Initiating Injectable Therapy in US Managed Care Patients With Diabetes Mellitus

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Type 2 diabetes mellitus (T2DM) is a progressive disease resulting from deficient insulin production or insulin resistance.[1] Throughout treatment, achieving targets of glycemic control is of paramount importance for decreasing the risk of short- and long-term complications.[2] As T2DM progresses, if monotherapy does not achieve target glycated hemoglobin A1c (A1C), a second agent should be added to the treatment regimen. This agent may be a second oral antidiabetic drug (OAD), a glucagon-like peptide 1 (GLP-1) receptor agonist, or basal insulin.[3] GLP-1 receptor agonists stimulate the secretion of insulin in a glucose-dependent manner.[4]

The 26-week LEAD-5 met+SU randomized controlled trial compared the efficacy and safety of open-label GLP-1 receptor agonists liraglutide with the efficacy and safety of insulin glargine and liraglutide placebo in patients with T2DM. All 3 interventions were prescribed as once-daily subcutaneous injections and in combination with metformin and glimepiride. Study data showed that once-daily treatment with liraglutide had a greater A1C-reducing effect than insulin glargine and also had a beneficial effect on patients' body weight and systolic blood pressure. The proportions of patients with hypoglycemia were similar in the liraglutide and insulin glargine groups, whereas liraglutide users were more likely than insulin glargine users to report gastrointestinal adverse events.[5] However, there is a need to supplement the data from randomized controlled clinical studies—which have relatively small cohorts of patients with predefined characteristics and study durations that may be too short to detect small or cumulative effects—with data from T2DM patients using liraglutide and insulin glargine in real-world practice settings. Currently, there are limited data assessing how these injectable treatments are being used in real-world settings and what the cost implications for either treatment option are.

The aims of the current study were 2-fold. First, we planned to examine treatment patterns—defined as a descriptive comparison of patient clinical characteristics, healthcare

ABSTRACT

Objective: To examine treatment patterns and outcomes of initiation of injectable pen therapy with either insulin glargine or liraglutide, and to evaluate comparative effectiveness.

Study Design: Retrospective analysis of information from the national managed care IMPACT database. Adults with type 2 diabetes mellitus initiating injectable pen therapy with insulin glargine or liraglutide were evaluated.

Methods: Clinical and economic measures were compared between cohorts at baseline and over 1 year. Those patients with poor glycemic control (glycated hemoglobin target glycated A1c (A1c) ≥7.0%) were matched using propensity score matching for comparative effectiveness analysis.

Results: A total of 1574 patients were identified; 756 and 818 initiated therapy with insulin glargine and liraglutide, respectively. There were significant differences in demographics and clinical characteristics at baseline; insulin glargine initiators were sicker, had longer hospitalizations, had a higher mean A1C (9.7% vs 7.9%; P <.0001), and had higher baseline costs. In patients who had poorer glycemic control, 698 with comparable baseline characteristics were matched. During 1-year follow-up of this subset, there was little difference in utilizations and clinical outcomes between cohorts. However, compared with liraglutide initiators, insulin glargine initiators had significantly lower diabetes-related pharmacy costs ($2832 vs $4027; P <.0001) and total diabetes-related costs ($5305 vs $7501; P = .0005).

Conclusions: Significant real-world differences, particularly in A1C level, existed at baseline between those initiating injectable therapy with insulin glargine versus liraglutide. The matched-cohort analysis suggests that the use of the insulin glargine pen was associated with clinical outcomes similar to those with liraglutide, but with lower diabetes-related costs.

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PRACTICAL IMPLICATIONS

There are limited real-world data to assess the use of the injectable therapies insulin glargine and liraglutide in type 2 diabetes mellitus patients.

- At baseline there were significant differences in clinical and demographic characteristics between patients initiating therapy with insulin glargine versus liraglutide.
- Comparative effectiveness analysis in matched patients with inadequate glycemic control showed that patients in both cohorts had similar clinical outcomes, but insulin glargine patients had lower diabetes-related costs.
- These results highlight variation in real-world prescribing of injectable therapies for type 2 diabetes, and the challenges this poses to comparative effectiveness studies.

utilization, and costs—associated with initiation of injectable pen therapy with either insulin glargine pen (SoloSTAR) or liraglutide (Victoza) in injectable-naive T2DM patients. Second, we aimed to evaluate the comparative effectiveness of insulin glargine and liraglutide with respect to clinical and economic outcomes among those initiators who previously did not achieve glycemic control using OADs. Data were obtained from a large US managed care healthcare claims database.

METHODS

Study Design and Patients

This was a retrospective analysis of data from the IMPACT national managed care database. The IMPACT database is an administrative insurance claims database that comprises approximately 50 US healthcare plans and contains medical claims, pharmacy claims, eligibility data, and laboratory results for 107 million patients, of whom 73% had pharmacy benefits and 18% had laboratory results (**Figure 1**).

