Use of Antidiabetic Drugs in the U.S., 2003–2012

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OBJECTIVE

To describe market trends for antidiabetic drugs, focusing on newly approved drugs, concomitant use of antidiabetic drugs, and effects of safety concerns and access restrictions on thiazolidinedione use.

RESEARCH DESIGN AND METHODS

Nationally projected data on antidiabetic prescriptions for adults dispensed from U.S. retail pharmacies were extracted from IMS Health Vector One National and Total Patient Tracker for 2003–2012 and from Encuity Research Treatment Answers and Symphony Health Solutions PHAST Prescription Monthly for 2012.

RESULTS

Since 2003, the number of adult antidiabetic drug users increased by 42.9% to 18.8 million in 2012. Metformin use increased by 97.0% to 60.4 million prescriptions dispensed in retail pharmacies in 2012. Among antidiabetic drugs newly approved for marketing between 2003 and 2012, the dipeptidyl peptidase-4 (DPP-4) inhibitor sitagliptin had the largest share with 10.5 million prescriptions in 2012. Rosiglitazone use plummeted to <13,000 prescriptions dispensed in retail or mail-order pharmacies in 2012. Concomitancy analyses showed that 44.9% of metformin use was for monotherapy. Between 33.4 and 48.1% of sulfonylurea, DPP-4 inhibitor, thiazolidinedione, and glucagon-like peptide 1 analog use was not accompanied by metformin.

CONCLUSIONS

The antidiabetic drug market is characterized by steady increases in volume, and newly approved drugs experienced substantial uptake, especially DPP-4 inhibitors. The use of rosiglitazone has been negligible since restrictions were put in place in 2011. Further study is needed to understand why one-third to one-half of other noninsulin antidiabetic drug use was not concomitant with metformin use despite guidelines recommending that metformin be continued when other agents are added to treatment.

In 2010, 18.8 million adults in the U.S. had been diagnosed with diabetes mellitus, 7.0 million additional Americans were affected by undiagnosed diabetes, and an estimated 1.9 million adults received a new diagnosis of diabetes during that year (1). The number of Americans with diabetes who have or have not received a diagnosis is expected to increase to 44.1 million in 2034 (2). In 2012, the total cost of diabetes was estimated at $245 billion, including $176 billion in direct medical costs and $69 billion in reduced productivity (3). Spending on antidiabetic drugs accounted for $18.3 billion (3).

Although intensive lifestyle interventions (4) and bariatric surgery in obese diabetic patients (5–7) have been shown to improve or even reverse diabetes mellitus, most patients require pharmaceutical management of their disease (8). Indeed, between 2007 and 2010, only 52.2% of diabetic patients had HbA$_{1c}$ levels <7.0%, and only 14.3% met the combined goal of controlled HbA$_{1c}$ level, blood pressure, and LDL cholesterol level, and nonsmoking status (8).

The antidiabetic drug market is characterized by a number of new drugs that have been introduced during the last decade. These are the amylin analog pramlintide (approved in 2005); glucagon-like peptide 1 (GLP-1) analogs (exenatide immediate release, 2005; liraglutide, 2010; exenatide extended release, 2012); dipeptidyl peptidase-4 (DPP-4) inhibitors (sitagliptin, 2006; saxagliptin, 2009; linagliptin, 2011; alogliptin, 2013); a bile acid sequestrant (colesevelam, 2009); a dopamine agonist (bromocriptine, 2009); and a sodium glucose transport protein-2 inhibitor (canagliflozin, 2013). Several of these agents were also approved as combination products containing metformin or simvastatin.

The field of antidiabetic drugs experienced not only the addition of new drugs, but also emerging safety concerns of established drugs. In 2007, a meta-analysis (9) raised concerns regarding the cardiovascular safety of rosiglitazone, which was later pulled from the European market (10), and its use was severely restricted in the U.S. (11). Safety concerns also arose about the other remaining thiazolidinedione, pioglitazone, regarding its role in heart failure (12) and bladder cancer (13).

This study describes the U.S. market trends for prescription antidiabetic drugs from 2003 through 2012. We highlight the market uptake of drugs approved during this decade and how the use of thiazolidinediones was affected by recent safety concerns. Additional details by active ingredients are provided for all antidiabetic drugs for the year 2012, including an analysis of concomitant use.

