



Utilization of antidiabetic drugs among Medicare beneficiaries with diabetes, 2006-2009

Diabetes Treatment

Data Points #9

Diabetes mellitus, a condition characterized by high blood glucose, is a major public health burden. The condition affects an estimated 7.8 percent (23.6 million persons) of the United States population and accounts for more than \$174 billion annually in excess health care costs.¹ Type 2 diabetes, where the pancreas gradually loses the ability to produce insulin in response to meals and peripheral tissues fail to properly respond to insulin (insulin resistance), comprises the vast majority of all cases of diabetes in the U.S. It is strongly associated with obesity and age over 45 years. Older people with diabetes are more likely to experience cognitive disorders, urinary incontinence, and physical disabilities such as impaired mobility and tremor than the general population.^{2,3} They are more likely to suffer cognitive decline and inadequate physical function than people in younger age categories, even after adjusting for preexisting conditions.^{2,3} Additionally, older adults with diabetes are more likely to have multiple medical conditions and are twice as likely to have depression than nondiabetic elders. Finally, they are also significantly more likely to be affected by hypoglycemia.^{3,4}

There are currently six classes of oral antidiabetic medications: alpha-glucosidase inhibitors, biguanides, dipeptidyl peptidase-4 inhibitors, meglitinides, sulfonylureas, and thiazolidinediones. Several types of insulin and other injectable drugs such as amylin analogs and glucagon-like peptide-1 receptor agonists are also available. The American Diabetes Association (ADA) guidelines and the Effective Healthcare Program generally suggest metformin as a first-line therapy for treating type 2 diabetes until kidney function has declined to a certain point.^{5,6} Second-line therapies include combinations of metformin and insulin, or metformin and a sulfonylurea.⁵



Biguanides (i.e., metformin) were the most commonly used antidiabetic drug class among Medicare beneficiaries from 2006 to 2009, followed by sulfonylureas, insulins, and thiazolidinediones. Approximately 37 percent of diabetic beneficiaries had a claim for a biguanide in 2009.

Sulfonylurea use generally increased with age. Among Medicare beneficiaries age 85 years or older, sulfonylureas were used more frequently than both biguanides and insulins from 2006 to 2009.

From 2006 to 2009, thiazolidinedione use decreased dramatically overall and uniformly across all health care referral regions in the U.S. This trend was consistent among all age groups.

Metformin is also frequently avoided in older adults due to declines in renal function as indicated by product labeling, though some data suggest that this precaution is not warranted.⁷ Additionally, sulfonylurea use in older adults is associated with increased risk of hypoglycemia also due to decreasing renal function.²

Recent findings regarding rosiglitazone also have implications for older people. In 2007, rosiglitazone, a thiazolidinedione, was found to be associated with myocardial infarction, major adverse cardiovascular events, mortality from cardiovascular causes, and all-cause mortality.⁸ A more recent study comparing rosiglitazone with pioglitazone, also a thiazolidinedione, confirms these results.⁹ However, pioglitazone has been associated with a small but significantly increased risk of developing heart failure.¹⁰ Prescription patterns for rosiglitazone changed dramatically when the 2007 meta-analysis⁹ was published and the Food and Drug Administration initially issued warnings about the safety of rosiglitazone.¹¹ A recent study showed up to a 54 percent decrease in rosiglitazone prescription claims across nine commercial plans covering 9 million eligible members, though pioglitazone use was not shown to have changed significantly.¹²

The goals of this report are to: (1) present general antidiabetic drug utilization patterns among the Medicare Parts A and B fee-for-service (FFS) population enrolled in Medicare Part D; and (2) focus on the utilization of the four most frequently dispensed antidiabetic drug classes in this same population: biguanides, sulfonylureas, insulins, and thiazolidinediones.

FINDINGS

We studied the population of beneficiaries who were continuously enrolled for at least a 12-month period in Medicare Parts A and B FFS and in Part D. A population with continuous enrollment may have more stable medication patterns than a population without continuous enrollment. Biguanides, sulfonylureas, insulins, and thiazolidinediones were the most frequently dispensed antidiabetic medication classes in 2006-2009 (Table 1). Alpha-glucosidase inhibitors, amylin analogs, dipeptidyl peptidase-4 inhibitors, glucagon-like peptide-1 receptor agonists, and meglitinides were significantly less frequently dispensed.

