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SYMPOSIUM

Predictors of Initiating Rapid-Acting Insulin Analog Using Vial/Syringe, Prefilled Pen, and Reusable Pen Devices in Patients with Type 2 Diabetes

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Abstract

Background:

Limited data are available on the predictors of insulin delivery device choice. This study assessed the patient- and health-care-system-related factors that predict the initiation of one rapid-acting insulin analog (RAIA) delivery system over another.

Methods:

A retrospective analysis using a claims database (January 1, 2007, through March 31, 2009) was conducted. Patients were required to be diagnosed with type 2 diabetes mellitus, and have ≥12 months of continuous eligibility prior to their first prescription of a RAIA on or after January 1, 2008. The three cohorts in the study were vial/syringe (n = 6820), prefilled pen (n = 5840), and reusable pen (n = 2052). Multiple factors were examined using stepwise logistic regression.

Results:

Factors that increased the likelihood of initiating RAIA using prefilled pen versus vial/syringe included endocrinologist visit [odds ratio (OR) = 3.13, 95% confidence interval (CI) = 2.56, 3.82], prior basal insulin use with pen (OR = 4.85, 95% CI = 4.21, 5.59), and use of ≥1 oral antihyperglycemic agents (OR = 1.32, 95% CI = 1.20, 1.45). Factors that decreased the likelihood included inpatient admission (OR = 0.76, 95% CI = 0.70, 0.83), nursing home visit (OR = 0.22, 95% CI = 0.18, 0.27), and obesity (OR = 0.67, 95% CI = 0.53, 0.83). There were fewer differences between prefilled and reusable pen initiators. Factors that increased the likelihood of initiating with prefilled versus reusable pen included endocrinologist visit (OR = 1.87, CI = 1.50, 2.34) and inpatient admission (OR = 1.46, 95% CI = 1.30, 1.64).

Conclusion:

Significant differences in predictors were observed between prefilled pen and vial/syringe initiators. The differences were fewer between prefilled and reusable pen initiators. These differences should be taken into consideration when evaluating outcomes associated with specific insulin delivery systems.

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Abbreviations: (CCI) Charlson Comorbidity Index, (CI) confidence interval, (DACON) daily average consumption, (HbA1c) hemoglobin A1c, (MPR) medication possession ratio, (OHA) oral antihyperglycemic agent, (OR) odds ratio, (RAIA) rapid-acting insulin analog, (T2DM) type 2 diabetes mellitus

Keywords: insulin, pen device, type 2 diabetes mellitus, vial

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Background

Diabetes is a common and costly disease. In 2007, there were 23.6 million people in the United States with diagnosed and undiagnosed diabetes (7.8% of the total population).[1] Studies show that the overall costs for treating diabetes are lower in individuals with optimal glycemic control (hemoglobin A1c [HbA1c] <7.0%) than those with suboptimal control and that optimal control results in decreased progression of the disease and mortality.[2–5]

Insulin is an effective pharmacotherapy for lowering glycemia.[6,7] Despite the well-documented effectiveness of insulin and other antihyperglycemic agents, a large number of patients with type 2 diabetes mellitus (T2DM) do not achieve HbA1c <7.0%.[8] Less than optimal adherence to prescribed therapies may be a contributing factor. According to Cramer,[9] adherence to oral antihyperglycemic agents (OHAs) and insulin range from 36–93% and 62–64%, respectively. Several treatment-, patient-, and physician-related factors have been identified to be associated with nonadherence to antihyperglycemic agents.[10–12] Examples of treatment-related factors include the complexity of the drug regimen, incorrect dose titration, or frequency; patient-related factors may include fear of hypoglycemia, needle use, or unwanted weight gain; and physician-related factors may include concern that patients may not be able to use the therapies properly.[10,13,14] Other research found that patients feared social stigma, reduced quality of life, injection pain, the permanence and restrictiveness of insulin, as well as the side effects of insulin, namely, hypoglycemia and weight gain.[12,15]

To date, three studies compared the real-world patient outcomes of prefilled pen devices to traditional vial/syringe. Lee *et al.*[16] and Cobden *et al.*[17] reported significant improvements in insulin adherence and reductions in diabetes-related and total health care expenditures after patients switched from vial/syringe to a pen.[16,17] Pawaskar *et al.*[18] compared the outcomes of either initiating or switching from vial/syringe to a pen versus those who initiated or remained on vial/syringe. The study found that diabetes-related medication adherence was greater in the pen cohort than the vial/syringe cohort for the pen-naïve comparison, but not for the insulin-naïve comparison.[18] Both diabetes-related and total health care expenditures were significantly lower in the pen cohort than the vial/syringe cohort for the insulin-naïve comparison, but not for the pen-naïve comparison.[18]

