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ORIGINAL RESEARCH

Glycemic and Economic Outcomes in Elderly Patients with Type 2 Diabetes Initiating Dulaglutide Versus Basal Insulin in a Real-World Setting in the United States: The DISPEL-Advance Study

Meredith Hoog · Rosirene Paczkowski · Ahong Huang · Rachel Halpern · Erin Buysman · Sydnie Stackland · Yiran Zhang · Ruth Wangia-Dixon

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ABSTRACT

Introduction: Treatments like glucagon-like peptide-1 receptor agonists carry low hypoglycemia risk and are recommended for elderly patients with type 2 diabetes (T2D), while some routine treatments, like insulin, increase hypoglycemia risk. The DISPEL-Advance (Dulaglutide vs Basal InSulin in Injection Naïve Patients with Type 2 Diabetes: Effectiveness in ReaL World) study compared glycemic outcomes, healthcare resource utilization, and costs in elderly patients with T2D who initiated treatment with dulaglutide versus those initiating treatment with basal insulin.

Methods: This observational, retrospective cohort study used data from the Optum Research Database. Medicare Advantage patients (≥ 65 years) with T2D were assigned to dulaglutide or basal insulin cohorts based on pharmacy claims and propensity score matched on demographic and baseline characteristics. Change in HbA1c, 12-months follow-up HbA1c, and follow-up all-cause and diabetes-related healthcare resource utilization and costs were compared.

Results: Propensity score matching yielded well-balanced cohorts with 1891 patients each (mean age: dulaglutide, 72.09 years; basal insulin, 72.56 years). The dulaglutide cohort had significantly greater mean HbA1c reduction from baseline to follow-up than basal insulin cohort (− 0.95% vs − 0.69%; $p < 0.001$). The dulaglutide cohort had significantly lower mean all-cause and diabetes-related medical costs (all-cause: $8306 vs $12,176; diabetes-related: $4681 vs $7582 respectively; $p < 0.001$) and lower mean all-cause total costs ($18,646 vs $20,972, respectively; $p = 0.007$) than basal insulin cohort. The dulaglutide cohort had significantly lower all-cause and diabetes-related total costs per 1% change in HbA1c than basal insulin

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M. Hoog (✉)
Eli Lilly and Company, Indianapolis, IN, USA
e-mail: meredith.hoog@lilly.com

R. Paczkowski
GSK, Collegeville, PA, USA

A. Huang
Tigermed-BDM, Somerset, NJ, USA

R. Halpern · E. Buysman · Y. Zhang
Optum Inc., Eden Prairie, MN, USA

S. Stackland
Panalgo, Boston, MA, USA

R. Wangia-Dixon
Elevance Health, Atlanta, GA, USA

cohort (all-cause: $19,729 vs $30,334; diabetes-related: $12,842 vs $17,288, respectively; $p < 0.001$).
Conclusions: Elderly patients with T2D initiating dulaglutide had greater HbA1c reduction, lower mean all-cause medical and total costs, lower diabetes-related medical costs, and lower total all-cause and diabetes-related costs per 1% change in HbA1c than patients initiating basal insulin. Future studies assessing medications that do not increase hypoglycemia risk could help inform therapeutic strategies in elderly patients.

Keywords: Aged; Diabetes mellitus; Type 2; Retrospective studies; Glycated Hemoglobin; Dulaglutide; Insulin; Glucagon-like peptide-1 receptor

Key Summary Points

Why carry out this study?

Elderly patients with type 2 diabetes (T2D) are at higher risk of developing hypoglycemia compared to other age groups.

While treatments that do not increase hypoglycemia risk, such as glucagon-like peptide 1 receptor agonists (GLP-1 RAs), are recommended for elderly patients, they are often prescribed traditional medications like insulin, which potentially increase the risk of hypoglycemia. Little is known about the effects of these treatments on glycemic control, healthcare costs, and resource utilization in elderly patients.

What was learned from the study

This study showed that elderly patients initiating dulaglutide, a GLP-1 RA, had greater HbA1c reduction, lower mean all-cause and diabetes-related medical costs and healthcare utilization after 12 months of follow-up, and lower follow-up total all-cause and diabetes-related costs per 1% decrease in HbA1c compared with those initiating basal insulin.

When considering treatment strategies to improve glycemic control in elderly patients with T2D, it is important to weigh the treatment benefits against the risk of hypoglycemia. The results of this study could help inform T2D treatment strategies in elderly patients.

INTRODUCTION

The estimated prevalence of diabetes in older individuals (aged ≥ 65 years) in the USA in 2019 was approximately 16 million [1]. The cost of diagnosed diabetes in the USA in 2017 was $237 billion for direct medical costs, while the total cost was $327 billion; around 61% of diabetes-related costs in the USA were associated with patients aged ≥ 65 years [1, 2].

