Trends in Insulin Initiation and Treatment Intensification Among Patients with Type 2 Diabetes

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BACKGROUND: Many patients with type 2 diabetes eventually require insulin, yet little is known about the patterns and quality of pharmacologic care received following insulin initiation. Guidelines from the American Diabetes Association and the European Association for the Study of Diabetes recommend that insulin secretagogues such as sulfonylureas be discontinued at the time of insulin initiation to reduce the risk of hypoglycemia, and that treatment be intensified if HbA1c levels remain above-target 3 months after insulin initiation.

OBJECTIVE: To describe pharmacologic treatment patterns over time among adults initiating insulin and/or intensifying insulin treatment.

DESIGN: Observational study.

SUBJECTS: A large commercially insured population of adult patients without recorded type 1 diabetes who initiated insulin.

MAIN MEASURES: We evaluated changes in non-insulin antidiabetic medication use during the 120 days immediately following insulin initiation, rates of increase in insulin dose and/or dosing frequency during the 270 days following an insulin initiation treatment period of 90 days, and rates of insulin discontinuation.

KEY RESULTS: Seven thousand, nine hundred and thirty-two patients initiated insulin during 2003–2008, with the majority (61 %) initiating basal insulin only. Metformin (55 %), sulfonylureas (39 %), and thiazolidinediones (30 %) were commonly used prior to insulin initiation. Metformin was continued by 64 % of patients following mixed or mealtime insulin initiation; the continuation rate was nearly as high for sulfonylureas (58 %). Insulin dose and/or dosing frequency increased among 22.9 % of patients. Insulin was discontinued by 27 % of patients.

CONCLUSIONS: We found evidence of substantial departures from guideline-recommended pharmacotherapy. Insulin secretagogues were frequently co-prescribed with insulin. The majority of patients had no evidence of treatment intensification following

insulin initiation, although this finding is difficult to interpret without HbA1c levels. While each patient's care should be individualized, our data suggest that the quality of care following insulin initiation can be improved.

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Type 2 diabetes is common and costly.¹ An estimated 25.8 million people in the United States—8.3 % of the population—have diabetes, including 18.8 million with diagnosed disease and another 7 million yet undiagnosed; type 2 diabetes accounts for approximately 95 % of these cases.² The economic burden of type 1 and type 2 diabetes has been estimated at \$245 billion, including direct medical costs and indirect costs related to disability, work loss, and premature mortality.¹ These estimates are projected to increase with rising obesity rates and an aging population.³

While treatment algorithms developed by the American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD) recommend metformin as the initial choice for patients with type 2 diabetes, over time, many patients will require intensification of therapy with medications including insulin. Among patients initially achieving diabetes control on a single oral medication in the United Kingdom Prospective Diabetes Study (UKPDS), 50 % and 75 % required the addition of a second drug after 3 and 9 years, respectively.⁴ The 2006 and 2009 ADA/EASD guidelines recommend that metformin treatment be followed by the addition of basal insulin or a sulfonylurea as second-step therapy if HbA1c levels remain $\geq 7\%$ after 2–3 months; the guidelines were updated in 2012 to include dipeptidyl peptidase-4 (DPP-4) inhibitors, GLP-1 receptor agonists, and thiazolidinediones as alternative second-step therapies, and to include regimens of twice daily pre-mixed insulin or basal plus mealtime insulin as initial insulin regimens for patients with severely elevated HbA1c levels.^{5,6} If HbA1c levels remain $\geq 7\%$ after another 3 months, the initiation or intensification of insulin is recommended as a third treatment step. Because insulin secretagogues such as sulfonylureas and meglitinides

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increase the risk of hypoglycemia,⁷ the ADA and EASD recommend that these agents be discontinued at prandial insulin initiation.

Despite the availability of guidelines and compelling evidence regarding the benefits of glucose control, US-based studies typically find only a third of patients at their target HbA1c.^{6–9} Recent work has focused on documenting delays in initiating insulin or intensifying oral therapy,^{8,9} and exploring patient and physician barriers to insulin initiation.^{10–12} Very little is known about patterns of treatment intensification among individual patients once insulin is initiated. Limited data from studies conducted in the United Kingdom and by Kaiser Permanente Northwest suggest that 75–90 % of patients are persistent with insulin, dose increases are far more common than changes in medications, and glycemic control remains suboptimal.^{13–15} In the absence of empirical evidence on the best approach to insulin initiation and intensification, it is important to understand current treatment patterns. We sought to describe treatment patterns among a large commercially insured population of adults initiating insulin, specifically evaluating changes in medication use following insulin initiation, including insulin intensification and adding or discontinuing non-insulin antidiabetic medications.

