ORIGINAL RESEARCH

Adherence to Insulin Pen Therapy Is Associated with Reduction in Healthcare Costs Among Patients with Type 2 Diabetes Mellitus

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BACKGROUND: Type 2 diabetes mellitus is a chronic metabolic disorder that poses a significant economic burden on the US healthcare system associated with direct and indirect medical costs, loss of productivity, and premature mortality.

OBJECTIVES: To determine whether increased adherence to therapy among patients with type 2 diabetes who use an insulin pen is associated with reduced healthcare costs, and to describe the overall healthcare costs of patients with type 2 diabetes.

METHODS: This retrospective claims database analysis used the Truven Health MarketScan Commercial and Medicare Supplemental databases to identify patients diagnosed with type 2 diabetes with at least 1 insulin pen prescription claim between January 2006 and September 2010. Insulin pen adherence was measured using the medication possession ratio (MPR). The cost outcomes included all-cause and type 2 diabetes–related costs by type of service (ie, inpatient, outpatient medical, outpatient pharmacy), which were calculated in 2011 US dollars. Insulin adherence and overall healthcare costs were evaluated over the 12-month postindex period.

RESULTS: A total of 32,361 patients met the study inclusion criteria, with an average MPR of 0.63 (standard deviation [SD], 0.29). Overall, patients with type 2 diabetes who used an insulin pen had an average annual healthcare cost of $19,612, which was driven by inpatient costs (37.2%) and outpatient pharmacy costs (24.4%). There is a significant difference in the average annual per-patient healthcare expenditures between the least adherent group (MPR <0.20; 11.0% of patients) and the most adherent group (MPR >0.80; 34.6% of patients) $26,310 versus $23,839, respectively (*P* = .007). Patients with the greatest insulin adherence had higher overall pharmacy costs than patients with the lowest insulin adherence ($10,174 vs $5395, respectively; *P* <.001).

CONCLUSIONS: The total healthcare expenditures of patients with type 2 diabetes who utilized insulin pens decreased with improvement in adherence, suggesting that higher rates of medication adherence may present an opportunity to curb healthcare costs in insulin pen users. The average sample MPR for our study population was 0.63 (SD, 0.29), indicating that insulin adherence continues to be a challenge for successful diabetes management. More research is needed to better characterize the relationship between medication adherence and healthcare costs among insulin users with type 2 diabetes and to identify the key drivers of adherence among this patient group.

KEY WORDS: type 2 diabetes, type 1 diabetes, insulin pen, healthcare cost, medical costs, pharmacy costs, insulin adherence, diabetes management

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Diabetes mellitus is a chronic metabolic disorder posing a significant economic burden on the US healthcare system. According to the American Diabetes Association, an estimated 22.3 million people in the United States were diagnosed with diabetes in 2012, representing approximately 7% of the population.[1]

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The prevalence of diabetes increased by 23% from 2007 to 2012 and is projected to increase to 1 in 3 adults by 2050.[1] In 2012, the total estimated cost of diagnosed diabetes was $245 billion, including $176 billion in direct medical costs and $69 billion in lost productivity.[1]

The most common long-term complications of diabetes mellitus are retinopathy, with a potential loss of vision; nephropathy leading to renal failure; peripheral neuropathy, which is associated with the risk for foot ulcers and amputation; and cardiovascular-related morbidity and mortality.[2] Patients with diabetes often progress toward numerous metabolic abnormalities, leading to a high risk for cardiovascular-related morbidity and mortality, with greater disease severity associated with higher risk.[3]

Diabetes is classified into type 1, type 2, and gestational disease. Type 1 diabetes accounts for approximately 5% to 10% of all cases of diabetes in the United States, whereas type 2 diabetes accounts for 90% to 95% of all cases.[2]

Glycemic control is crucial for preventing or minimizing the long-term complications associated with diabetes. To achieve and maintain optimal glycemic control, type 1 diabetes is generally managed through lifestyle changes. Similarly, type 2 diabetes management may also require lifestyle changes (including diet), but the disease may progress to require a combination of oral medications, noninsulin injectables, and/or insulin therapy in addition to lifestyle changes.[4]

The American College of Endocrinology (ACE) and American Association of Clinical Endocrinologists (AACE) suggest lifestyle management for all phases of type 2 diabetes, intensifying at higher hemoglobin (Hb) A_{1c} levels. The ACE/AACE guidelines also recommend initiating oral antidiabetic medications when the HbA_{1c} level is between 6% and 7%, and adding insulin therapy when the HbA_{1c} level exceeds 8% among therapy-naïve patients, typically beginning with basal (ie, long-acting) insulin, and adding bolus (ie, short-acting) insulin if further intervention is needed.[4]

Because of the substantial human and economic burdens of type 2 diabetes, there is interest in understanding real-world patient adherence to, and persistence with, insulin therapy in this patient population; adherence measures the use of a medication as directed during treatment, and persistence measures treatment duration.[5] Previous research has described poor adherence to oral medications and to insulin therapy.[6] Similarly, insulin persistence is low, ranging from 26% to 52% in the year after the initiation of basal insulin, and even lower, at 19% to 42%, for bolus insulin.[7]