Patients were included in the analysis if they were 18 years or older with a diagnosis of T2DM, defined as having 1 or more inpatient visits or 2 or more physician visits (≥30 days apart) with a primary or secondary diagnosis of T2DM (*International Classification of Diseases, 9th Revision, Clinical Modification* [*ICD-9-CM*] codes 250.x0 or 250.x2). Included patients also initiated either insulin glargine or liraglutide by pen device between January 2010 and September 2010; had continuous medical and prescription drug coverage for 6 months prior to the initiation date of injectable therapy (the baseline period) and for 1 year after initiation (follow-up); had A1C data at baseline; and were injectable-naïve and receiving at least 1 OAD at baseline. An exclusion criterion was initiation of insulin glargine by both pen and vial and syringe on the same day.

Those identified from the treatment pattern analysis whose baseline A1C was 7.0% or greater were also included in a comparative effectiveness analysis of patients with inadequate glycemic control.

Baseline Measures

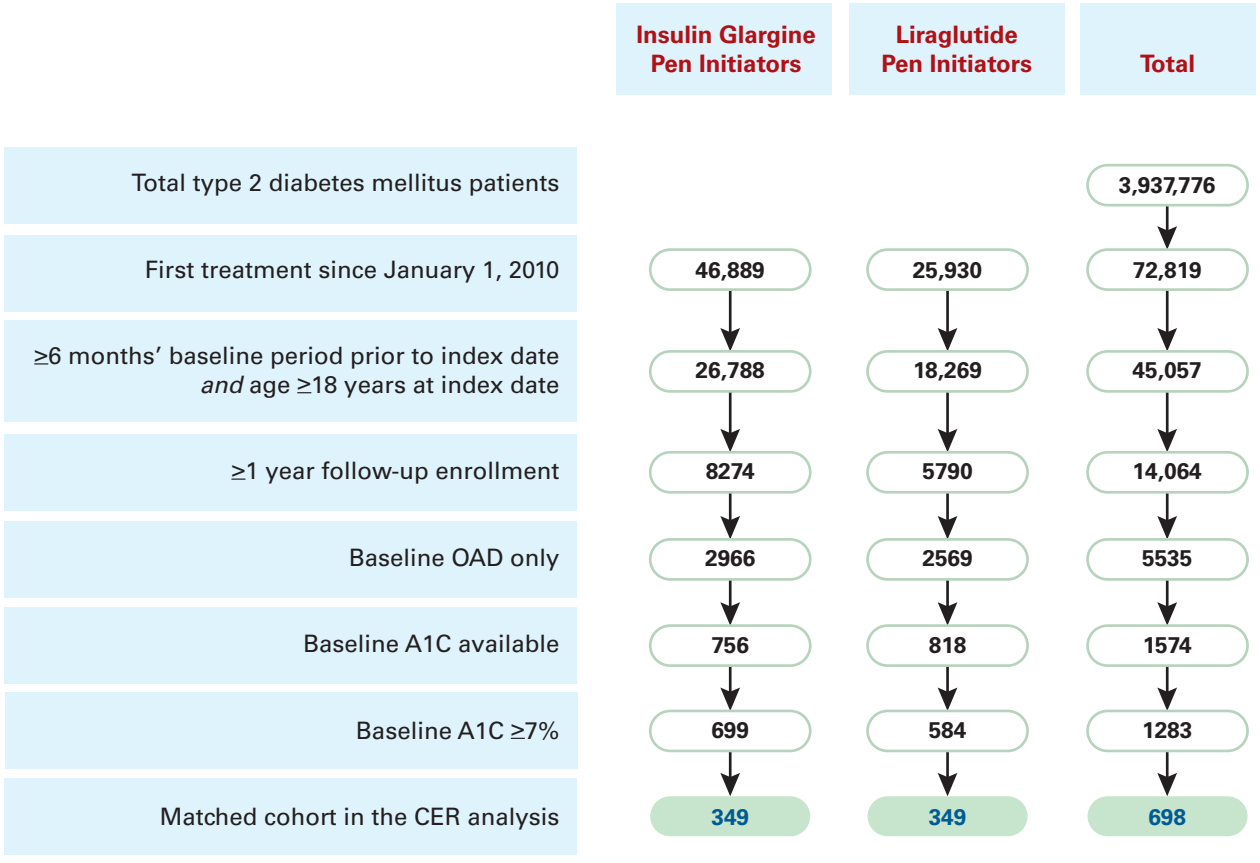
Patient demographics included sex, age group, and age at initiation of injectable therapy. Clinical variables consisted of comorbidities, Charlson Comorbidity Index score, prescription drug usage, and laboratory test results, when available, for the 6-month baseline period.