Studies that examine the factors that increase or decrease the likelihood of introducing one insulin injection delivery system versus another are limited. In 2008, a study by Rubin and Peyrot[19] found that, when patients felt encouraged by their physicians to use a pen, patients were over 100 times more likely to use a pen compared to patients with physicians who did not discuss pen use or were described as discouraging pen use.[19] Patients who felt that the use of a pen facilitates self-care were 20 times more likely to use the pen than vial/syringe.[19] The purpose of this study was to determine the key patient- and health-care-system-related factors that predict the initiation of rapid-acting insulin analog (RAIA) using vial/syringe, prefilled pen, or reusable pen devices in patients with T2DM.

Methods

Data Source

Medical insurance claims from January 1, 2007, to March 31, 2009, were extracted from the Thomson Reuters MarketScan® Research databases (Ann Arbor, MI,). These databases contain claims of over 22 million individuals who were insured with a variety of commercial health plans during the study period, over half of which are large self-insured employers. All study data were compliant to the Health Insurance Portability and Accountability Act and statistically de-identified for research purposes. Therefore, Institutional Review Board approval was not required.

Study Population

Patients were required to have ≥12 months of eligibility and continuous enrollment for medical and pharmacy benefits, and have ≥1 diagnosis of T2DM (International Classification of Disease, 9th Edition, Clinical Modification [ICD-9-CM] 250.x0, 250.x2) during the 12-month period prior to the index date. The index date was the date of first prescription of a RAIA (i.e., insulin aspart, insulin lispro and insulin glulisine) on or after January 1, 2008. Patients initiating a RAIA were further categorized into (1) prefilled pen cohort (Humalog KwikPen, Novolog® FlexPen®, or Apidra® Solostar®), (2) vial/syringe cohort, and (3) reusable pen cohort. Patients were excluded if they had at least one prescription of RAIA, type 1 diabetes (ICD-9-CM: 250.x1, 250.x3), claims for insulin pumps or pump supplies, inhaled insulin, or evidence of

pregnancy or gestational diabetes (ICD-9-CM: 630-679 or V codes, which are supplementary classification factors for pregnancy) during the 12-month pre-index period.

Definition of Variables

Demographic characteristics examined in the study included age, gender, insurance plan type, geographic region, population density (urban/rural), census-based median household income, and proportion of college graduates in patient's five-digit zip code. Insurance plan type included capitated versus noncapitated and Medicare versus commercial. Provider type was identified by reviewing each patient's outpatient claims on the same day or within 7 days prior to the index date. The provider type nearest in time to the index prescription was chosen for each patient as a proxy for the provider type who prescribed the index RAIA.

Comorbidities and prior medication use were assessed during the 12-month pre-index period. Individual comorbidities, including renal and eye disorders, were assessed using ICD-9-CM codes on inpatient and outpatient claims. A full list of individual comorbidities is included in **Table 1**. Overall comorbid status was measured using the Deyo Charlson Comorbidity Index (CCI)[20] during the 12-month pre-index period. Pharmacy claims were used to identify individual OHA, insulin, device type, diabetes-related medications, and noninsulin antihyperglycemic injectables (hereafter, exenatide/pramlintide; administered with vial/syringe or pen). A full list of individual medications is included in **Table 2**. Insulin and device type were categorized as (1) analog basal or human intermediate-acting insulin used with any pen device (basal pen), (2) analog basal or human intermediate-acting insulin used with vial/syringe (basal vial), (3) other human or analog insulin (e.g., premixture) used with any pen device (other pen), (4) other human or analog insulin (e.g., premixture) used with vial/syringe (other vial), and (5) insulin naïve.

Two proxy variables were created to (1) assess availability of insulin pen at the insurance level (hereafter, index pen utilization) and (2) adherence to antihyperglycemic agents. The first variable was created at the health plan level and expressed in deciles after computing the proportion (insulin pen claims/total insulin claims) for each health plan from January 1, 2007, to March 31, 2009. Patients with higher values were insured in health plans that had higher proportions of insulin pen availability than vial/syringe for all of their enrollees. The second proxy, adherence to antihyperglycemic agents (hereafter, insulin and/or OHAs) during the pre-index year was created by first combining estimates of insulin and OHA adherence and then creating a binary measure (poor versus adequate to good adherence). Insulin adherence was estimated using daily average consumption (DACON).[21,22] Patients were categorized as "low" (<10th percentile, <21 U/day), "normal" (≥21 U/day), or "no insulin." Oral antihyperglycemic agent adherence was estimated using medication possession ratio (MPR; calculation = number of days of medication supplied within the refill interval/number of days in refill interval).[16–18,23] Patients were categorized as "low" (<10th percentile, MPR <0.73), "normal," or "no OHA." The overall adherence proxy was categorized as poor if a patient had (1) low DACON and either low or no OHA or (2) no insulin and low OHA. All other patients—those with normal DACON, normal OHA, or no antihyperglycemic agents—were categorized as having adequate to good adherence.

