A Real-World Study of Patients With Type 2 Diabetes Initiating Basal Insulins via Disposable Pens

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ABSTRACT

Introduction: Real-world data comparing outcomes of type 2 diabetes mellitus (T2DM) patients initiating different insulin regimens can help with treatment decisions and patient management. Clinical and economic outcomes following initiation with insulin glargine disposable pen (GLA-P) or insulin detemir disposable pen (DET-P) in T2DM patients were compared over 1-year follow-up. **Methods:** This retrospective cohort analysis was conducted on data in a US national managed care claims database (July 2006 to September 2010) from patients initiating insulin treatment with GLA-P or DET-P. Treatment persistence, adherence, glycated hemoglobin (A1C), hypoglycemic events, and healthcare costs during follow-up

were compared. **Results:** In all, 1682 patients were identified; 1016 (60.4%) started using GLA-P, 666 (39.6%) started using DET-P. After 1:1 propensity score matching, each cohort comprised 640 patients. Patients initiating GLA-P were significantly more likely to persist and adhere to treatment, and used a lower daily consumption dose. Over the last quarter of follow-up, fewer GLA-P users switched to DET-P compared with those switching from DET-P to GLA-P. GLA-P was associated with lower A1C levels and higher reduction of A1C levels from baseline, with no significant difference in the number of patients having hypoglycemic events. Patients in both cohorts had similar total and diabetes-related healthcare costs, but healthcare costs were lower in the GLA-P cohort for each 1% reduction in A1C from baseline. **Conclusion:** This real-world study demonstrates that patients initiating GLA-P were more likely to persist with and adhere to treatment, with better glycemic control and similar overall hypoglycemia rate at no increase in healthcare cost.

Keywords: clinical outcomes, economic outcomes, insulin glargine, insulin detemir, type 2 diabetes mellitus

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INTRODUCTION

The global prevalence of type 2 diabetes mellitus (T2DM) in 2010 was estimated to be 6.4% and this is expected to rise to 8% by 2030¹ due to an increasing aging population, increasing physical inactivity, prevalence of overweight people, and obesity.^{2,3} In the United States (US), diabetes affects an estimated 25.8 million people, equivalent to 8.3% of the US population,⁴ with T2DM comprising 90% to 95% of all diagnosed cases of diabetes.⁵ Untreated, T2DM can lead to several important clinical sequelae. Of particular significance is the established association between T2DM and an increased risk of cardiovascular complications, including coronary artery disease, peripheral artery disease, and carotid artery disease. In addition, microvascular complications leading to damage to the eyes, kidneys, or nerves, are also important in T2DM.⁶ As a chronic, progressively worsening disease, T2DM also carries an economic burden. In the USA, the total cost of diabetes was an estimated US\$174 billion in 2007.⁵ This includes both direct medical costs (estimated at US\$116 billion) and indirect costs (US\$58 billion) incurred through treating the consequences of inadequate glycemic control and other complications of diabetes as well as costs associated with disability, work loss, and premature mortality.^{5,7,8}

Tight (or intensive) glycemic control is beneficial in reducing the complications associated with diabetes^{6,9,10} and may, therefore, help reduce diabetes-related healthcare costs. Although oral medication is initially recommended for most patients with T2DM, insulin therapy is indicated once this is insufficient or if patients present with severe hyperglycemic signs or symptoms.^{11,12} Among adults with diagnosed diabetes, approximately 27.9% used insulin therapy to manage and control their disease in 2008, either as

monotherapy (15.5%) or in combination with oral medication (12.4%), whereas 48.5% used oral medicine only, and 23.6% were not using medication.¹³ The supplementation of oral glucose-lowering drugs with basal insulin analogs, such as insulin glargine and insulin detemir, can provide clinically important improvements in glycemic control with low risk of hypoglycemia.¹⁴ Although there are few comparative clinical trials, the two agents, insulin glargine and insulin detemir, have shown similar efficacy in terms of overall glycemic control, as well as similar tolerability profiles in terms of incidence of hypoglycemia.^{15–17} These results were also confirmed in one observational study that compared these insulin analogs in routine clinical practice. Insulin glargine and insulin detemir had improved efficacy results (glycemic control) compared with neutral protamine Hagedorn (NPH).¹⁸ It has been suggested that the similar degree of efficacy achieved with insulin glargine to insulin detemir can, however, be achieved with lower doses.^{19,20}