Table 1. Yearly prevalence (%) of antidiabetic drug class utilization among diabetic Medicare beneficiaries with continuous enrollment in Parts A and B FFS and Part D, 2006-2009

Variable	Year	Biguanides	Insulins	Sulfonylureas	Thiazolidinediones	
Overall	2006	33.13	24.40	33.02	22.05	
	2007	34.84	22.43	32.01	19.46	
	2008	36.03	22.83	30.74	14.56	
	2009	37.24	23.45	29.37	13.03	
Age	Under 45	2006	34.62	27.65	20.67	19.15
		2007	36.14	28.19	19.81	17.19
		2008	36.88	28.57	18.77	13.24
		2009	37.86	29.30	17.72	11.60
	45 to 54	2006	38.14	29.23	27.19	23.66
		2007	39.70	29.19	26.50	21.09
		2008	40.97	29.87	25.20	16.18
		2009	42.17	30.78	23.84	14.31
	55 to 64	2006	38.85	32.11	32.06	26.04
		2007	40.63	31.16	31.29	22.97
		2008	41.62	31.75	29.91	17.24
		2009	42.58	32.62	28.18	15.25
	65 to 74	2006	39.55	22.86	35.46	25.36
		2007	41.54	20.81	33.73	22.14
		2008	42.85	21.26	32.35	16.55
		2009	43.99	21.90	30.72	14.84
	75 to 84	2006	29.10	22.20	34.59	20.32
		2007	30.79	19.98	33.31	17.92
		2008	32.07	20.30	32.10	13.36
		2009	33.49	20.77	30.96	12.05
85 to 94	2006	17.79	22.91	32.11	14.44	
	2007	19.26	20.46	31.56	13.08	
	2008	20.24	20.62	30.40	9.65	
	2009	21.35	20.98	29.41	8.62	
95 and over	2006	9.78	21.17	27.01	9.18	
	2007	10.83	19.49	26.94	8.40	
	2008	11.70	19.70	26.04	6.26	
	2009	12.36	20.24	25.40	5.51	

Table 1. Continued from previous page

Variable	Year	Biguanides	Insulins	Sulfonylureas	Thiazolidinediones	
Gender	Male	2006	33.38	23.38	34.10	22.79
		2007	35.05	21.80	33.14	20.33
		2008	36.44	22.38	32.03	15.58
		2009	37.80	23.09	30.69	14.04
	Female	2006	32.99	25.00	32.38	21.61
		2007	34.71	22.84	31.27	18.89
		2008	35.76	23.12	29.88	13.89
		2009	36.86	23.69	28.48	12.36
Race/ Ethnicity	White	2006	33.17	23.42	33.09	21.47
		2007	34.86	21.25	31.96	18.83
		2008	36.10	21.65	30.68	14.00
		2009	37.28	22.25	29.28	12.45
	African American	2006	30.62	30.91	30.99	21.36
		2007	32.58	29.58	30.72	19.23
		2008	33.46	30.09	29.56	14.34
		2009	34.59	30.72	28.38	12.83
	Asian	2006	37.08	13.53	37.83	27.63
		2007	38.11	13.84	36.13	25.65
		2008	39.00	14.15	34.35	19.89
		2009	40.45	14.72	32.90	18.29
	Hispanic	2006	37.60	24.34	35.36	27.51
		2007	39.18	24.90	34.41	25.32
		2008	40.22	25.81	32.95	19.77
		2009	41.73	26.74	31.46	18.46
American Indian/ Alaska Native	2006	31.87	27.57	29.26	23.61	
	2007	34.85	27.88	30.35	23.61	
	2008	36.61	28.87	29.88	20.51	
	2009	38.43	30.83	29.23	19.33	

Biguanides were the most frequently used class of antidiabetic medications. Among the study population with prevalent diabetes, approximately 33 percent, 35 percent, 36 percent, and 37 percent of beneficiaries had a claim for a biguanide in 2006-2009, respectively (Table 1). Biguanide utilization varied with age. In 2009, 44 percent of beneficiaries ages 65 to 74 had a claim for a biguanide, compared with 21 percent and 12 percent among those ages 85 to 94 and 95 and over, respectively (Table 1).