Recent research suggests that patients with type 2 diabetes who start therapy or are converted to insulin therapy with a pen demonstrate comparable or improved medication adherence versus patients who receive insulin with a vial or syringe.[8-10] Health resource utilization, based on claims for hypoglycemic events, emergency department visits, physician visits, and annual medication costs, was found to be lower in patients using insulin pens.[8-10] Compared with syringes, insulin pen devices have been shown to provide more reliable, accurate, and simplified dosing.[11-13]

Insulin delivery systems other than a vial or a syringe have the potential to improve factors such as patient treatment satisfaction, treatment adherence, and clinical outcomes.[9] The use of these systems, such as prefilled insulin pens, in the United States has lagged behind other countries.[9]

The substantial and growing burden of type 2 diabetes and opportunities to curb its associated costs have been the focus of policymakers, payers, and nonprofit organizations. Strategies to improve medication adherence and its potential to lower healthcare resource utilization and costs for patients with type 2 diabetes are of interest to a wide variety of stakeholders.[14,15] Consequently, there is significant interest in understanding the association between insulin adherence and healthcare costs for patients with type 2 diabetes who are insulin pen users.

KEY POINTS

- Type 2 diabetes mellitus carries a major economic burden stemming from direct and indirect medical costs, loss of productivity, and premature mortality.
- This retrospective claims-based analysis investigated whether improved adherence to insulin pen therapy could mitigate healthcare costs in patients with type 2 diabetes.
- The average annual per-patient healthcare expenditures in the least adherent cohort was 1.53 times higher ($27,707) than in the most adherent group of patients ($18,068).
- In the postindex period, the total all-cause expenditures were significantly (P = .007) lower for the most adherent group ($23,839) versus the least adherent group ($26,310).
- Patients with the greatest insulin adherence had almost double the overall pharmacy costs compared with patients with the lowest adherence ($10,174 vs $5395, respectively; P <.001).
- According to this real-world pharmacy and medical analysis, the total healthcare cost of patients with type 2 diabetes who used insulin pens decreased with improvement in adherence.
- More research is needed to characterize the exact relationship between insulin adherence and healthcare costs.

The objectives of this study were to determine if higher insulin pen adherence among patients with type 2 diabetes who are insulin pen users was associated with lower healthcare costs, and to describe the overall healthcare costs of patients with type 2 diabetes. This study may provide insights to payers and providers to guide future analyses in identifying ways to improve diabetes care outcomes and to lower the associated healthcare expenditures.[16]

Methods

Study Design

In this retrospective claims database study we analyzed privately insured patients diagnosed with type 2 diabetes between January 2006 and September 2010. In this study, we evaluated the impact of adherence to insulin therapy on healthcare costs among patients with type 2 diabetes using insulin pens.

For this study, we used 2 MarketScan research databases from Truven Health—the Commercial Claims and Encounters (commercial) database and the Medicare Supplemental and Coordination of Benefits (Medicare supplemental) database. The commercial database contains the inpatient, outpatient, emergency department, and outpatient prescription drug experiences of several million individuals and their dependents in the United States. The overall database includes individuals from more than 100 self-insured employers and health plans. The Medicare supplemental database contains the healthcare data of individuals with Medicare supplemental insurance paid for by employers. The MarketScan research databases contain the healthcare data of privately insured individuals covered under a variety of fee-for-service, fully capitated, and partially capitated health plans. The health plans include preferred provider organizations, point of service plans, indemnity plans, and HMOs.

Inclusion Criteria

The Truven Health MarketScan Research Databases were used to identify adults (aged ≥18 years) with at least 1 insulin pen prescription claim (ie, the index event) between January 2006 and September 2010. They were also required to have continuous medical and pharmacy benefits for 12 months before and after the index event. Patients were required to have a diagnosis of type 2 diabetes mellitus (*International Classification of Diseases, Ninth Revision, Clinical Modification* [*ICD-9-CM*] code 250.x0 or 250.x2) and the use of any oral antidiabetes agent in the 12 months before the index event. Patients were excluded if they had a diagnosis of type 1 diabetes mellitus (*ICD-9-CM* code 250.x1 or 250.x3) or gestational diabetes (*ICD-9-CM* code 648.8x), or if they used an insulin pump or oral or inhaled insulin during the study period.

The demographic characteristics were defined at the index event, including age, sex, geographic region, and insurance plan type, as shown in **Table 1**. The clinical characteristics were defined separately for the 12 months before and after the index event based on the presence of nondiagnostic or nonancillary claims for microvascular conditions (ie, diabetic retinopathy, macular edema, diabetic neuropathy, amputation, ulceration, renal disease), macrovascular conditions (ie, myocardial infarction, ischemic heart disease, congestive heart failure, peripheral vascular disease, cerebrovascular disease), and other general comorbid conditions (ie, anxiety, depression, dyslipidemia, hypertension).

The use of biguanides, sulfonylureas, meglitinides, thiazolidinediones, alpha-glucosidase inhibitors, fixed-dose therapies, antihyperlipidemics, antihypertensives, antidepressants, antiobesity medications, antiemetic/antinausea medications, exenatide, and liraglutide was also reported separately in the 12 months before and after the index event.