Adequate control of T2DM helps to prevent the clinical sequelae and limit the financial consequences associated with the disease. In order to further characterize the healthcare outcomes associated with insulin glargine and insulin detemir in a real-world setting, an analysis of data from patients initiating insulin treatment with these agents was performed. It is important to note that this study was conducted with patients using disposable pen delivery devices for both therapies. Comparative studies have demonstrated that insulin pens have advantages over traditional vial and syringe injections in terms of patient preferences, discretion, ease of use, ease of reading the dose, improved accuracy for delivering small doses, and the ease of accurate dosing for older patients.^{21–24} Therefore, treatment comparisons using different delivery device mechanisms

may not reflect actual differences between therapies. The clinical outcomes and healthcare costs associated with use of the insulin glargine disposable pen (GLA-P: SoloSTAR®; Sanofi-Aventis, Paris, France) and the insulin detemir disposable pen (DET-P: FlexPen®; Novo Nordisk, Bagsværd, Denmark) in patients using these devices for initiating T2DM therapy were compared.

Methods

This was a retrospective analysis of data from over 40 US healthcare plans collected in the Innovus IMPACT national managed care database between 2006 and 2010. This database contains information on medical claims, pharmacy claims, eligibility data, and laboratory results for 86.4 million patients, of whom 74% had pharmacy benefits and 15% had laboratory results.

Patient records were included in the analysis if they matched the following criteria: patients were diagnosed with T2DM, defined as having at least one inpatient visit or two physician visits dated at least 30 days apart with primary or secondary diagnosis of International Classification of Diseases, 9th Revision, Clinical Modification (ICD-9-CM) codes 250.x0 (T2DM or unspecified type not stated as uncontrolled) or 250.x2 (T2DM or unspecified type uncontrolled); patients were on one or more oral antidiabetic drugs (OAD) or glucagon-like peptide-1 (GLP-1) medication; initiated insulin treatment using the GLA-P or DET-P device; aged 18-79 years old; and had continuous enrollment in a health plan for 6 months prior to the start of the GLA-P or DET-P use (the baseline period) and for 12 months after the initiation (the follow-up period). In addition, glycated hemoglobin (A1C) data were required at baseline and at the end of the 1-year follow-up for records to be included.

Patient cohorts were determined by their use of either GLA-P or DET-P for insulin delivery at initiation.

Study Endpoints

A number of comparisons were made between the GLA-P and DET-P cohorts, including treatment persistence, defined as remaining on therapy without discontinuation during the 1-year follow-up from initiation. Study medication was considered discontinued if the prescription was not refilled within the expected time of medication coverage, defined as the 90th percentile of the time, stratified by the metric quantity supplied between first and second fills among patients with at least one refill. Sensitivity analyses of medication persistence were conducted using the 75th or 95th percentiles of time-to-refill to define treatment discontinuation among patients with at least one refill and allow for longer-than-usual time between refills.

Also compared were: time-to-discontinuation, measured as days of being persistent with initiated therapy from the index date; treatment adherence, measured by both the traditional medication possession ratio (MPR), and the adjusted MPR taking into account the differences in insulin device package size during the 1-year follow-up, with the adjusted MPR calculated by multiplying the traditional MPR (the total days' supply of all prescriptions in the analysis period as registered by the pharmacy when the insulin prescription is filled, divided by the number of days in the analysis period) by the average days between prescription refills for patients using insulin, divided by the average days' supply for patients using insulin;²⁵ daily average consumption (DACon), measured during the 1-year follow-up period in units per day; glycemic control, measured by A1C level at the end of

1-year follow-up and the change from baseline A1C level; and hypoglycemic events, defined as a healthcare encounter (outpatient, inpatient or emergency department [ED] visit) with ICD-9-CM codes for the primary or secondary diagnosis for hypoglycemia during the 1-year follow-up period (250.8: diabetes with other specified manifestations; 251.0: hypoglycemic coma; 251.1: other specified hypoglycemia; and 251.2: unspecified hypoglycemia).

Additionally, healthcare utilization, including the number of office visits, ED visits and endocrinologist visits, and the number and total duration of hospital admissions, were compared. Both total and diabetes-related healthcare costs were assessed from the perspective of US healthcare plan administrators during the 1-year follow-up. Costs were measured as standardized allowed payment (adjusted for inflation in 2009 US\$) by the health plan to the provider. Total cost was the sum of inpatient, outpatient, ED, and pharmacy prescription costs. Diabetes-related cost included inpatient, outpatient, and ED care for T2DM, as well as diabetes medications and diabetes consumable items (needles, blood glucose test devices, etc).

