

# Diabetes dilemma

U.S. trends in diabetes medication use



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**A NOTE FROM GLEN STETTIN, MD**

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## Delivering quality care for people with diabetes

For nearly two decades, the U.S. healthcare system has grappled with the meteoric rise of diabetes. Endless research has sought to understand the causes of this nationwide epidemic and to improve prevention and treatment of diabetes. Today, people with diabetes have access to significant advances in treatment that improve their health and quality of life, and reduce the risk of diabetes-related complications.

Diabetes remains one of the most costly conditions for payers. Yet lifestyle changes and wise use of diabetes medications are among the most important levers for reducing the human suffering and costs associated with this disease.

Our mission at Express Scripts is to put medicine within reach for members. We conducted this analysis of 26 million commercially insured members to identify new opportunities to work with plans to deliver safer, more effective and more affordable diabetes treatment.

**Key findings:**

**1. 11.6 million Americans with commercial insurance used medication to treat diabetes in 2016:**

- More than 5% of commercially insured Express Scripts members, including privately insured retirees, used diabetes medication. This extrapolates to nearly 11.6 million Americans with private health insurance being treated for diabetes.
- Oral diabetes medications were used by more than 84% of people treated for diabetes, with 69% using *only* these drugs to treat diabetes.
- One in four individuals with diabetes used insulin as part of their treatment regimen; nearly one in 10 used insulin only.
- More than 11% of people treated for diabetes were concomitant users of non-insulin oral drugs and insulin.

**2. Adherence to oral diabetes medication had a significant impact on patient health and costs:**

- Patients who were adherent to their oral diabetes medications had 235 fewer ER visits and 50 fewer inpatient hospitalizations per 1,000 patients.
- These patients spent nearly \$500 less on healthcare costs than nonadherent patients, which extrapolates to an estimated \$210 million in savings for 2016.
- In 2016, people with diabetes who were nonadherent to their non-insulin oral diabetes drugs had 1.3 times higher medical costs per person compared to those who were adherent.
- While not all diabetes-related complications are avoidable, among people with diabetes who had related complications, those adherent to their oral diabetes drugs averaged 9.4% lower total healthcare costs than those who were nonadherent.

**3. Diabetes was associated with higher healthcare costs for payers and individuals in 2016:**

- Payers spent more than \$9,000 in total medical expenses per person with diabetes – nearly three times higher than spending for individuals without diabetes.
- Inpatient hospitalization costs were more than four times higher, and costs for ER visits were twice as high for people with diabetes.
- Prescription plan costs for people who are using oral and/or non-insulin injectable diabetes drugs were three times higher than costs for people using non-diabetes drugs.
- Health plans and employers spent nearly six times more for people using only insulin to treat their diabetes than for people using medications for conditions other than diabetes.

Payers, providers and patients have a substantial opportunity to reduce pharmacy and medical costs by:

- **Increasing their efforts around the prevention of type 2 diabetes**
- **Implementing meaningful and sustainable lifestyle modifications**
- **Boosting adherence to diabetes medications**

At the Express Scripts Lab, we're partnering with more than 300 plans to test new ideas that address important issues in diabetes care. These include solutions such as connected glucometers, which allow for remote monitoring and counseling by diabetes pharmacists, and our collaboration with **Mango Health**, whose mobile health platform is designed to unlock our members' good intentions and get them on the road to better outcomes.

In addition, our **Diabetes Care Value Program<sup>SM</sup>** provides payers with condition-specific cost management and a quality pharmacy network – supported by the Express Scripts Diabetes Therapeutic Resource Center (TRC) – that can boost the average medication adherence rate for enrolled patients by 5%.

Together, we believe we can ease the burden of diabetes for payers and give people with diabetes a pathway for living a healthier life that is not defined by their condition.



**Glen Stettin, M.D.**

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# Background

**Diabetes is one of the most prevalent and expensive medical conditions requiring prescription therapy.**

The Centers for Disease Control and Prevention (CDC) estimates that more than 30 million Americans have diabetes, and another 84 million Americans have prediabetes – a condition in which blood sugar (glucose) levels are consistently elevated, but not high enough for a diabetes diagnosis.<sup>1</sup> That means roughly **one out of every three people in the U.S.** has the potential to need treatment for diabetes.