Health care resource utilization and expenditure variables were assessed during the 12-month pre-index period. Binary measures (any visit versus no visit) were created for previous inpatient admission, emergency room visit, and nursing home visit. Number of HbA1c tests and number of visits to ophthalmologists, podiatrists, dietitians, and visits for diabetes outpatient self-management training (hereafter, self-management training) were captured. Diabetes outpatient self-management training was identified using Health Care Common Procedure Coding System codes G0108 and G0109. Diabetes-related health care expenditures were identified by any medical claim with a primary diagnosis of diabetes (ICD-9-CM: 250.xx) or a pharmacy claim for insulin or OHA. Total health care expenditures included payments to providers made by insurance plans and patient out-of-pocket expenditures. Patient out-of-pocket expenditures included total patient copayment, co-insurance, and deductibles.

Statistical Analyses

Baseline characteristics of prefilled pen initiators were compared to vial/syringe initiators and to reusable pen initiators using t-tests for continuous variables and chi-square tests for binary variables. Two multivariate logistic regression models were (1) prefilled pen versus vial/syringe and (2) prefilled pen versus reusable pen. All of the pre-index period variables defined earlier were considered as potential predictors in the models. Additionally, pairwise interactions of significant main effects, as well as interactions of age with all significant variables, were tested for significance. Stepwise regression with a 5% significance threshold was used to select the final variables for inclusion in each model. All statistical tests were conducted using SAS (version 9.2).

Table 1.
Demographic and Clinical Characteristics at Baseline

	Prefilled pen (*n* = 5840)	Vial/syringe (*n* = 6820)	*p* value[a]	Reusable Pen (*n* = 2052)	*p* value[a]
	A	B	A versus B	C	A versus C
Male	54.5%	51.2%	0.000	54.5%	0.950
Mean age (standard deviation)	58.5 (12.3)	62.9 (14.1)	0.000	58.6 (12.4)	0.891
Urban	83.1%	80.1%	0.000	82.6%	0.560
Western region[b]	12.4%	18.7%	0.000	18.7%	0.000
Capitated insurance	13.6%	14.8%	0.055	16.0%	0.008
Medicare coverage	22.2%	36.4%	0.000	21.8%	0.678
Percent college graduate in patient's zip code	24.7%	23.7%	0.000	24.2%	0.232
Median income in patient's zip code (mean, standard deviation)	$47,148 ($16,335)	$46,231 ($16,062)	0.002	$47,346 ($16,353)	0.636
Physician type					
Primary care	25.4%	26.3%	0.246	31.8%	0.000
Endocrinologist	8.9%	2.3%	0.000	4.8%	0.000
Nurse practitioner or physician assistant	0.68%	0.70%	0.899	0.44%	0.222
Other specialists[c]	7.1%	7.9%	0.126	6.6%	0.391
Other providers	25.8%	27.9%	0.009	20.4%	0.000
Unknown	32.0%	34.9%	0.001	35.9%	0.001
Individual comorbidities					
Ischemic heart disease	25.4%	29.4%	0.000	21.7%	0.001
Diseases of arteries, arterioles, and capillaries	9.4%	12.0%	0.000	7.2%	0.003
Cerebrovascular diseases	2.7%	6.3%	0.000	1.9%	0.055
Hypertension	44.0%	48.7%	0.000	39.0%	0.000
Disorders of lipid metabolism	23.6%	20.4%	0.000	23.5%	0.910
Eye disorders	32.2%	35.0%	0.001	31.4%	0.499
Renal diseases	17.0%	21.4%	0.000	14.7%	0.015
Peripheral circulatory diseases	3.2%	4.7%	0.000	2.5%	0.148
Obesity	3.1%	4.0%	0.005	3.1%	0.934
Depression	6.1%	8.4%	0.000	6.3%	0.778
Diseases of esophagus, stomach, duodenum	10.3%	12.0%	0.003	8.6%	0.026
Neurological diseases	16.7%	18.7%	0.004	15.2%	0.116
Osteoarthritis	8.8%	12.1%	0.000	10.0%	0.099
Rheumatoid arthritis	1.3%	1.6%	0.115	1.3%	0.952
Conditions that affect mobility[d]	2.6%	4.4%	0.000	2.4%	0.540
Hypoglycemia[e]	1.8%	3.0%	0.000	1.1%	0.037
CCI (mean, standard deviation)	2.5 (2.0)	2.8 (2.3)	0.000	2.3 (2.0)	0.001
Index of pen utilization[f] (mean, standard deviation)	36.2 (8.7)	33.1 (8.7)	0.000	35.2 (8.7)	0.000