Among diabetic beneficiaries who received at least one prescription for an antidiabetic medication, approximately 50 percent, 53 percent, 55 percent, and 57 percent of the population had a claim for a biguanide in 2006-2009, respectively. Further, among beneficiaries having at least one biguanide claim, about 21 percent also had a claim for an insulin, between 52 percent (2006) and 44 percent (2009) had a claim for a sulfonylurea, and

between 35 percent (2006) and 20 percent (2009) had a claim for a thiazolidinedione, the latter representing a considerable decreasing trend in utilization over time. In 2009, insulins were the most frequently used antidiabetic class among beneficiaries who did not use biguanides (about 55 percent).

The geographic distribution of biguanide use per year, based on Dartmouth Atlas of Health Care (www.dartmouthatlas.org) hospital referral regions (HRRs), is presented in Figure 1. Geographic variation in utilization by year is evident. Biguanide utilization was most prevalent in the western States, but its use increased across all States.

Sulfonylureas were the second most frequently used class of antidiabetic medications under study. Among the study population with prevalent diabetes, approximately 33 percent, 32 percent, 31 percent, and 29 percent of beneficiaries had a claim for a sulfonylurea in 2006-2009, respectively (Table 1). Sulfonylurea utilization varied by age. In 2009, nearly 31 percent of beneficiaries ages 65 to 84 had a claim for a sulfonylurea, compared with a low of less than 18 percent of beneficiaries under the age of 45 years (Table 1). Among diabetic beneficiaries who received at least one prescription claim for an antidiabetic medication, approximately 49 percent, 49 percent, 47 percent, and 45 percent had a claim for sulfonylurea in 2006-2009, respectively. In contrast to biguanides, use of sulfonylureas decreased over time. Beneficiaries with prescription claims for sulfonylureas also frequently had prescription claims for biguanides and insulins. Maps of the geographic distribution of sulfonylurea use per year, based on Dartmouth Atlas of Health Care HRRs, are in an online supplement.

Insulins were the third most frequently used antidiabetic class. Among the study population with prevalent diabetes, approximately 24 percent, 22 percent, 23 percent, and 23 percent of beneficiaries had a prescription claim for an insulin agent in 2006-2009, respectively (Table 1). With respect to race/ethnicity, Asians were much less likely to use insulin (15 percent) compared with Whites, Hispanics, African Americans, and American Indians/Alaska Natives (22 percent, 27 percent, 31 percent, and 31 percent, respectively) in 2009 (Table 1). Among diabetic beneficiaries who received at least one prescription for an antidiabetic medication, approximately 37 percent, 34 percent, 35 percent, and 36 percent of the population had a claim for an insulin product in 2006-2009, respectively. Further, in 2009, among beneficiaries having at least one insulin claim, about 33 percent also had a claim for a biguanide, 28 percent had a claim for a sulfonylurea, and between 26 percent (2006) and 14 percent (2009) had a claim for a thiazolidinedione, the latter representing a considerable decreasing trend in utilization over time.

Biguanides were the most frequently dispensed antidiabetic class of drugs among beneficiaries who did not have a claim for an insulin product (about 69 percent in 2009). Further, among beneficiaries with no insulin claim, between 61 percent (2006) and 54 percent (2009) had a claim for a sulfonylurea and 37 percent (2006) and 23 percent (2009) had a claim for a thiazolidinedione, both representing decreasing trends in utilization over time. Maps of the geographic distribution of insulin use per year, based on Dartmouth Atlas of Health Care HRRs, are in an online supplement.

Thiazolidinediones were the fourth most frequently used antidiabetic medication class, and their use varied greatly, particularly by calendar year. A pronounced reduction in claims occurred from 2007 to 2009, likely driven by highly publicized concerns about increased mortality with rosiglitazone use observed in a large randomized clinical trial.^{7,10} Approximately 22 percent, 19 percent, 15 percent, and 13 percent of the study population with prevalent diabetes had a claim for an agent in this class in 2006-2009, respectively (Table 1). The decrease in thiazolidinedione claims was also noted among diabetic beneficiaries in the study population who had at least one claim for an antidiabetic medication. About 33 percent, 30 percent, 22 percent, and 20 percent of these beneficiaries had a claim for an agent in this class in 2006-2009, respectively.