Compared with basal insulin, glucagon-like peptide 1 receptor agonists (GLP-1 RAs) result in more effective glycemic control in patients with type 2 diabetes mellitus (T2D) [3]. The DISPEL (Dulaglutide vs Basal InSulin Injection Naïve Patients with Type 2 Diabetes: Effectiveness in ReaL World) study compared changes in glycated hemoglobin (HbA1c) and costs in adult (aged ≥ 18 years) patients with T2D who initiated the GLP-1 RA dulaglutide with those who initiated basal insulin [4]. The study reported greater HbA1c reduction and lower diabetes-related costs per 1% reduction in HbA1c in patients treated with dulaglutide compared with patients treated with basal insulin [4].

Older individuals with T2D are likely to have a number of age-related conditions, such as frailty and cognitive impairments, as well as comorbidities, such as cardiovascular, renal, or hepatic diseases [5]. These factors increase the complexity of diabetes management in elderly patients who are especially prone to hypoglycemia, which can result in physical or cognitive deficits, disability, or even fatal cardiovascular episodes [5, 6]. Therefore, for elderly patients with T2D, the American Diabetes Association (ADA) guidelines recommend treatments that are associated with a low risk of

hypoglycemia, such as GLP-1 RAs and sodium-glucose cotransporter 2 inhibitors [5]. In addition, the ADA recommends glycemic targets of HbA1c < 7.0% to 7.5% (53–58 mmol/mol) for otherwise healthy older adults with T2D [5]. For those with multiple comorbidities, the ADA recommends less stringent glycemic targets, such as HbA1c < 8.0% (64 mmol/mol) [5].

Despite these recommendations, in clinical practice, elderly patients with T2D are routinely prescribed conventional glucose-lowering medications that increase the risk of hypoglycemia, such as sulfonylureas and insulin [7]. Diabetes-related renal complications result in significant medical costs among patients aged ≥ 65 years, and up to 18% of total complication costs are attributed to congestive heart failure [8]. Despite the rapidly growing population of older individuals with T2D, very few studies have assessed glucose-lowering treatments for this age group. There are also limited real-world data comparing glycemic outcomes and healthcare resource utilization in elderly patients initiating either dulaglutide or basal insulin to date.

To help fill the gap, the DISPEL-Advance study was designed to develop real-world data similar to that collected in the DISPEL study, but in a population of older individuals with T2D. Using data from US health insurance claims, this study aimed to describe the clinical characteristics, compare glycemic outcomes in terms of HbA1c changes, and compare healthcare resource utilization and costs, in patients aged ≥ 65 years with T2D who were initiating treatment with dulaglutide or basal insulin.

METHODS

Data Source

This observational, retrospective cohort study used administrative claims data from the Optum Research Database (ORD). The ORD contains US-based claims data with linked enrollment, laboratory test results, and sociodemographic information for commercial and Medicare Advantage enrollees. Medical claims data include International Classification of Diseases, Ninth and Tenth Revisions, Clinical Modifications diagnosis and procedure codes, Current Procedural Terminology and Healthcare Common Procedure Coding System codes, site of service codes, provider specialty codes, and paid amounts. Pharmacy claims data include National Drug Code, dosage form, drug strength, fill date, days' supply, and paid amounts.

All study data were accessed in compliance with US patient confidentiality requirements, including the Health Insurance Portability and Accountability Act (HIPAA) of 1996. As this study used only de-identified data compliant with the HIPAA from the ORD, it was exempt from institutional review board approval. The study was performed in accordance with the Helsinki Declaration of 1964, and its later amendments.

Study Sample

The study sample consisted of elderly commercial and Medicare Advantage enrollees with at least one pharmacy claim for dulaglutide or basal insulin during the identification period of January 1, 2015 through February 28, 2019 (Supplementary Fig. 1). The index date was the date of the first dulaglutide or basal insulin pharmacy claim during the identification period. The index therapy was the medication on the index date.

Patients were included if they met these criteria: (i) aged ≥ 66 years in the index year (i.e., ≥ 65 years during the baseline period); (ii) continuous enrollment with medical and pharmacy benefits during the 6-month baseline and 12-month follow-up periods; (iii) at least one baseline T2D diagnosis code; and (iv) at least one HbA1c laboratory test result at baseline and during 4 to 12 months of follow-up. Patients were excluded if they had (i) a diagnosis of type 1 diabetes or claims for injectable antihyperglycemic medications (insulin, GLP-1 RA, and pramlintide) at baseline; (ii) medical claims with diagnosis or procedure codes for secondary diabetes, bariatric surgery, or other procedures for morbid obesity at baseline or follow-up; (iii) pharmacy claims for both dulaglutide and basal insulin on the index date; or (iv) missing or

invalid demographic information (Supplementary Fig. 1). Patients were assigned to the dulaglutide or basal insulin cohorts on the basis of the index therapy claim. A total of 18 months of data were captured for each patient over the baseline and follow-up periods.

