulting Patient Counts

A1c=hemoglobin A1c; BMI=body mass index; EMR=electronic medical record; ESRD=end-stage renal disease; GLP-1RA=glucagon-like peptide-1 receptor agonist; OAD=oral antidiabetic drug; T1DM=type 1 diabetes mellitus; T2DM=type 2 diabetes mellitus.

Effect of Weight Change on Economic Outcomes Among Persons with Type 2 Diabetes Mellitus in the United States: Beyond Glycemic Control

TABLE 1 Baseline Demographic and Clinical Characteristics of the Study Sample

Characteristics	Overall Sample (N = 1,407)	
Age at index date (years)		
Mean	55.2	
SD	9.3	
Median	56.0	
Gender (n, %)		
Male	777	55.2
Female	630	44.8
U.S. census region (n, %)		
Northeast	737	52.4
Midwest	297	21.1
South	293	20.8
West	80	5.7
Health plan type (n, %)		
Consumer-directed health plan	4	0.3
Health maintenance organization	266	18.9
Indemnity	68	4.8
Point-of-service	47	3.3
Preferred provider organization	1,022	72.6
Primary payer type (n, %)		
Commercial	660	46.9
Medicaid	1	0.1
Medicare Risk	18	1.3
Self-insured	728	51.7
Physician specialty at index (n, %)		
General practice/family practice	442	31.4
Internal medicine	344	24.4
Endocrinology	37	2.6
Other	481	34.2
Unknown	103	7.3
CCI score (excluding T1DM and T2DM)		
Mean	0.3	
SD	0.7	
Median	0.0	
Adapted Diabetes Complications Severity Index score		
Mean	0.4	
SD	0.9	
Median	0.0	

Characteristics	Overall Sample (N = 1,407)	
Comorbidities of interest (n, %) ^a		
Dyslipidemia, hypertriglyceridemia	877	62.3
Gastroesophageal reflux disease	144	10.2
Hypertension	853	60.6
Obesity	202	14.4
Obstructive sleep apnea	170	12.1
Prediabetes	382	27.1
Sleep apnea	179	12.7
Concomitant medications (n, %)		
Antihypertensive medications	772	54.9
Lipid-lowering therapy	744	52.9
Other cardiovascular medications	128	9.1
Sedatives, hypnotics	115	8.2
Antibiotics	440	31.3
NSAIDs	227	16.1
Neuropathy treatment	326	23.2
Anti-obesity	5	0.4
Number of pre-index antidiabetic classes used		
Mean	0.7	
SD	1.0	
Median	0.0	
BMI (kg/m ²)		
Mean	35.0	
SD	6.7	
Median	34.2	
Weight (kg)		
Mean	102.2	
SD	22.9	
Median	99.7	
A1c (%)		
Mean	7.4	
SD	1.6	
Median	6.9	
A1c, n (%)		
<6.0%	112	8.0
6.0%-6.9%	611	43.4
7.0%-7.9%	378	26.9
8.0%-9.0%	135	9.6
>9.0%	171	12.2

^aList of comorbidities: anorexia; asthma; cachexia; chronic kidney disease and related renal conditions; chronic nonalcoholic liver disease (includes nonalcoholic liver disease and nonalcoholic steatohepatitis); congestive heart failure; connective tissue/rheumatic disease; chronic obstructive pulmonary disease; Cushing syndrome; depression; diabetes with other coma; dyslipidemia and hypertriglyceridemia; dyspepsia; epilepsy; gallbladder disease; gastroesophageal reflux disease; human immunodeficiency virus/acquired immunodeficiency syndrome; hypertension; hypoglycemia; inflammatory bowel diseases (Crohn's disease or ulcerative colitis); liver disease; metabolic syndrome; myocardial infarction; nutritional deficiencies (except for vitamin deficiency); obesity; obesity hypoventilation syndrome; obstructive sleep apnea; osteoarthritis; osteoporosis; peptic ulcer; pneumonia; Prader-Willi syndrome; prediabetes; renal disease; severe psychiatric disorder (schizophrenia, other psychotic disorder, or bipolar disorder); sleep apnea; and stroke.