Healthcare resource utilizations were described and included outpatient visits, emergency department (ED) visits, inpatient admissions, inpatient length of stay, and endocrinologist visits in the 6-month baseline period. Diabetes-related healthcare resource utilization included claims with a primary or secondary diagnosis of diabetes (*ICD-9-CM* 250.xx). Healthcare costs were computed as plan-paid amounts of adjudicated claims in the 6-month baseline period. Diabetes-related healthcare costs included costs from medical claims with a primary or secondary diagnosis of diabetes (*ICD-9-CM* 250.xx), antidiabetic medications, glucose meters, and test strips.

End Point Measures

Clinical outcomes included A1C at 1-year follow-up, A1C change from baseline at 1-year follow up, and treatment persistence. Based on previously published studies, an empirical approach was used to estimate treatment persistence using 2 measures: 1-year follow-up treatment persistence as a dichotomous measure and treatment persistence days within 1-year follow-up as a continuous measure.[6-9] During the 1-year follow-up from initiation, patients were considered persistent with treatment if they remained on therapy without discontinuation or switching. Study medication was considered discontinued if the prescription was not refilled within the expected time of medication coverage (the 90th percentile of the time, stratified by the metric quantity supplied, between first and second fills among patients with at least 1 refill). Patients who restarted their initial medication after a period without it during follow-up were considered nonpersistent. Treatment persistence days were defined as the number of days from the initiation until discontinuation/switching. Sensitivity analyses were also conducted using the 75th and 95th percentiles of the time. The daily average consumption (DACON) was calculated as the total amount of medication (units or milligrams)

Figure 1. IMPACT Database: Attrition of Patient Population Investigated During the Study Period January 1, 2009, to September 30, 2011



A1C indicates glycated hemoglobin; CER, comparative effectiveness research; OAD, oral antidiabetic drug.

dispensed before the last refill of study drug, divided by the total number of days between initiation and the last refill during the follow-up. Hypoglycemia was defined as a healthcare encounter (outpatient, inpatient, or ED visit) with a primary or secondary *ICD-9-CM* diagnosis code for hypoglycemia (*ICD-9* code 250.8–diabetes with other specified manifestations, 251.0–hypoglycemic coma, 251.1–other specified hypoglycemia, or 251.2–hypoglycemia unspecified).[10]

Healthcare resource utilization was described and included outpatient visits, ED visits, inpatient admissions, inpatient length of stay, and endocrinologist visits for the 1-year follow-up period. Diabetes-related healthcare resource utilization included claims with a primary or secondary diagnosis of diabetes *(ICD-9-CM* 250.xx). Healthcare costs were computed as plan-paid amounts of adjudicated claims in the 1-year follow-up period. Diabetes-related healthcare costs included costs from medical claims with a primary or secondary diagnosis of diabetes (*ICD-9-CM* 250.xx), antidiabetic medications, glucose meters, and test strips.

Statistical Analysis

Treatment Pattern Analysis. Baseline variables were compared using the student *t* test or Fisher's exact test, depending on the distribution of the measure. Follow-up outcomes were descriptively examined for both cohorts. Within each cohort, baseline and follow-up healthcare costs were compared using paired student *t* tests.

Comparative Effectiveness Analysis. To compare risk adjusted outcomes, stringent propensity score matching (PSM; 1:1 ratio)[11] was used to match insulin glargine patients with liraglutide patients to remove observed differences in baseline demographics and clinical characteristics. Baseline characteristics, clinical outcomes, and economic parameters were summarized and compared among matched patients, with *P* values provided by the student *t* test or χ^2 test where appropriate.

RESULTS

Treatment Pattern Analysis

Patient Demographics, Clinical Characteristics, and Healthcare Utilization at Baseline. A total of 1574

T2DM patients were identified; of these patients, 756 initiated insulin glargine and 818 initiated liraglutide (Table 1). There were differences in the patient demographics; patients in the insulin glargine group were less likely to be women (43.2% vs 50.6%; $P = .0035$) and were less likely to live in the Southern states of the United States. The average co-payment was higher for liraglutide patients, most likely because liraglutide was launched in January 2010.

There were significant differences in the baseline clinical characteristics of the 2 cohorts (Table 1). Compared with liraglutide patients, those in the insulin glargine cohort were sicker (Charlson Comorbidity Index score 0.62 vs 0.37; $P < .0001$), with significantly greater rates of diabetes-related comorbidities (eg, neuropathy, renal disease, retinopathy), but were less likely to be obese. Mean A1C was substantially lower for liraglutide patients than for insulin glargine patients (mean 7.9% vs 9.7%; $P < .0001$). Additionally, A1C was lower than 7.0%, the American Diabetes Association (ADA) target in most patients, for 28.6% of liraglutide patients compared with 7.5% of insulin glargine patients. High baseline A1C (≥9.0%) was evident in 23.3% of liraglutide patients versus 58.2% of insulin glargine patients (Table 1). A lower proportion of liraglutide patients than insulin glargine patients reported hypoglycemic events (1.8% vs 4.2%; $P = .0052$). Baseline OAD use was also significantly different between the cohorts. The mean number of OADs was 2.22 for insulin glargine initiators and 2.06 for liraglutide initiators ($P = .0003$). The insulin glargine cohort were more often on sulfonylureas (64.0% vs 44.3%; $P < .0001$), but less often receiving metformin (80.9% vs 85.5%, $P = .0139$).