Diabetes results from the body's inability to make or regulate insulin, an essential hormone that regulates blood glucose.<sup>2</sup> Chronic diabetes is associated with long-term damage, dysfunction and failure of various organs, especially the eyes, kidneys, nerves, heart and blood vessels. The complications of diabetes, including heart attack, stroke, kidney failure, neuropathy and amputation, are both disabling and deadly. Not only is diabetes the seventh leading cause of death in the U.S. but roughly **two-thirds of those with diabetes die from heart disease or stroke.**<sup>1</sup>

People with diabetes face clinical challenges in managing their disease to prevent complications. Frequent monitoring may be needed to help ensure blood glucose levels are maintained at safe levels. Glycosylated hemoglobin levels (a measure of longer-term blood glucose control) need to be checked at least twice per year with a laboratory test called a hemoglobin A1C (HbA1c) test.<sup>3</sup> Other required monitoring includes blood pressure, cholesterol and urine tests to detect kidney damage.

While insulin and non-insulin medications are extremely effective in controlling blood glucose for people with diabetes, they are only one component in the treatment equation. Behavior modification, diet control and exercise are also important parts of an effective diabetes control plan. **For a summary of medication therapies for type 1 and type 2 diabetes, please see the Glossary on pages 23-25.**

As the following sections will highlight, diabetes is a complex chronic condition that exerts a significant economic burden on people managing this disease. The diabetes-related drug market is robust as the demand for medications, devices and supplies continues to increase with the rising prevalence of diabetes and associated comorbidities. The recently expanded drug mix for treating diabetes further compounds the complexity.

In this analysis, we examined usage of oral and/or non-insulin injectable diabetes medications and insulins.

## Type 1 diabetes

- Nonpreventable, autoimmune disease that destroys cells in the pancreas that make insulin.
- Often called Juvenile Diabetes, as the condition is frequently discovered in childhood.
- Accounts for only a small fraction of the overall diabetes population.
- Patients are dependent on insulin for life and do not use other diabetes drugs.

## Type 2 diabetes

- A disease in which the patient's pancreas doesn't produce enough insulin, and/or the body resists insulin that's produced.
- May be prevented, delayed and even reversed with sustained modifications to diet and exercise.
- Most people use oral and/or non-insulin injectable diabetes medications.
- Cases more difficult to control may require the use of insulin.

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# Diabetes medication use in the U.S.

## As the population ages, diabetes drug utilization increases

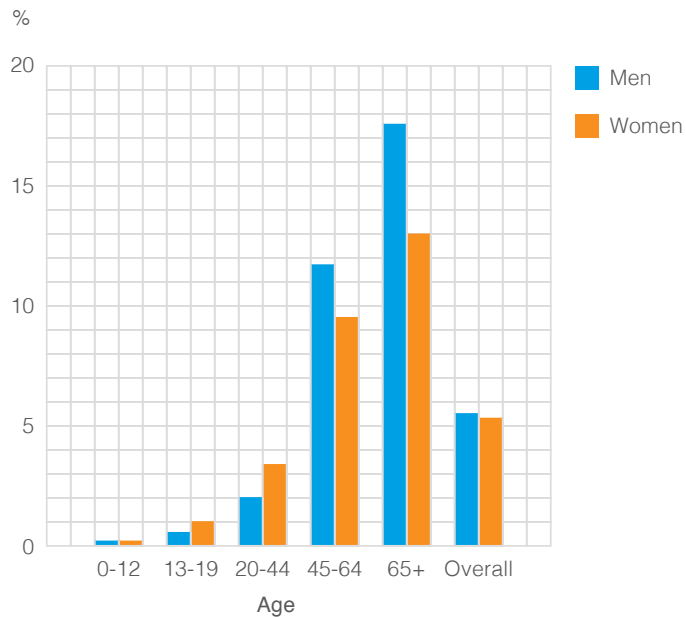
More than 5% of commercially insured members, including retirees with private health insurance, used diabetes medications in 2016, a rate that has remained relatively steady over the past three years. When our findings are extrapolated to the U.S. population, we estimate that 11.6 million Americans with private health insurance used diabetes medications.<sup>4</sup>

In 2016, overall use of diabetes medications was high among older adults, mirroring the prevalence of type 2 diabetes in the U.S. population.<sup>5</sup> Overall, prevalence of diabetes medication use was higher among men than women, with ages 45 to 64 years and 65 years or older having the highest utilization.