A1c = hemoglobin A1c; BMI = body mass index; CCI = Charlson Comorbidity Index; NSAID = nonsteroidal anti-inflammatory drug; SD = standard deviation; T1DM = type 1 diabetes mellitus; T2DM = type 2 diabetes mellitus.

\$800, and \$1,100 in savings, respectively) versus no weight change. Greater magnitude of weight loss resulted in greater savings. All-cause annual total health care costs were 15%-20% lower (CR=0.80-0.85; $P<0.05$) among patients with weight loss versus weight gain (resulting in up to ~\$2,000 in savings).

Differences in annual all-cause total health care costs can be attributed to differences in all-cause outpatient costs, which were significantly lower among patients with weight loss versus no weight change and among patients with weight loss versus weight gain. T2DM-related annual total costs were 7%-19%

**Effect of Weight Change on Economic Outcomes Among Persons with
Type 2 Diabetes Mellitus in the United States: Beyond Glycemic Control**

TABLE 2 All-Cause and T2DM-Related HCRU of the Study Sample

Characteristics	Baseline (N = 1,407)		Evaluation Period				Outcomes Measurement Period			
			1-6 Months Post-Index (N = 1,407)		7-12 Months Post-Index (N = 1,407)		13-18 Months Post-Index (N = 1,407)		13-24 Months Post-Index (N = 1,407)	
All-cause visits/services used										
Pharmacy (including all pharmacy prescriptions and infusion administrations)										
Patients with pharmacy scripts (n, %)	1,289	91.6	1,346	95.7	1,342	95.4	1,346	95.7	1,364	96.9
Mean	15.6		19.4		18.6		18.4		37.0	
SD	14.0		14.6		14.7		14.2		27.7	
Median	12.0		16.0		15.0		15.0		30.0	
ED visits										
Patients with visits (n, %)	135	9.6	168	11.9	153	10.9	120	8.5	218	15.5
Mean	0.1		0.2		0.1		0.1		0.2	
SD	0.4		0.5		0.5		0.4		0.6	
Median	0.0		0.0		0.0		0.0		0.0	
Inpatient visits										
Patients with visits (n, %)	50	3.6	81	5.8	47	3.3	51	3.6	98	7.0
Mean	0.0		0.1		0.0		0.0		0.1	
SD	0.2		0.3		0.3		0.3		0.4	
Median	0.0		0.0		0.0		0.0		0.0	
Average length of stay among patients with inpatient visits										
Mean	3.2		3.7		3.6		3.7		3.6	
SD	1.7		2.3		2.9		1.8		2.4	
Median	3.0		3.0		2.0		3.0		3.0	
Outpatient visits										
Patients with visits (n, %)	1,385	98.4	1,405	99.9	1,400	99.5	1,368	97.2	1,398	99.4
Mean	21.3		25.3		22.6		20.5		41.0	
SD	18.2		20.2		19.4		19.3		33.4	
Median	16.0		20.0		17.0		15.0		32.0	
T2DM-related visits/services used										
Pharmacy (including all pharmacy prescriptions and infusion administrations)										
Patients with pharmacy scripts (n, %)	706	50.2	1,096	77.9	1,041	74.0	1,043	74.1	1,111	79.0
Mean	2.5		4.8		4.2		4.1		8.2	
SD	4.2		4.8		4.5		4.4		8.5	
Median	1.0		4.0		3.0		3.0		6.0	
ED visits										
Patients with visits (n, %)	23	1.6	81	5.8	84	6.0	50	3.6	95	6.8
Mean	0.0		0.1		0.1		0.0		0.1	
SD	0.2		0.3		0.3		0.3		0.4	
Median	0.0		0.0		0.0		0.0		0.0	
Inpatient visits										
Patients with visits (n, %)	3	0.2	11	0.8	8	0.6	8	0.6	13	0.9
Mean	0.0		0.0		0.0		0.0		0.0	
SD	0.0		0.1		0.1		0.1		0.1	
Median	0.0		0.0		0.0		0.0		0.0	
Average length of stay among patients with inpatient visits										
Mean	2.7		4.0		2.0		4.6		3.3	
SD	2.9		4.5		1.1		3.3		3.1	
Median	1.0		3.0		2.0		3.5		2.0	
Outpatient visits										
Patients with visits (n, %)	518	36.8	1,393	99.0	1,299	92.3	1,189	84.5	1,309	93.0
Mean	3.4		11.3		8.7		7.6		15.1	
SD	6.4		8.3		7.5		7.5		12.4	
Median	0.0		10.0		7.0		6.0		14.0	