There were significant differences in baseline healthcare utilization and costs between the 2 cohorts (Table 1). Compared with patients in the liraglutide group, insulin glargine patients had longer mean hospitalization duration (0.80 vs 0.08 days; $P < .0001$) and were more likely to be hospitalized or to visit the ED. As a result of these differences, insulin glargine patients had significantly higher annualized costs in the baseline period ($16,206 vs $10,466; $P < .0001$).

Clinical Outcomes

During the 1-year follow-up, the treatment persistence (90th percentile) was 51.3% for insulin glargine initiators and 45.3% for liraglutide initiators. The insulin glargine cohort was persistent for a mean of 278 days, whereas the liraglutide cohort was persistent for a mean of 250 days. Sensitivity analyses using the 75th and 95th percentiles yielded similar results. At the 75th percentile, 26.5% of insulin glargine initiators were persistent, with a mean of 201 persistent days, and 21.6% of liraglutide initiators were persistent, with a mean of 174 persistent days. At the 95th percentile, 63.2% of insulin glargine initiators were persistent, with a mean of 308 persistent days, and 56.1% of liraglutide initiators were persistent, with a mean of 287 persistent days. The DACON was 29.15 U/day for those initiating with insulin glargine and 1.13 mg/day for those initiating with liraglutide.

For those with data available, A1C at 1-year follow-up was 8.4% for insulin glargine initiators (n = 331) and 7.4% for liraglutide initiators (n = 358). The reduction in A1C from baseline was –1.4% for insulin glargine and –0.5% for liraglutide. The prevalence of hypoglycemia was also low, with 7.2% of insulin glargine initiators and 3.4% of liraglutide initiators reporting at least 1 hypoglycemic event, with hypoglycemia event rates of 23.28 and 6.48 events per 100 patient-years, respectively.

The proportion of patients initiating rapid-acting insulin within 3 months of initiating injectable therapy was 14.9% for insulin glargine initiators (11.4% initiated within 30 days of insulin glargine) and 0.3% of liraglutide initiators. Of these, 12.5% and 2.3%, respectively, were still on rapid-acting insulin during the last 3 months of the follow-up period. At the end of 1-year follow-up, 4.6% of insulin glargine patients either added or switched to GLP-1 receptor agonist therapy (exenatide 1.3%; liraglutide 3.3%), and 8.0% of liraglutide patients added or switched to basal insulin therapy (insulin glargine 4.5%; insulin detemir 3.4%).

Healthcare Utilization and Cost Outcomes

There was a small, nonsignificant increase in the annualized total healthcare costs for insulin glargine patients during follow-up ($16,206 to $17,101; $P = .5834$). There was a significant increase in pharmacy costs, offset by a decrease in medical costs, mainly driven by a decrease in inpatient costs. A similar pattern was observed for diabetes-related healthcare costs (Figure 2A).

For liraglutide patients, the annualized total healthcare costs increased by 44% ($10,466 to $15,039; $P < .0001$), and diabetes-related healthcare costs almost doubled during follow-up (Figure 2B). This was mostly driven by increased pharmacy costs due to the high cost of medications under investigation.