Measurements

The Charlson/Deyo Comorbidity Index, which measures the severity of comorbid conditions, was calculated and reported separately for the 12 months before and after the index insulin pen claim.[17] Adherence to insulin was measured using the medication possession ratio (MPR), which is a standard measure for assessing treatment adherence as the extent to which a patient acts in accordance with the prescribed dosing interval and dose of a regimen. Persistence is defined as the duration of time from the initiation of a therapy to its discontinuation. In this analysis, adherence is used as an overarching term to describe adherence to therapy and persistence with therapy. MPR is a frequently used measure of adherence.[18] Because of the data source, however, MPR is actually measuring refill adherence, because the data source does not contain information on whether the medication was actually used by the patient.

The MPR was calculated using the days' supply filled of the insulin prescription claims, which was adjusted to account for variations in time between insulin refills.[19] The MPR was reported as a continuous measure. The patients were also stratified by MPR quintile, ranging from least compliant (MPR, 0-0.20) to most compliant (MPR, 0.81-1.00). Insulin nonpersistence was previously defined as the presence of a 90-day gap in prescription claims for insulin.[20,21]

The annual direct medical costs were calculated by summing the patient and payer portions of all health insurance claims for the year before and the year after the index claim. The total costs were reported, as were the inpatient, outpatient, emergency department, and out-

Table 1 Demographic Characteristics of Study Participants

	Medication possession ratio					
Patient demographics	0.0-0.20 (N = 3560)	0.21-0.40 (N = 4093)	0.41-0.60 (N = 5973)	0.61-0.80 (N = 7529)	0.81-1.00 (N = 11,206)	Total (N = 32,361)
Age, yrs, mean (SD)	57.5 (13.0)	58.0 (12.7)	58.8 (12.2)	59.6 (11.3)	59.8 (10.4)	59.1 (11.6)
Age-group, N (%)						
18-24 yrs	14 (0.4)	13 (0.3)	7 (0.1)	11 (0.1)	7 (0.1)	52 (0.2)
25-34 yrs	103 (2.9)	123 (3.0)	128 (2.1)	112 (1.5)	121 (1.1)	587 (1.8)
35-44 yrs	449 (12.6)	441 (10.8)	558 (9.3)	535 (7.1)	603 (5.4)	2586 (8.0)
45-54 yrs	875 (24.6)	1023 (25.0)	1432 (24.0)	1699 (22.6)	2535 (22.6)	7564 (23.4)
55-64 yrs	1223 (34.4)	1415 (34.6)	2230 (37.3)	3009 (40.0)	4859 (43.4)	12,736 (39.4)
65-74 yrs	470 (13.2)	598 (14.6)	888 (14.9)	1353 (18.0)	2029 (18.1)	5338 (16.5)
75-84 yrs	357 (10.0)	408 (10.0)	620 (10.4)	695 (9.2)	942 (8.4)	3022 (9.3)
≥85 yrs	69 (1.9)	72 (1.8)	110 (1.8)	115 (1.5)	110 (1.0)	476 (1.5)
Sex, N (%)						
Male	1744 (49.0)	2036 (49.7)	2939 (49.2)	3963 (52.6)	6272 (56.0)	16,954 (52.4)
Female	1816 (51.0)	2057 (50.3)	3034 (50.8)	3566 (47.4)	4934 (44.0)	15,407 (47.6)
Geographic region, N (%)						
Northeast	368 (10.3)	438 (10.7)	597 (10.0)	859 (11.4)	1390 (12.4)	3652 (11.3)
North Central	1070 (30.1)	1253 (30.6)	1977 (33.1)	2627 (34.9)	4069 (36.3)	10,996 (34.0)
South	1632 (45.8)	1737 (42.4)	2438 (40.8)	2903 (38.6)	4029 (36.0)	12,739 (39.4)
West	459 (12.9)	643 (15.7)	914 (15.3)	1094 (14.5)	1659 (14.8)	4769 (14.7)
Unknown	31 (0.9)	22 (0.5)	47 (0.8)	46 (0.6)	59 (0.5)	205 (0.6)
Health plan type, N (%)						
Capitated[a]	719 (20.2)	778 (19.0)	1149 (19.2)	1284 (17.1)	1723 (15.4)	5653 (17.5)
Noncapitated/fee for service[b]	2739 (76.9)	3200 (78.2)	4645 (77.8)	6033 (80.1)	9177 (81.9)	25,794 (79.7)
Unknown	102 (2.9)	115 (2.8)	179 (3.0)	212 (2.8)	306 (2.7)	914 (2.8)

[a]Capitated plans include HMO and capitated POS.
[b]Noncapitated plans include PPO, noncapitated POS, basic medical, comprehensive, and consumer-driven healthcare plans.
POS indicates point of service; PPO, preferred provider organization; SD, standard deviation.

patient pharmacy costs. The all-cause and diabetes-related costs before and after the index claim were reported separately. The diabetes-related costs were defined as the paid amount (health plan and payer portions) on claims with a primary diagnosis of type 2 diabetes in any setting of care. All costs were adjusted to 2011 US dollars using the medical component of the Consumer Price Index.