About  
**11.6M** privately  
 insured  
 Americans  
 used diabetes  
 medications  
 in 2016

## Percent of people using diabetes medications

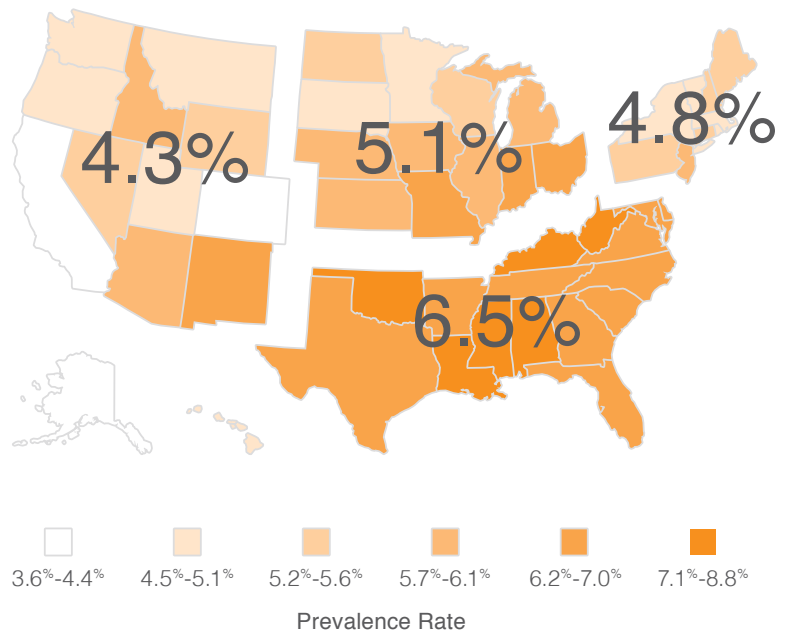
BY AGE AND GENDER, 2016



Diabetes medication usage varies significantly around the country, with the highest concentration of diabetes medication users residing in southern states. In 2016, the age- and gender-adjusted prevalence of use of diabetes medication was 6.5% in the South, compared with 4.3% in the West. Alabama had the highest prevalence among U.S. states (7.7%) and Colorado had the lowest (4.2%).

### Geographic prevalence of diabetes medication use

2016



Note: Geographic comparisons were adjusted for age and gender using 2010 U.S. Census data

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# Diabetes costs

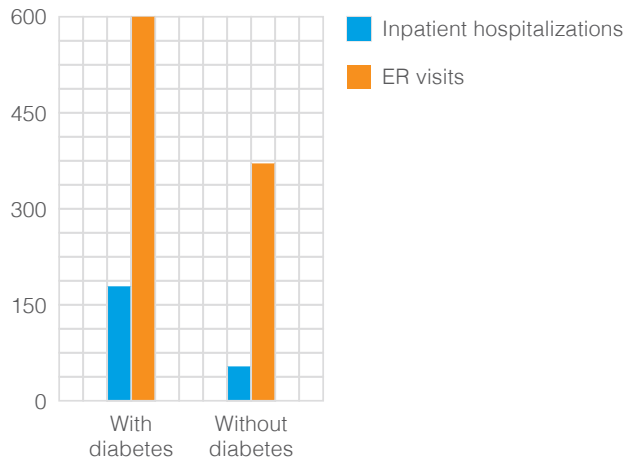
## Comorbid conditions and complications drive higher costs for people with diabetes

Diabetes-related medical costs contribute to making diabetes one of the costliest chronic conditions to treat. The American Diabetes Association estimates that direct medical spending on diabetes is \$176 billion in 2012 U.S. dollars.<sup>6</sup>

People with diabetes are at increased risk for serious comorbid conditions and complications, which can predispose them to greater likelihood of inpatient hospitalizations or emergency room (ER) visits. When examining inpatient hospitalizations for all diagnoses, including diabetes and all-cause ER visits among people with and without diabetes, we found that patients with diabetes had more than three times higher inpatient visits and 1.6 times higher ER visits versus people without diabetes (identified using the International Classification of Diseases, 9th and 10th Revision, Clinical Modification coding system).