Comparative Effectiveness Analysis

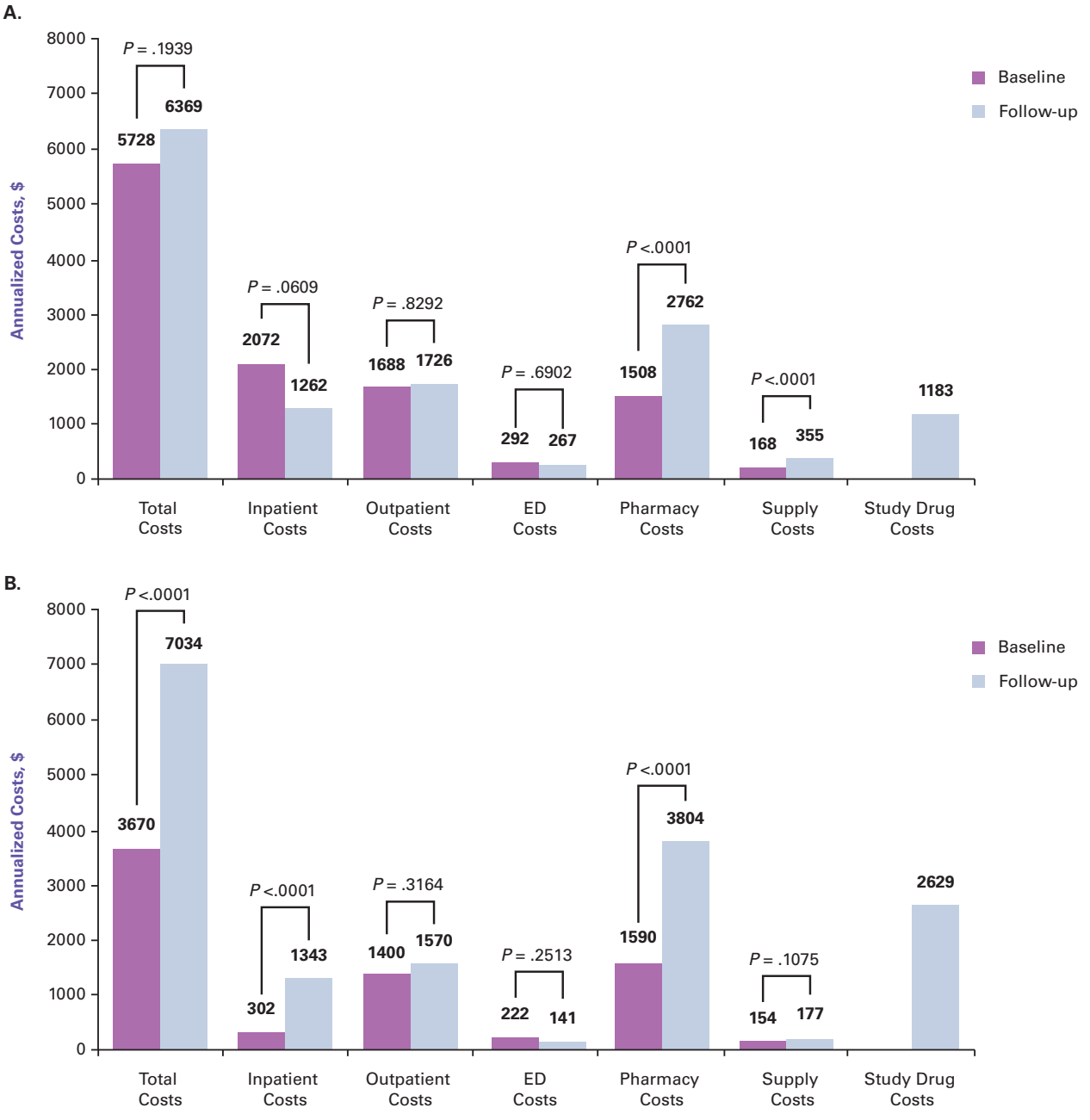
Patient Demographics, Clinical Characteristics, and Healthcare Utilizations at Baseline. After eliminating those achieving good glycemic control (defined as A1C <7.0%), 1283 patients remained. After those 1283 patients were matched by 1:1 PSM, 698 patients remained (349 in each cohort). The cohorts were well balanced

Table 1. Treatment Pattern Analysis: Patient Demographics, Clinical Characteristics, Healthcare Resource Utilization, and Costs at Baseline

Characteristic	Insulin Glargine Pen Initiators (n = 756)	Liraglutide Pen Initiators (n = 818)	*P*
Women, n (%)	327 (43.2)	414 (50.6)	.0035
Age, y, n (%)			
18–39	67 (8.8)	67 (8.1)	.1735
40–64	640 (84.6)	712 (87.0)	
65–74	46 (6.0)	39 (4.7)	
75+	3 (0.3)	0 (0.0)	
Mean (SD)	53 (9)	53 (9)	.5616
A1C, %, mean (SD)	9.7 (2.1)	7.9 (1.5)	<.0001
Patients, %			
A1C <7.0%	7.5	28.6	<.0001
A1C 7.0 to <8.0%	13.3	29.3	
A1C 8.0 to <9.0%	20.8	18.7	
A1C ≥9.0%	58.2	23.3	
Any hypoglycemia, n (%)	32 (4.8)	15 (1.8)	.0052
Comorbidity, n (%)			
Renal disease	47 (6.2)	22 (2.6)	.0006
Neuropathy	79 (10.4)	51 (6.2)	.0024
Obesity	83 (10.9)	136 (16.6)	.0012
Nephropathy	37 (4.8)	25 (3.0)	.0611
Retinopathy	58 (7.6)	37 (4.5)	.0088
Charlson Comorbidity Index score, mean (SD)	0.62 (1.30)	0.37 (0.80)	<.0001
Health plan, n (%)			
HMO	134 (17.7)	135 (16.5)	.0374
POS	570 (75.3)	597 (72.9)	
PPO	52 (6.8)	86 (10.5)	
Region, n (%)			
Northeast	105 (13.8)	87 (10.6)	.0439
South	482 (63.7)	564 (68.9)	
Midwest	113 (14.9)	98 (11.9)	
West	56 (7.4)	69 (8.4)	
Total hospitalization days, mean (SD)	0.80 (4.12)	0.08 (0.52)	<.0001
Healthcare utilizations, n (%)			
Any hospitalization	77 (10.1)	21 (2.5)	<.0001
Diabetes-related hospitalization	70 (9.2)	14 (1.7)	<.0001
ED visit	166 (21.9)	116 (14.1)	<.0001
Endocrinologist visit	193 (25.5)	231 (28.2)	.2259
Number of OADs, mean (SD)	2.22 (0.89)	2.06 (0.93)	.0003
Costs, mean $ (SD)			
Total healthcare cost	8103 (15,228)	5233 (5909)	<.0001
Total diabetes-related cost	2864 (5646)	1835 (2405)	<.0001
Total prescription costs	2198 (2938)	2319 (2141)	.3560