Variables and Outcomes

The 6-month baseline period was used to measure and evaluate clinical characteristics and variables for propensity score matching. HbA1c outcomes, costs, and healthcare resource utilization were measured in the 12-month follow-up period. Demographic characteristics included age, sex, US Census region, race/ethnicity, education level, household income, index year, and insurance type. Baseline clinical characteristics included comorbid conditions, use of cardiovascular and oral antihyperglycemic medications, Quan-Charlson Comorbidity Index (QCCI) score [9, 10], Diabetes Complications Severity Index (DCSI) score [11–13], and baseline HbA1c, defined as the HbA1c value closest to or on the index date. Table 1 presents the outcomes evaluated in this study.

Statistical Analyses

Patients in the initial pre-match dulaglutide and basal insulin cohorts were exact matched on the following baseline HbA1c categories: (i) $< 7.0\%$, (ii) 7.0 to $< 8.0\%$, (iii) 8.0 to $< 9.0\%$, (iv) 9.0 to $< 10.0\%$, and (v) $\geq 10.0\%$. They were then propensity score matched on demographic and baseline characteristics in a 1:1 ratio using logistic regression and "greedy" matching without replacement. Matches were identified with a caliper of 0.2 $\times$ standard deviation of the logit [14]. Supplementary Table 1 presents the variables in the final propensity score matching model. Matching success was evaluated by comparing all demographic and baseline variables between cohorts using standardized differences, variance ratios, and propensity score histograms.

P values for differences in follow-up all-cause and diabetes-related total costs per 1% change in HbA1c between cohorts were calculated with a variance-stabilized bootstrap-t method using 5000 samples. All other outcomes were compared between the matched cohorts using Student's two-sided *t* tests for continuous variables and chi-square statistics for binary and categorical variables. Statistical significance was defined as $p < 0.05$.

Change in HbA1c and follow-up diabetes-related total costs were modeled with multivariable regression on the cohort. Change in HbA1c was modeled with ordinary least squares (OLS) regression controlling for baseline continuous HbA1c. Follow-up diabetes-related total costs were modeled with a generalized linear model with gamma distribution and log link controlling for baseline continuous diabetes-related total cost. Sensitivity analyses for the regressions were conducted by controlling for additional variables on which patients were not well matched after propensity score matching: index year, baseline all-cause total costs, race, and household income. All analyses were generated using SAS® software Version 9.4 (2016; SAS Institute Inc., Cary, NC, USA).

RESULTS

Baseline Demographic and Clinical Characteristics

The initial pre-match sample included 9001 patients after the selection criteria were applied: 2013 (22.36%) in the dulaglutide cohort and 6988 (77.64%) in the basal insulin cohort (Supplementary Fig. 1). Propensity score matching resulted in a final sample of 3782 patients: 1891 patients in each cohort. The propensity score matched cohorts were well balanced on all demographic and baseline variables except baseline all-cause total cost (post-match standardized difference − 10.58%) and index year (post-match standardized differences − 67.78% to 30.54%). The cohorts also remained unbalanced for patients of White race and those with a household income of $<$ \$40,000 (post-match standardized differences 10.21% and − 13.91%, respectively). Sociodemographic variables were used to describe the sample. These variables were not used for

Table 1 Outcomes evaluated in the study

Outcome	Definition
Follow-up HbA1c	HbA1c value 4 to 12 months after the index date and closest to the end of the follow-up period
Change in HbA1c	Difference between follow-up and baseline HbA1c values
Follow-up all-cause and diabetes-related healthcare resource utilization: office visits, outpatient visits, emergency room visits, inpatient visits, and home health visits	All-cause utilization was measured from all medical claims, irrespective of diagnosis codes
	Diabetes-related utilization was measured from medical claims with diagnosis codes for diabetes in any position on the claim
Follow-up all-cause and diabetes-related healthcare costs: medical costs, pharmacy costs, total costs (medical + pharmacy)	All-cause costs were the sum of health plan and patient paid amounts on medical and pharmacy claims, irrespective of diagnosis codes on medical claims or of medications
	Diabetes-related costs were the sum of health plan and patient paid amounts from medical claims with diagnosis codes for diabetes in any position and medical and pharmacy claims for antihyperglycemic medications
Total follow-up cost per 1% change in HbA1c	Sum of total all-cause or diabetes-related costs divided by the sum of change in HbA1c value across all patients by cohort

HbA1c glycated hemoglobin

propensity score matching because they were not considered confounders of the treatment effect.