Figure 1. Utilization of biguanides per 100 diabetic Medicare beneficiaries with continuous enrollment in Parts A and B FFS and Part D, by HRR, 2006-2009

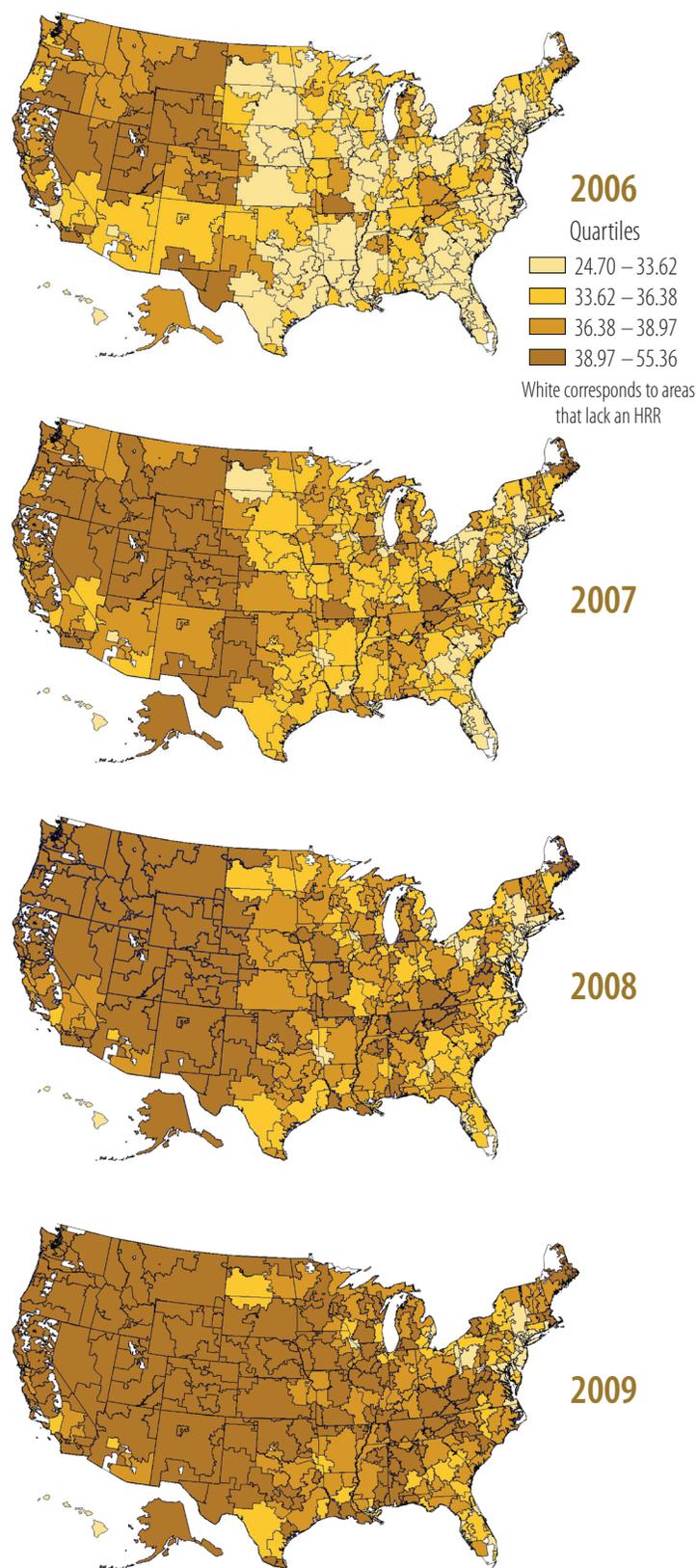
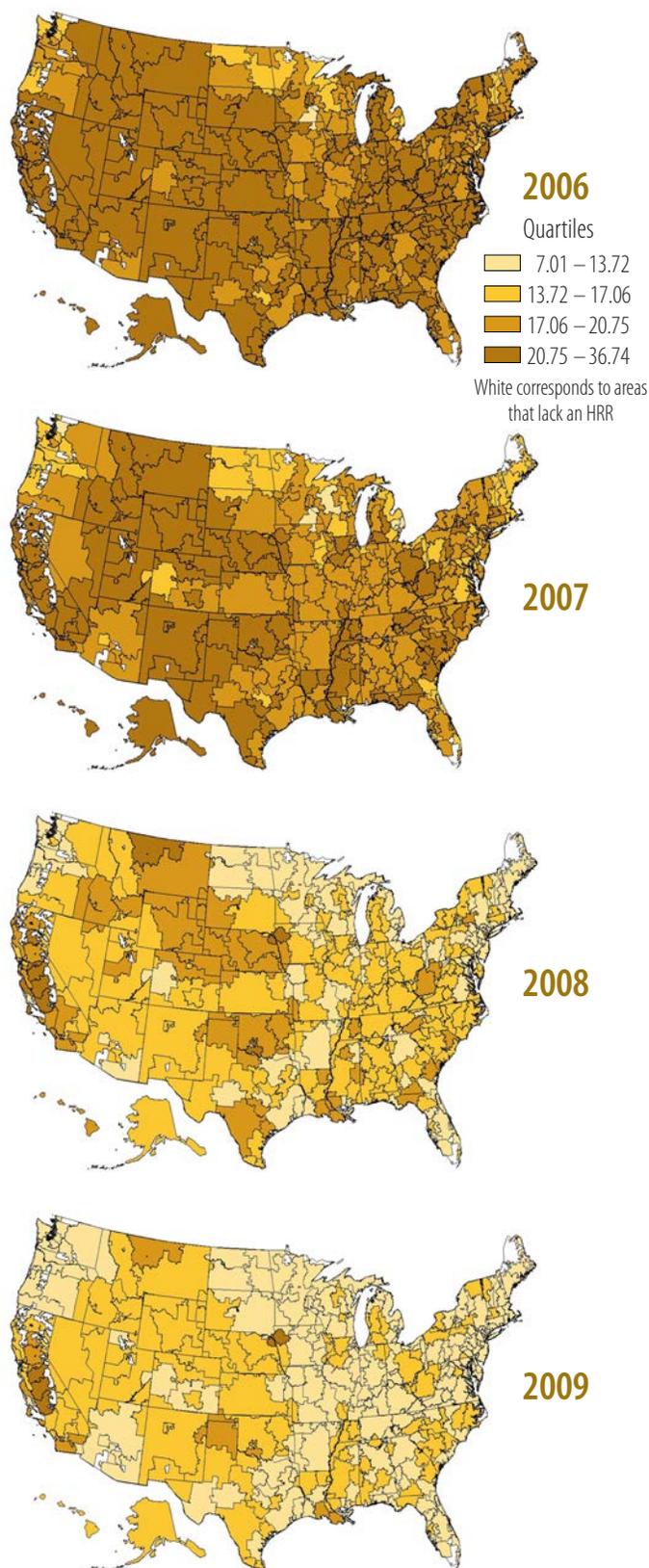


