Clinical and Economic Outcomes of Patients with Type 2 Diabetes on Multiple Daily Injections of Basal-bolus Insulin (MDI) Therapy: A Retrospective Cohort Study

Diana Brixner, RPh, PhD[1]; Anastasia Ermakova, PharmD[2]; Yan Xiong, MS[2]; Ray Sieradzan, PharmD[3]; Naomi Sacks, PhD[4]; Philip Cyr, MPH[4]; and Stephanie D. Taylor, PhD[2]

[1]*University of Utah College of Pharmacy, Salt Lake City, UT, USA;* [2]*Health Economics and Outcomes Research, Becton Dickinson, Franklin Lakes, NJ, USA;* [3]*Medical Affairs, Becton Dickinson, Franklin Lakes, NJ, USA; and* [4]*Precision Xtract, Boston, MA, USA*

ABSTRACT

Purpose: Therapy for patients with type 2 diabetes (T2DM) not achieving hemoglobin (Hb) A_{1c} targets may progress from an oral antidiabetic drug (OAD) to added basal insulin and then to multiple daily injections of basal-bolus insulin (MDI); however, the relative clinical and economic burden experienced by patients prescribed MDI for T2DM is not well quantified. The intent of this work was to describe direct medical costs, health care resource utilization, and glycemic control in patients with T2DM exposed to MDI in a clinical practice setting.

Methods: This retrospective cohort study used administrative claims data (2012–2015, United States) from patients aged 18 to 64 years with T2DM prescribed OAD, basal insulin, or MDI therapy. Eligible patients had continuous enrollment from ≥6 months before to 12 months after the date of the index prescription drug claim. Patients eligible for inclusion in the MDI cohort had ≥2 pharmacy claims each for basal and bolus insulin from the index date through the postindex period. Glycemic control, defined as an HbA1c value of <7% during the last 9 postindex months, was assessed in a subset of patients with HbA_{1c} data available from that period. Descriptive analyses were performed.

Findings: We identified 225,135 patients with T2DM and claims for an OAD (n = 188,230), basal insulin (n = 23,724), or MDI (n = 13,181). The mean age was 51 or 52 years in each cohort; 54% to 59% of patients in each cohort were men. The mean Charlson comorbidity index scores were 0.8, 1.4, and 1.8, respectively; the percentages of patients with obesity and diabetes-related complications were greatest in the MDI cohort compared with OAD and basal insulin cohorts. The mean direct medical costs (all-cause; year-2015 US $) were $9368 in the OAD cohort, $14,420 in the basal insulin cohort, and $25,624 in the MDI cohort; diabetes-related costs were $3396, $7285, and $13,538. In the OAD, basal insulin, and MDI cohorts, 7%, 9%, and 14% of patients had ≥1 hospitalization, and 17%, 20%, and 24% had ≥1 emergency department visit, while 5%, 7%, and 11% had ≥1 diabetes-related hospitalization, and 8%, 11%, and 15% had ≥1 diabetes-related emergency department visit. Glycemic control was found in 64%, 22%, and 15% of patients in the OAD, basal insulin, and MDI cohorts.

Implications: These findings suggest that patients prescribed MDI therapy for T2DM have greater disease burden, experience greater medical costs and health care resource utilization, and exhibit poorer glycemic control than do patients treated with OAD or basal insulin therapy. (*Clin Ther*. 2019;41:303–313) © 2019 Published by Elsevier Inc.

Keywords: basal insulin, glycemic control, health care resource utilization, medical costs, multiple daily injections, oral antidiabetic drug.

Accepted for publication December 23, 2018
https://doi.org/10.1016/j.clinthera.2018.12.014
0149-2918/$ - see front matter

INTRODUCTION

Diabetes is a chronic disease that affects 30.3 million people in the United States (9.4% of the population).[1] Type 2 diabetes mellitus (T2DM) accounts for 90% to 95% of all diabetes cases and is characterized by progressive loss of pancreatic β-cell function, excessive glucose production, deterioration of glycemic control, and, ultimately, the development of microvascular and macrovascular complications.[1,2] The economic impact of T2DM is substantial, and T2DM continues to present a considerable health care burden. In 2015, the total direct and indirect costs were estimated at over US $475 billion, 64% of which ($304 billion) was attributed to direct medical costs.[3] The direct medical costs had been estimated to rise in 2017 to $348 billion.[4]

Achieving and maintaining glycemic control reduces long-term complications and is an important goal of T2DM treatment.[5] Clinical guidelines from the American Diabetes Association and the European Association for the Study of Diabetes recommend initial pharmacologic management with an oral antidiabetic drug (OAD).[5] In patients not achieving hemoglobin (Hb) A_{1c} targets, intensification to combination therapy, including a basal insulin, may be required for glycemic goal attainment. However, an estimated 24% to 54% of patients with T2DM have residual hyperglycemia after the initiation of basal insulin therapy.[6]