### All-cause inpatient hospitalizations and ER visits

PER 1,000 PATIENTS, 2016



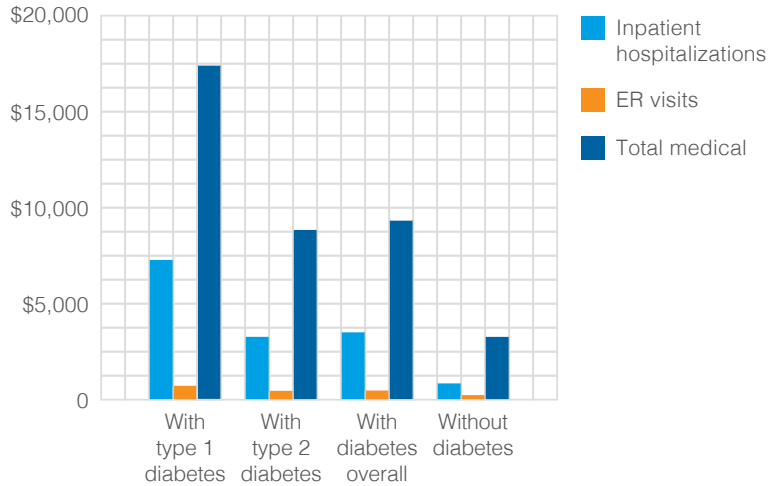
All-cause medical costs are higher among people with diabetes. Payers spent more than \$9,000 in total medical expenses per diabetes patient in 2016 – nearly three times higher than spending for individuals without diabetes. Medical costs were over five times higher for type 1 diabetes patients and nearly three times higher for type 2 patients than for people without diabetes. For those with diabetes overall, hospitalization costs were more than four times higher and ER visit costs were twice as high.



In 2016, each person with diabetes cost payers **\$9K+** in medical expenses – nearly three times more than those without diabetes

### All-cause medical plan costs

PER PATIENT, 2016



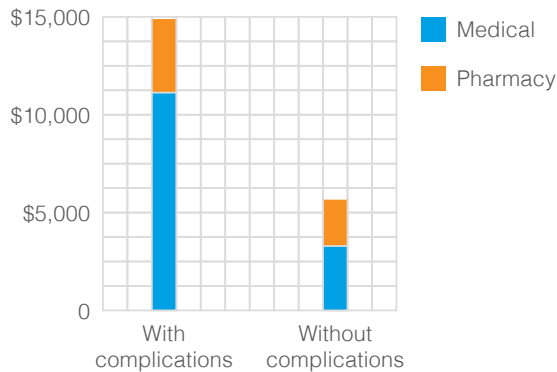
### Costs for people with diabetes-related complications

Along with chronic comorbidities that are associated with diabetes, such as high blood pressure and high cholesterol, individuals with diabetes may also suffer from other complications, including blindness, diabetic foot pain, nerve pain and chronic kidney disease – especially when diabetes is poorly controlled. The added physical and economic burdens of these complications can be significant.

People with diabetes and one or more complications incur about 2.4 times more in total healthcare costs for plans compared to people with uncomplicated diabetes (\$14,635 vs. \$6,140) due to three-times higher medical costs.