The mean (standard deviation [SD]) age in the matched dulaglutide and basal insulin cohorts was 72.09 (4.93) and 72.56 (5.15) years, respectively (standardized difference − 9.33%; Supplementary Table 2). Although statistically significant (data not shown), the difference in mean age was not clinically meaningful. The dulaglutide and basal insulin cohorts had similar distributions by sex (52.19% and 52.72% female, respectively; standardized difference − 1.06%) and insurance type (93.18% and 92.86% Medicare Advantage with Part D, respectively; standardized difference 1.25%). The matched cohorts also had similar baseline clinical characteristics (Supplementary Table 3). The mean (SD) QCCI scores in the dulaglutide and basal insulin cohorts were 1.29 (1.42) and 1.35 (1.52), respectively (standardized difference − 4.52%). The mean (SD) DCSI scores were 1.49 (1.51) in the dulaglutide cohort and 1.59 (1.56) in the basal insulin cohort (standardized difference − 6.38%). The most prevalent comorbid conditions were hypertension (dulaglutide 80.80%, basal insulin 82.71%; standardized difference − 4.93%) and hyperlipidemia (dulaglutide 77.15%, basal insulin 78.74%; standardized difference − 3.83%; Supplementary Table 3).

Follow-up Glycemic Outcomes

The matched dulaglutide cohort had a significantly lower mean (SD) follow-up HbA1c value compared with the basal insulin cohort: 7.39% (1.31) versus 7.72% (1.35), respectively; $p < 0.001$ (Table 2). The difference in mean follow-up HbA1c was because a significantly higher proportion of the dulaglutide cohort achieved glycemic control with a HbA1c of <

7.0% compared with the basal insulin cohort (43.47% vs 29.72%, respectively; $p < 0.001$) and significantly higher proportions of the basal insulin cohort had a follow-up HbA1c of $\geq 7.0\%$ and $< 10.0\%$ (all $p \leq 0.006$; Fig. 1a). The mean (SD) reduction in HbA1c from baseline to follow-up was greater in the dulaglutide cohort compared with the basal insulin cohort: − 0.95% (1.44) vs − 0.69% (1.68), respectively ($p < 0.001$; Table 2). Overall, a significantly larger proportion of the dulaglutide cohort had a ≥ 1.0% decrease in HbA1c compared with the basal insulin cohort (44.90% vs 35.54%, respectively; $p < 0.001$; Fig. 1b).

The OLS regression of change in HbA1c confirmed these results (Supplementary Table 4). The matched dulaglutide cohort had a larger improvement in HbA1c compared with the basal insulin cohort: − 0.30% (95% confidence interval [CI] − 0.38 to − 0.22; $p < 0.001$). The sensitivity analysis (additionally controlling for the variables not well matched) yielded similar results (data not shown). Thus, the dulaglutide cohort was strongly associated with a reduction in HbA1c from baseline to follow-up.

Table 2 Follow-up HbA1c and change in HbA1c from baseline to follow-up by post-match cohort

Variable	Dulaglutide (*N* = 1891)	Basal insulin (*N* = 1891)	*p* value
Follow-up HbA1c, %, mean (SD)[a]	7.39 (1.31)	7.72 (1.35)	< 0.001
Time from index date to follow-up HbA1c (days), mean (SD)	270.19 (70.59)	272.06 (69.72)	0.412
Change in HbA1c from baseline to follow-up, %, mean (SD)[a,b]	− 0.95 (1.44)	− 0.69 (1.68)	< 0.001

HbA1c glycated hemoglobin, *N* total number of patients, *SD* standard deviation

[a]Follow-up HbA1c was defined as HbA1c value 4 to 12 months after the index date and closest to the end of the follow-up period

[b]Baseline HbA1c was defined as the HbA1c value closest to or on the index date. Change in HbA1c was defined as difference between follow-up and baseline HbA1c values

Follow-up Healthcare Resource Utilization and Costs

The matched dulaglutide cohort had lower proportions of patients with one or more all-cause outpatient visits (65.79% vs 70.44%, respectively; $p = 0.002$), emergency room visits (27.39% vs 32.47%, respectively; $p < 0.001$), and inpatient stays (12.16% vs 18.51%, respectively; $p < 0.001$) compared with the basal insulin cohort (Fig. 2a). Similarly, the dulaglutide cohort had lower proportions of patients with one or more diabetes-related outpatient visits (37.81% vs 43.79%; $p < 0.001$), emergency room visits (17.56% vs 21.15%; $p = 0.005$), and inpatient stays (11.79% vs 17.87%; $p < 0.001$) compared with the basal insulin cohort (Fig. 2b). The dulaglutide cohort had significantly lower mean all-cause ($8306 vs $12,176; $p < 0.001$) and diabetes-related ($4681 vs $7582; $p < 0.001$) medical costs, as well as lower mean all-cause total costs ($18,646 vs $20,972; $p = 0.007$), compared with the basal insulin cohort (Fig. 2c). The dulaglutide cohort had higher mean all-cause pharmacy ($10,340 vs $8795; $p = 0.005$) and diabetes-related pharmacy ($7456 vs $4370; $p < 0.001$) costs. The mean diabetes-related total costs (medical + pharmacy) were not significantly different between the two cohorts (dulaglutide, $12,138; basal insulin, $11,952; $p = 0.714$; Fig. 2c).