[a] *p* values were computed using *t*-test for continuous variables and chi-squared test for categorical variables.
[b] Western region includes Alaska, Arizona, California, Colorado, Hawaii, Idaho, Montana, Nevada, New Mexico, Oregon, Utah, Washington, and Wyoming.
[c] Other specialists include but are not limited to surgery, geriatric medicine, neurology, and gastroenterology.
[d] Includes diseases that affect mobility, such as multiple sclerosis and cerebral palsy, as well as amputations.
[e] ICD-9-CM codes 251.0x, 251.1x, 251.2x, and 250.3x were used to identify hypoglycemia during pre-index period.
[f] Index of pen utilization assesses availability of insulin pen at the insurance level. It is expressed in deciles after computing the proportion (insulin pen/total insulin claims) for each health plan. Patients with higher values were insured in health plans that had higher proportions of insulin pen availability than vial/syringe for all of their enrollees during the study period.

Table 2.
Health Care Resource Utilization and Expenditures at Baseline

	Prefilled pen (*n* = 5840)	Vial/syringe (*n* = 6820)	*p* value[a]	Reusable pen (*n* = 2052)	*p* value[a]
	A	B	A versus B	C	A versus C
OHAs					
Biguanides	47.3%	37.2%	0.000	46.6%	0.563
Sulfonylureas	43.1%	34.8%	0.000	38.8%	0.001
Thiazolidinediones	25.9%	22.2%	0.000	26.8%	0.427
Alpha-glucosidase inhibitors	0.8%	0.9%	0.499	0.4%	0.117
Meglitinides	5.1%	3.8%	0.000	3.6%	0.005
Dipeptidyl peptidase-4 inhibitors	14.7%	8.1%	0.000	11.6%	0.001
Combination of biguanide and sulfonylureas	7.0%	4.5%	0.000	6.1%	0.173
Combination of biguanide and thiazolidinediones	4.5%	2.6%	0.000	4.4%	0.974
More than one OHA	52.7%	37.5%	0.000	48.4%	0.001
At least one OHA	76.7%	65.8%	0.000	74.4%	0.033
Noninsulin antihyperglycemic injectables					
Exenatide	14.8%	6.1%	0.000	14.1%	0.433
Pramlintide	1.2%	0.8%	0.041	1.0%	0.411
At least one exenatide or pramlintide	15.8%	6.8%	0.000	14.8%	0.280
Diabetes-related medications					
Angiotensin-converting enzyme inhibitors	44.8%	44.6%	0.847	46.2%	0.244
Angiotensin-receptor blockers	27.9%	25.7%	0.005	28.0%	0.934
Anticoagulants/antiplatelets	20.1%	26.6%	0.000	19.3%	0.441
Beta blockers	39.7%	44.5%	0.000	40.5%	0.549
Calcium-channel blockers	26.3%	28.4%	0.007	25.0%	0.247
Diuretics	36.9%	45.3%	0.000	37.5%	0.605
Statins	68.1%	62.8%	0.000	68.5%	0.778
Pre-index insulin and device type[b]					
Basal pen	32.4%	5.1%	0.000	32.9%	0.709
Other pen	7.5%	1.9%	0.000	5.9%	0.010
Basal vial	16.4%	35.3%	0.000	24.2%	0.000
Other vial	7.1%	15.4%	0.000	7.9%	0.291
Insulin naïve	36.6%	42.4%	0.000	29.3%	0.000
Daily consumption of insulin					
Below 21 U	9.0%	8.2%	0.105	10.5%	0.040
21 or more U	38.0%	37.1%	0.341	44.7%	0.000
Missing units or no insulin in preperiod	53.0%	54.7%	0.067	44.7%	0.000
Total daily insulin dose >90 U	1.9%	2.6%	0.012	2.0%	0.680