### Total healthcare plan costs for diabetes patients

PER PATIENT, 2016



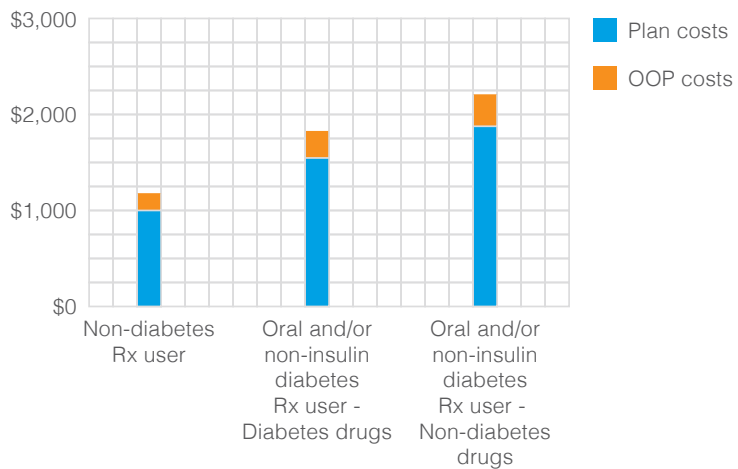
**Pharmacy costs for oral and/or non-insulin injectable diabetes medication users**

Employers and patients face considerable financial burdens related to lifelong management of their condition and treating additional diabetes-associated comorbidities. The annual prescription costs (diabetes and non-diabetes) for patients using oral and/or non-insulin injectable diabetes medications were three times higher (\$3,424.32) compared to costs for those who do not use any diabetes drugs (\$1,052.33). Even spending on just diabetes-related drugs and devices was higher compared to the overall drug spend of people not using a diabetes drug. Patient OOP costs were also considerably higher for those treated for diabetes.

Payers spent **three times more on drugs** for patients using oral and/or non-insulin injectable diabetes medications than those using non-diabetes drugs

**Plan and out-of-pocket costs for medication users**

PER UTILIZER, 2016



**Cost for insulin-only users**

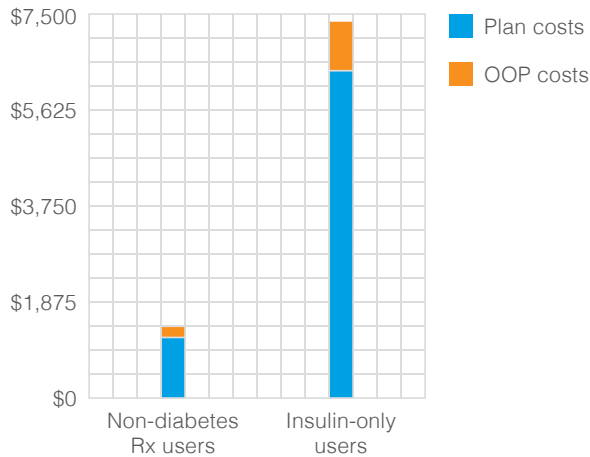
Brand inflation and lack of generic/biosimilar versions have contributed to increases in insulin cost. Some insulins increased in price by 150% or more between 2010 and 2015.<sup>7</sup> Although patents are long-expired for some insulin brands, no biosimilar/follow-on versions were approved until recently due to the complexity of insulin production and a lack of FDA guidelines for manufacturers. Basaglar® (insulin glargine), the first follow-on insulin approved in the U.S., launched in December 2016.

The skyrocketing costs for insulins have received considerable attention recently. Our analysis of medication users shows that total plan spend by health plans and employers for insulin-only users' prescription drugs was nearly six times the amount that was spent for people using drugs for conditions other than diabetes (\$5,682.70 vs. \$1,052.33). The annual patient OOP for medications averaged \$850.48 compared to \$180.08 for people who take non-diabetes drugs.

In 2016, plans spent **nearly six times more** on drugs for diabetes patients who used insulin than for those using non-diabetes drugs

**Plan and out-of-pocket costs for non-diabetes medication users and insulin-only users**

PER UTILIZER, 2016



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## Orals and non-insulins

### Medication usage, adherence and related costs

Medications to treat type 2 diabetes include oral drugs and/or non-insulin injectable diabetes medications.

We examined five classes of oral diabetes drugs – biguanides, sulfonylureas, dipeptidyl peptidase 4 (DPP-4) inhibitors, sodium-glucose cotransporter-2 (SGLT2) inhibitors and thiazolidinediones – and one class of non-insulin injectable diabetes medication – glucagon-like peptide-1 (GLP-1) receptor agonists – approved in the U.S.. Less than 1% of patients used meglitinides or alpha-glucosidase inhibitors, which were not included in our analysis. Each of the classes has different mechanisms of action and drugs from different classes may be taken together to achieve greater blood-sugar lowering effects.