Statistical Analysis

Comparing outcomes or deriving causal inference between patient cohorts in nonexperimental studies may have the possibility of overt bias, and results would be confounded by risk factors.²⁶ In order to overcome selection bias, propensity score matching at a matching ratio of 1:1 was applied to match patients in both cohorts, based on baseline demographic, comorbidity, A1C, OAD, and/or GLP-1 medication use, study drug copay, healthcare utilization, and cost data.

All analyses were conducted on the matched cohorts. All study variables, including baseline and outcome measures, were analyzed

descriptively. Percentages, means, SD, and *P* values were obtained and calculated using standard statistical tests and procedures. Time-to-discontinuation was analyzed using the Kaplan-Meier analysis.

RESULTS

Demographics

A total of 1682 eligible patient records were identified from the database. Of these, 1016 patients (60.4%) initiated with GLA-P and 666 patients (39.6%) initiated with DET-P. After propensity score matching, each cohort comprised 640 patients and there were no significant differences in demographic data, A1C, OAD, and/or GLP-1 medication use, comorbidities, hypoglycemia rates, healthcare utilizations, or healthcare costs between the GLA-P cohort and the DET-P cohort at baseline (multivariate analysis indicated *P* was nonsignificant for all baseline characteristics) (Table 1).

Treatment Persistence and Adherence

During the follow-up period, significantly more patients in the GLA-P cohort persisted with their treatment than those in the DET-P cohort (64.8% vs. 50.9%, $P<0.0001$). In addition, the mean $\pm$ SD number of days that patients persisted with their treatment was significantly higher in the GLA-P cohort than in the DET-P cohort (236.3 $\pm$ 118.8 days vs. 212.8 $\pm$ 114.9 days, respectively; $P=0.0003$). Kaplan-Meier analysis showed the GLA-P cohort were less likely to discontinue early than DET-P cohort ($P<0.001$) (Figure 1).

Sensitivity analyses of medication persistence using the 75th percentiles of time-to-refill showed similar findings, with a higher persistence in

Table 1. Baseline characteristics of the matched insulin glargine disposable pen (GLA-P) and insulin detemir disposable pen (DET-P) cohorts (*continued on next page*).

	GLA-P (<i>n</i> =640)	DET-P (<i>n</i> =640)	<i>P</i> value
Demographics:			
Men, <i>n</i> (%)	358 (55.9)	371 (58.0)	0.4630
Age, <i>n</i> (%):			
18-39 years old	53 (8.3)	47 (7.3)	0.5320
40-64 years old	507 (79.2)	517 (80.8)	0.4847
65-74 years old	57 (8.9)	50 (7.8)	0.4796
≥75 years old	23 (3.6)	26 (4.1)	0.6621
Mean±SD	55.00±10.1	54.81±10.2	0.7390
Health plan, <i>n</i> (%):			
HMO	154 (24.1)	156 (24.4)	0.8962
POS	337 (52.7)	323 (50.5)	0.4336
PPO	100 (15.6)	94 (14.7)	0.6400
Others	49 (7.7)	67 (10.5)	0.0797
Region, <i>n</i> (%):			
North East	148 (23.1)	143 (22.3)	0.7388
South	381 (59.5)	376 (58.8)	0.7762
Midwest	42 (6.6)	48 (7.5)	0.5119
West	68 (10.6)	72 (11.3)	0.7202
Other	1 (0.2)	1 (0.2)	1.0000
Laboratory tests, mean±SD:			
A1C	9.4±2.0	9.4±2.0	0.8948
Total cholesterol	176.3±77.8	173.7±59.8	0.5553
Comorbidities			
Charlson Comorbidity Index, mean score±SD	0.58±1.2	0.64±1.3	0.3859
Comorbidities, <i>n</i> (%):			
Hypertension	469 (73.3)	467 (73.0)	0.8997
Hyperlipidemia	491 (76.7)	492 (76.9)	0.9472
Myocardial infarction	13 (2.0)	17 (2.7)	0.4599
Congestive heart failure	32 (5.0)	31 (4.8)	0.8972
Peripheral vascular disease	24 (3.8)	33 (5.2)	0.2226
Renal disease	37 (5.8)	35 (5.5)	0.8083
Retinopathy	53 (8.3)	67 (10.5)	0.1794
Neuropathy	74 (11.6)	66 (10.3)	0.4737
Nephropathy	30 (4.7)	39 (6.1)	0.2653
Chronic pulmonary disease	57 (8.9)	62 (9.7)	0.6303
Cancer	34 (5.3)	39 (6.1)	0.5467
Mental illness	80 (12.5)	86 (13.4)	0.6177
Severe mental illness	23 (3.6)	22 (3.4)	0.8794

Table 1. (Continued) Baseline characteristics of the matched insulin glargine disposable pen (GLA-P) and insulin detemir disposable pen (DET-P) cohorts.