ED = emergency department; SD = standard deviation; T2DM = type 2 diabetes mellitus.

TABLE 3 All-Cause and T2DM-Related Costs of the Study Sample

Costs, \$	Baseline			Evaluation Period						Outcomes Measurement Period					
				1-6 Months Post-Index			7-12 Months Post-Index			13-18 Months Post-Index			13-24 Months Post-Index		
	Mean	Median	SD	Mean	Median	SD	Mean	Median	SD	Mean	Median	SD	Mean	Median	SD
All-cause costs															
Total costs	4,228	2,067	7,829	5,990	2,664	12,059	4,974	2,280	11,379	5,043	2,305	10,320	10,589	5,239	26,341
Prescription costs	1,307	613	2,827	1,596	823	3,830	1,592	850	3,449	1,578	815	3,359	3,277	1,713	6,603
ED costs	90	0	481	152	0	719	114	0	608	125	0	786	234	0	1,124
Inpatient costs	760	0	5,094	1,481	0	8,382	919	0	7,178	1,011	0	6,691	2,439	0	22,971
Outpatient costs	2,071	939	3,585	2,761	1,326	4,700	2,349	1,002	5,194	2,329	958	5,172	4,639	2,359	7,379
T2DM-related costs															
Total costs	550	10	2,119	1,498	783	2,856	1,251	495	3,941	1,211	472	3,878	2,450	1,004	4,998
Prescription costs	267	0	642	433	105	769	456	55	971	471	51	915	998	133	1,925
ED costs	16	0	175	80	0	565	58	0	429	62	0	647	127	0	938
Inpatient costs	5	0	162	10	0	274	1	0	19	3	0	43	23	0	726
Outpatient costs	262	0	1,781	976	501	2,558	737	312	3,669	675	287	3,629	1,303	614	4,063

ED=emergency department; SD=standard deviation; T2DM=type 2 diabetes mellitus.

lower (CR=0.81-0.93; $P<0.05$) among patients with weight loss (resulting in ~\$200, 300, and \$400 in savings, respectively) versus no weight change. A greater magnitude of weight loss resulted in greater savings: T2DM-related annual total costs were 23%-33% lower (CR=0.67-0.77; $P<0.05$) among patients with weight loss versus weight gain (resulting in up to ~\$800 savings). Weight loss did not affect all-cause prescription, inpatient, and ED costs in the long term. Overall, weight loss in T2DM resulted in significant reductions in all-cause and T2DM-related annual total health care costs, irrespective of the pattern in which weight loss occurred (Table 4).

During the 12-month follow-up period, the majority of T2DM patients used prescription services (all-cause=96.9%; T2DM-related=79.0%) and had ≥ 1 annual outpatient visit (all-cause=99.4%; T2DM-related=93.0%). Refer to Table 2 for additional details. After controlling for changes in time-varying confounders including A1c using SNMMs, weight loss did not affect annual all-cause inpatient and ED visits. However, annual all-cause outpatient visits were 5%-13% lower (VR=0.87-0.95; $P<0.05$) among patients with weight loss versus no weight change and 16%-23% lower (VR=0.77-0.84; $P<0.05$) among patients with weight loss versus weight gain (data not shown).