A1C indicates glycated hemoglobin; ED, emergency department; HMO, health maintenance organization; OAD, oral antidiabetic drug; POS, point-of-service; PPO, preferred provider organization.

Figure 2. Treatment Pattern Analysis: Annualized Diabetes-Related Costs for Patients at Baseline and Follow-up Initiating (A) Insulin Glargine or (B) Liraglutide



ED indicates emergency department.

for baseline demographics, clinical characteristics, and healthcare utilizations and costs (Table 2).

Clinical Outcomes. During the 1-year follow-up, there was little difference in outcomes between the cohorts (Table 3). Treatment persistence (90th percentile) was similar for insulin glargine and liraglutide initiators (53.0% vs 46.7%; P = .0958), although the insulin glargine cohort were persistent for longer (mean persistent days: 283 vs 252; P = .0002).

For those with data available, mean A1C at 1-year follow-up was not different between insulin glargine initiators (n = 155, 8.0%) and liraglutide initiators (n = 142, 8.1%; P = .8995); there was no difference between the groups in A1C reduction from baseline (–1.0% vs –1.0%; P = .7370). The DACON was 29.53 U/day for those initiating insulin glargine and 1.11 mg/day for those initiating liraglutide. Prevalence of hypoglycemia

Table 2. Comparative Effectiveness Analysis: Patient Baseline Demographics, Clinical Characteristics, Healthcare Utilizations, and Costs

Characteristic	Insulin Glargine Pen Initiators (n = 349)	Liraglutide Pen Initiators (n = 349)	*P*
Women, n (%)	164 (46.9)	153 (43.8)	.4030
Age, y, n (%)			
18–39	30 (8.5)	24 (6.8)	.6464
40–64	298 (85.3)	306 (87.6)	
65–74	21 (6.0)	19 (5.4)	
Mean (SD)	53 (9)	53 (9)	.3826
A1C, %, mean (SD)	9.1 (1.4)	9.0 (1.4)	.6214
Any hypoglycemia, n (%)	7 (2.0)	6 (1.7)	.7795
Comorbidity, n (%)			
Renal disease	9 (2.5)	7 (2.0)	.6130
Neuropathy	26 (7.4)	22 (6.3)	.5496
Obesity	42 (12.0)	36 (10.3)	.4710
Nephropathy	13 (3.7)	9 (2.5)	.3862
Retinopathy	26 (7.4)	17 (4.8)	.1565
Charlson Comorbidity Index score, mean (SD)	0.37 (0.92)	0.36 (0.81)	.9653
Total hospitalization days, mean (SD)	0.09 (0.62)	0.07 (0.48)	.6337
Healthcare utilizations, n (%)			
Any hospitalization	9 (2.5)	7 (2.0)	.6130
Diabetes-related hospitalization	7 (2.0)	6 (1.7)	.7795
ED visit	41 (11.7)	48 (13.7)	.4270
Endocrinologist visit	85 (24.3)	100 (28.6)	.1983
Number of OADs, mean (SD)	2.29 (0.88)	2.33 (0.93)	.5591
Costs, mean (SD)			
Total healthcare cost	5056 (7637)	4738 (5741)	.5347
Total diabetes-related cost	1752 (1987)	1897 (2396)	.3866
Total prescription costs	2062 (1991)	2263 (2212)	.2090

A1C indicates glycated hemoglobin; ED, emergency department; OAD, oral antidiabetic drug.

was low (insulin glargine 6.0% vs liraglutide 3.4%; P = .1085), as was the hypoglycemia event rate (10.60 vs 4.58 events per 100 patient-years [P = .0689], respectively, for insulin glargine and liraglutide). The percentage of patients experiencing severe hypoglycemia, an event with an ED or inpatient setting, was also very low (insulin glargine 1.4% vs liraglutide 1.4%; P >.99) with a correspondingly low event rate (1.43 vs 1.43 events per 100 patient-years [P >.99], respectively, for insulin glargine and liraglutide).