Patients who require further therapy to achieve postprandial glycemic control may be additionally prescribed rapid-acting prandial/bolus insulin, necessitating multiple daily injections of basal-bolus insulin (MDI). The requirement for escalation to MDI therapy likely represents substantial progression in the natural history of T2DM, and recent studies have suggested that patients prescribed and using MDI have longstanding disease and often fail to achieve glycemic targets.[7–9] However, the relative clinical and economic burdens experienced by patients prescribed MDI for T2DM are not well quantified.[10,11] The objectives of this study were: (1) to characterize the baseline demographic and clinical characteristics in patients prescribed MDI therapy for T2DM in a clinical practice setting; and (2) to describe clinical and economic outcomes in patients prescribed MDI therapy over a 1-year period. We contrasted the demographic and clinical characteristics and outcomes in patients prescribed MDI with those in patients likely earlier in the progression of T2DM who were prescribed OAD or basal insulin therapy.

MATERIALS AND METHODS

Data Source

This retrospective, cross-sectional cohort study used deidentified administrative claims data from the Truven Health MarketScan Commercial and Medicare Supplemental Claims and Encounters databases and the MarketScan Laboratory database for the 4-year period from January 1, 2012, through December 31, 2015 (*study period*).[12] The databases contain inpatient, outpatient, and prescription drug claims data and enrollment records from individuals with commercial and/or retiree health care coverage from >100 employers and health plans. The data include demographic and health plan membership information as well as diagnosis codes, procedure codes, and other health care encounter information. The 2012–2015 MarketScan database featured a geographically diverse population of ~92 million individuals from all 50 US states, and the MarketScan Laboratory database included laboratory testing results from >5.3 million individuals.[12]

The use of deidentified data from the MarketScan databases was compliant with the standards of the US Health Insurance Portability and Accountability Act of 1996.[13]

Study Population

Patients with data eligible for this study had T2DM, which we defined as ≥1 inpatient or ≥2 outpatient claims, dated 30 to 365 days apart, with a T2DM diagnosis (*International Classification of Disease, Ninth Revision—Clinical Modification* [ICD-9-CM] code 250.x0 or 250.x2, or ICD-10 code E11) in the first or second position in the claim. In addition, eligible patients with T2DM were aged 18 to 64 years on the index date of the first qualifying claim for an OAD, basal insulin, or MDI (*index claim*) and had continuous enrollment with medical and pharmacy benefits for ≥6 months before the index date (*baseline period*) to ≥12 months after the index date (*postindex period*).

The following exclusion criteria could apply at any time during the study period. Patients were excluded from the analyses if they were prescribed continuous subcutaneous insulin infusion, an insulin pump, or a glucagon-like peptide 1 (GLP-1) receptor agonist. We excluded GLP-1 receptor agonists because: (1) the rate of prescribing of these agents was low during the first years of the study and thus uneven during the study period; and (2) we wanted to restrict our analysis to only 1 type of injectable agent (insulin). Patients were also excluded if they had ≥1 inpatient or outpatient claim with a diagnosis of type 1 diabetes; evidence of pregestational diabetes, gestational diabetes, or pregnancy/labor and delivery diabetes; or a diagnosis of cancer or malignant tumor (see Supplemental Appendix in the online version at doi:10.1016/j.clinthera.2018.12.014 for the list of diagnosis codes).

In each of the 3 mutually exclusive study cohorts, the first *qualifying index claim* for an OAD, basal insulin, or MDI was considered the index claim. A qualifying index claim in the OAD cohort was the first claim for an OAD in any of the following therapeutic classes: biguanide, sulfonylurea, thiazolidinedione, dipeptidyl peptidase 4 inhibitor, or sodium-glucose cotransporter 2 inhibitor; patients in the OAD cohort had no claims for insulin in the database. A qualifying index claim in the basal insulin cohort was the first claim for basal insulin; patients in the basal insulin cohort had no claims for bolus insulin or premixed insulin in the database.

A qualifying index claim for MDI was defined as the earliest claim for bolus insulin that was followed by ≥2 claims for basal insulin and 1 additional claim for bolus insulin within the 12-month postindex period. Patients in the MDI cohort could also have received an OAD but no premixed insulin during the study period; there was no requirement for other antidiabetic therapies preceding the date of the MDI index claim.