Discussion

In this study, controlling for time-varying covariates resulted in significant reductions in all-cause and T2DM-related annual total health care costs, irrespective of weight loss pattern. Also, weight loss significantly decreased T2DM-related total health care costs in the short term. Previous studies, such as retrospective database analysis by Bell et al. (2014), evaluated the effect of weight change (weight loss $>3\%$ or weight gain $>3\%$ vs. weight neutral [change $\leq 3\%$]) among 2,110 T2DM patients in the first 6 months after initiating noninsulin antidiabetic medication on health care costs incurred in the following 12

months.²² That study reported that the weight-loss cohort, compared with the weight-neutral cohort, had significantly lower annual all-cause (\$2,200) and T2DM-related total costs (\$440; $P<0.05$ for both), and weight gain was found to be associated with significantly higher (\$3,400) all-cause annual total costs.²² Mukherjee et al. (2016) reported that a decrease in weight change over a 6-month period was associated with lower T2DM-related costs ($P=0.039$) over the subsequent 12-month period.²⁵ Yu et al. (2007) conducted a retrospective cohort study using health maintenance organization data on 458 T2DM patients from 1997-2005 and reported that every 1 percentage point of weight loss over a 6-month period was associated with a 3.6% decrease in all-cause total costs (\$256; $P<0.05$) and a 5.8% decrease (\$131; $P<0.01$) in T2DM-related total costs in the subsequent 12-month period.²⁸ Findings from this current study are, therefore, consistent with previous evidence linking weight loss among T2DM patients with significant savings in health care costs and reduced resource use. Additionally, in this study, the effect of weight loss was assessed after adjusting for changes in A1c to evaluate the incremental effect of weight loss. To our knowledge, this is the first study to determine the savings in health care costs and reduced resource use attributable to weight loss, beyond achieving glycemic control.

We observed consistent results as previous U.S.-based studies even though the patients were at different stages in their treatment pathway. For example, Bell et al. only included patients receiving noninsulin antidiabetic medications, and Mukherjee et al. only included patients who added to or switched from metformin monotherapy—where both populations were possibly earlier in the disease course, before complications occurred—whereas our study included patients receiving any antidiabetic medication class (OADs, GLP-1RAs, or insulin) without any medication washout period, thus,

Effect of Weight Change on Economic Outcomes Among Persons with Type 2 Diabetes Mellitus in the United States: Beyond Glycemic Control

TABLE 4 Effect of Weight Loss on Health Care Costs

	Weight Loss Pattern		Short-Term T2DM-Related Total Costs (6 Months Follow-up)		Long-Term T2DM-Related Total Costs (12 Months Follow-up)		Long-Term All-Cause Outpatient Costs (12 Months Follow-up)		Long-Term All-Cause Total Costs (12 Months Follow-up)	
	1-6 Months %	7-12 Months %	Savings per Patient vs. No Weight Change, \$	Savings per Patient vs. Weight Gain ^a , \$	Savings per Patient vs. No Weight Change, \$	Savings per Patient vs. Weight Gain ^a , \$	Savings per Patient vs. No Weight Change, \$	Savings per Patient vs. Weight Gain ^a , \$	Savings per Patient vs. No Weight Change, \$	Savings per Patient vs. Weight Gain ^a , \$
3% weight loss	3	0	81.30	232.50 ^b	215.53 ^b	597.55 ^b	187.28	656.82 ^b	486.54 ^b	1,539.44 ^b
	0	3	63.29	216.91 ^b	162.48 ^b	553.56 ^b	245.32 ^b	708.74 ^b	489.23 ^b	1,541.85 ^b
	1.5	1.5	72.33 ^b	224.74 ^b	189.16 ^b	575.69 ^b	216.39 ^b	682.87 ^b	487.88 ^b	1,540.65 ^b
5% weight loss	5	0	132.44	276.80 ^b	348.59 ^b	707.86 ^b	307.91	764.73 ^b	798.41 ^b	1,818.81 ^b
	0	5	103.63	251.85 ^b	264.76 ^b	638.36 ^b	401.61 ^b	848.55 ^b	802.76 ^b	1,822.71 ^b
	2.5	2.5	118.13 ^b	264.41 ^b	307.08 ^b	673.45 ^b	355.02 ^b	806.87 ^b	800.59 ^b	1,820.76 ^b
7% weight loss	7	0	181.27	319.09 ^b	473.72 ^b	811.60 ^b	425.27	869.71 ^b	1,100.66 ^b	2,089.56 ^b
	0	7	142.56	285.56 ^b	362.48 ^b	719.38 ^b	552.35 ^b	983.39 ^b	1,106.56 ^b	2,094.85 ^b
	3.5	3.5	162.09 ^b	302.48 ^b	418.86 ^b	766.12 ^b	489.30 ^b	926.99 ^b	1,103.61 ^b	2,092.20 ^b