Healthcare Utilization and Cost Outcomes. During the 1-year follow-up there was no statistically significant difference between the cohorts in healthcare utilization (Table 3). Between insulin glargine and liraglutide there were no differences in mean hospitalization duration (0.54 vs 0.59 days; P = .8094) or the number of patients with any hospitalization (8.8% vs 9.4%, P = .7931), an ED visit (24.9% vs 27.2%, P = .4904), or an endocrinologist visit (32.9% vs 34.3%, P = .6888).

There was a significant difference in diabetes-related costs between the 2 cohorts (**Figure 3**). Compared with liraglutide initiators, insulin glargine initiators had significantly lower study drug costs ($1192 [median $991] vs $2642 [$2684]; P <.0001), resulting in lower diabetes-related pharmacy costs ($2832 [$2433] vs $4027 [$3742]; P <.0001) and lower total diabetes-related costs ($5305 [$4150] vs $7501 [$5415]; P = .0005). There was no statistically significant difference in total costs between insulin glargine initiators and liraglutide initiators ($13,727 [$7560] vs $15,211 [$10,107]; P = .3081).

DISCUSSION

Data from the treatment pattern analysis show that when initiating injectable therapy, there are differences

Table 3. Comparative Effectiveness Analysis: Clinical and Economic Outcomes During 1-Year Follow-Up

Characteristic	n	Insulin Glargine Pen Initiators	n	Liraglutide Pen Initiators	*P*
A1C					
A1C, %, mean (SD)	155	8.0 (1.7)	142	8.1 (1.7)	.8995
Change in A1C, %, mean (SD)	155	–1.0 (2.0)	142	–1.0 (1.8)	.7370
Hypoglycemia prevalence, n (%)	349	21 (6.0)	349	12 (3.4)	.1085
Hypoglycemia incidence rate, events per 100 patient-years	349	10.60	349	4.58	.0027
Persistence, n (%)	349	185 (53.0)	349	163 (46.7)	.0958
Persistence days	349	283 (96)	349	252 (117)	.0002
DACON[a]	349	29 (33)	349	1.11 (0.44)	NA
Healthcare utilizations, n (%)					
Any hospitalization	349	31 (8.8)	349	33 (9.4)	.7931
ED visit	349	87 (24.9)	349	95 (27.2)	.4904
Endocrinologist visit	349	115 (32.9)	349	120 (34.3)	.6888

A1C indicates glycated hemoglobin; DACON, daily average consumption; ED, emergency department; NA, not applicable. [a]DACON are expressed in units per day; for liraglutide, units are expressed in milligrams per day.

in the prescribing patterns of physicians, which may be derived from patient characteristics, patient behavior, and disease status. Approximately one-third of liraglutide initiators had an A1C lower than 7.0% at baseline and so, according to the ADA guidelines, were satisfactorily managing their blood glucose with their baseline therapy.[12] The relatively new approval of liraglutide (January 2010) may also have had an impact on prescribing patterns. Physicians may have chosen to prescribe the more established treatment (insulin glargine) to those patients who were the sickest or had the poorest glycemic control. Initiation of liraglutide at lower A1C may relate to the perception of liraglutide as beneficial to weight loss,[13] which is supported by the finding in this study of a higher level of obesity at baseline in the liraglutide cohort, although this study lacks weight and body mass index data to confirm this observation. Liraglutide is also being investigated as a treatment for obesity.[14]