Study Measures

The Truven MarketScan database was used to identify patients' demographic data as of the index date. Medical claims during the 6-month baseline period were used to calculate diabetes-related comorbid conditions and complications, including obesity, hyperlipidemia, hypertension, diabetic neuropathy, renal disease, retinopathy, acute myocardial infarction, stroke, and ischemic heart disease, as well as the Charlson comorbidity index score based on ICD-9-CM/10 diagnosis codes, with a higher score indicating greater comorbidity.[14]

Total direct medical costs and diabetes-related costs per patient during the 12-month postindex period were calculated. *Medical costs* included the amounts paid to health care providers by insurers, as reported on medical and pharmacy claims. Medical claims for services containing a code for a diagnosis of T2DM (ICD-9-CM codes 250.x0 and 250.x2, and ICD-10 code E-11) at any position on the claim were considered diabetes related, as were pharmacy claims for medications or supplies in antidiabetic agent therapeutic classes or diabetes-related supplies. Per-annum total direct medical costs, based on inpatient, outpatient, and pharmacy claims, are reported. Costs of emergency department (ED) visits in which patients were not admitted to the hospital were calculated and are reported separately and also are included in the reporting of outpatient costs. All costs were adjusted to year-2015 US $ using the medical care component of the Consumer Price Index.[15]

Health care resource utilization (HCRU) and diabetes-related HCRU were reported by identifying the percentages of patients with ≥1 hospitalization, ≥1 ED visit, and ≥1 outpatient visit in each category of HCRU (all-cause and diabetes related).

Glycemic control during the postindex period was assessed in a subset of patients who had ≥1 HbA_{1c} laboratory value recorded at ≥3 months after the index date. If >1 HbA_{1c} value were recorded, the mean of all HbA_{1c} values was utilized.[7] Patients with a mean HbA_{1c} level of <7% were considered to have had glycemic control.[16] Additional HbA_{1c} values were categorized using the following cut-points: 7.0% to <8.0%, 8.0% to <9.0%, and ≥9%.

Statistical Analyses

Descriptive analyses were conducted to characterize patient demographic and clinical characteristics and all outcomes measures. Frequencies and percentages are reported for categorical variables, while median (interquartile range [IQR]) and/or mean (SD) were calculated for continuous and count variables in each cohort.

With regard to medical costs, where the distribution was highly skewed, we report the median costs. In addition, we report the mean costs as recommended in the reporting guideline from the Enhancing the Quality and Transparency of Health Research (EQUATOR) Network,[17] because the means can be multiplied by a target population to estimate total costs and hence are of most use to policymakers.

All data analyses were conducted using the SAS software package version 9.4 (SAS Institute Inc, Cary, North Carolina).

RESULTS

Patient Characteristics

Of the 3,413,106 patients with T2DM in the database during the study period, we identified a total of 225,135 eligible patients based on the inclusion and exclusion criteria with claims for OAD (n = 188,230), basal insulin (n = 23,724), or MDI (n = 13,181) (Figure 1).

The mean ages were 50.6 and 51.4 years in the OAD and basal insulin cohorts, respectively, and slightly older in the MDI cohort (52.0 years); over half of patients in each cohort (range, 54%–59%) were men (Table I).

The presence of comorbidities, as measured by the Charlson comorbidity index score, was numerically greatest in the MDI cohort. Moreover, the percentages of patients with obesity, comorbidities, and recorded diabetes-related complications, including neuropathy, retinopathy, and renal disease, were greater in the MDI cohort than in the other 2 cohorts. In the MDI cohort, 13%, 12%, and 9% of patients had a record of renal disease, neuropathy, and retinopathy, respectively, and 3% had a diagnosis of acute myocardial infarction in the 6-month baseline period (Table I).

In the basal insulin cohort, biguanides and sulfonylureas were the antidiabetic drugs most commonly prescribed during the 6-month preindex period, with 64% and 44% of patients having ≥1 claim for a biguanide and a sulfonylurea, respectively (Table I). In the MDI cohort, claims for basal insulin (58% of patients) and a biguanide (51%) were most common during that time period.

Medical Costs and HCRU

Total direct medical costs and diabetes-related costs, by treatment cohort, are summarized in Table II. The total mean direct medical costs per patient in the 12 months after the index claim in the OAD and basal insulin cohorts were $9368 and $14,420, respectively, as compared with $25,624 in the MDI cohort (Table II). The mean diabetes-related costs in the OAD and basal insulin cohorts were $3396 and $7285, respectively, and $13,538 per patient in the MDI cohort (Table II). The mean diabetes-related costs represented 36%, 51%, and 53% of total medical costs in the OAD, basal insulin, and MDI cohorts, respectively.

Numerically lower percentages of the non-MDI than the MDI cohort had ≥1 hospitalization or ≥1 ED visit, both overall and related to T2DM, as depicted in Figure 2. In the OAD and basal insulin cohorts, >99% of patients had ≥1 outpatient visit, and 93% and 97%, respectively, had ≥1 diabetes-related outpatient visit. In the MDI cohort, nearly all had ≥1 outpatient visit (all-cause) and ≥1 diabetes-related outpatient visit (99% and 97%, respectively).