This was a descriptive study and, as such, standard descriptive tests were used, where appropriate, to identify significant differences across the MPR categories; Fisher's exact tests were used for comparing the means between the cohorts, and chi-square tests were used for tests of proportions. The cohort demographics, resource utilization before and after the index claim, and the expenditures were compared across the MPR categories.

Results

Patient Demographics

A total of 32,361 patients met the study criteria. The average patient age was 59.1 years (standard deviation [SD], 11.6) years, and 52.4% of the patients were male. Of the sample, 97.1% had a capitated, noncapitated, or fee-for-service health plan. As shown in Table 1, the MPR does not appear to differ by region or plan type; however, the MPR does appear to differ by age, with the highest MPR among patients aged 55 to 64 years.

Table 2 Baseline Clinical Characteristics of Study Participants

Patient baseline characteristics	Medication possession ratio 0-0.20 (N = 3560)	0.21-0.40 (N = 4093)	0.41-0.60 (N = 5973)	0.61-0.80 (N = 7529)	0.81-1.00 (N = 11,206)	Total (N = 32,361)
Charlson/Deyo Comorbidity Index, mean (SD)	2.3 (2.0)	2.0 (1.8)	2.0 (1.7)	2.0 (1.7)	2.0 (1.7)	2.0 (1.7)
Microvascular complications, N (%)						
Eye conditions (diabetic retinopathy and macular edema)	208 (5.8)	299 (7.3)	498 (8.3)	634 (8.4)	975 (8.7)	2614 (8.1)
Diabetic neuropathy	538 (15.1)	551 (13.5)	865 (14.5)	1131 (15.0)	1682 (15.0)	4767 (14.7)
Amputation and ulceration	118 (3.3)	155 (3.8)	193 (3.2)	243 (3.2)	358 (3.2)	1067 (3.3)
Renal disease	584 (16.4)	570 (13.9)	785 (13.1)	1000 (13.3)	1510 (13.5)	4449 (13.7)
Macrovascular complications, N (%)						
Myocardial infarction	115 (3.2)	113 (2.8)	120 (2.0)	152 (2.0)	233 (2.1)	733 (2.3)
Ischemic heart disease	766 (21.5)	780 (19.1)	1084 (18.1)	1501 (19.9)	2298 (20.5)	6429 (19.9)
Congestive heart failure	309 (8.7)	346 (8.5)	435 (7.3)	582 (7.7)	809 (7.2)	2481 (7.7)
Peripheral vascular disease	232 (6.5)	224 (5.5)	341 (5.7)	453 (6.0)	599 (5.3)	1849 (5.7)
Cerebrovascular disease	338 (9.5)	353 (8.6)	427 (7.1)	560 (7.4)	816 (7.3)	2494 (7.7)
Other comorbidities, N (%)						
Hypertension	1700 (47.8)	1693 (41.4)	2424 (40.6)	3030 (40.2)	4398 (39.2)	13,245 (40.9)
Anxiety	177 (5.0)	170 (4.2)	211 (3.5)	254 (3.4)	329 (2.9)	1141 (3.5)
Dyslipidemia	1110 (31.2)	1177 (28.8)	1632 (27.3)	2036 (27.0)	3028 (27.0)	8983 (27.8)
Depression	236 (6.6)	211 (5.2)	299 (5.0)	387 (5.1)	455 (4.1)	1588 (4.9)
Obesity	271 (7.6)	208 (5.1)	317 (5.3)	363 (4.8)	480 (4.3)	1639 (5.1)
Hypoglycemia	245 (6.9)	262 (6.4)	350 (5.9)	406 (5.4)	551 (4.9)	1814 (5.6)
Hyperglycemia	3359 (94.4)	3719 (90.9)	5388 (90.2)	6718 (89.2)	10,157 (90.6)	29,341 (90.7)
Outpatient medications of interest, N (%)						
Biguanides (metformin)	2036 (57.2)	2169 (53.0)	3248 (54.4)	4045 (53.7)	6254 (55.8)	17,752 (54.9)
Sulfonylureas	1709 (48.0)	1983 (48.4)	2840 (47.5)	3635 (48.3)	5620 (50.2)	15,787 (48.8)
Meglitinides	158 (4.4)	224 (5.5)	315 (5.3)	428 (5.7)	625 (5.6)	1750 (5.4)
Thiazolidinediones	1012 (28.4)	1257 (30.7)	1878 (31.4)	2357 (31.3)	3543 (31.6)	10,047 (31.0)
Alpha-glucosidase inhibitors	32 (0.9)	56 (1.4)	66 (1.1)	89 (1.2)	149 (1.3)	392 (1.2)
Fixed-dose therapies	606 (1.07)	771 (18.8)	1052 (17.6)	1238 (16.4)	1920 (17.1)	5587 (17.3)
Antihyperlipidemics	2209 (62.1)	2584 (63.1)	3929 (65.8)	5210 (69.2)	8300 (74.1)	22,232 (68.7)
Antihypertensives	2688 (75.5)	3066 (74.9)	4583 (76.7)	5968 (79.3)	9337 (83.3)	25,642 (79.2)
Antidepressants	980 (27.5)	1064 (26.0)	1559 (26.1)	2100 (27.9)	3106 (27.7)	8809 (27.2)
Antiobesity medications	9 (0.3)	13 (0.3)	14 (0.2)	24 (0.3)	32 (0.3)	92 (0.3)
Antiemetics/antinausea medications	345 (9.7)	297 (7.3)	398 (6.7)	484 (6.4)	705 (6.3)	2229 (6.9)
Exenatide	452 (12.7)	549 (13.4)	878 (14.7)	1243 (16.5)	2052 (18.3)	5174 (16.0)
Liraglutide	21 (0.6)	23 (0.6)	42 (0.7)	58 (0.8)	88 (0.8)	232 (0.7)

SD indicates standard deviation.