The results of the generalized linear model regression of diabetes-related total costs were consistent with the descriptive analysis. There was no significant difference in diabetes-related total costs between the cohorts, with a non-

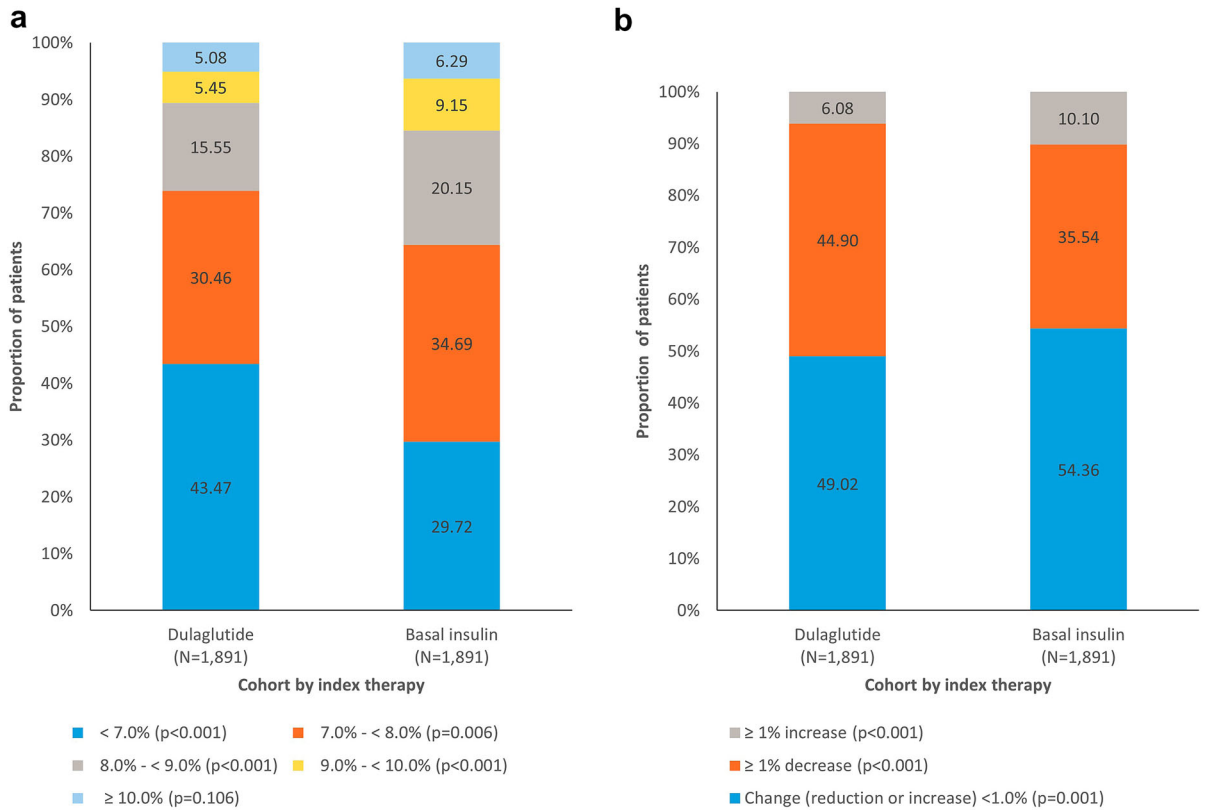


Fig. 1 **a** Follow-up HbA1c values by post-match cohort. Follow-up HbA1c was defined as the HbA1c value 4 to 12 months after the index date and closest to the end of the follow-up period. **b** Change in HbA1c from baseline to follow-up by post-match cohort. Change in HbA1c was defined as the difference between follow-up and baseline HbA1c values. Follow-up HbA1c was defined as the HbA1c value 4 to 12 months after the index date and closest to the end of the follow-up period. Baseline HbA1c was defined as the HbA1c value closest to or on the index date. *HbA1c* glycated hemoglobin, *N* total number of patients in the cohorts