RESEARCH DESIGN AND METHODS

Study Cohort

We identified patients initiating insulin between July 2003 and December 2008 within data from Horizon Blue Cross Blue Shield of New Jersey. The Horizon database contains longitudinal claims for all filled prescriptions and clinical encounters. We defined insulin initiation as having no insulin prescriptions during the 180-day baseline period prior to filling an insulin prescription. We required that patients have continuous plan enrollment in the 180 days prior to insulin initiation, with at least one inpatient or outpatient medical claim and one prescription drug claim to demonstrate healthcare system use.¹⁶ We further restricted our cohort to patients aged 18–64 years without evidence of type 1 diabetes (ICD-9-CM code of 250.x1 or 250.x3) or gestational diabetes (ICD-9-CM code of 648.8x) during the baseline period. Patients aged 65 years and over were excluded, because claims for services covered by Medicare are not available within the database. Because medication usage patterns have likely changed over the 6-year study period in part due to the approval of agents representing new classes of medications, such as exenatide in April 2005 and sitagliptin in October 2006, we conducted a secondary analysis in which we split our study period at its mid-point, January 2006. We also evaluated medication use before and after the May 2007 publication of a meta-analysis suggesting that rosiglitazone increases cardiovascular risk.¹⁷

Baseline Characteristics

Using data from the 180 days prior to insulin initiation, we identified demographic and clinical characteristics of the study population, including diabetic complications and common comorbid conditions by ICD-9/CPT-4 code (code detailed in Appendix 1, available online). We also evaluated patterns of health care system use, including other elements of diabetes care, such as diabetes education, podiatry and ophthalmology visits.

Insulin Regimens

We classified each initiated insulin regimen based on the prescription(s) filled on the index date. Regimens were classified as basal only, basal plus mealtime, mixed, mealtime only, or other combinations. Insulin formulations were categorized as outlined in Appendix 2, available online. For example, patients filling only a prescription for an intermediate-acting human insulin such as neutral protamine Hagedorn (NPH) or a longer-acting analog such as insulin detemir or insulin glargine were classified as initiating a basal insulin-only regimen. Patients filling a prescription for a basal insulin plus a short-acting insulin such as regular insulin or insulin aspart were classified as initiating a basal-plus-mealtime insulin regimen.

Oral and Injected Medication Use Prior to Insulin Initiation

We defined classes of oral medications based on mechanism of action: biguanides, sulfonylureas, thiazolidinediones, meglitinides, alpha-glucosidase inhibitors, and DPP-4 inhibitors. Self-injected non-insulin medications included glucagon-like peptide 1 (GLP-1) analogs and amylin analogs (see Appendix 2). We calculated the number of classes used during the baseline period and evaluated the use of combinations of medications recommended as second step therapy by the ADA/EASD consensus statement.^{5,18} We defined concurrent use as having an overlap of ≥ 15 days on at least one occasion, based on dispensing dates and days supply.

Changes in Oral and Non-insulin Injected Medication Use at Insulin Initiation

Changes in oral and non-insulin injected medication use immediately following insulin initiation are of interest in that the ADA/EASD guidelines recommend the discontinuation of insulin secretagogues such as sulfonylureas and meglitinides, due to increased hazard of hypoglycemia. We identified the medication classes filled by each patient

during the 120 days immediately prior to insulin initiation and the classes filled during the 120 days immediately following the insulin initiation date. We determined whether each patient continued or discontinued each medication taken prior to insulin initiation (depicted in Fig. 1a).

Treatment Intensification Following Insulin Initiation

Given ADA/EASD recommendations that treatment be intensified if HbA1c levels remain above target after

3 months of insulin treatment, medication patterns following insulin initiation are of interest. Insulin intensification is defined as switching from basal insulin to premixed insulin, adding mealtime bolus doses, and/or increasing the frequency of dosing. For this analysis, we defined an “insulin initiation” phase as the 90 days following insulin initiation, and a “treatment intensification phase” as the 90 to 270 days following insulin initiation (depicted in Fig. 1b). We identified the addition of oral or non-insulin injected medications by comparing prescriptions filled at any point during the treatment intensification phase to those filled at any point during the insulin initiation phase. We identified