Clinical Characteristics

Overall, the average sample MPR was 0.63 (SD, 0.29). **Table 2** summarizes the baseline clinical characteristics of the study population, stratified by MPR. The baseline Charlson/Deyo comorbidity score was 2.0 (SD, 1.7).

The most common comorbidities included hypertension (40.9%), dyslipidemia (27.8%), ischemic heart disease (19.9%), diabetic neuropathy (14.7%), and renal disease (15.9%); 5.1% of patients had a claim with an *ICD-9-CM* code for obesity. The patients frequently continued to fill oral antidiabetes medication prescriptions after initiating an insulin pen, with the most common being biguanides (54.9%) and sulfonylureas (48.8%).

Healthcare Costs

The patients' expenditures before and after the index claim were analyzed by MPR quintiles, wherein patients were stratified from least adherent (MPR, 0-0.20) to most adherent (MPR, 0.81-1.00). **Table 3** summarizes the preindex annual healthcare expenditures of the study patients.

The mean preindex all-cause annual per-patient expenditures totalled $19,612 (SD, $40,571). The mean preindex diabetes-related annual per-patient expenditures totaled $2866 (SD, $5187). The preindex outpatient annual per-patient pharmacy costs were higher for the most adherent patients compared with the least adherent patients ($5683 vs $3852, respectively); the outpatient pharmacy costs also accounted for a larger proportion (31%) of the preindex total costs among the most adherent patients versus the least adherent patients (14%).

In the preindex period, the mean all-cause annual per-patient expenditures in the least adherent group were $27,707 (SD, $53,270), whereas the mean all-cause expenditures were $18,068 (SD, $38,504) in the most adherent group, or 1.53 times (P <.001) higher in the least adherent subgroup.

Table 4 summarizes the postindex annual per-patient healthcare expenditures. The mean all-cause annual per-patient expenditures for insulin pen users during the study period were $24,680 (SD, $44,005). The mean diabetes-related annual per-patient expenditures totaled $4952 (SD, $5209) and significantly increased after the index for all MPR groups, except the least adherent. For the least adherent group, we observed that the inpatient costs were 29% of the total all-cause expenditures versus 19% of the total all-cause expenditures for the most adherent group, which are likely driven by differences in the proportion of patients with an inpatient stay (37.3% vs 25.3%; P <.001).

The postindex outpatient annual per-patient pharmacy costs were higher for the most adherent patients than for the least adherent patients ($10,174 vs $5395, respectively; P <.001); the outpatient pharmacy costs also represented a larger proportion of the total postindex healthcare costs among the most adherent patients (43%) compared with the least adherent patients (21%). In the postindex period, the total all-cause annual per-patient expenditures were 9.4% (P = .007) lower for the most adherent group ($23,839; SD, $33,617) than for the least adherent group ($26,310; SD, $49,026).

Discussion

This study evaluated the relationship of insulin adherence to healthcare costs for a population of patients with type 2 diabetes using an insulin pen. Poor adherence is of particular concern in patients with type 2 diabetes, because previous studies have demonstrated that improved adherence to insulin therapy may substantially reduce the direct and indirect medical costs of type 2 diabetes for these patients.[22,23] Poor adherence not only increases the risk for poor diabetes-related clinical outcomes, but it may also heighten the likelihood of concomitant renal and cardiovascular damage.[24]

In our analysis, patients with type 2 diabetes in the lowest quintile of adherence (by MPR) had total healthcare expenditures of >$26,000 annually compared with <$24,000 in the most adherent quintile, nearly a 10% difference that is highly statistically significant. These differences in total expenditures remain, despite the finding that outpatient pharmacy–related costs in the most adherent subgroup were much higher than for the least adherent quintile (>$10,000 vs ~$5400, respectively). These relationships strongly suggest benefits of improved adherence to prescribed medical therapies in the population with type 2 diabetes.

A systematic review of the literature on adherence and persistence of pharmacotherapeutic diabetes management found that patients frequently fail to comply with lifestyle management plans and treatment for diabetes, including insulin, noninsulin injectables, and oral hypoglycemic agents.[6] The reasons for poor adherence are multifactorial, including communication between patient and provider, inadequate patient knowledge about antidiabetes medications, complex treatment regimens and their required follow-up, and insulin (and needle) resistance.[25-28] In addition to being more user-friendly and convenient, insulin pens offer improved dose accuracy; superior portability; and easier, less painful injections than vial and syringe methods.[29-31]

The burden of poorly managed type 2 diabetes includes costs directly associated with type 2 diabetes as well as related conditions that are associated with poorly managed type 2 diabetes. As part of a large survey of US Medicare beneficiaries with self-reported diabetes, Stuart and colleagues found that greater medication adherence