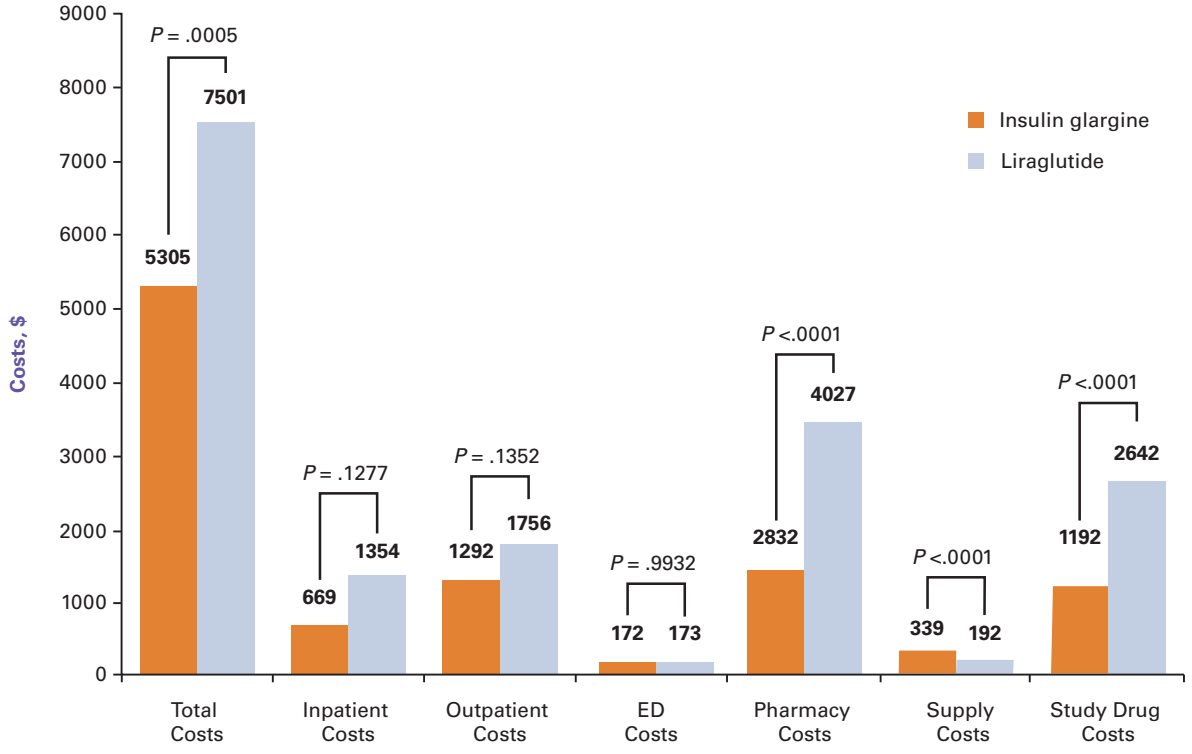
There were dramatic differences in the change in healthcare costs for insulin glargine and liraglutide initiators. After initiation, the higher cost for insulin glargine was offset by lower medical costs among insulin glargine initiators. In contrast, liraglutide patients had a significant increase in total healthcare cost after initiation, mainly because of the higher drug cost, without lower medical costs. Unfortunately, the differences in baseline characteristics make it difficult to compare the properties of these treatments and determine whether the increases in costs are related to improvements in outcomes. The comparative effectiveness analysis aimed to address these questions.

In patients with inadequate glycemic control, as measured by A1C of 7.0% or greater, PSM was used to match patients initiating insulin glargine with patients initiating liraglutide so that the cohorts had comparable characteristics at baseline. During 1-year follow-up, there was little difference in healthcare utilization and clinical outcomes between the cohorts; a mean A1C reduction of 1.0% was seen for both. This result differs from the findings of the 26-week LEAD-5 study, which found that A1C was reduced by 1.33% with liraglutide 1.8 mg/day, whereas A1C was reduced by 1.09% with insulin glargine (average dose 24 U/day).[5] The LEAD-5 study was, however, limited by its short duration and use of the highest dose for liraglutide but a low insulin glargine dose. In this real-world study, the average dose of liraglutide was 1.11 mg/day and the average dose of insulin glargine was 29 U/day, which may account for the variation in A1C reduction between the studies.

Diabetes-related costs and total pharmacy costs were significantly higher for the liraglutide than for the insulin glargine cohort. This difference was driven by the significantly higher study drug cost for liraglutide. Thus, insulin glargine may be the more cost-effective option because during 1-year follow-up, insulin glargine patients had lower healthcare costs than liraglutide patients, with similar clinical outcomes.

Our study was based on real-world data, using both clinical and economic data from patients with T2DM from a large national US claims database. Statistical analyses (eg, the use of PSM) were used to overcome the observed differences at baseline. However, our study has some limitations. It was a retrospective observational study; therefore, the data may have been subject to selection bias and confounding, and the causality of drug effect on observed

Figure 3. Comparative Effectiveness Analysis: Diabetes-Related Costs for the Patients at 1-Year Follow-up



ED indicates emergency department.

outcomes cannot be established. The analyses were also based on data from a managed care population and may not be representative of other populations. Although pharmacy claims provide information on the medication prescribed, no information was available regarding the actual usage of medication; therefore, treatment persistence could only be estimated. Further, data on patients' body weight were not available from the database. Because of the availability of the data, our study was limited to 1-year follow-up. Many different factors contribute to total healthcare costs besides those related to diabetes. Cost data are well known for their extreme values, skewed distribution, and large standard deviations; therefore, the descriptive statistical tests used in this study may not be appropriate for cost comparisons. Finally, after PSM, a moderate number of patients remained for inclusion in each group. Future studies are needed to validate the findings from this study in larger patient cohorts.

In conclusion, in this real-world study of T2DM patients initiating their first injectable therapy using insulin glargine or liraglutide, the treatment pattern analysis showed there were significant differences in the baseline clinical and demographic characteristics of those initiating injectable therapy. A significant portion of patients initiated liraglutide at A1C lower than 7.0%, and the 2 cohorts showed distinctive follow-up healthcare cost patterns compared with their baselines. The comparative effectiveness analysis suggested that among the matched patients with inadequate glycemic control, the use of the insulin glargine pen was associated with clinical outcomes similar to those seen with liraglutide, but lower diabetes-related costs because of lower drug costs. These findings will be further explored by the ongoing INITIATOR (The Initiation of New Injectable Treatment Introduced after Antidiabetic Therapy with Oral-only Regimens) study.[15,16]

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