Figure 1. Diagrams of study design. **a** Study design for treatment initiation analysis. Changes in oral and non-insulin injected medication use immediately following insulin initiation were evaluated by comparing the medication classes filled by each patient during the 120 days immediately prior to insulin initiation to the classes filled during the 120 days immediately following the insulin initiation date. *Met* metformin prescription filled, *sulf* sulfonylurea prescription filled. **b** Study design for treatment intensification analysis. Changes in medication patterns following insulin initiation were evaluated by defining an “insulin initiation” phase as the 90 days following insulin initiation, and a “treatment intensification phase” as the 90 to 270 days following insulin initiation. We identified the addition of oral or non-insulin injected medications by comparing prescriptions filled at any point during the treatment intensification phase to those filled at any point during the insulin initiation phase. Insulin intensification is defined as switching from basal insulin to premixed insulin, adding mealtime bolus doses, and/or increasing the frequency of dosing. *Basal* basal insulin prescription filled, *Met* metformin prescription filled, *glit* thiazolidinediones prescription filled. The last basal insulin fill during the initiation phase (*basal#*) is used to calculate the initiation dose. Intensification phase doses are compared to this dose. *Basal** denotes a dose change.

the addition of mealtime insulin to basal or mixed insulin regimens, and switches from basal to mixed insulin in a similar manner. To assess increases in dose and/or dosing frequency within a formulation, we calculated the dose for the last insulin prescription dispensed during the insulin initiation phase and compared this to doses dispensed during the treatment intensification phase. Doses were calculated from dispensed quantity, units, and days supply. The analysis was restricted to patients who had ≥ 180 days of follow-up data available following insulin initiation, and were on basal, mixed, or basal + mealtime regimens during the insulin-initiation phase. In a sensitivity analysis, we used the 30 days following insulin initiation to define insulin regimens and initial doses.

Statistical Analysis

We calculated descriptive frequencies for categorical variables and mean $\pm$ standard deviation for continuous variables. Binomial proportions were compared using chi-square tests and means were compared using t-tests.

The study was approved by the Brigham and Women's Hospital Institutional Review Board.

RESULTS

We identified 7,932 eligible patients who initiated insulin during the study period. The mean age was 50 years, and 46.8 % were female (Table 1). Patients filled an average of 1.5 non-insulin diabetes medications during the baseline period, 17 % had a visit with an endocrinologist, 18.6 % saw an ophthalmologist, and 2.8 % saw a podiatrist. Neuropathy was recorded for 9.1 % of patients, retinopathy for 7.1 %, skin ulcers for 6.1 %, and renal impairment for 5.2 %. Hypertension (57.4 %) and hypercholesterolemia (42.3 %) were common comorbidities. The majority (61 %) initiated basal insulin only, while 14 % initiated mixed insulin, 13 % initiated basal plus mealtime, 11 % initiated mealtime only, and 1 % initiated combinations of mealtime plus mixed, basal plus mixed, or all three.

Metformin was the most commonly used oral medication (55 %) during the 180 days prior to insulin initiation, followed by sulfonylureas (39 %), thiazolidinediones (30 %), meglitinides (9 %), and DPP-4 inhibitors (6 %) (Table 2). Non-insulin injected medications were used by 8 % of patients. Among patients initiating insulin in 2006–2008, 9.9 % used exenatide, and 8.3 % used a DPP-4 inhibitor. Rates of thiazolidinediones use decreased from 35.6 % prior to June 2007 to 23.4 % thereafter. The majority of patients used one (22 %) or two classes (27 %), with 18 % using three, and 5 % using four or more. Among the 4,355 patients taking metformin, 11 % concurrently used a sulfonylurea and

Table 1. Characteristics of 7,932 Patients Assessed in a 180-Day Baseline Period

Characteristic	N/mean*	Percent/std*
Demographics		
Female	3,714	46.8
Age (mean, std)	50.23	9.5
Healthcare system use		
Number of medications prescribed (mean, std)	9.26	5.7
Number of physician office visits (mean, std)	4.81	4.7
Hospitalization	1,651	20.8
Number of diabetes medication classes prescribed (mean, std)	1.52	1.3
Endocrinology visit	1,349	17.0
Ophthalmology visit	1,472	18.6
Podiatry visit	220	2.8
Diabetes education	113	1.4
Nutritional counseling	319	4.0
Diabetic complications		
Hypoglycemia	246	3.1
Hyperglycemia	169	2.1
Diabetic ketoacidosis	131	1.7
Diabetic nephropathy	78	1.0
Diabetic neuropathy	723	9.1
Diabetic retinopathy	561	7.1
Skin ulcer	483	6.1
Macular edema	143	1.8
Renal impairment	411	5.2
End-stage renal disease	114	1.4
Ulcer of lower limb	196	2.5
Amputation	23	0.3
Comorbid conditions		
Charlson comorbidity score (mean, std)	1.75	1.7
Hypercholesterolemia	3,351	42.3
Hypertension	4,551	57.4
Ischemic heart disease	609	7.7
Congestive heart failure	301	3.8
Peripheral vascular disease	33	0.4
Stroke and/or transient ischemic attack	140	1.8
Coronary atherosclerosis	1,102	13.9
Dysrhythmia	618	7.8
Depression	548	6.9