continued →

Table 2. Continued

	Prefilled pen (*n* = 5840)	Vial/syringe (*n* = 6820)	*p* value[a]	Reusable pen (*n* = 2056)	*p* value[a]
	A	B	A versus B	C	A versus C
Proxy of poor adherence to insulin and/or OHAs					
Poor adherence	21.4%	21.6%	0.809	20.4%	0.339
Adequate to good adherence	78.6%	78.4%	0.809	79.6%	0.339
Number of HbA1c tests (mean, standard deviation)	1.49 (1.5)	1.03 (1.4)	0.000	1.45 (1.5)	0.278
Health care provider visits (mean, standard deviation)					
Ophthalmologist	0.82 (1.6)	0.81 (1.6)	0.739	0.79 (1.5)	0.573
Podiatrist	0.52 (1.5)	0.68 (1.7)	0.000	0.54 (1.6)	0.612
Dietitian	0.06 (0.52)	0.04 (0.49)	0.026	0.03 (0.29)	0.021
Diabetes self-management training	0.09 (0.47)	0.04 (0.31)	0.000	0.06 (0.39)	0.003
Health care facility visits					
Inpatient admission	35.1%	51.2%	0.000	26.7%	0.000
Emergency room visit	36.9%	47.4%	0.000	32.9%	0.001
Nursing home visit	2.9%	16.7%	0.000	2.8%	0.756
Health care expenditures (mean, standard deviation)					
Out-of-pocket medication expenditure	$802 ($661)	$737 ($675)	0.000	$796 ($663)	0.716
Total out-of-pocket expenditure	$1,889 ($3,732)	$1,902 ($2,971)	0.824	$1,707 ($2,252)	0.037
Diabetes-related health care expenditure	$1,670 ($3,762)	$1,999 ($9,501)	0.013	$1,548 ($3,711)	0.207
Total health care expenditure	$26,274 ($52,203)	$36,990 ($70,888)	0.000	$19,957 ($37,179)	0.000

[a] *p* values were computed using *t*-test for continuous variables and chi-squared test for categorical variables.
[b] Pre-index insulin and device type were categorized as (1) analog basal or human intermediate-acting insulin used with any pen device (basal pen), (2) analog basal or human intermediate-acting insulin used with vial/syringe (basal vial), (3) other human or analog insulin (e.g., premixture) used with any pen device (other pen), (4) other human or analog insulin (e.g., premixture) used with vial/syringe (other vial), and (5) insulin naïve.

Results

A total of 149,620 patients were identified as having a claim for RAIA as of January 1, 2008. Study sample attrition is shown in **Figure 1**. After applying inclusion and exclusion criteria, the final study sample included 14,712 patients who were initiated on RAIA with vial/syringe, prefilled pen, or reusable pen (**Figure 1**).

Descriptive Results

Prefilled Pen versus Vial/Syringe

Significant differences in baseline characteristics were observed between the prefilled pen and vial/syringe cohorts (**Tables 1** and **2**). The majority of demographic and socioeconomic variables were different between the two cohorts, including age, gender, Medicare coverage, urban residence, and median household income (**Table 1**). More prefilled pen patients than vial/syringe patients visited an endocrinologist within 7 days prior to index (8.9% versus 2.3%, $p < .001$). All individual comorbidities, hypoglycemia, and CCI were lower among prefilled pen patients than vial/syringe patients except for disorders of lipid metabolism. Utilization of any single OHA (except for alpha-glucosidase inhibitor) and ≥1 OHA was higher in the prefilled pen cohort than the vial/syringe cohort (**Table 2**). Use of diabetes-related medications was lower in the prefilled pen cohort than the vial/syringe cohort except for angiotensin-converting enzyme inhibitors, angiotensin-receptor blockers, and statins. In terms of insulin and device use, the prefilled pen cohort had fewer patients using a high total daily insulin dose (>90 U/day) than those in the vial/syringe cohort.