RESEARCH DESIGN AND METHODS

We queried the IMS Health Vector One National and Total Patient Tracker databases for prescription antidiabetic drug use in the U.S. adult population (ages ≥20 years), annually from 2003 through 2012. The IMS Health databases are large commercial prescription and patient databases of drugs dispensed from outpatient retail pharmacies. IMS Health contracts with retail pharmacies, software providers, and pharmacy claims aggregators to obtain dispensed prescription data from two-thirds of the ~59,000 U.S. retail pharmacies, accounting for approximately one-half of all retail prescriptions dispensed in the U.S. On an ongoing basis, IMS Health projects these data to the national level by using a proprietary method incorporating geography, pay type, and class of trade (e.g., retail, independent, mass merchandisers).

Based on IMS Health data and U.S. Census Bureau population estimates, we calculated the annual population-adjusted rates of antidiabetic drug users, and the proportion of insulin users and users of noninsulin antidiabetic drugs. These categories were not mutually exclusive, and users of noninsulin antidiabetic drugs included patients who used insulin in addition to their noninsulin antidiabetic drug. Next, we obtained the annual number of prescriptions dispensed by class for all antidiabetic drug classes and prescriptions dispensed by active ingredient for noninsulin antidiabetic drugs that were newly introduced to the market during the observation period. Additional analyses in the IMS Health databases focused on the annual use of thiazolidinediones, and, for the year 2012, the number of prescriptions and users by active ingredient. To investigate a shift from retail to mail-order pharmacies as a consequence of restricted distribution of rosiglitazone, we accessed the Symphony Health Solutions PHAST Prescription Monthly database, which, unlike the IMS Health databases used in our primary analyses, also contains mail-order prescriptions. This analysis was not restricted to adult use.

We further extracted information on the concomitant use of antidiabetic drugs during the year 2012 using the Encuity Research Treatment Answers database. This database includes data from a survey of >3,200 office-based physicians representing 30 specialties across the U.S. who report on all patient activity during 1 typical workday per month. Encounter forms include basic patient demographic information, diagnoses, and treatments. Physicians are recruited by region and specialty based on the American Medical Association mailing list, which includes member and nonmember physicians. No filter is applied with regard to physician affiliation, and physicians in large health care systems are also invited to participate. We interpreted an office visit where more than one antidiabetic drug was mentioned as concomitant use of these drugs. In this context, drugs mentioned during an office visit include ongoing therapy, issuance of prescriptions, or the dispensing of drug samples. Combination products were treated as concomitant use of two antidiabetic drugs. The Treatment Answers database was also used to investigate diagnoses associated with the use of metformin. All data are nationally projected.

Our analyses included all antidiabetic drugs available in 2012, with the exception of colesevelam. Colesevelam was approved for treatment of type 2 diabetes in 2009, but it also carries an established indication for hypercholesterolemia, thus not permitting us to analyze its use for the treatment of diabetes in the IMS Health database. Bromocriptine was also approved for type 2 diabetes in 2009, and it is an established therapy for Parkinson's disease, hyperprolactinemia, and acromegaly. However, one bromocriptine product (Cycloset; Santarus, San Diego, CA) is exclusively indicated for the treatment of type 2 diabetes mellitus, and we included Cycloset in our analyses.

Summary statistics and linear regression analysis to describe longitudinal trends in the total number of antidiabetic drug users were computed in Excel 2010 (Microsoft, Redmond, WA). Population rates of drug use were calculated using U.S. Census Bureau estimates of the U.S. adult population (14).

RESULTS

Longitudinal Trends in Antidiabetic Drug Use

According to IMS Health data, ~18.8 million adults filled antidiabetic drug prescriptions from U.S. retail pharmacies in 2012. This number represents a 42.9% increase from 13.2 million in 2003, and an average annual increase

by 650,229 (95% CI 519,490–780,968). On a per capita level, 81.3 per 1,000 adults filled antidiabetic drug prescriptions in 2012, a 28.9% relative increase from 63.1 per 1,000 adults in 2003. Although rates of antidiabetic drug use have increased since 2003, the proportion of insulin users (27.1% in 2012) and the proportion of noninsulin antidiabetic drug users (86.7% in 2012) among all antidiabetic drug users remained constant over time.