*N and % are reported for binary variables; mean and standard deviation (std) are reported for continuous variables and are noted in row labels

pioglitazone, 26 % used a sulfonylurea, 11 % used pioglitazone, 8 % used a DPP-4 inhibitor, and 26 % used an alpha-glucosidase inhibitor, meglitinide, or exenatide. More than a quarter of patients (28 %) had no anti-diabetic agent use prior to insulin initiation. Compared to patients with prior oral or injected medication use, these patients were more likely to have been hospitalized during the baseline period (26.1 % versus 15.3 %, $p < 0.0001$), less likely to have seen an endocrinologist (11.4 % versus 20.6 %, $p < 0.0001$), and less likely to have a prior diagnosis of hypercholesterolemia (26.4 % versus 47.1 %, $p < 0.0001$) or hypertension (45.5 % versus 60.6 %, $p < 0.0001$).

Patients initiating basal insulin only continued their oral medications at higher rates than those initiating mealtime or mixed insulin (Table 3). Metformin was continued by 82 % of current users initiating basal insulin, thiazolidinediones by 76 %, DPP-4 inhibitors by 69 %, exenatide by 66 %, and alpha-glucosidase inhibitors by 72 %. Among patients initiating mealtime or mixed regimens, continuation rates were 64 % for

Table 2. Oral and Injected Medication Use in the 180 Days Prior to Insulin Initiation

Class	Overall		Initiation pre-June 2007*		Initiation post-June 2007*		p value†
	N	%	N	%	N	%	
Oral medications							
Metformin	4,355	54.9	2,484	54.6	1,871	55.3	0.5188
Sulfonylureas	3,120	39.3	1,804	39.7	1,316	38.9	0.5067
Thiazolidinediones	2,405	30.3	1,614	35.5	791	23.4	< 0.0001
DPP-4 inhibitors	504	6.4	49	1.1	455	13.5	< 0.0001
Meglitinides	725	9.1	474	10.4	251	7.4	< 0.0001
Alpha-glucosidase inhibitors	137	1.7	96	2.1	41	1.2	0.0024
Injected medications							
Exenatide	607	7.7	197	4.3	410	12.1	< 0.0001
Pramlintide	21	0.3	4	0.1	17	0.5	0.0004

*Medication use is reported before and after the publication of a meta-analysis suggesting that rosiglitazone increases cardiovascular risk
†p values compare proportions pre versus post-June 2007

metformin, 67 % for thiazolidinediones, 47 % for DPP-4 inhibitors, 47 % for exenatide, and 57 % for alpha-glucosidase inhibitors. Insulin secretagogues—sulfonylureas and meglitinides—which ADA/EASD guidelines recommend should be stopped at initiation of a prandial insulin regimen, were continued by 75 % (sulfonylureas) and 70 % (meglitinides) of patients initiating basal insulin and 58 % and 47 % of patients initiating mealtime or mixed insulin regimens.

A total of 5,570 patients (70 % of the original sample) had sufficient follow-up data (≥ 180 days) for inclusion in the treatment intensification analysis (Table 4). There was evidence of treatment intensification among 38.1 % of patients, with similar rates of intensification in patients initiating basal-only, mixed, and basal-plus-mealtime regimens. Among patients initiating basal insulin only, 20.4 % increased the dose or frequency of basal insulin, 7.6 % added mealtime insulin, and 2.0 % added or switched to mixed insulin. Mixed insulin dose and/or dose frequency was increased for 20.5 % of patients initiating mixed insulin, and 6.8 % added mealtime insulin. Among patients initiating basal + mealtime regimens, dose and/or dose frequency was increased for 31.3 %. An

insulin secretagogue was added in 5.7 % of patients, another oral agent was added in 10.9 %, and an injected agent was added in 2.7 %.