Table 3 Preindex Annual Healthcare Expenditures Per Patient

Healthcare expenditures	Medication possession ratio 0.0-0.20 (N = 3560) Mean (SD), $	0.21-0.40 (N = 4093) Mean (SD), $	0.41-0.60 (N = 5973) Mean (SD), $	0.61-0.80 (N = 7529) Mean (SD), $	0.81-1.00 (N = 11,206) Mean (SD), $	Total (N = 32,361) Mean (SD), $
All-cause expenditures						
Inpatient admissions	13,424 (42,333)	8776 (30,953)	6742 (25,515)	6553 (28,717)	5608 (31,808)	7298 (31,403)
Emergency department visits	491 (1553)	391 (1328)	315 (1131)	308 (1281)	269 (1767)	327 (1480)
Outpatient office visits	975 (954)	903 (938)	877 (784)	890 (843)	906 (804)	904 (845)
Primary care physician	477 (508)	435 (449)	449 (481)	442 (460)	461 (476)	453 (474)
Endocrinologist	68 (168)	78 (181)	75 (169)	75 (172)	80 (174)	76 (173)
Nurse practitioner	6 (48)	6 (51)	6 (52)	7 (51)	7 (52)	6 (51)
Other physicians	360 (585)	316 (661)	289 (458)	298 (475)	298 (477)	305 (513)
Outpatient laboratory and radiology						
Laboratory services	789 (2118)	654 (1802)	569 (1542)	538 (1236)	520 (1384)	580 (1539)
Radiology services	1407 (5965)	809 (2376)	854 (3325)	806 (3120)	727 (2337)	854 (3296)
Other outpatient services	6769 (17,813)	5531 (18,502)	4803 (18,461)	4375 (11,697)	4354 (13,340)	4857 (15,334)
Outpatient prescriptions (pharmacy)	3852 (4859)	3924 (6259)	4331 (8013)	4755 (4560)	5683 (5062)	4793 (5798)
Total expenditures	27,707 (53,270)	20,989 (43,392)	18,491 (38,161)	18,225 (36,192)	18,068 (38,504)	19,612 (40,571)
Diabetes-related expenditures						
Inpatient admissions	672 (7364)	408 (4605)	420 (5453)	265 (2791)	271 (3907)	359 (4609)
Emergency department visits	45 (264)	42 (337)	26 (192)	25 (229)	19 (160)	27 (224)
Outpatient office visits	282 (264)	310 (306)	318 (280)	325 (296)	339 (296)	322 (292)
Primary care doctor	172 (204)	184 (223)	193 (227)	194 (225)	206 (237)	194 (227)
Endocrinologist	60 (154)	73 (171)	70 (161)	71 (164)	76 (168)	71 (165)
Nurse practitioner	2 (25)	3 (30)	3 (33)	3 (35)	4 (38)	3 (34)
Other physicians	31 (111)	31 (115)	33 (110)	34 (120)	33 (113)	33 (114)
Outpatient laboratory and radiology						
Laboratory services	135 (272)	140 (282)	140 (273)	135 (263)	139 (261)	138 (268)
Radiology services	11 (112)	7 (62)	7 (73)	7 (88)	6 (67)	7 (79)
Other outpatient services	272 (1446)	275 (1427)	256 (1027)	289 (1574)	254 (852)	267 (1229)
Outpatient prescriptions	987 (1179)	1233 (1329)	1523 (1521)	1778 (1669)	2268 (1946)	1745 (1721)
Total expenditures	2405 (7632)	2415 (5113)	2690 (5907)	2825 (3778)	3298 (4595)	2866 (5187)

SD indicates standard deviation.

was significantly associated with lower medical costs and a reduced risk for hospitalization; each additional antidiabetes drug prescription was associated with a net $71 decrease in Medicare spending, which incorporates the cost of the prescription.[32] These findings are substantively similar to our analysis, albeit in a more aged patient population (Medicare beneficiaries) and using older data (1997-2004).

According to a study conducted in 2012 by the American Diabetes Association examining the economic burden of diabetes care, the most influential factors in driving costs stem from the inpatient setting, from increased hospitalization rates and longer average lengths of stay.[1] Together, these 2 factors accounted for more than 40% of the medical cost of diabetes.[1] In our current analysis, the presence and length of inpatient stays were significant cost-drivers. The patients in the least adherent quintile had an average inpatient admission cost of $7543, which was $3058 greater than the cost in the most adherent quintile ($4485); the patients in the most expensive quintile (MPR, 21-40) had an inpatient cost ($8674) that was nearly twice that of the most adherent quintile.