Glycemic Control

Results of HbA_{1c} tests conducted at ≥3 months after the index date were available from 10,971 (6%), 1614 (7%), and 907 (7%) patients in the OAD, basal insulin, and MDI cohorts, respectively. The mean HbA_{1c} laboratory values during the last 9 months of the postindex period were 7.0%, 8.4%, and 8.7%, respectively. The percentages of patients with glycemic control (HbA_{1c} <7%) in the OAD and basal insulin cohorts were greater than among patients prescribed MDI (64%, 22%, and 15%, respectively) (Figure 3). Conversely, the percentages of patients with HbA1c values ≥9% in the OAD and basal insulin cohorts were lower compared with that in the MDI cohort (8%, 32%, and 40%, respectively).

DISCUSSION

These clinical practice study findings highlight important differences in patient characteristics and in direct medical costs, HCRU, and disease burden between patients prescribed MDI as compared with OAD or basal insulin therapy for T2DM. Patients prescribed MDI therapy had numerically greater total and diabetes-related medical costs and greater rates of all-cause and diabetes-related inpatient hospitalizations and ED visits. The mean per-patient diabetes-related costs in the MDI cohort were 4-fold greater than those in the OAD cohort and nearly double (1.9-fold) those in patients treated with basal insulin. These differences between cohorts were not unexpected, as treatment intensification to MDI therapy for T2DM usually occurs in conjunction with substantial progression in the natural history of T2DM.

These findings depict the economic burden experienced by patients prescribed MDI therapy relative to OAD and basal insulin therapy and support the findings of high MDI-related costs and HCRU reported in 2 prior, smaller-scale observational studies that examined outcomes after the initiation of MDI