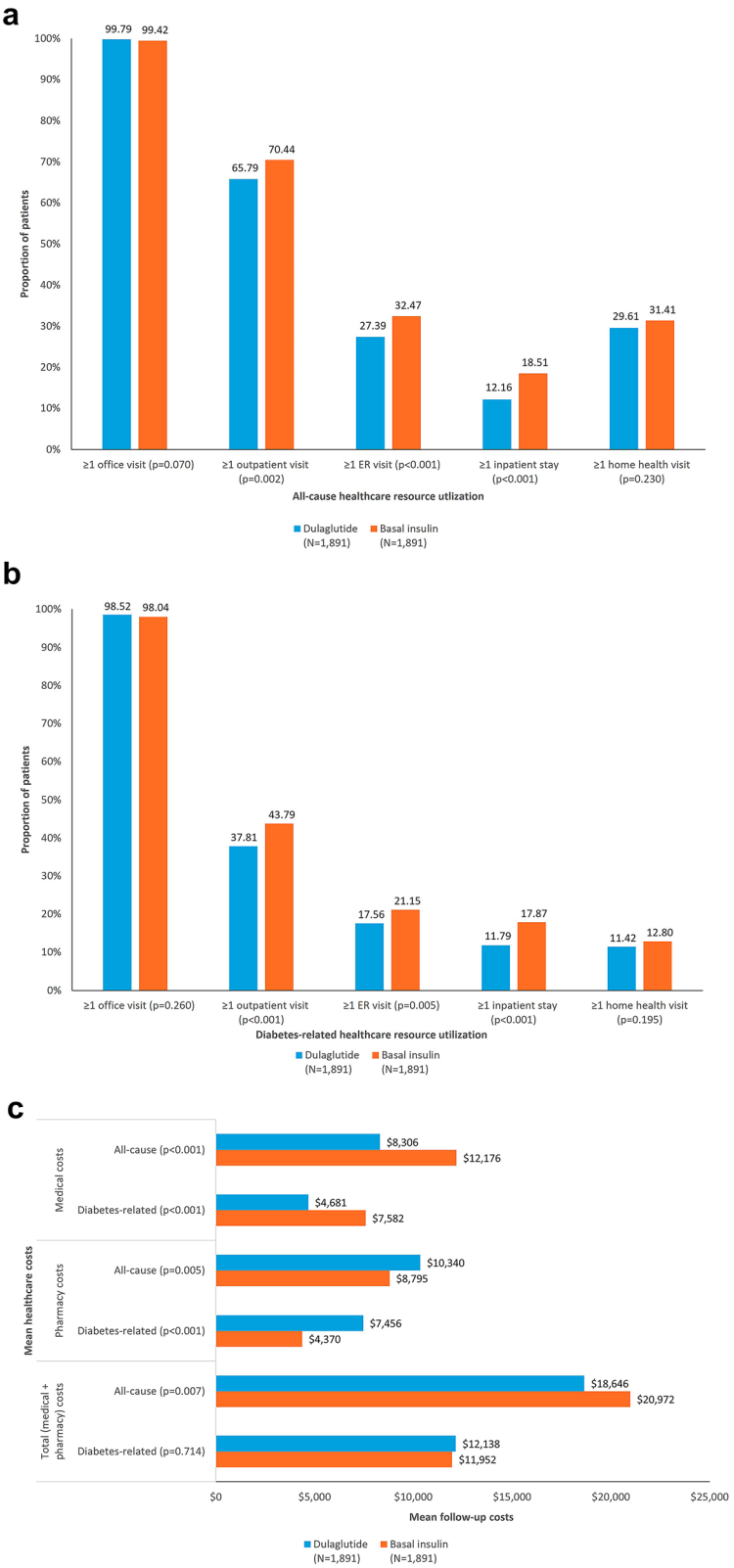
significant cost ratio (1.03; 95% CI 0.95–1.12; $p = 0.483$) associated with the dulaglutide cohort (Supplementary Table 5). The predicted costs were \$12,572 for the dulaglutide cohort and \$12,204 for the basal insulin cohort. Results were similar in the sensitivity analysis (results not shown).

The dulaglutide cohort had significantly lower all-cause total costs per 1% change in HbA1c compared with the basal insulin cohort (\$19,729 vs \$30,334; $p < 0.001$; Table 3). Similarly, diabetes-related total costs per 1% change in HbA1c were significantly lower in the dulaglutide cohort than in the basal insulin cohort (\$12,842 vs \$17,288 respectively; $p < 0.001$; Table 3).

DISCUSSION

In this claims-based cohort study, the dulaglutide and basal insulin cohorts were matched successfully and were unbalanced on only a few characteristics, which were not propensity score matching covariates. Patients were unbalanced on index year, as expected given dulaglutide was approved for the US market in late 2014. However, index year was not considered a confounder of the treatment effect. Overall, patients in the matched dulaglutide cohort had comparatively better glycemic outcomes and used fewer healthcare resources than the basal insulin cohort.