Note: Only significant findings were included in this table. Costs calculated as: Mean total cost–(cost ratio in the SNMM × mean total cost).

^aThose who gained 3.5% in 1-6 months and gained another 3.5% in 7-12 months post-index.

^bP<0.05.

SNMM = structural nested mean model; T2DM = type 2 diabetes mellitus.

analyzing a more heterogeneous and more advanced T2DM population.^{22,25}

In addition, all-cause annual outpatient visits and costs were significantly lower among patients with weight loss versus those with no weight change or weight gain. Lower A1c levels and better control of cardiovascular risk factors and diabetes-related comorbidities and complications among patients with weight loss may decrease the need for physicians to closely monitor these patients, thereby decreasing outpatient health care utilization and costs.^{18,25} An unexpected finding from our study was that ED visits in the short term were significantly higher among patients with weight loss compared with no weight change and weight gain. T2DM patients with obesity and hypertension are reported to have significantly more ED visits compared with those with T2DM alone.³³

Finally, irrespective of the timing or pattern in which weight loss occurred over the study period, losing weight was associated with significant reductions in all-cause and T2DM-related annual total health care costs.

Our study adds to the current body of literature and further strengthens the importance of weight loss and maintenance of weight loss in management of patients with T2DM beyond glycemic improvements vis-à-vis A1c lowering. Because our study quantifies the benefits associated with weight loss, findings can help health care decision makers with cost-containment strategies that incorporate more than drug acquisition factors. Guidelines recommend intensive intervention programs and frequent follow-up for weight reduction among T2DM patients who are overweight and obese.^{6,12} However, more than 80% of patients with T2DM continue to be overweight or obese.¹ There

is clearly an unmet need for weight management among T2DM patients. Although intensive programs may help achieve weight loss goals in clinical trials, it is difficult to adhere to and deliver these programs in the real world.^{34,35} Per American Association of Clinical Endocrinologists guidelines, adding medication to lifestyle change for chronic weight loss should be considered among patients who are unable to lose weight or maintain their weight loss using diet and exercise alone.^{12,34}

Our study findings also have clinical implications. Although A1c control is often the primary therapeutic goal for patients with T2DM, there is a need to recognize the importance of avoiding medication-related weight gain among these patients and overall cardiovascular risk reduction.¹² As different anti-diabetic medications have different weight change profiles, previous studies and guidelines suggest that physicians should individualize medication therapy based on each patient's weight loss goals, consider the effect of antidiabetic agents on weight (in addition to clinical effectiveness) among patients receiving combination therapy, and opt for weight-neutral medications if possible.^{4,6,12,35,36} This may also potentially affect medication adherence, per previous evidence that T2DM patients who lose weight on a treatment regimen are more likely to adhere to their regimen compared with patients who gain weight with their medication.¹⁵ According to our study, even a modest weight loss (3%) can result in significantly lower annual all-cause and T2DM-related health care costs. Focusing on weight loss early in the disease progression pathway may enable patients to reap advantages from early lines of therapy that provide good A1c control in addition to weight loss benefits.²⁵

Limitations

The results of this study should be viewed in the context of potential limitations. First, claims and EMR databases are not primarily designed for research purposes. Internal validity is typically not good enough to infer causality due to the lack of randomization and to make a strong conclusion regarding whether measurable or unmeasurable factors affect the outcomes of interest. External validity is not high due to the fact that the study employs small samples and may not be generalizable to the other populations like uninsured patients.