Figure 2. Utilization of thiazolidinediones per 100 diabetic Medicare beneficiaries with continuous enrollment in Parts A and B FFS and Part D, by HRR, 2006-2009



The decrease in utilization of this class of medication was geographically uniform over time (Figure 2).

Among the study population with prevalent diabetes, claims for dipeptidyl peptidase-4 inhibitors increased from 2006-2009 (0.1 percent to 5 percent), but overall use remained low. Claims for meglitinides decreased from 2006-2009 (3 percent to 2 percent). Similarly, claims for alpha-glucosidase inhibitors decreased from 0.6 percent to 0.4 percent. Finally, amylin analogs, the least used antidiabetic class, remained consistently very low, with claims in around 0.14 percent of diabetic beneficiaries.

DATA SOURCE

Files utilized for this analysis included the Medicare Enrollment Database (EDB, current through May 2010), the Common Working File (CWF, 1/1/2005-6/11/2010), and monthly Medicare Part D Prescription Drug Event data (1/1/2006-5/31/2010). The years were chosen based on the availability of Medicare Part D in 2006.

STUDY PERIOD

The study period over which diabetes and antidiabetic agents were examined included 2006-2009.

DEFINITIONS AND METHODS

Population of Beneficiaries

Beneficiaries in this *Data Points* brief were derived from the Medicare Parts A and B FFS and Medicare Part D populations. A beneficiary was included in the enrollment population for a given year if he or she had at least a 12-month period of continuous enrollment in Parts A and B, entering in any of the months in a given year, and was continuously enrolled in Medicare Part D throughout the calendar year. Enrollment status as well as gender, race/ethnicity, and age were identified in the EDB.