	GLA-P (<i>n</i> =640)	DET-P (<i>n</i> =640)	<i>P</i> value
Oral antidiabetic medication, <i>n</i> (%):			
Metformin	532 (83.1)	526 (82.2)	0.6578
Sulfonylureas	440 (68.8)	442 (69.1)	0.9039
DPP4	190 (29.7)	177 (27.7)	0.4217
GLP-1	135 (21.1)	126 (19.7)	0.5324
Thiazolidinediones	242 (37.8)	262 (40.9)	0.2526
Meglitinides	37 (5.8)	36 (5.6)	0.9041
Alpha-glucosidase	8 (1.3)	8 (1.3)	1.0000
Any hypoglycemia at baseline, <i>n</i> (%)	18 (2.8)	16 (2.5)	0.7281
Healthcare utilization, <i>n</i> (%):			
Any hospitalization	48 (7.5)	67 (10.5)	0.0633
Any ED visit	113 (17.7)	130 (20.3)	0.2257
Any office visit	637 (99.5)	635 (99.2)	0.4781
Any endocrinologist visit	205 (32.0)	204 (31.9)	0.9522
Diabetes-related healthcare utilization, <i>n</i> (%):			
Any diabetes-related hospitalization	37 (5.8)	46 (7.2)	0.3070
Any diabetes-related ED visit	42 (6.6)	47 (7.3)	0.5827
Any diabetes-related office visit	625 (97.7)	625 (97.7)	1.0000
Total cost (US\$), mean±SD:			
Total cost	6736±11,343	7915±13,702	0.0938
Inpatient cost	1849±8836	2486±10,160	0.2311
Outpatient cost	2522±4335	2946±6116	0.1519
ED cost	220±750	260±827	0.3667
Treatment cost	2146±2022	2222±2210	0.5169
Total diabetes-related cost (US\$), mean±SD:			
Diabetes-related total cost	2671±4706	3246±7412	0.0975
Diabetes-related inpatient cost	827±4101	1221±5498	0.1467
Diabetes-related outpatient cost	818±1357	1010±3495	0.1956
Diabetes-related ED cost	119±539	110±519	0.7398
Diabetes-related treatment cost	832±716	829±717	0.9482
Diabetes supply cost	75±137	77±128	0.7527

A1C=glycated hemoglobin; DPP4=dipeptidyl peptidase-4; ED=emergency department; GLP-1=glucagon-like peptide-1; HMO=Health Maintenance Organization; POS=point-of-service plan; PPO=preferred provider organization.

the GLA-P cohort (at 75th percentiles: 41.0% vs. 31.2%; *P*=0.0002; at 95th percentiles: 74.3% vs. 61.2%; *P*<0.0001).

At the end of the 1-year follow-up, fewer patients in the GLA-P cohort switched to

DET-P compared with patients in the DET-P cohort who switched to GLA-P (1.4% vs. 5.9%; *P*<0.0001).

Patient adherence to treatment was also significantly higher in the GLA-P cohort

Figure 1. Kaplan-Meier curve for time-to-discontinuation of initiated insulin therapy among the matched insulin glargine disposable pen (GLA-P) and insulin detemir disposable pen (DET-P) cohorts. Medication persistence was measured using the 90th percentiles of time-to-refill.

compared with the DET-P cohort (MPR: 0.48 ± 0.26 vs. 0.44 ± 0.28 ; $P=0.0049$; adjusted MPR: 0.70 ± 0.30 vs. 0.63 ± 0.33 ; $P<0.0001$). In addition, among patients in the GLA-P cohort, significantly more had an adjusted MPR ≥ 0.8 than that in the DET-P cohort (48.3% vs. 41.6%; $P=0.0157$).