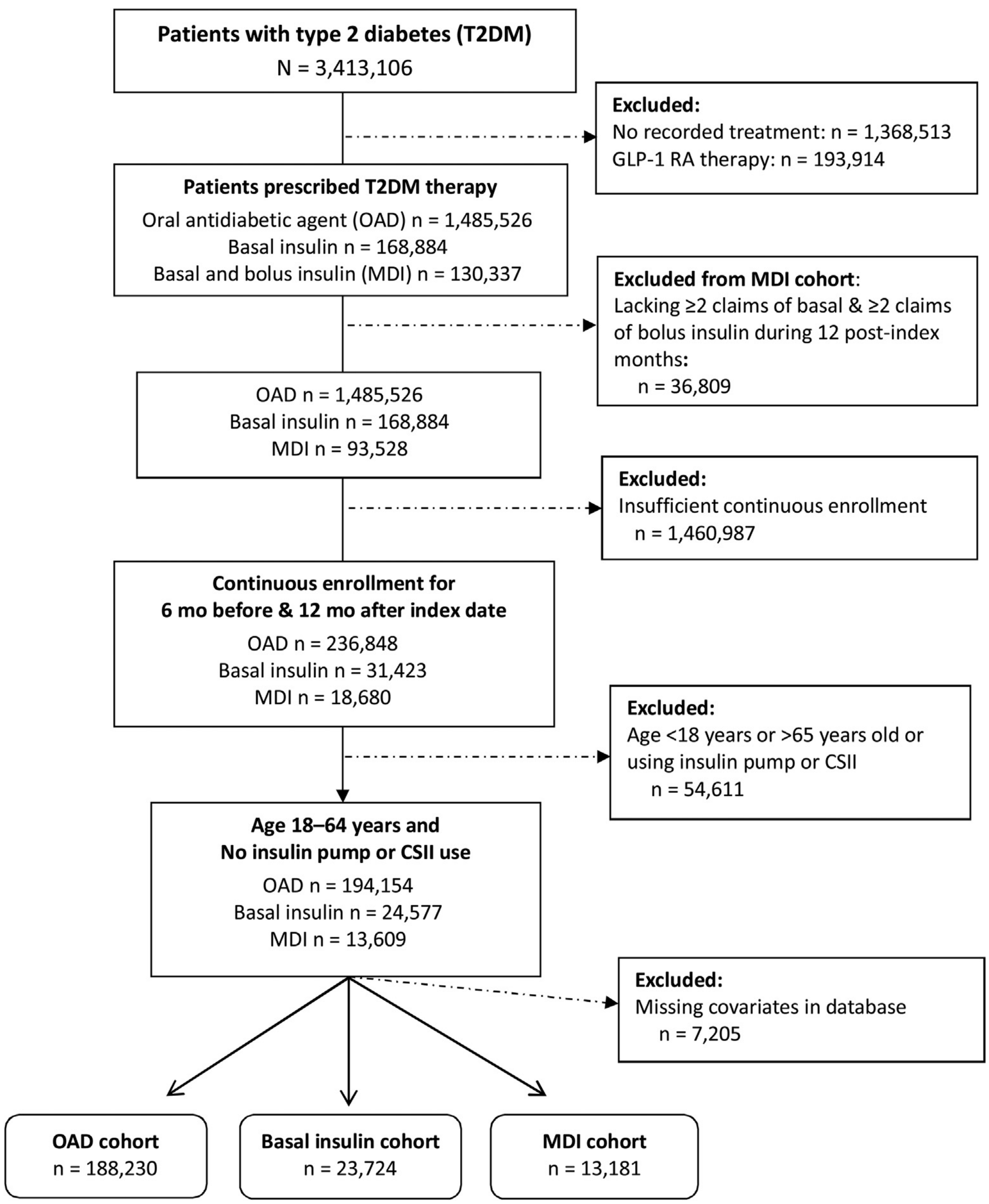

Figure 1. Patient selection from the database. CSII = continuous subcutaneous insulin infusion; GLP-1 RA = glucagon-like peptide-1 receptor agonist; MDI = multiple daily injections of basal-bolus insulin; OAD = oral antidiabetic drug.

therapy for T2DM.[10,11] Moreover, these results support previous findings that patients treated with MDI have advanced disease,[7] as evidenced in their Charlson comorbidity index scores and rates of cardiovascular and other diabetes-related complications in the months before the MDI index claim.

The clinical outcomes results in the subgroup of patients with recorded HbA_{1c} values were consistent with those from studies that have reported suboptimal glycemic control in patients prescribed MDI, including estimates of the percentages of patients with HbA1c <7% (ie, control) that range from 15.5% in clinical

Table I. Demographic and clinical characteristics at baseline of patients with type 2 diabetes, by antidiabetic treatment at index date. Data are given as number (%) of patients unless otherwise noted.

Characteristic	OAD (n = 188,230)	Basal insulin (n = 23,724)	MDI (n = 13,181)
Age at index, mean (SD), y	50.6 (8.6)	51.4 (8.3	52.0 (8.2
Male	102,490 (54)	14,035 (59)	7431 (56)
Region			
Northeast	27,386 (15)	3241 (14)	1739 (13)
Midwest	40,758 (22)	5084 (21)	3405 (26)
South	89,247 (47)	10,465 (44)	5379 (41)
West	30,839 (16)	4934 (21)	2658 (20)
Insurance plan type			
HMO	25,584 (14)	4141 (17)	2313 (18)
PPO	114,140 (61)	13,661 (58)	7702 (58)
Other	48,506 (26)	5922 (25)	3166 (24)
CCI			
Mean (SD) score	0.74 (0.87)	1.39 (1.15)	1.78 (1.48)
Score group			
0	83,258 (44)	2911 (12)	1261 (10)
1	83,092 (44)	14,496 (61)	6733 (51)
2	14,199 (8)	2818 (12)	1817 (14)
3	5252 (3)	2250 (9)	1870 (14)
4	2429 (1)	1249 (5)	1500 (11)
Comorbidities/complications			
Hypertension	82,321 (44)	11,718 (49)	6828 (52)
Disorder of lipid metabolism	74,347 (40)	10,762 (45)	6233 (47)
Obesity	21,582 (11)	2700 (11)	1745 (13)
Ischemic heart disease	12,400 (7)	2565 (11)	2169 (16)
Neuropathy	5105 (3)	1787 (8)	1608 (12)
Retinopathy	3815 (2)	1210 (5)	1164 (9)
Renal disease	3799 (2)	1686 (7)	1661 (13)
Stroke	3333 (2)	638 (3)	524 (4)
Acute myocardial infarction	1721 (1)	435 (2)	438 (3)
Hypoglycemia	766 (<1)	67 (<1)	81 (1)
Preindex claims[a]			
Biguanide	0	15,183 (64)	6674 (51)
Sulfonylurea	0	10,504 (44)	3866 (29)
Dipeptidyl peptidase-4 inhibitor	0	6445 (27)	2220 (17)
Thiazolidinedione	0	277 (1)	99 (1)
SGLT-2 inhibitor	0	1 (<1)	1 (<1)
Basal insulin	0	0	7652 (58)

CCI = Charlson comorbidity index; HMO = health maintenance organization; MDI = multiple daily injections of basal-bolus insulin; OAD = oral antidiabetic drug; PPO = preferred provider organization; SGLT-2 = sodium-glucose cotransporter-2.
[a] Some patients had claims for >1 antidiabetic agent during the 6-month preindex period.