Figure 1A shows an increase in the total number of prescriptions for noninsulin antidiabetic drugs by 36.2%, from 88.8 million prescriptions in 2003 to 120.9 million in 2012. During this decade, the use of biguanides (metformin) increased by 97.0% to 60.4 million

prescriptions in 2012. The use of sulfonylureas remained constant in terms of prescription volume, but their share among noninsulin antidiabetic drug prescriptions decreased from 36.3% in 2003 to 26.7% in 2012. During this period, the use of thiazolidinediones decreased by 64.0%.

Among the noninsulin antidiabetic drugs that were newly introduced to the market between 2003 and 2012, the DPP-4 inhibitor sitagliptin gained the largest share with 10.5 million prescriptions (single ingredient or combination products) in 2012 (Fig. 1B). Among GLP-1 analogs, immediate-release exenatide (Byetta; Bristol-Myers Squibb, New York, NY) first entered the marked in 2005, and its use peaked in 2008 at 2.5

million prescriptions. An increase in the use of liraglutide, which first assumed leadership of the GLP-1 analog market in 2011, was paralleled by a 49.5% decline in the use of exenatide-containing products. A once-weekly extended-release version of exenatide (Bydureon; Bristol-Myers Squibb) was approved by the U.S. Food and Drug Administration (FDA) in January 2012 and represented 20.3% of all exenatide prescriptions in 2012 (data from both exenatide products are combined in Fig. 1B).

The use of thiazolidinediones is characterized by recent steep declines (Fig. 2). Rosiglitazone-containing products declined from their peak in 2006, when 12.7 million prescriptions were dispensed, to <1,000 prescriptions dispensed by retail pharmacies in 2012. The use of pioglitazone-containing products started a slow decline following its peak in 2008 when 14.2 million prescriptions were dispensed. This decline accelerated in recent years, and 6.8 million prescriptions were dispensed in 2012, down 52.1% from the peak in 2008. Using the Symphony Health Solutions PHAST Prescription Monthly database, we found 12,597 prescriptions of rosiglitazone-containing products dispensed in a retail or mail-order setting in 2012. Unlike analyses based on IMS Health data, this estimate was not restricted to adult use.

Antidiabetic Drug Use in 2012
In 2012, 154.5 million prescriptions were dispensed for antidiabetic drugs, 78.4% of which were for noninsulin antidiabetic drugs (Table 1). About one in every two noninsulin antidiabetic drug prescriptions was for single-ingredient metformin, which was used by 11.8 million of 16.3 million noninsulin antidiabetic drug users (72.3%). More than one-quarter of noninsulin antidiabetic drug prescriptions was for sulfonylureas, and almost all of them were divided between three second-generation sulfonylureas (glipizide, glimepiride, and glyburide). DPP-4 inhibitors dominated the new class of incretin mimetic drugs, which also includes the GLP-1 analogs. In comparison, the use of some other drugs that were recently introduced to the diabetic market, such as pramlintide and bromocriptine, was infrequent.