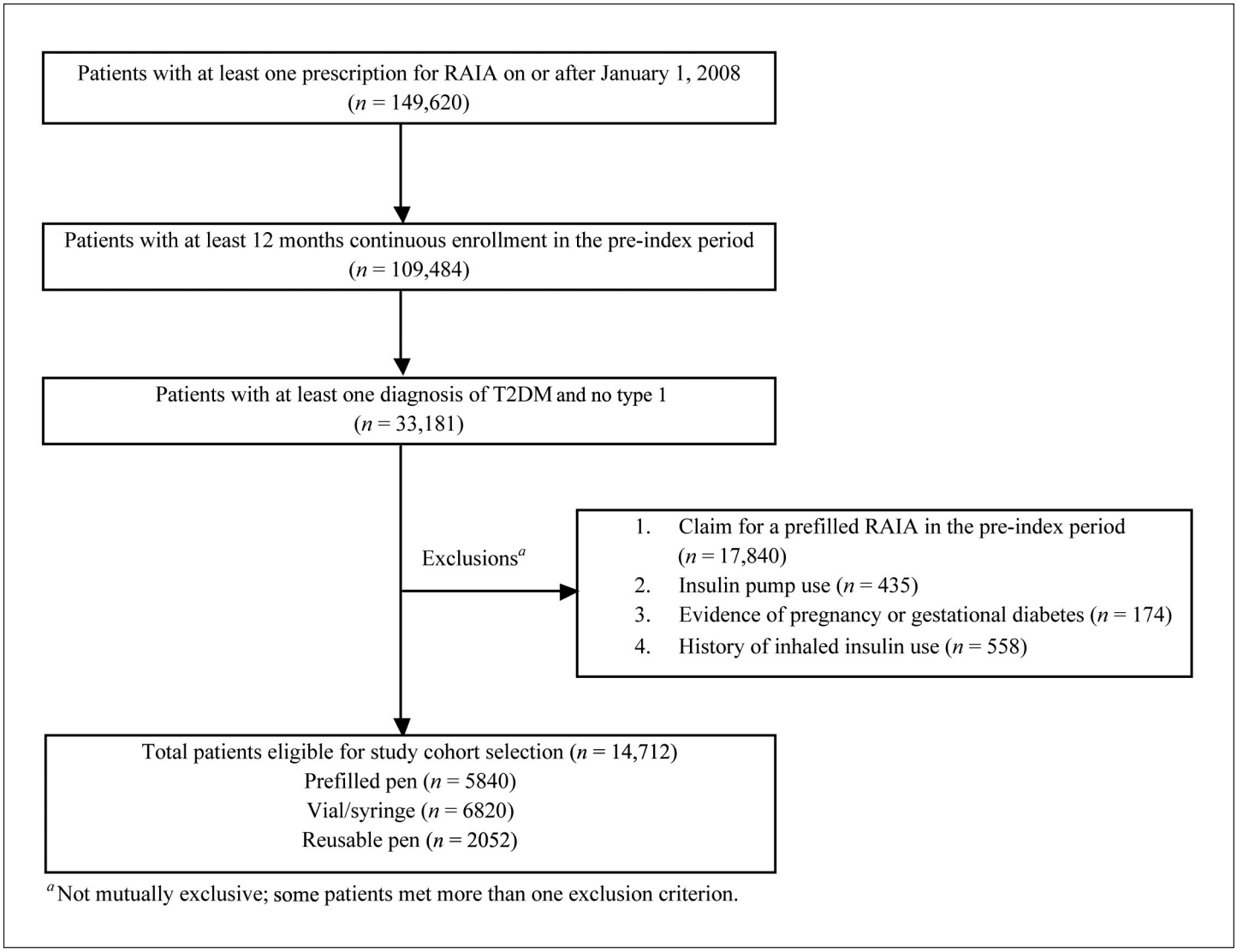

Figure 1. Study sample flow.

Patients in the prefilled pen cohort used more basal pen (32.4% versus 5.1%, $p < .001$) and other pen (7.5% versus 1.9%, $p < .001$), but a lower proportion were insulin naïve when compared to those in the vial/syringe cohort (36.6% versus 42.4%, $p < .001$). The number of HbA1c tests, dietitian visits, and self-management training visits were higher in the prefilled pen cohort than the vial/syringe cohort. Conversely, health care facility visits as well as diabetes-related and total pre-index period health care expenditures were lower in the prefilled cohort than the vial/syringe cohort.

Prefilled Pen versus Reusable Pen

Fewer significant differences in baseline characteristics were observed when comparing the prefilled and reusable pen cohorts (**Tables 1** and **2**). No differences were observed in age, gender, urban residence, or Medicare coverage. However, more prefilled pen patients than reusable pen patients visited an endocrinologist within 7 days prior to index (8.9% versus 4.8%, $p < .001$). Several individual comorbidities, including ischemic heart disease and hypertension, as well as the CCI, were higher among prefilled pen patients than reusable pen patients (**Table 1**). Utilization of certain OHAs, such as dipeptidyl peptidase-4 inhibitors and more than one OHA, was higher in the prefilled pen cohort than the reusable pen cohort. Use of other pen and the proportion of insulin-naïve patients were higher in the prefilled pen cohort than the reusable pen cohort. The number of visits to dietitians and for self-management training was higher in the prefilled pen cohort than the reusable pen cohort (**Table 2**). Prefilled pen patients had higher rates of inpatient admissions (35.1% versus 26.7%, $p < .001$) and total pre-index period health care expenditures but did not have

significantly different diabetes-related expenditures compared to the reusable pen patients.