Clinical Outcomes

A1C Levels

At the end of the 1-year follow-up, patients who initiated with GLA-P had significantly lower A1C levels as well as significantly greater reductions in A1C levels from baseline. Mean A1C for the GLA-P users at the end of the 1-year follow-up was $8.1 \pm 1.6\%$ compared with $8.4 \pm 1.8\%$ for the DET-P users ($P=0.0260$) (Figure 2). Patients in the GLA-P cohort had a mean change in A1C from baseline levels of -1.23 (95% CI, -1.39% , -1.06%) whereas patients in the DET-P cohort had a change from baseline of -1.00 (95% CI, -1.16% , -0.84% ; $P=0.0467$) (Figure 2). There was no significant difference in the proportion of patients achieving A1C $< 7.0\%$ (23.9% vs. 23.3%; $P=0.79$).

DACON

The DACON dose of insulin was significantly lower in the GLA-P cohort than in the DET-P cohort (29.0 ± 19.1 units/days vs. 31.8 ± 23.3 units/days, respectively; $P=0.03$). Due to the higher A1C reduction in the GLA-P cohort (-1.23% vs. -1.00%), population-wise, for each 1% reduction in A1C the mean required DAICON dose was 23.6 units/days in the GLA-P cohort compared with 31.8 units/days in the DET-P cohort.

During the follow-up period, rapid-acting insulin was used by 118 patients (18.4%) in the GLA-P cohort and 117 patients (18.3%) in the DET-P cohort. The mean DAICON dose of rapid-acting insulin was lower in the patients in the GLA-P cohort compared with patients in the DET-P cohort; this difference did not reach statistical significance (35.2 ± 28.7 units/days vs. 40.4 ± 33.9 units/days; $P=0.2074$).

Hypoglycemia

The proportion of patients who incurred a hypoglycemic event during the 1-year follow-up was low and similar in both patient cohorts (7.9% in the GLA-P cohort and 5.9% in the DET-P cohort; $P=0.1531$), as was the mean number of hypoglycemic events per patient per year (0.23 ± 1.26 vs. 0.13 ± 0.87 ; $P=0.09$). The mean number of hypoglycemia-related ED visits or hospitalizations per patient per year was low, but was statistically significantly higher in the GLA-P cohort compared with the DET-P cohort (0.04 ± 0.24 vs. 0.02 ± 0.13 , respectively; $P=0.0455$).

Overall, both a higher DAICON dose and a higher number of hypoglycemic events during the 1-year follow-up were significantly correlated with a higher reduction in A1C (correlation coefficient: -0.091 ; $P=0.0012$, and correlation coefficient: -0.098 ; $P=0.0012$, respectively).

Figure 2. Glycated hemoglobin (A1C) reduction from baseline (left) and A1C levels (right) after 1-year follow-up associated with insulin glargine disposable pen (GLA-P) compared with insulin detemir disposable pen (DET-P) treatment. *Error bars are 95% confidence intervals.

Economic Outcomes

There were no significant differences in healthcare utilization outcomes between the GLA-P cohort and the DET-P cohort for the percentage of patients with hospitalization (all-cause healthcare utilization 13.9% vs. 12.5%; diabetes-related healthcare utilization: 10.2% vs. 8.0%, for GLA-P and DET-P, respectively), the percentage of patients with any office visits (all cause: 100% vs. 99.8%; diabetes related: 99.4% vs. 99.7%), or for the percentage of patients with ED visits (all cause: 28.3% vs.

24.2%; diabetes related: 10.2% vs. 7.8%). The mean number of office visits per patient over the 1-year follow up was similar for GLA-P and DET-P users (all cause: 18.9 vs. 17.9; diabetes related: 7.7 vs. 7.9), as was the number of endocrinologist visits (3.1 vs. 2.8). The mean number of hospitalizations or ED visits per patient, whether all cause or diabetes related, was below 0.8 in either cohort. Patients also had similar total and diabetes-related healthcare costs across both cohorts (Figure 3). Study drug costs were similar too (US\$1066±773 vs. US\$1016±907; $P=0.2878$).

Figure 3. The 1-year outcomes of overall (all-cause) and diabetes-related healthcare costs associated with insulin glargine disposable pen (GLA-P) compared with insulin detemir disposable pen (DET-P) treatment. ED=emergency department.

However, due to the higher A1C reduction in the GLA-P cohort (-1.23% vs. -1.00%), population-wise, for each 1% reduction in A1C the total and diabetes-related healthcare costs were US\$13,059 and US\$5732 in the GLA-P cohort compared with US\$15,350 and US\$6287 in the DET-P cohort.