Second, the analytic focus of this study was on patients who met continuous observation criteria (180 days pre-index and 720 days post-index), with a potential to eliminate subjects who may have had different weight change patterns coincident with observation patterns. Also, patients with >15% weight loss for any 6-month period or with >25% weight loss for 12-month cumulative period were excluded from this study, which is possible among patients with very low-calorie diets. This may influence generalizability of the study findings to this unique group of patients.

Third, because of the time-varying nature of weight, for patients with >1 weight measurement in both 6-month periods, the measurement closest to the end of the time interval was considered the post-index weight instead of the average weight. Also, data entry errors may exist at the site of care, contributing to survey bias. The reverse trend was observed in ED visits, where a higher percentage of visits with weight loss versus no weight change or weight gain can be because of the low sample size of patients with these visits.

Finally, this study could only evaluate a few patterns of weight change, and other weight change patterns may have a different effect on annual health care costs and HCRU.

Conclusions

Weight loss among patients with T2DM resulted in significant reductions in all-cause and T2DM-related annual total health care costs compared with no weight change or weight gain, irrespective of weight loss pattern. Greater weight loss resulted in greater cost savings. This study helps link weight loss to outcomes that matter to health care decision makers and will help reinforce the value of weight loss in T2DM. Future research should evaluate the effect of weight loss, beyond glycemic control, on economic outcomes using longer follow-up periods.

Authors

SWAPNA KARKARE, MS; JINGSONG LU, MS; and MITCH DEKOVEN, MHSA, IQVIA, Real World Insights, Falls Church, Virginia. MOSHE FRIDMAN, PhD, AMF Consulting, Los Angeles, California. TAM DANG-TAN, PhD; B. GABRIEL SMOLARZ, MD, MS, FACE; and NEERAJ N. IYER, PhD, Novo Nordisk, Plainsboro, New Jersey.

AUTHOR CORRESPONDENCE: Neeraj N. Iyer, PhD, Director, Value Evidence & Outcomes, Clinical, Medical & Regulatory Affairs, Novo Nordisk, 800 Scudders Mill Rd., Plainsboro, NJ 08536. Tel.: 609.786.4899; E-mail: nriy@novonordisk.com.

DISCLOSURES

This study was funded by Novo Nordisk. Dang-Tan, Smolarz, and Iyer are employees of Novo Nordisk. Karkare and DeKoven (employees of IQVIA) and Fridman (employed by AMF Consulting) were contracted by Novo Nordisk to conduct this study. Fridman also reports personal fees from Shire, GSK, and CSL Behring, outside of the submitted work. Lu, an employee of IQVIA, accessed the database and conducted the statistical analysis for this study.