Multivariate Results

Prefilled Pen versus Vial/Syringe

Significant results of prefilled pen versus vial/syringe multivariate regression model are shown in **Table 3**. Prefilled pen initiators were more likely to be men and live in locations where the percentage of college graduates was higher but were less likely to live in the Western region of the United States or receive Medicare benefits. The provider type was a significant predictor in the model; the odds of initiating a prefilled pen over vial/syringe in patients with an endocrinologist visit in the 7 days prior to index were three times those with a primary care or other specialist visit [odds ratio (OR) = 3.13, 95% confidence interval (CI) = 2.56, 3.82]. Prior use of antihyperglycemic agents was a significant predictor of prefilled pen use. Specifically, patients were more likely to initiate a prefilled pen than vial/syringe if they had received exenatide/pramlintide or had received ≥1 OHA (OR = 1.42, 95% CI = 1.23, 1.63 and OR = 1.32, 95% CI = 1.20, 1.45, respectively). Compared to insulin naïve, basal pen and other pen use increased the odds of receiving a prefilled pen over vial/syringe by 385% (OR = 4.85, 95% CI = 4.21, 5.59) and 255% (OR = 3.55, 95% CI = 2.84, 4.45), respectively. Compared to insulin-naïve patients, those who used basal vial or other vial in the preperiod were significantly less likely to initiate with a prefilled pen than with vial/syringe.

Table 3.
Multivariate Regression Results of Prefilled Pen versus Vial/Syringe[a]

Variables	Reference group	Odds ratio	95% confidence interval	
Male	Female	1.15	1.06	1.24
Urban	Rural	1.21	1.09	1.34
Western region	All other U.S. regions	0.70	0.62	0.78
Percent college graduate	Continuous variable	1.01	1.00	1.01
Uncapitated insurance	Capitated insurance	1.14	1.01	1.28
Medicare	Commercial insurance	0.82	0.74	0.91
Endocrinologist	All other physician types, including primary care and other specialists	3.13	2.56	3.82
Obesity	At least 1 ICD-9-CM code indicating obesity versus no ICD-9-CM code	0.67	0.53	0.83
At least one OHA	At least one OHA versus no OHA	1.32	1.20	1.45
Exenatide or pramlintide	At least one prescription of exenatide or pramlintide versus none	1.42	1.23	1.63
Insulin and device type				
Basal pen	Insulin naïve	4.85	4.21	5.59
Basal vial	Insulin naïve	0.38	0.34	0.43
Other pen	Insulin naïve	3.55	2.84	4.45
Other vial	Insulin naïve	0.46	0.40	0.53
Proxy of poor adherence to insulin and/or OHAs	Poor versus adequate to good adherence	0.89	0.80	0.99
Index of pen utilization in patient's health plan	Continuous variable	1.02	1.01	1.02
Number of HbA1c tests	Continuous variable	1.05	1.02	1.08
Inpatient admission	Any inpatient admission versus none	0.76	0.70	0.83
Nursing home visit	Any nursing home visits versus none	0.22	0.18	0.27
Diabetes-related health care expenditure (log)	Continuous variable	1.11	1.06	1.17

[a] All variables in were significant at alpha ≤0.05.

Index pen utilization and poor adherence to insulin and/or OHAs were significant predictors of prefilled pen use, but the 95% CIs were close to 1.0 (OR = 1.02, 95% CI = 1.01, 1.02 and OR = 0.89, 95% CI = 0.80, 0.99, respectively). The only comorbidity that was a significant predictor was obesity, which lowered the odds of receiving a prefilled pen by 33% (OR = 0.67, 95% CI = 0.53, 0.83). Inpatient admission and nursing home visits reduced the odds of initiating a prefilled pen device by 24% (OR = 0.76, 95% CI = 0.70, 0.83) and 78% (OR = 0.22, 95% CI = 0.18, 0.27), respectively. Patients who had more HbA1c tests were more likely to initiate a prefilled pen over vial/syringe. Patients with 172% higher diabetes-related health care expenditures had 11% higher odds of receiving a prefilled pen versus vial/syringe.

Prefilled Pen versus Reusable Pen

Significant results of prefilled pen versus reusable multivariate regression model are shown in **Table 4**. Fewer variables were significant in this comparison. The odds of initiating a prefilled pen versus a reusable pen were almost twice as high in patients with an endocrinologist visit within the 7 days prior to index than a primary care or other specialist visit (OR = 1.87, 95% CI = 1.50, 2.34). Patients who received ≥1 OHAs and those who used other pen had higher odds of initiating a prefilled pen than a reusable pen (OR = 1.20, 95% CI = 1.06, 1.35 and OR = 1.48, 95% CI = 1.15, 1.92, respectively). Patients with inpatient admissions had higher odds of initiating a prefilled pen over a reusable pen (OR = 1.46, 95% CI = 1.30, 1.64).