Table II. Medical and type 2 diabetes mellitus (T2DM)-related costs, by antidiabetic treatment at index date. Data are given as year-2015 $ US, per patient per annum.

Cost type	OAD (n = 188,230)		Basal insulin (n = 23,724)		MDI (n = 13,181)	
	All medical costs	T2DM costs	All medical costs	T2DM costs	All medical costs	T2DM costs
Outpatient[a]						
Mean (SD)	4874 (10,704)	1594 (4474)	6084 (17,344)	2329 (6632)	10281 (29,462)	3653 (9672)
Median (IQR)	1946 (797–5105)	550 (261–1171)	2095 (873–5592)	795 (403–1726)	3372 (1280–9225)	1092 (520–2792)
Emergency department[b]						
Mean (SD)	294 (1654)	129 (834)	349 (1696)	195 (1114)	528 (2961)	305 (1434)
Inpatient hospitalization[b]						
Mean (SD)	2049 (13,093)	1282 (8817)	3387 (22,937)	2189 (12,925)	6377 (34,021)	4320 (25,192)
Pharmacy						
Mean (SD)	2445 (6344)	520 (1071)	4949 (8095)	2767 (2377)	8966 (11,644)	5565 (3968)
Median (IQR)	992 (363–2661)	97 (31–422)	3392 (1671–6075)	2123 (968–3959)	6703 (4024–10645)	4657(2801–7284)
Total						
Mean (SD)	9368 (20,339)	3396 (10,437)	14420 (32,951)	7285 (15,587)	25624 (52,112)	13538 (29,143)
Median (IQR)	3939 (1746–8841	910 (415–2399)	6940 (3707–13110)	3774 (2027–6718)	12433 (7185–23,874)	7320 (4426–12,488)

MDI = multiple daily injections of basal-bolus insulin; OAD = oral antidiabetic drug.

[a] Outpatient costs include costs of emergency department visits.

[b] All median (IQR) costs of emergency department visits and inpatient hospitalizations were $0.

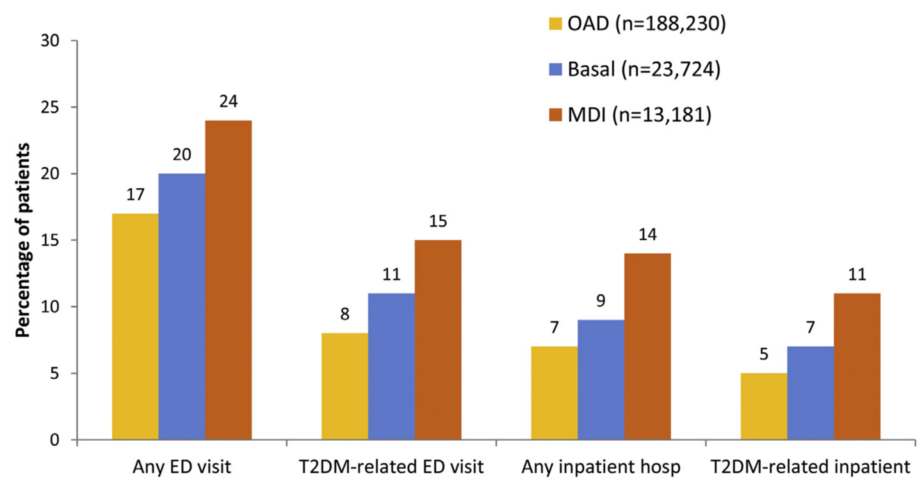

Figure 2. Percentages of patients with ≥1 emergency department (ED) visit and ≥1 inpatient hospitalization (hosp), all-cause (any) and related to T2DM. MDI = multiple daily injections of basal-bolus insulin; OAD = oral antidiabetic drug.

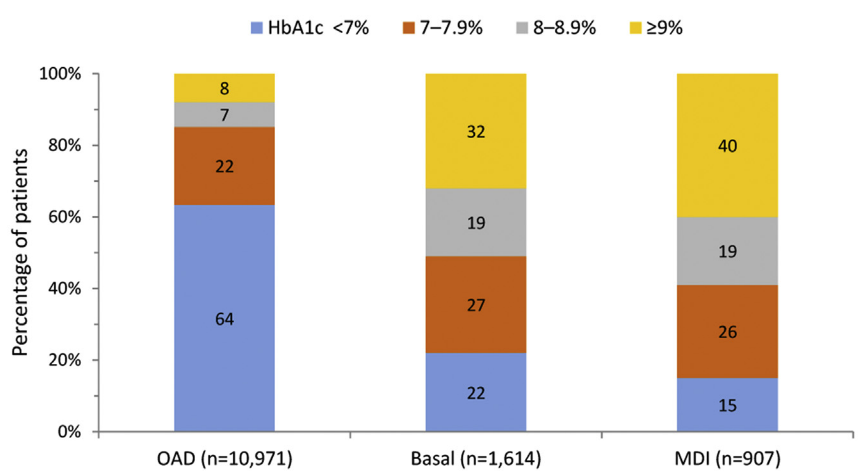

Figure 3. Percentages of patients with hemoglobin (Hb) A_{1c} results available in each HbA_{1c} category, from 3 to 12 mo (multiple values averaged), by treatment cohort. MDI = multiple daily injections of basal-bolus insulin; OAD = oral antidiabetic drug.