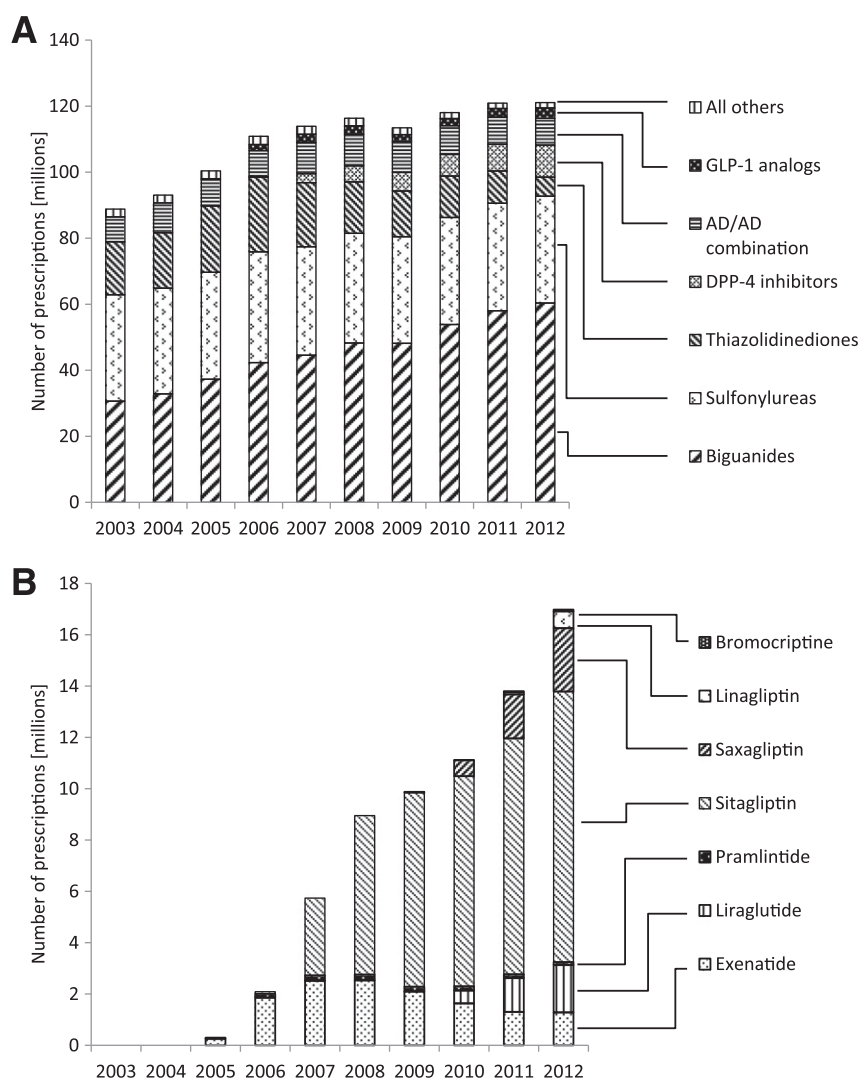In 2012, 33.4 million insulin prescriptions were dispensed to 5.1 million

Figure 1—A: Trends in noninsulin antidiabetic drug prescriptions filled in U.S. retail pharmacies 2003–2012. B: Prescriptions of recently approved noninsulin antidiabetic drugs filled in U.S. retail pharmacies, 2003–2012. AD, antidiabetic drugs. Source: IMS Health Vector One National.
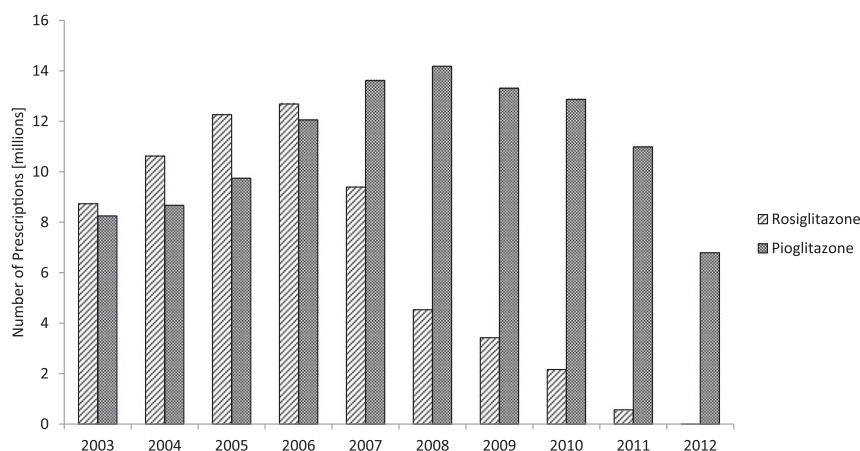
Figure 2—Thiazolidinedione prescriptions filled in U.S. retail pharmacies, 2003–2012. Source: IMS Health Vector One National.

patients. The insulin market was dominated by long-acting human analog insulin, mostly insulin glargine, followed by fast-acting human analog insulin, mostly insulin aspart and insulin lispro.

In 2012, metformin was predominantly used for the treatment of diabetes-related diagnoses (97.6%). Other uses were for gynecologic diagnoses (1.8%, predominantly for polycystic ovary disease), disorders related to obesity (0.1%), or other diagnoses (0.5%).

Concomitant Antidiabetic Drug Use in 2012

Concomitant use of more than one antidiabetic drug class in 2012 is displayed in Table 2 for the most commonly used antidiabetic drug classes. This table shows that 44.9% of metformin use was for monotherapy, 22.1% was concomitant with the use of sulfonylureas, 22.0% was concomitant with the use of DPP-4 inhibitors, and 9.7% was concomitant with the use of long-acting insulin. In contrast, between 51.9% (GLP-1 analogs) and 66.6% (thiazolidinediones) of noninsulin antidiabetic drug use was concomitant with the use of metformin. Almost one-third of long-acting insulin use was concomitant with the use of fast-acting insulin, and, conversely, almost two-thirds of fast-acting insulin use was concomitant with the use of long-acting insulin.