DISCUSSION

The results from this real-world study showed that, after 1-year follow-up, patients with T2DM initiating insulin treatment with GLA-P were more likely to persist with and adhere to treatment compared with patients initiating with DET-P. In addition, patients initiating with GLA-P had better A1C reduction at the end of follow-up, associated with a lower daily average consumption of insulin, and similar overall hypoglycemia rates, without additional healthcare costs or healthcare resource

utilization during the 1-year follow-up period. Therefore, the insulin dose required and the costs needed to achieve a 1% A1C reduction were lower with GLA-P than with DET-P.

The results of this study are important because they provide a comprehensive real-world comparison of the two basal insulin analogs (including both clinical and economic outcomes) using delivery devices with similar mechanisms, and can help optimize the management of patients with T2DM. Individual randomized clinical trials have reported similar efficacy and rates of hypoglycemia of insulin glargine and insulin detemir in insulin-naïve patients.^{14,16,19,27} A recently published Cochrane review confirmed these findings but also showed significant heterogeneity across studies.³⁰ Prespecified sensitivity analysis was used to address this issue and found that the mean difference in endpoint A1C levels between the two insulin analogs was statistically significant

in favor of insulin glargine (mean difference: 0.16%; 95% CI, 0.01, 0.32%). Our study reported a larger difference at 0.23%; this may relate to differences between controlled and real-world settings, such as patients' persistence or compliance with therapies.

With respect to economic and healthcare utilization, the results from this study showed that, although the costs associated with either treatment are comparable, GLA-P may be a more cost-effective option than DET-P as measured by the cost to achieve an A1C reduction of 1%. These results are suggestive because there has been limited published data in the literature and the current study's design was not necessarily compatible with the study design of published work. A German study found that the annual treatment costs associated with insulin glargine were 36% lower compared with those with insulin detemir.²⁸ In a Canadian study, the cost savings associated with lifetime insulin glargine use were CA\$4659 per patient compared with once-daily insulin detemir, and CA\$8709 per patient compared with twice-daily insulin detemir.²⁹

The limitations of this study include that the population being examined was from a managed care setting, and is therefore not representative of the US population as a whole. Claims data submitted by healthcare providers to insurance companies are subject to possible coding errors. Data on weight is not available, and weight gain during therapy is a concern for patients and a possible event associated with treatment. With regards to the pharmacy claim data used in this study, they may not accurately reflect daily insulin dose as patients may discard unused insulin portions at the in-use expiration date or skip doses, and this might artificially inflate or deflate the dose results, and also may affect the accuracy of persistence measurement. Dosing information (eg, once-daily dose or

twice-daily dose) was not available in this database.

A review of data from randomized controlled trials suggested that 13.6% to 57.2% of patients on insulin detemir were injecting twice daily at the end of the trial, whereas insulin glargine was mostly injected once daily. In addition, the proportion of patients with injection-site reactions was significantly lower with insulin glargine than with insulin detemir.³⁰ This could have an implication on patient compliance with insulin treatment in the routine practice, and possibly explain the difference in persistence and adherence observed in the current study.

Diabetes duration was not available in the dataset and would improve the matching. However, the authors believe that many variables, such as the number of oral antidiabetes medications and A1C that were controlled for in the propensity score matching, were also correlated with diabetes duration. Therefore, the diabetes duration was controlled indirectly. Finally, as with any retrospective studies, the findings from the current study are only hypothesis generating, and no causality can be established until randomized pragmatic clinical trials are conducted to confirm these hypotheses. Although propensity score matching can control for the observed bias, hidden bias might still be available due to the unavailable variables, such as disease severity. To the extent that severity is more correlated with one group, relative to the other, our results will be biased. Pearl suggests that hidden bias actually increases because matching bias on observed variables may unleash bias due to dormant observed confounders.³¹ There are other statistical techniques available to control for the hidden bias, such as instrumental variable approach. However, these methods are also bounded with their own limitations.³²

CONCLUSION

The current study in real-world T2DM patients initiating insulin treatment via disposable pen suggests that, comparing with insulin detemir, the use of insulin glargine may be associated with better persistence and compliance with treatment, and higher A1C reduction with a similar overall rate of hypoglycemia, at no increased cost, and, therefore, may be a more cost-effective treatment option. These data may assist the clinical decision-making process in routine practice settings for the treatment of patients with T2DM and help optimize patient management. However, these findings need to be confirmed with future randomized pragmatic clinical trials.

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OB is the guarantor for this article, and takes responsibility for the integrity of the work as a whole.

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