Insulin was discontinued entirely by 26.5 % of patients (Table 4); 11.8 % took no diabetes medications, 10 % continued previously used non-insulin medications, and 4 % added new non-insulin medications. Compared to patients continuing insulin, these patients were more likely to have been hospitalized during the baseline period (25.0 % versus 15.6 %, $p < 0.0001$) and were more likely to have no use of oral or injected medications during the baseline period (38.5.3 % versus 21.1 %, $p < 0.0001$).

In a sensitivity analysis where insulin regimens and doses were assessed over the first 30 days instead of the first 90 days following initiation, increases in insulin dose/and or dose frequency as well as changes in regimen were slightly more common. For example, among patients initiating basal insulin, 25.0 % increased the dose or frequency of basal insulin, 10.4 % added mealtime insulin, and 2.6 % added or switched to mixed insulin (Appendix 3, available online).

Table 3. Changes in Oral and Non-Insulin Injected Medication Use During Insulin Initiation

	N filling prescription during 120 days before insulin initiation	Pattern during 120 days following insulin initiation			
		Continue (%)	Continue and add new class (%)	Discontinue (%)	Discontinue and switch to different class (%)
Among patients initiating basal insulin only					
Metformin	2,124	61.9	20.5	13.2	4.4
Sulfonylureas	1,531	55.9	19.2	16.0	8.9
Thiazolidinediones	1,151	54.0	21.9	16.6	7.5
Meglitinides	342	49.1	20.5	19.6	10.8
DPP-4 inhibitors	256	51.2	18.0	23.4	7.4
Exenatide	252	47.2	18.7	22.2	11.9
Alpha-glucosidase inhibitors	63	41.3	30.2	17.5	11.1
Among patients initiating mealtime or mixed insulin					
Metformin	839	47.0	17.2	30.8	5.1
Sulfonylureas	626	42.8	15.5	33.2	8.5
Thiazolidinediones	449	49.4	17.4	24.9	8.2
Meglitinides	111	36.0	10.8	44.1	9.0
DPP-4 inhibitors	81	28.4	18.5	43.2	9.9
Exenatide	99	33.3	14.1	41.4	11.1
Alpha-glucosidase inhibitors	14	21.4	35.7	28.6	14.3

Table 4. Treatment Intensification Patterns Following a 90-Day Insulin Initiation Phase

Insulin Regimen During Initiation Phase	N	Changes in medication use during intensification phase, N (% of total population)									
		Continue insulin and:						Any treatment intensification	Stop insulin and:		
		Increase insulin dose/ frequency	Add mealtime insulin	Add mixed insulin	Add insulin secretagogues	Add other oral agent	Add injected therapy		Take no diabetes meds	Continue non-insulin meds	Add non-insulin meds
Basal only	3,445	702 (20.4)	260 (7.6)	69 (2.0)	233 (6.7)	399 (11.6)	96 (2.8)	1334 (38.7)	342 (9.9)	389 (11.3)	178 (5.2)
Mixed only	848	174 (20.5)	58 (6.8)	—	41 (4.8)	95 (11.2)	21 (2.5)	302 (35.6)	125 (14.7)	72 (8.5)	36 (4.6)
Basal + mealtime	1,277	399 (31.3)	—	—	45 (3.5)	114 (8.9)	34 (2.7)	484 (37.9)	193 (15.1)	96 (7.5)	43 (3.4)
Total	5,570	1275 (22.9)	318 (5.7)	69 (1.2)	319 (5.7)	608 (10.9)	151 (2.7)	2120 (38.1)	660 (11.8)	557 (10)	221 (4)

DISCUSSION

Our study provides novel data on treatment patterns among a large cohort of commercially insured patients with type 2 diabetes initiating insulin. A total of 61 % of patients initiated basal insulin, while more than a third of the patients in our study initiated a regimen including a short-acting insulin. Surprisingly, we found that among patients initiating mealtime or mixed-insulin regimens, 48 % of patients continued sulfonylureas and 38 % continued meglitinides. Further, sulfonylureas and meglitinides were started by 29 % and 11 % of patients adding a new oral agent following insulin initiation. While approximately one-third of patients had evidence of treatment intensification, the majority did not. Nearly one-third of patients discontinued insulin within 90 days.