practice settings to 73% in clinical trials,[7,8,11,18] with an estimated mean across clinical trials of 53.0% (95% CI, 47%–59%) in a recent systematic review.[18] In our study, nearly two thirds of patients with HbA_{1c} results in the OAD cohort achieved glycemic control. By contrast, the percentage of patients achieving glycemic control was low in the basal insulin cohort (22%) and lower still in the MDI cohort (15%). Findings of a recent observational study using data from US electronic medical records indicated that the percentage of patients with HbA_{1c} values of >9% (poor control) was 9% versus 28% in a non-MDI versus MDI cohort, respectively[19] (in our study, 8% and 32% in the non-MDI cohorts vs 40% in the MDI cohort had HbA_{1c} values of ≥9%). These findings together suggest that achieving and maintaining glycemic control is increasingly challenging as diabetes progresses, especially among patients utilizing MDI therapy.

Insulin is recognized as the most effective glucose-lowering agent for T2DM when used as directed, and a guideline from the American Diabetes Association recommends treatment with basal and bolus insulins in patients who fail to achieve glycemic control with OAD and basal insulin therapy.[16] Nonetheless, instituting an MDI regimen introduces several challenges for patients, including multiple daily injections, the use of different insulin preparations, an increased risk for hypoglycemia, the need for frequent dose adjustments, and resultant interference with activities of daily living.[20] Both providers and patients consider insulin therapy to be restrictive, citing the same 5 most common reasons for lack of adherence and missed insulin doses: busy schedules, travel, skipped meals, stress/emotional problems, and public embarrassment.[21] One third of patients on insulin-containing regimens report not taking insulin as prescribed on a mean of 3.3 days per month.[21,22] Not surprisingly, adherence with insulin-containing regimens reportedly decreases with more prescribed injections and as regimens become more complex.[23,24] One-year rates of persistence with MDI are reported to be as low as 21% in the clinical practice setting.[25]

Alternative delivery and management options can be considered when patients on MDI are no longer achieving glycemic control. Insulin pumps, insulin delivery systems, continuous glucose monitoring, and other technologies, while associated with up-front costs, can potentially reduce the complexity of insulin therapy, improve adherence and persistence, and subsequently glycemic control, potentially delaying the progression of diabetes-related complications and related health care costs.[9,26,27] In the OpT2mise (A Randomized Controlled Trial To Compare Insulin Pump Therapy With Multiple Daily Injections in the Treatment of Type 2 Diabetes) randomized clinical trial, continuous subcutaneous insulin infusion was shown to improve glycemic control and reduce the total daily dose of insulin in patients with suboptimally controlled T2DM. The patients with T2DM uncontrolled on MDI who were switched to a durable insulin pump experienced a 1.1% decrease in HbA_{1c} levels that was sustained at 1 year and was significantly greater ($p<0.001$) than the 0.4% decrease observed in patients continuing on MDI.[9,28]

Study Strengths and Limitations

The use of a large-scale claims database enabled us to examine clinical and economic outcomes in >225,000 patients with T2DM, including >13,000 patients prescribed MDI therapy. The Truven MarketScan databases are well-managed claims databases commonly used to study HCRU and costs.[12,23] For the eligibility criteria, we restricted the list of concurrent antidiabetic medications in each treatment cohort in order to study mutually exclusive cohorts with no overlap; the use of a GLP-1 receptor agonist was an exclusion criterion in all 3 cohorts. We followed up each patient for 12 months after the index claim date to capture HCRU and both all-cause and diabetes-related costs. We relied on descriptive analyses to characterize patients and provide a 1-year snapshot of outcomes in the 3 treatment cohorts.

The use of claims data is limited, however, by the absence of detailed prescribing information, such as total daily insulin dose and number of insulin injections per day. The Truven database represents insured, employed individuals and their families; thus, the study cohorts are not representative of a national cohort of patients with T2DM, which would include patients with Medicaid or Medicare coverage. Moreover, the clinical outcomes data were analyzed only in the small-scale subpopulation with available laboratory test results, limiting the generalizability of these findings. The subsets of patients with available HbA_{1c} data were a convenience sample; therefore, we cannot rule out selection bias for this outcome.