Several studies have demonstrated the greater efficacy of GLP-1 RA treatment compared with basal insulin [4, 15–19]. A systematic


a
Proportion of patients
100%
90%
80%
70%
60%
50%
40%
30%
20%
10%
0%
99.79
99.42
65.79
70.44
27.39
32.47
12.16
18.51
29.61
31.41
≥1 office visit (p=0.070)
≥1 outpatient visit (p=0.002)
≥1 ER visit (p<0.001)
≥1 inpatient stay (p<0.001)
≥1 home health visit (p=0.230)
All-cause healthcare resource utilization
Dulaglutide (N=1,891)
Basal insulin (N=1,891)
b
Proportion of patients
98.52
98.04
37.81
43.79
17.56
21.15
11.79
17.87
11.42
12.80
≥1 office visit (p=0.260)
≥1 outpatient visit (p<0.001)
≥1 ER visit (p=0.005)
≥1 inpatient stay (p<0.001)
≥1 home health visit (p=0.195)
Diabetes-related healthcare resource utilization
Dulaglutide (N=1,891)
Basal insulin (N=1,891)
c
Mean healthcare costs
Medical costs
Pharmacy costs
Total (medical + pharmacy) costs
All-cause (p<0.001)
Diabetes-related (p<0.001)
All-cause (p=0.005)
Diabetes-related (p<0.001)
All-cause (p=0.007)
Diabetes-related (p=0.714)
$8,306
$12,176
$4,681
$7,582
$10,340
$8,795
$7,456
$4,370
$18,646
$20,972
$12,138
$11,952
$0
$5,000
$10,000
$15,000
$20,000
$25,000
Mean follow-up costs
Dulaglutide (N=1,891)
Basal insulin (N=1,891)

◀**Fig. 2** **a** Follow-up all-cause healthcare resource utilization by post-match cohort. All-cause utilization was measured from all medical claims, irrespective of diagnosis codes. **b** Follow-up diabetes-related healthcare resource utilization by post-match cohort. Diabetes-related utilization was measured from medical claims with diagnosis codes for diabetes in any position on the claim. **c** Follow-up mean all-cause and diabetes-related medical, pharmacy, and total healthcare costs by post-match cohort. All-cause costs were the sum of health plan and patient paid amounts on medical and pharmacy claims, irrespective of diagnosis codes on medical claims or of medications. Diabetes-related costs were the sum of health plan and patient paid amounts from medical claims with diagnosis codes for diabetes in any position and medical and pharmacy claims for antihyperglycemic medications. *ER* emergency room, *N* total number of patients in the cohorts

Table 3 Cost per 1% change in HbA1c

Follow-up costs	Dulaglutide (*N* = 1891)	Basal insulin (*N* = 1891)	*p* value
All-cause total cost ($)			
Cost per 1% decrease[a] in HbA1c	19,729	30,334	< 0.001
Lower 95% CI	18,211	26,869	
Upper 95% CI	21,306	34,830	
Diabetes-related total cost ($)			
Cost per 1% decrease in HbA1c	12,842	17,288	< 0.001
Lower 95% CI	11,858	15,256	
Upper 95% CI	13,884	19,735	

CI confidence interval, *HbA1c* glycated hemoglobin
[a]Change in HbA1c was defined as difference between follow-up and baseline HbA1c values. Most changes were reductions in HbA1c as shown in Fig. 1b

review and meta-analysis of the clinical efficacy of GLP-1 RAs demonstrated that treatment with once-weekly GLP-1 RAs, such as dulaglutide, was associated with a significant reduction in HbA1c when compared with basal insulin [19]. The AWARD-2 trial reported improved HbA1c for patients treated with dulaglutide, with more patients achieving an HbA1c of < 7.0% (53 mmol/mol), compared with treatment with basal insulin [17]. In the real-world setting, the DISPEL study demonstrated improved glycemic outcomes in terms of HbA1c reductions for adult patients initiating dulaglutide compared with those initiating basal insulin [4]. The results of the present study are consistent with these studies [4, 15–19]. Patients in the dulaglutide cohort had significantly better glycemic outcomes than patients in the basal insulin cohort, with a lower follow-up HbA1c, greater reduction in HbA1c, including a ≥ 1% decrease, and higher proportions of patients with a follow-up HbA1c of < 7.0%. Multivariable regression analyses controlling for baseline HbA1c confirmed a significantly larger decrease in HbA1c in the dulaglutide cohort compared with the basal insulin cohort. In a subgroup analysis of patients aged ≥ 65 years in the DISPEL study, HbA1c levels reduced by 1.10% in the dulaglutide cohort, compared with a 0.54% reduction in the basal insulin cohort [4]. The current study showed the same order of magnitude of HbA1c reduction (0.95% and 0.69% in the dulaglutide and basal insulin cohorts, respectively).