REFERENCES

1. National Center for Chronic Disease Prevention and Health Promotion, Division of Diabetes Translation. National diabetes statistics report, 2017. Centers for Disease Control and Prevention. Available at: <https://www.cdc.gov/diabetes/pdfs/data/statistics/national-diabetes-statistics-report.pdf>. Accessed January 13, 2019.
2. American Diabetes Association. Economic costs of diabetes in the U.S. in 2017. *Diabetes Care*. 2018;41(5):917-28.
3. American Diabetes Association. Improving care and promoting health in populations: standards of medical care in diabetes-2018. *Diabetes Care*. 2018;41(Suppl 1):S7-S12.
4. American Diabetes Association. Economic costs of diabetes in the U.S. in 2012. *Diabetes Care*. 2013;36(4):1033-46.
5. Inzucchi SE, Bergenstal RM, Buse JB, et al. Management of hyperglycemia in type 2 diabetes, 2015: a patient-centered approach: update to a position statement of the American Diabetes Association and the European Association for the Study of Diabetes. *Diabetes Care*. 2015;38:140-49.
6. Centers for Disease Control and Prevention. Prevalence of overweight and obesity among adults with diagnosed diabetes—United States 1988-1994 and 1999-2002. *Morbid Mortal Wkly Rep*. 2004;53(45):1066-68. Available at: <https://www.cdc.gov/mmwr/preview/mmwrhtml/mm5345a2.htm>. Accessed January 13, 2019.
7. Anderson JW, Kendall CW, Jenkins DJ. Importance of weight management in type 2 diabetes: review with meta-analysis of clinical studies. *J Am Coll Nutr*. 2003;2:331-39.
8. American Diabetes Association. Standards of medical care for patients with diabetes mellitus. *Diabetes Care*. 2003;26(Suppl 1):S33-S50.
9. Van Gaal LF, Mertens IL, De Block CE. Mechanisms linking obesity with cardiovascular disease. *Nature*. 2006;444:875-80.
10. Franz MJ, Boucher JL, Rutten-Ramos S, VanWormer JJ. Lifestyle weight-loss intervention outcomes in overweight and obese adults with type 2 diabetes: a systematic review and meta-analysis of randomized clinical trials. *J Acad Nutr Diet*. 2015;115(9):1447-63.
11. American Diabetes Association, Bantle JP, Wylie-Rosett J, et al. Nutrition recommendations and interventions for diabetes: a position statement of the American Diabetes Association. *Diabetes Care*. 2008;31(Suppl 1):S61-78.
12. Garber AJ, Abrahamson MJ, Barzilay JI, Blonde L et al. Consensus statement by the American Association of Clinical Endocrinologists and American College of Endocrinology on the comprehensive type 2 diabetes management algorithm—2018 executive summary. *Endocr Pract*. 2018;24(1):91-120.
13. Wing RR, Lang W, Wadden TA, et al. Benefits of modest weight loss in improving cardiovascular risk factors in overweight and obese individuals with type 2 diabetes. *Diabetes Care*. 2011;34(7):1481-86.
14. Feldstein AC, Nichols GA, Smith DH et al. Weight change in diabetes and glycemic and blood pressure control. *Diabetes Care*. 2008;31:1960-65.
15. Grandy S, Fox KM, Hardy E; SHIELD Study Group. Association of weight loss and medication adherence among adults with type 2 diabetes mellitus: SHIELD (Study to Help Improve Early evaluation and management of risk factors Leading to Diabetes). *Curr Ther Res Clin Exp*. 2013;75:77-82.
16. Look AHEAD Research Group; Wing RR. Long-term effects of a lifestyle intervention on weight and cardiovascular risk factors in individuals with type 2 diabetes mellitus: four-year results of the Look AHEAD trial. *Arch Intern Med*. 2010;170:1566-75.
17. Ryan DH, Yockey SR. Weight loss and improvement in comorbidity: differences at 5%, 10%, 15%, and over. *Curr Obes Rep*. 2017;6(2):187-94.

Effect of Weight Change on Economic Outcomes Among Persons with Type 2 Diabetes Mellitus in the United States: Beyond Glycemic Control