CONCLUSIONS

This study adds current and nationally projected estimates to previous studies describing the use of antidiabetic drugs (15–19). We documented a steady increase

in the number of patients who used antidiabetic drugs and in the number of dispensed prescriptions in U.S. retail pharmacies. Our estimate of 18.8 million antidiabetic drug users in 2012 is identical to the Centers for Disease Control and Prevention estimate (1) of patients in whom diabetes has been diagnosed (18.8 million in 2010). However, our number should not be taken as the actual number of diabetic patients because not every patient who receives a diagnosis of diabetes uses antidiabetic drugs, the number of patients with diagnosed diabetes likely increased during the 2 years between the Centers for Disease Control and Prevention estimate and our estimate, and not all antidiabetic drugs are used solely for diabetes. Nevertheless, the fact that these numbers are so similar, although obtained through very different methodology, provides reassurance regarding data validity.

Our study illustrated the roles that different antidiabetic drugs play in the management of diabetes; chief among them was metformin, which represents one of every two prescriptions for noninsulin antidiabetic drugs. This marks the continuation of a remarkable trend: in 1996, the year after metformin was approved in the U.S., 19.0% of all oral antidiabetic drug prescriptions were for metformin, and this proportion increased to 32.7% in 2001 (19). Almost 11.8 million patients (62.7% of all patients who received antidiabetic drugs) used single-ingredient metformin in 2012 (Table 1), and 44.9% of patients to whom metformin was dispensed

used the drug as monotherapy (Table 2), consistent with recommendations by the American Diabetes Association and the European Association for the Study of Diabetes to use metformin as first-line therapy (20). Although metformin was used for other indications, the vast majority of prescriptions was for the treatment of diabetes.

While the share of sulfonylurea use decreased, antidiabetic drugs that were approved during the last decade quickly gained significant market share. The most commonly prescribed new class was the DPP-4 inhibitors, which are available as oral tablets. Injectable GLP-1 analogs have also been widely used; however, between them, liraglutide has continued to gain market share while the use of exenatide declined. Liraglutide requires one daily injection, compared with twice-daily injections required for immediate-release exenatide, which may partially explain this trend. An extended-release version of exenatide, which requires only one weekly injection, was approved by the FDA in January 2012, and it reached a 20% share of all exenatide prescriptions during that year.

During the last decade, several combination products were approved, and their early rise in prescriptions has been documented before (15). Alexander et al. (15) found that 15% of treatment visits in 2004 were associated with oral combination products (first introduced in 2000), but this increase did not continue (13% in 2007). We found that in 2012, only 6.7% of noninsulin antidiabetic drug prescriptions were for combination products, predominantly combinations of metformin with either sitagliptin or glyburide. While combination products using metformin represented a substantial share of DPP-4 inhibitor–containing products, they played a smaller role among sulfonylureas or thiazolidinediones.

Our analysis of the concomitant use of antidiabetic drugs in 2012 showed that only one-half to two-thirds of sulfonylurea, DPP-4 inhibitor, thiazolidinedione, and GLP-1 analog use was concomitant with metformin use. This occurred despite guideline recommendations of continuing metformin use when adding another noninsulin antidiabetic drug to therapy, unless metformin is contraindicated or not well-tolerated