The GLP-1 receptor agonists, also known as incretin mimetics, simulate the action of GLP-1 receptors, stimulating insulin production. At the same time, they reduce the liver's glucose output and slow gastric emptying. Apart from reducing A1c, they also may reduce appetite and promote weight loss. Additionally, their risk of causing low blood sugar is not as high as for some other classes.

### Oral medications

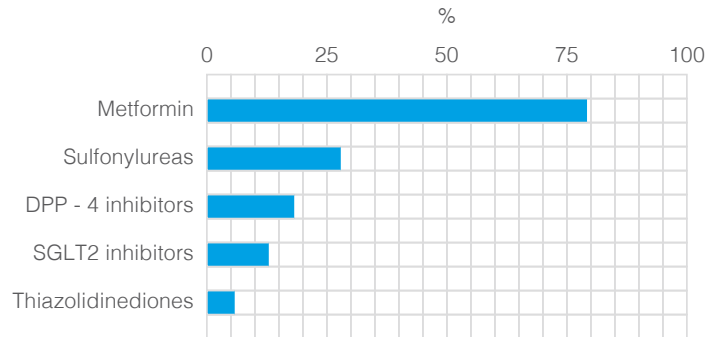
In 2016, oral diabetes medications were used by 84.4% of people treated for diabetes, with 69% using *only* oral drugs to treat diabetes. Use of oral diabetes medications was greatest among patients 45 and older (87.6%) compared to those under 45 (74.1%). Two older classes of oral diabetes medications, biguanides – metformin is the only one approved in the U.S. – and sulfonylureas, such as glipizide, were most frequently used, at 79.2% and 27.9% of users, respectively.

The first DPP-4 inhibitor, Januvia® (sitagliptin), came to market in 2006. The first SGLT2 inhibitor, Invokana® (canagliflozin), came to market in 2013. Since then, use of SGLT2 inhibitors has seen a steady uptick from 6.6% prevalence of use in 2014 to 12.9% in 2016.

**84.4% of people  
with diabetes  
used oral  
medications  
in 2016**

## Prevalence of use for oral diabetes drug classes

PERCENT OF ORAL DIABETES RX USERS, 2016



**More than 36% of people taking oral diabetes drugs were taking two or more diabetes medications**

Among patients using oral diabetes medications, nearly two-thirds (63.1%) used only one drug. More than 36% of oral Rx users were taking two or more medications, with over 3% taking four or more.

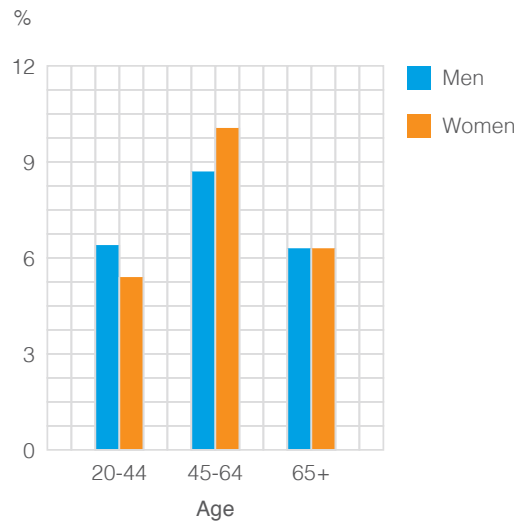
Many people with type 2 diabetes may also require insulin to control their blood glucose. We found that 11.4% of people treated for diabetes used both oral drugs and insulin together for treatment.

### Non-insulin injectables

Use of GLP-1 agonists has been rising steadily from about 6% of adults with diabetes (ages 20 and over) in 2014 to over 8% in 2016. A higher proportion of women than men with diabetes aged 45 to 64 years were using a GLP-1 drug in 2016.