According to research by the National Institute of Diabetes and Digestive and Kidney Diseases, each percentage point reduction in HbA_{1c} reduced the risk for microvascular complications by 40%.[33] In another study, 78% of

Table 4 Postindex Annual Healthcare Expenditures Per Patient

Healthcare expenditures	Medication possession ratio 0.0-0.20 (N = 3560) Mean (SD), $	0.21-0.40 (N = 4093) Mean (SD), $	0.41-0.60 (N = 5973) Mean (SD), $	0.61-0.80 (N = 7529) Mean (SD), $	0.81-1.00 (N = 11,206) Mean (SD), $	Total (N = 32,361) Mean (SD), $
All-cause expenditures						
Inpatient admissions	7543 (27,815)	8674 (46,659)	7465 (38,569)	5889 (24,291)	4485 (21,542)	6228 (30,581)
Emergency department visits	548 (2880)	432 (1494)	427 (1740)	369 (1509)	315 (1223)	389 (1675)
Outpatient office visits	1138 (1073)	1091 (932)	1109 (913)	1156 (997)	1158 (875)	1138 (942)
Primary care physician	528 (569)	506 (508)	526 (522)	537 (525)	548 (527)	534 (528)
Endocrinologist	80 (178)	93 (194)	99 (199)	105 (214)	118 (231)	104 (212)
Nurse practitioner	8 (54)	7 (50)	8 (56)	11 (80)	9 (63)	9 (64)
Other physicians	438 (689)	395 (618)	389 (583)	407 (598)	402 (556)	404 (595)
Outpatient laboratory and radiology						
Laboratory services	901 (2694)	781 (2615)	719 (2233)	685 (1933)	645 (1867)	713 (2160)
Radiology services	1576 (6706)	1232 (5035)	1099 (4123)	1108 (4907)	978 (3543)	1129 (4612)
Other outpatient services	9208 (27,778)	7792 (25,265)	7236 (20,182)	6695 (18,253)	6084 (17,264)	6998 (20,552)
Outpatient prescriptions	5395 (7509)	6017 (7130)	6913 (7144)	8303 (5798)	10,174 (6108)	8085 (6775)
Total expenditures	26,310 (49,026)	26,019 (60,894)	24,968 (50,935)	24,206 (37,794)	23,839 (33,617)	24,680 (44,005)
Diabetes-related expenditures						
Inpatient admissions	274 (4335)	247 (3540)	281 (3162)	231 (3627)	161 (3079)	223 (3441)
Emergency department visits	22 (184)	20 (160)	22 (166)	22 (222)	18 (315)	20 (240)
Outpatient office visits	308 (286)	341 (290)	367 (311)	394 (329)	414 (324)	380 (317)
Primary care physician	182 (225)	190 (226)	203 (235)	216 (244)	227 (257)	210 (243)
Endocrinologist	72 (166)	86 (183)	92 (185)	99 (205)	111 (212)	97 (198)
Nurse practitioner	3 (32)	3 (35)	4 (43)	5 (48)	5 (49)	5 (44)
Other physicians	33 (105)	38 (129)	42 (130)	45 (137)	45 (138)	42 (132)
Outpatient laboratory and radiology						
Laboratory services	134 (361)	142 (303)	151 (269)	160 (397)	160 (284)	153 (322)
Radiology services	6 (52)	9 (98)	10 (108)	8 (84)	9 (100)	9 (93)
Other outpatient services	441 (2801)	391 (1224)	461 (1652)	523 (2270)	537 (3123)	491 (2477)
Outpatient prescriptions	1449 (1235)	2154 (1307)	2932 (1499)	3824 (1837)	5237 (2548)	3676 (2371)
Total expenditures	2634 (5830)	3304 (4144)	4224 (4099)	5162 (4885)	6536 (5549)	4952 (5209)

SD indicates standard deviation.

diabetes-related inpatient costs, 47% of physician office visit costs, 82% of emergency department visit costs, and 52% of hospital outpatient costs were attributed to a combination of only a few diabetes-related medical and cardiovascular conditions.[1] Similarly, in a 2011 review, Asche and colleagues reported that diabetic patients with an MPR of <80% have a 2.5 times greater risk for hospitalization related to diabetes than patients with an MPR of >80% (odds ratio, 2.53; 95% confidence interval, 1.38-4.64), a finding mirrored in this current analysis.[34,35]

Limitations

This analysis is subject to limitations inherent in the data source. First, it does not include socioeconomic status, anthropometric information, race or ethnicity, and mortality information. The data source also lacked data on clinical characteristics, such as HbA_{1c} levels, body weight, and body mass index or obesity, all of which may impact diabetes management and healthcare costs. Likewise, hypoglycemia during a hospitalization may have contributed to the discontinuation of insulin and could not be accounted for as a result of *ICD-9* coding limitations. Economic factors, such as barriers to obtaining pharmacy benefits, were also not accounted for.

The data for this study came mainly from large US employers and health plans, and therefore may not be generalizable to patients covered by other types of health plans, such as those with no insurance coverage or patients who are covered through the Veterans Affairs.

Finally, our observational study design does not allow any causal inferences to be made regarding our findings; this study is not designed to describe a direct causal relationship between insulin MPR and healthcare costs. It is instead intended to present descriptive analyses of insulin pen adherence and the potential association with healthcare costs. The presence of differences in preindex costs for patients with higher or lower insulin pen adherence underlies the complexity of the relationship between diabetes management and healthcare costs.