Table 1—Antidiabetic drug dispensing in U.S. retail pharmacies, 2012

Drug class	Total prescriptions (N)	Prescriptions, share in NIAD or insulin (%)	Patients (N)*	Drug	Prescriptions, share in class (%)	Patients (N)*
Noninsulin antidiabetic drugs	121,055,250	100	16,316,580			
Biguanides	60,368,335	49.9	11,792,980	Metformin	100.0	11,792,980
Sulfonylureas	32,341,020	26.7	6,121,488	Glipizide	44.7	2,757,532
				Glimepiride	33.0	2,064,241
				Glyburide	22.3	1,457,504
				Chlorpropamide	<0.1	3,235
				Tolbutamide	<0.1	1,099
				Tolazamide	<0.1	938
				Acetohexamide	<0.1	2
DPP-4 inhibitors	9,703,821	8.0	1,870,819	Sitagliptin	76.4	1,431,124
				Saxagliptin	17.3	331,983
				Linagliptin	6.4	160,825
AD/AD combination	8,109,413	6.7	1,504,542	Sitagliptin/metformin	38.5	600,099
				Glyburide/metformin	35.1	521,878
				Pioglitazone/metformin	11.8	180,681
				Saxagliptin/metformin	9.8	165,633
				Glipizide/metformin	3.5	57,467
				Pioglitazone/glimepiride	0.8	11,408
				Linagliptin/metformin	0.5	14,398
				Repaglinide/metformin	0.1	1,267
				Rosiglitazone/metformin	<0.1	252
				Rosiglitazone/glimepiride	<0.1	62
Thiazolidinediones	5,770,131	4.8	1,083,193	Pioglitazone	100.0	1,082,938
				Rosiglitazone	<0.1	350
GLP-1 analogs	3,136,564	2.6	673,367	Liraglutide	59.1	415,075
				Exenatide	40.9	286,613
Meglitinides	1,079,356	0.9	226,628	Repaglinide	54.0	122,959
				Nateglinide	46.0	106,235
α-Glucosidase inhibitors	356,852	0.3	80,506	Acarbose	92.0	74,794
				Miglitol	8.0	6,044
Amylin analogs	110,373	0.1	28,809	Pramlintide	100.0	28,809
Dopamine receptor agonist	66,999	0.1	17,808	Bromocriptine	100.0	17,808
AD/non-AD combination	12,386	0.0	3,571	Sitagliptin/simvastatin	100.0	3,571
Insulins and insulin analogs	33,406,589	100	5,088,495			
Analog human long-acting	17,311,225	51.8	3,650,111	Insulin glargine	81.3	2,974,373
				Insulin detemir	18.7	767,443
Analog human fast-acting	9,056,523	27.1	2,172,770	Insulin aspart	51.8	1,212,208
				Insulin lispro	43.8	969,550
				Insulin glulisine	4.4	101,156
Analog human insulin combinations	2,590,153	7.8	519,504	Insulin aspart protamine/insulin aspart	63.4	345,653
				Insulin NPL/insulin lispro	19.4	91,009

Table 1—Continued

Drug class	Total prescriptions (N)	Prescriptions, share in NIAD or insulin (%)	Patients (N)*	Drug	Prescriptions, share in class (%)	Patients (N)*
Human insulin combinations	1,884,245	5.6	371,341	Insulin lispro protamine/lispro	17.2	109,526
				Insulin human/insulin NPH human	100.0	371,579
Human insulin intermediate-acting	1,400,094	4.2	317,341	Insulin NPH human recombinant	62.9	207,487
				Insulin NPH human semi-synthesized	37.1	126,908
Human insulin fast-acting	1,164,300	3.5	343,360	Insulin regular human recombinant	67.1	229,552
				Insulin regular human semi-synthesized	32.9	127,267
Other insulins	49	<0.1	43	Animal insulins, human insulin long-acting, insulin zinc, insulin human (isophane/regular)	100.0	49
Total	154,461,839		18,810,311			

AD, antidiabetic drugs; NIAD, noninsulin antidiabetic drug; TZD, thiazolidinedione; NPL, neutral protamine lispro; NPH, neutral protamine Hagedorn. Source: IMS Health Vector One National and Total Patient Tracker. *Patient counts across drugs in one class may not add up to total patient counts for that class because patients could have used more than one member of the drug class in 2012, but would only be counted once on the class level.

(20). Previous studies (21–25) have identified the presence of contraindications among users of metformin; however, whether contraindications or lack of tolerability explain why metformin is not used more often with second-line antidiabetic drugs is subject to further research.