In addition, medical and pharmacy claims do not provide access to all relevant patient characteristics, including weight and body mass index, or information about lifestyle modifications and other health behaviors that could have an impact on clinical and economic outcomes. Additionally, study outcomes were not analyzed by demographic characteristics of the sample.

The identification of patients with T2DM relied on diagnosis codes in medical claims, and therefore on the accuracy of the coding on those claims. The medication claims used to identify patients in each cohort were limited to prescription drug fills that were adjudicated by health insurance. For the determination of diabetes-related HCRU and costs, the T2DM diagnosis code could have been in any position in the claims; therefore, this approach could have resulted in overestimation of the T2DM-related costs. Nonetheless, the costs reported in this study do not reflect the full range of costs related to T2DM, because indirect costs, such as lost productivity and absenteeism, were not included. Finally, the 12-month study timeframe could not detect the long-term impact of diabetes control on diabetes-related complications and comorbidities.

CONCLUSIONS

These descriptive findings contrast the demographic and clinical characteristics and outcomes of patients prescribed MDI with those of patients likely earlier in the progression of T2DM who are prescribed OAD or basal insulin therapy. Patients prescribed MDI therapy have a greater disease burden and experience greater medical costs and HCRU than do patients treated with OAD or basal insulin therapy. Among the limited number of patients with available HbA_{1c} values after the index date, poor rates of glycemic control were evident among patients prescribed MDI, with only 15% achieving recommended goals for glycemic control during the postindex year. These findings highlight the economic and clinical burdens of T2DM during a year of therapy with MDI.

Conflicts of Interest

This work, and writing and editorial assistance, were supported by Becton, Dickinson and Company (BD, Franklin Lakes, New Jersey).

D. Brixner has received consultation fees from BD, Abbott, and AbbVie; has served on the advisory boards of AstraZeneca and Avexis; and has received research grants to the University of Utah from Bristol-Myers Squibb, Novartis, AstraZeneca, Myriad Genetics, and Sanofi. A. Ermakova, Y. Xiong, R. Sieradzan, and S.D. Taylor are employees and stockholders of BD. N. Sacks is an employee of Precision Xtract, which has received consultation fees from BD for both the conduct of this study and apart from the submitted work. P. Cyr is an employee of Precision Xtract, which has received consultation fees from BD for both the conduct of this study and apart from the submitted work, and he owns stock options in Precision Medicine Group. The authors have indicated that they have no other conflicts of interest with regard to the content of this article.

ACKNOWLEDGMENTS

Medical writing and editorial assistance was provided by Elizabeth V. Hillyer, DVM.

The study sponsor participated in the study design. All of the authors, including those employed by the study sponsor, participated in the analysis and interpretation of the data; in the writing of the manuscript; and in the decision to submit the manuscript for publication. All of the authors approved the final manuscript. D. Brixner provided conceptualization, writing-reviewing, and editing. A. Ermakova, R. Sieradzan, and S.D. Taylor provided conceptualization, methodology, writing-reviewing, and editing. Y. Xiong provided conceptualization, methodology, formal analysis, writing-reviewing, and editing. N. Sacks provided writing of the original draft. P. Cyr provided writing-reviewing.

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Address correspondence to: Stephanie D. Taylor, PhD, Health Economics and Outcomes Research, Becton, Dickinson and Company, 1 Becton Drive, Franklin Lakes, NJ 07417, USA. E-mail: Stephanie.Taylor@bd.com

APPENDIX I

International Classification of Disease, Ninth Revision, Clinical Modification (ICD-9-CM) and ICD, Tenth Revision (ICD-10-CM) diagnostic codes used in the study.

- Type 2 diabetes diagnosis (inclusion criterion)
  - ICD-9-CM codes 250.x0 or 250.x2
  - ICD-10-CM code E11
- Type 1 diabetes diagnosis (exclusion criterion)
  - ICD-9-CM codes 250.x1, 250.x3
  - ICD-10-CM code E10
- Evidence of pregestational diabetes, gestational diabetes, or diabetes with pregnancy/labor and delivery (exclusion criterion)
  - ICD-9-CM codes 630.xx-679.xx, 648.0x, 648.8x,
    V220, V221, V222
  - ICD-10-CM codes O00-O16, O20-O48, O60-O77, O80-O82, O85-O92, O94-O99, O9A, Z33, Z34, Z3A
- Diagnosis of cancer/malignant tumors (exclusion criterion)
  - ICD-9-CM codes 140.xx-172.xx, 174.xx-195.xx, 196.xx-198.xx, 199.xx, 200.xx-208.xx, 209.0x-209.3x, 230.xx-234.xx
  - ICD-10-CM codes C00-D49 (excluding D10-D36 and D3A)