Conclusions

This study adds to a growing body of literature describing the burden of poor management of type 2 diabetes, including poor insulin adherence. Our study results are consistent with the published literature in describing the benefits of better insulin adherence in terms of healthcare costs. As expected, increased adherence was associated with increased outpatient pharmacy costs; previous research has demonstrated that the increased costs associated with increased adherence were more than offset by associated reductions in other medical and pharmacy costs.[32]

The average sample MPR for our study population was 0.63 (SD, 0.29), indicating that the average adherence to insulin was still relatively poor and continues to be a challenge for the successful management of diabetes. A plausible goal for MPR is at least 0.8, which was obtained by approximately 33% of patients in this analysis.

More research is needed to identify specific characteristics of better adherence as well as strategies or technologies that can lead to improved adherence among patients with type 2 diabetes. Further research should focus on the development of adherence measures that capture the effects of human and economic factors that can influence medication adherence. Furthermore, future analysis should focus on the interplay among insulin pen adherence and other antihyperglycemic therapies; this descriptive analysis focuses only on insulin pen adherence. ■

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Author Disclosure Statement

Dr Bonafede is an employee of Truven Health Analytics, which was contracted by Becton Dickinson to conduct this study; Ms Chandran is, Ms Nigam was, and Ms Saltiel-Berzin is an employee of Becton Dickinson; Dr Hirsch is an employee of and holds stocks in Becton Dickinson, as well as in Merck; Ms Lahue is an employee of and holds stocks in Becton Dickinson.

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STAKEHOLDER PERSPECTIVE

Adherence to Antihyperglycemic Treatment Regimen Also Reduces Overall Costs

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There are currently 14 classes of antihyperglycemic medications available for treating type 2 diabetes.[1] Despite the extensive and diverse treatment options, more than 50% of patients with type 2 diabetes are still not achieving glycemic goals of hemoglobin (Hb) A_{1c} levels <7%,[2-5] as recommended by the American Diabetes Association and the American Association of Clinical Endocrinologists (AACE). The reasons for the failure to achieve glycemic control are multifactorial; however, medication nonadherence is one major issue frequently encountered in this population.[6] In patients receiving oral medications for glycemic control, the rate of adherence has been reported to be as low as 65%.[7] The adherence rate for patients receiving insulin is even lower, ranging from 26% to 52% in the year after the initiation of basal insulin, and 19% to 42% for bolus insulin.[8,9]

PATIENTS/PROVIDERS: Glycemic control in patients with type 2 diabetes is important to prevent long-term micro- and macrovascular complications, especially when the control is achieved early in the disease process.[1,10] The recently updated "AACE/ACE Comprehensive Diabetes Management Algorithm 2015" recognized that there is a continuum of risk for poor health outcomes in the progression from normal glucose tolerance to overt type 2 diabetes.[5] Early interventions, combining lifestyle modifications, weight-loss control, and early use of antihyperglycemic agents is recommended for all at-risk patients, especially those who are over-

STAKEHOLDER PERSPECTIVE *Continued*

weight or obese, or in patients with prediabetes.

Because diabetes is a progressive disease, most patients will require pharmacologic therapy that will need to be intensified over time. The success of the treatment regimen depends on the patient's adherence to the recommended therapy. One study demonstrated an inverse relationship between prescribed oral antihyperglycemic drugs and HbA_{1c} levels: with each 10% increase in adherence rate, a decrease of 0.1% in HbA_{1c} was observed.[11] The common reasons for medical nonadherence include fear of treatment side effects (weight gain, hypoglycemia), needle anxiety, complexity of the treatment regimen, and costs or formulary issues.[12-14]

The emergence of the latest 3 classes of drugs—glucagon-like peptide (GLP)-1 receptor agonists; dipeptidyl peptidase (DPP)-4 inhibitors; and sodium-glucose cotransporter 2 (SGLT2) inhibitors—offers treatment options that may alleviate the fear of hypoglycemia and weight gain that initially plagued the older diabetes drugs.

These 3 classes have low hypoglycemic risks, and the GLP-1 receptor agonists and SGLT2 inhibitors can promote weight-loss effects when used alone or in combination.[15] The SGLT2 and DPP-4 inhibitors are once-daily oral medications, and are available in combination with metformin to decrease pill burden. The GLP-1 receptor agonists are available as injection pens, with treatment frequency ranging from twice-daily to weekly injections. The use of insulin pens over syringes may also improve the adherence rate.[13]

In the current retrospective claims database analysis, Chandran and colleagues demonstrated a significant, nearly 10% difference in total healthcare expenditures (>$26,000 vs <$24,000) between the lowest adherence quintile and the highest adherence quintile in patients using insulin pens.[9] This relationship remains despite the findings that outpatient pharmacy costs in the most adherent subgroup were higher than in the least adherent quintile.[9] These findings suggest the benefits of improved glycemic control and lower complication rates with improved adherence to prescribed medical therapies.

PAYERS: The rates of nonadherence to type 2 diabetes treatments are similar to the corresponding rates for other chronic diseases.[16,17] Advances in delivering and monitoring devices, combination therapies, and more convenient treatment frequencies are new strategies that have emerged only within the past 3 or 4 years. The benefits of these interventions are yet to be fully appreciated.

Chandran and colleagues demonstrated an important concept in their study, showing that although the patients with the greatest insulin adherence rate had a higher overall outpatient pharmacy cost compared with patients with the lowest insulin adherence rate, the total healthcare expenditures for the highest adherence group were significantly lower.[9] ■

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