A steep decline in the use of rosiglitazone-containing products after the publication of the meta-analysis by Nissen and Wolski (9) reporting an association between rosiglitazone and cardiovascular events has been well-documented, both in the U.S. (26–32) and abroad (33–35). However, to our knowledge, our study is the first to also evaluate thiazolidinedione use patterns after rosiglitazone restrictions were implemented by the FDA in May 2011 (11). Since then, rosiglitazone-containing products have been limited to patients already being successfully treated with these medicines, and to patients whose blood glucose level cannot be controlled with other antidiabetic drugs and who, after consulting with their health care providers, do not wish to use pioglitazone-containing medicines. To implement this restriction, since November 2011, health care providers and patients had to be enrolled in a special access program, and rosiglitazone-containing products could be obtained only through specially certified mail-order pharmacies. Our analysis found 12,597 prescriptions of rosiglitazone-containing products dispensed in a retail or mail-order setting in 2012. Compared with <1,000 rosiglitazone prescriptions detected in our primary analysis based on retail pharmacies, this number indicates that the majority of rosiglitazone was obtained through mail order. Nevertheless, the overall use of rosiglitazone-containing products in 2012 was almost negligible. Pioglitazone-containing products represented almost all thiazolidinedione use, with 6.8 million dispensed prescriptions in 2012. Yet, this number reached only half of the peak use in 2008, despite the approval of the first generic form of pioglitazone in August 2012, highlighting the impact of potential safety concerns. In November 2013, the FDA announced the removal of restrictions for rosiglitazone on patients, prescribers, and pharmacies (36). Future research should describe the impact of relaxing

Table 2—Concomitant therapy among the most common antidiabetic drug classes, 2012

Use of this class	Concomitant with							
	No other antidiabetic drug	Biguanides	Sulfonylureas	DPP-4 inhibitors	TZDs	GLP-1 analogs	Insulin, analog human long-acting	Insulin, analog human fast-acting
Biguanides	44.9	—	22.1	22.0	8.0	4.0	9.7	2.4
Sulfonylureas	28.0	61.0	—	15.4	9.4	3.7	10.3	1.9
DPP-4 inhibitors	25.5	65.1	16.4	—	5.3	1.3	8.7	2.7
TZD	19.4	66.6	28.5	14.9	—	5.6	7.9	<1.0*
GLP-1 analogs	37.3	51.9	17.3	5.5	8.7	—	18.7	3.2
Insulin, analog human	—	—	—	—	—	—	—	—
Long-acting	32.7	31.7	12.3	9.7	3.1	4.8	—	31.4
Fast-acting	25.7	16.1	4.6	6.2	<1.0*	1.7	64.1	—

Data are given as %. Row totals can exceed 100% because of patients using more than two antidiabetic drugs. TZD, thiazolidinedione. Source: Encuity Research Answer Generator. *Shares <1.0% are not displayed.

prescription requirements on rosiglitazone use.

One strength of this study is the use of nationally projected data, without being limited to a certain health care setting or population. However, we were able to provide data only on antidiabetic drug prescriptions dispensed from U.S. retail pharmacies. Using wholesale sales data obtained from the IMS Health National Sales Perspective, we estimated that in 2012, 68% of noninsulin antidiabetic drug containers were shipped to retail pharmacies, while 21% were shipped to mail-order pharmacies and 11% to nonretail settings, including, among others, clinics, hospitals, and long-term care facilities. For insulin, 59%, 23%, and 18% of drug containers were shipped to retail pharmacies, mail-order pharmacies, or the nonretail setting, respectively. We expect that the total number of antidiabetic drug users is still a valid estimate, as most patients will fill a prescription for at least one antidiabetic drug in a retail pharmacy in a given year and, thus, would be included in our analysis. However, users of our data should keep in mind that the total number of prescriptions dispensed applies only to the retail setting. Similarly, our data did not capture the use of over-the-counter insulin. Further, while the sample of retail pharmacies is large, representativeness is not necessarily guaranteed, and changes in the sampling scheme could affect trend data.

This study documented a 42.9% increase in the number of patients who filled antidiabetic drug prescriptions in U.S. retail pharmacies between 2003 and 2012. Among 154.5 million antidiabetic drug prescriptions in 2012, metformin was the dominant noninsulin antidiabetic drug. Since 2003, several new classes of antidiabetic drugs have gained significant market share, most prominently DDP-4 inhibitors and GLP-1 analogs. This study further provided patterns of thiazolidinedione use after restrictions were placed on rosiglitazone in 2011. In 2012, the use of rosiglitazone was almost negligible, and the use of pioglitazone decreased to half of its peak level from 2008. Finally, our concomitancy analysis found that about one-third to one-half of sulfonylurea, DPP-4 inhibitor, thiazolidinedione, and GLP-1 analog use was not accompanied by metformin use, despite recommendations in diabetes treatment guidelines.

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