Definition of Diabetes

A beneficiary was determined to have diabetes if he or she had two or more claims with International Classification of Diseases (ICD-9) codes consistent with diabetes or at least one inpatient claim with ICD-9 codes consistent with diabetes (250.00-03, 250.10-13, 250.20-23, 250.30-33, 250.40-43, 250.50-53, 250.60-63, 250.70-73, 250.80-83, 250.90-93) in the 12-month period of continuous enrollment. Diagnostic codes were identified in the CWF. Beneficiaries included both incident and prevalent users of anti-diabetic agents.

Generation of Maps

Maps were generated using Dartmouth Atlas of Health Care (www.dartmouthatlas.org) HRRs. Beneficiary Zip Code of residence, as of December 31 of the given year, was extracted from the EDB and linked to HRRs. The percentages of beneficiaries with diabetes and use of antidiabetic drugs were grouped into quartiles and mapped accordingly. Geographic regions that did not correspond to an HRR were mapped in white. Regions with fewer than 11 beneficiaries contributing to the proportions presented were mapped in gray.

Definition of Antidiabetic Medications Used

Medications were identified using National Drug Codes (NDCs) for agents used to treat hyperglycemia. These agents were grouped into the following classes, as used by Facts & Comparisons (www.factsandcomparisons.com):

alpha-glucosidase inhibitors: acarbose, miglitol

amylin analog: pramlintide

biguanides: metformin, metformin-glipizide, metformin-glyburide, metformin-pioglitazone, metformin-rapaglinide, metformin-rosiglitazone, metformin-sitagliptin

dipeptidyl peptidase-4 inhibitors: saxagliptin, sitagliptin, sitagliptin-metformin

glucagon-like peptide-1 receptor agonist: exenatide

insulins: insulin aspart, insulin aspart-insulin aspart protamine, insulin detemir, insulin glargine, insulin glulisine, insulin inhalation rapid acting, insulin isophane, insulin isophane-insulin regular, insulin lispro, insulin lispro-insulin lispro protamine, insulin regular, insulin zinc, insulin zinc extended

meglitinides: nateglinide, rapaglinide, rapaglinide-metformin

sulfonylureas: acetohexamide, chlorpropamide, glimepiride, glimepiride-rosiglitazone, glimepiride-pioglitazone, glipizide, glipizide-metformin, glyburide, glyburide-metformin, tolazamide, tolbutamide

thiazolidinediones: pioglitazone, pioglitazone-glimepiride, pioglitazone-metformin, rosiglitazone, rosiglitazone-glimepiride, rosiglitazone-metformin

Definition of Antidiabetic Drug Users Among Beneficiaries With Diabetes

Beneficiaries with diabetes were classified as an antidiabetic drug user if they had a claim for one or more antidiabetic drugs in a given year.

ADDITIONAL FINDINGS AVAILABLE ONLINE

The following additional tables and maps are available online:

Prevalence of Drugs by Antidiabetic Class, Among Medicare Parts A, B, and D FFS Population With Diabetes, by Age, Gender, and Race, 2006-2009

Prevalence of Drugs by Antidiabetic Class, Among Medicare Parts A, B, and D FFS Population With Diabetes and At Least One Antidiabetic Drug Order, by Age, Gender, and Race, 2006-2009

Prevalence of Drugs by Antidiabetic Class, Among Medicare Parts A, B, and D FFS Population With Diabetes and At Least One Insulin Claim, by Age, Gender, and Race, 2006-2009

Prevalence of Drugs by Antidiabetic Class, Among Medicare Parts A, B, and D FFS Population With Diabetes and No Insulin Claim, by Age, Gender, and Race, 2006-2009

Prevalence of Drugs by Antidiabetic Class, Among Medicare Parts A, B, and D FFS Population With Diabetes and At Least One Biguanide Claim, by Age, Gender, and Race, 2006-2009

Prevalence of Drugs by Antidiabetic Class, Among Medicare Parts A, B, and D FFS Population with Diabetes and No Biguanide Claim, by Age, Gender, and Race, 2006-2009

Utilization of Antidiabetic Drugs, Among Medicare Parts A, B, and D FFS Population With Diabetes, by Drug Class and Hospital Referral Region (HRR), 2006-2009

Utilization of Sulfonylureas per 100 Diabetic Medicare Beneficiaries With Continuous Enrollment in Parts A and B FFS and Part D, by HRR, 2006-2009

Utilization of Insulins per 100 Diabetic Medicare Beneficiaries With Continuous Enrollment in Parts A and B FFS and Part D, by HRR, 2006-2009

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