18. Ross SA, Dzida G, Vora J, Khunti K, Kaiser M, Ligthelm RJ. Impact of weight gain on outcomes in type 2 diabetes. *Curr Med Res Opin.* 2011;27(7):1431-38.
19. Wilding JPH. The importance of weight management in type 2 diabetes mellitus. *Int J Clin Pract.* 2014;68(6):682-91.
20. Williamson DF, Thompson TJ, Thun M, Flanders D, Pamuk E, Byers T. Intentional weight loss and mortality among overweight individuals with diabetes. *Diabetes Care.* 2000;23(10):1499-504.
21. Blak BT, Rigney U, Sternhufvud C, Davis J, Hammar N. Weight change and health care resource use in English patients with type 2 diabetes mellitus initiating a new diabetes medication class. *Int J Clin Pract.* 2016;70:45-55.
22. Bell K, Parasuraman S, Shah M, et al. Economic implications of weight change in patients with type 2 diabetes mellitus. *Am J Manag Care.* 2014;20:e320-e9.
23. Dilla T, Valladares A, Nicolay C, Salvador J, Reviriego J, Costi M. Healthcare costs associated with change in body mass index in patients with type 2 diabetes mellitus in Spain: the ECOBIM study. *Appl Health Econ Health Policy.* 2012;10(6):417-30.
24. Davis WA, Bruce DG, Davis TME. Economic impact of moderate weight loss in patients with type 2 diabetes: the Fremantle Diabetes Study. *Diabet Med.* 2011;28:1131-35.
25. Mukherjee J, Sternhufvud C, Smith N, et al. Association between weight change, clinical outcomes, and health care costs in patients with type 2 diabetes. *J Managed Care Specialty Pharm.* 2016;22(5):449-66. Available at: <https://www.jmcp.org/doi/10.18553/jmcp.2016.22.5.449>.
26. Nichols GA, Bell K, Kimes TM, O'Keeffe-Rosetti M. Medical care costs associated with long-term weight maintenance versus weight gain among patients with type 2 diabetes. *Diabetes Care.* 2016;39(11):1981-86.
27. Sabale U, Bodegard J, Svennblad B, et al. Weight change patterns and health care costs in patients with newly-diagnosed type-2 diabetes in Sweden. *Prim Care Diabetes.* 2017;11(3):217-25.
28. Yu AP, Wu EQ, Birnbaum HG, et al. Short-term economic impact of body weight change among patients with type 2 diabetes treated with anti-diabetic agents: analysis using claims, laboratory, and medical record data. *Curr Med Res Opin.* 2007;23(9):2157-69.
29. DerSarkissian M, Bhak RH, Huang J, et al. Maintenance of weight loss or stability in subjects with obesity: a retrospective longitudinal analysis of a real-world population. *Curr Med Res Opin.* 2017;33(6):1105-10.
30. Romano PS, Roos LL, Jollis JG. Adapting a clinical comorbidity index for use with ICD-9-CM administrative data: differing perspectives. *J Clin Epidemiol.* 1993;46(10):1075-79.
31. Chang HY, Weiner JP, Richards TM, Bleich SN, Segal JB. Validating the adapted Diabetes Complications Severity Index in claims data. *Am J Manag Care.* 2012;18(11):721-26.
32. Almirall D, Ten Have T, Murphy SA. Structural nested mean models for assessing time-varying effect moderation. *Biometrics.* 2009;66(1):131-39.
33. Green AJ, Bazata DD, Fox KM, Grandy S. Quality of life, depression, and healthcare resource utilization among adults with type 2 diabetes mellitus and concomitant hypertension and obesity: a prospective survey. *Cardiol Res Pract.* 2012;2012:404107.
34. Anderson DA, Wadden TA. Treating the obese patient. Suggestions for primary care practice. *Arch Fam Med.* 1999;8(2):156-67.
35. Van Gaal L, Scheen A. Weight management in type 2 diabetes: current and emerging approaches to treatment. *Diabetes Care.* 2015;38(6):1161-72.
36. Carls GS, Tan R, Zhu JY. Real-world weight change among patients treated with glucagon-like peptide-1 receptor agonist, dipeptidyl peptidase-4 inhibitor and sulfonylureas for type 2 diabetes and the influence of medication adherence. *Obes Sci Pract.* 2017;3(3):342-51.

APPENDIX Study Time Period

A1c = hemoglobin A1c; HCRU = health care resource utilization.