The treatment patterns we observed suggest that insulin is being initiated in a heterogeneous manner that may place some patients at increased risk of hypoglycemia while leaving others at risk of suboptimal glycemic control. The continuation of sulfonylureas with mixed and mealtime insulin is problematic in that patients taking insulin are already at an increased risk of hypoglycemia, with severe events occurring at a rate of 1–3 per 100 person-years of treatment in patients with type 2 diabetes,^{19–23} and increasing rates with tighter glucose control. Sulfonylureas can increase the risk of hypoglycemia by as much as 4–9 percentage points,⁷ and for this reason the ADA/EASD guidelines state that insulin secretagogues should be discontinued at the time of prandial insulin initiation.⁵ The frequent initiation of insulin as a mixed or mealtime regimen is also discordant with the ADA/EASD guidelines in place during the study period, which recommend that insulin be initiated with a single low daily dose of basal insulin. While there is evidence to suggest that mixed and mealtime formulations improve glucose control, these formulations are also associated with an increased risk of hypoglycemia, as well as increased weight gain, and are not generally recommended as initial therapy.^{5,24–27} The 2012 updated guidelines make an exception for patients with HbA1c levels $\geq 9\%$.⁶

The low rates of treatment intensification and high rates of insulin discontinuation observed in this study suggest that patients remain at risk of inadequate glycemic control following insulin initiation. In the absence of data on HbA1c values, it is difficult to know what proportion of patients' treatment should have been intensified. However, given the ADA/EASD recommended-practice of initiating insulin at a low dose of 10 units or 0.2 units per kilogram, titrating upwards based on fasting glucose levels measured at least weekly, and intensifying insulin after 2–3 months if HbA1c levels remain above target,^{5,28} one would expect to see evidence of treatment intensification in most patients. Insulin discontinuation may be appropriate in some patients, such as those initiating insulin following steroid use or severe illness, and a quarter of patients discontinuing insulin had been hospitalized in the 180 days prior to insulin initiation. However, it is likely that the high rates of insulin discontinuation we observed also reflect patient non-adherence and/or guideline-discordant care.

Our study adds novel information to an extremely limited literature on treatment patterns at the time of insulin initiation. Three prior studies have reported discontinuation rates in the range of 12–25 %, ^{13–15} with some variation by insulin formulation.¹⁴ Several studies also suggest that treatment intensification does not occur as often as clinically indicated.^{13,15} A study of patients receiving insulin monotherapy in the UK and Germany found that 75 % had HbA1c values above target,²⁹ while a study of visits to US academic medical center ambulatory clinics found that 66 % of patients with type 1 or type 2 diabetes were not achieving their HbA1c goals; only 40 % of these patients had a change in therapy in their subsequent visit.⁹ Other studies have also found that only 30–35 % of patients reach their target HbA1c, highlighting the frequency with which therapy is not intensified sufficiently.³⁰

Our study has several limitations. The analysis was conducted within the Horizon Blue Cross Blue Shield New Jersey health plan, and thus may not be representative of the

general population. However, many of the medication utilization patterns we observed were consistent with those documented in recent studies conducted in CVS Caremark data³¹ and in the nationally-representative National Disease and Therapeutic Index data.³² In the absence of lab test values, our ability to assess the appropriateness of care is limited. For example, we do not know what percent of patients had indications for treatment intensification based on inadequate glycemic control. Without data on written prescriptions, our ability to assess changes in insulin dose and dosing frequency is imperfect and reliant on the accuracy of days supply information entered at the pharmacy. While we attempted to exclude patients with type 1 diabetes through the use of diagnosis codes, it is possible that our cohort includes some patients with type 1 diabetes. We did not evaluate rates of hypoglycemia. Finally, there is controversy surrounding optimal HbA1c target levels. While there may be valid treatment approaches other than those advocated in the ADA/EASD guidelines, our study provides valuable data on the treatment patterns of patients initiating insulin in the United States, regardless of which algorithm might be optimal for guiding overall treatment.

Among a large cohort of commercially insured patients with diabetes, we found evidence that insulin is frequently initiated in a manner that is inconsistent with the ADA/EASD guidelines. The co-prescribing of insulin secretagogues with short-acting insulin places patients at an increased risk of hypoglycemia; at the same time, the majority of patients had no evidence of treatment intensification, and a quarter of patients discontinued insulin following initiation. While each patient's care should be individualized, our data suggest that the quality of care following insulin initiation can be improved to insure that greater numbers of patients achieve glycemic control without unnecessarily increasing the risk of hypoglycemia.

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Conflict of Interest: The authors declare that they do not have a conflict of interest.

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