Discussion

In patients with T2DM who newly initiated a RAIA, the variable with the highest OR for the choice of a prefilled pen over vial/syringe was the type of insulin delivery system previously used. Patients who used an insulin pen previously were three to five times more likely to use a prefilled pen versus vial/syringe when initiating a RAIA than vial/syringe. Several hypotheses for this include (1) patients and/or the treating health care provider may have already been familiar with insulin pens, (2) patients may have been insured by health plans that had a comprehensive coverage of insulin pens, and/or (3) patients and/or the treating health care provider may have developed a preference for pen delivery systems.

Table 4.
Multivariate Regression Results of Prefilled Pen versus Reusable Pen[a]

Variables	Reference group	Odds ratio	95% confidence interval	
Western region	All other U.S. regions	0.67	0.58	0.77
Uncapitated insurance	Capitated insurance	1.15	1.00	1.33
Endocrinologist	All other physician types, including primary care and other specialists	1.87	1.50	2.34
Interaction term: both endocrinologist and vial/syringe[b]	Did not have both endocrinologist and vial/syringe	0.70	0.60	0.82
Osteoarthritis	At least one ICD-9-CM code indicating osteoarthritis versus no ICD-9-CM code	0.81	0.68	0.96
At least one OHA	At least one OHA versus no OHA	1.20	1.06	1.35
Insulin and device type[c]				
Basal pen	Insulin naïve	1.06	0.89	1.25
Basal vial	Insulin naïve	0.82	0.67	1.01
Other pen	Insulin naïve	1.48	1.15	1.92
Other vial	Insulin naïve	1.07	0.84	1.37
Inpatient admission	Any inpatient admission versus none	1.46	1.30	1.64

[a] All variables were significant at alpha ≤0.05.
[b] This variable compares patients who had both an endocrinologist visit and previous insulin use with vial/syringe versus those who did not have both.
[c] This variable was significant since ≥1 category within the variable (other pen versus insulin naïve) was significant.

Another key predictor with a large impact on the choice of prefilled pen over vial/syringe was an endocrinologist visit. One hypothesis is that endocrinologists may be more likely than other provider types to prescribe newer insulin devices, because they may have had more experience with them or because they may have had more support staff to recommend and discuss diabetes care options with patients. This seems likely in the context of a survey study by Rubin and Peyrot[19] that found that the dominating factor in the choice of a pen was physician recommendation. Our findings also indicate that increased use of diabetes-specific health care resources (e.g., number of HbA1c tests, use of OHAs, exenatide/pramlintide) were associated with the choice of a prefilled pen over vial/syringe. A hypothesis from this finding is that the increased health care utilization may have created more opportunities for interaction with health care providers and hence more opportunities to discuss alternative insulin delivery device options. Previous research has shown that patients who receive diabetes care from a multidisciplinary environment improve self-efficacy and self-care practices.[24]

Patients who had been hospitalized during the pre-index period were not as likely to receive a prefilled pen as vial/syringe. Although the timing or cause of hospitalization relative to RAIA initiation was not evaluated in this study, it is possible that some patients may have been recently hospitalized and were in a phase where their regimen was being adjusted and reevaluated. Poor adherence to insulin and/or OHAs was a significant predictor of prefilled pen use, but the 95% CI was close to 1.0. The effects of adherence to insulin and/or OHAs on device choice could be studied more explicitly in a population where all patients had previous insulin or OHAs.

There are several limitations to this study. As observed in other retrospective claims database analyses, the most completely recorded data are those that affect reimbursement. Hence it is expected that the capture of previous medications is highly accurate, whereas there is a potential for under-ascertainment of individual comorbidities. Also, information about whether a health care provider discussed pens as an option with a patient is not directly captured in a claims database. In this study, we created a proxy for prescriber by using the prescriber information on the patient's most proximate medical claim prior to initiating RAIA, within a limit of 7 days. Certain clinical variables such as duration of diabetes and HbA1c results were also not captured.

Conclusions

Significant differences in patient- and health-care-system-related factors were identified in the choice of insulin delivery system when initiating a RAIA in patients with T2DM . Previous pen use, endocrinologist visit, and increased diabetes-specific resource utilization were particularly significant. These differences should be taken into consideration when evaluating outcomes associated with the use of specific insulin delivery systems.

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