Previous studies have reported the cost-effectiveness of dulaglutide as a medication for diabetes [4, 18, 20–22]. The DISPEL study reported lower medical costs and higher pharmacy costs for patients initiating dulaglutide compared with those initiating basal insulin [4]. Data from a real-world study in Spain reported lower total annual healthcare costs for patients initiating dulaglutide compared with patients initiating other GLP-1 RAs [18]. In the current study, patients in the dulaglutide cohort used fewer all-cause and diabetes-related healthcare resources compared with the basal insulin cohort, including the higher-cost categories such as outpatient visits, emergency room visits, and inpatient stays. Furthermore, the dulaglutide cohort had significantly lower total all-cause and diabetes-related costs per 1% decrease in HbA1c from baseline to follow-up compared with the basal insulin cohort. These

findings are aligned with a literature review of real-world studies, which found that dulaglutide was associated with lower healthcare costs per 1% reduction in HbA1c compared with other GLP-1 RAs or basal insulin [20]. Mean follow-up pharmacy costs in the current study were higher in the dulaglutide cohort and this difference contributed to the similar follow-up diabetes-related total costs between the two cohorts. These results are consistent with those from the DISPEL study, which also demonstrated that the total diabetes-related costs between patients initiating dulaglutide and basal insulin were not significantly different [4].

This study has some limitations which should be considered when interpreting the results. Because patients in the initial pre-match basal insulin cohort were exact matched on baseline HbA1c and in a 1:1 ratio with patients in the dulaglutide cohort, changes in HbA1c observed in the basal insulin cohort cannot be generalized to all patients who initiate basal insulin therapy. Patients in the matched basal insulin cohort may have had systematically less improvement in HbA1c than those in the initial pre-match basal insulin cohort who were excluded during matching. Furthermore, patients on insulin are likely to have more severe T2D [23], and the cohorts were propensity score matched to allow for a direct comparison, thus limiting the basal insulin cohort to patients who had less severe T2D than the average patient on basal insulin. It is possible that diagnosis codes on claims may be miscoded and medications may not be used as prescribed, a limitation common in real-world evidence studies utilizing claims data. In addition, important clinical variables that could inform multivariable regression analysis, such as severity of diabetes, are not available in claims data. Although the risk of hypoglycemia is a key clinical factor that motivated this study, hypoglycemia cannot be fully captured using claims data. Results of this analysis may not be generalizable to individuals who are uninsured, fee-for-service Medicare beneficiaries, or who reside in institutions such as nursing homes.

Understanding the specific needs of older individuals with T2D is important for effective diabetes management. Owing to comorbidities and age-related complications such as frailty, elderly patients are more likely to be overprescribed medications which could result in an increased risk of drug interactions and drug-related adverse effects [24]. Older individuals are also more prone to hypoglycemia, highlighting the need to weigh the benefits of improved glycemic control against the risk of hypoglycemia [6, 24, 25].

CONCLUSIONS

The paucity of clinical trials of diabetes treatments specifically in older patients, coupled with the heterogeneous nature of the elderly population, makes it difficult to extrapolate the results of most clinical trials to older patients with T2D. The present study sought to address this gap and provide real-world evidence in this population. Elderly patients with T2D who initiated dulaglutide had better glycemic outcomes, lower mean all-cause and diabetes-related medical costs, and lower total all-cause and diabetes-related costs per 1% change in HbA1c compared with those initiating basal insulin in this real-world study. Additional research is needed to validate the results of this study in a broader patient population who might have more severe T2D. Further research using alternative methods to assess the risk of hypoglycemia evaluating the long-term effectiveness of medications for glycemic control that do not increase the risk of hypoglycemia in elderly patients with T2D could help inform therapeutic choices for diabetes management in these patients.

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Declarations

Conflict of Interest. Meredith Hoog is an employee and stockholder of Eli Lilly and Company. Rosirene Paczkowski is an employee of GSK and was an employee of Eli Lilly and Company during this research. Ahong Huang is an employee of Tigermed-BDM. Rachel Halpern, Erin Buysman, and Yiran Zhang are employees of Optum, Inc. Ruth Wangia-Dixon is an employee of Elevance Health and was an employee of Optum, Inc. during this research. Sydnie Stackland was an employee of Optum, Inc. during this research.

Ethical Approval. All study data were accessed with protocols compliant with the US patient confidentiality requirements, including the HIPAA of 1996. As this study used only de-identified data compliant with the HIPAA from the ORD, it was exempt from institutional review board approval. The study was performed in accordance with the Helsinki Declaration of 1964, and its later amendments.

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