### Prevalence of use for non-insulin injectables

BY GENDER AND AGE GROUP, 2016



### Adherence to oral diabetes medications

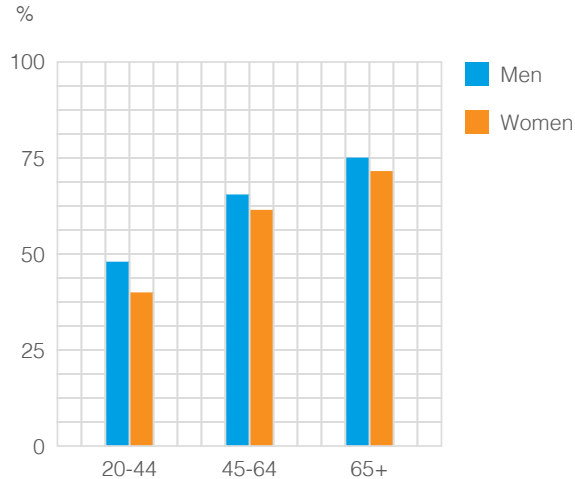
Medication adherence is estimated based on possession of medications within a defined period using pharmacy claims data. Previous studies have found that adherence is associated with greater control of blood glucose and lower use of healthcare resources.<sup>8-10</sup> And, as adherence increases, hemoglobin A1c levels – a measure of long-term blood glucose control – decrease.<sup>11</sup>

**Only 63% of people aged 20+ were adherent to their diabetes drug regimen in 2016**

Given the progressive nature of the disease, managing diabetes becomes even more critical as individuals age. However, in 2016, only 63% of all commercially insured adults 20 years or older using oral diabetes medications were adherent to their drug regimen. Among individuals treated for diabetes, about two-thirds aged 45-64 and nearly three-quarters aged 65 or older were adherent. Gender disparities in adherence to diabetes drugs existed too, with women being less adherent than men across age groups, representing another critical gap in care for diabetes patients.

### Percent of patients adherent to oral diabetes medications

BY GENDER AND AGE GROUP, 2016



Typically, adherence increases as the number of non-diabetes drugs taken increases

**Adherence among users of multiple drug regimens**

Interestingly, as the number of oral diabetes drugs being used by people treated for diabetes increases, adherence also tends to increase, with a few exceptions. These findings are consistent with results from our previous studies, which showed that the proportion of individuals adherent to their medications is higher among people who have diabetes, hypertension and high cholesterol, as opposed to people who have only one of these three chronic conditions.<sup>12,13</sup>

**Percent of adherent patients who take oral diabetes and non-diabetes drugs**

BY NUMBER OF ORAL DIABETES DRUGS, 2016

		Number of oral diabetes drugs			
		1	2 to 3	4+	Total
Number of non-diabetes drugs	0	43.2%	48.1%	52.8%	44.7%
	1 to 2	56.5%	59.6%	60.7%	57.6%
	3 to 5	62.5%	64.2%	62.7%	63.1%
	6+	65.0%	65.3%	60.3%	64.9%
	Total	62.5%	63.9%	61.2%	63.0%

**Adherence among patients treated for diabetes by pharmacy channels and dispensing days' supply**

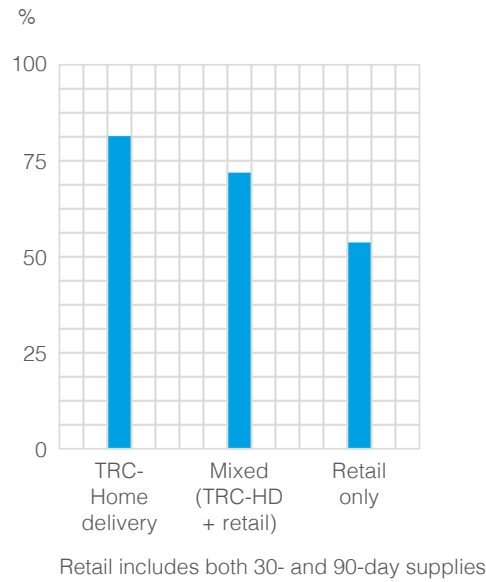
Previous Express Scripts research showed that commercially insured individuals who filled prescriptions through the Express Scripts Diabetes Therapeutic Resource Center/home delivery (TRC-HD), or a mix of retail and TRC-HD, had a higher likelihood of being adherent compared to those who filled their medications only at retail pharmacies.<sup>18</sup> Other researchers also found home delivery pharmacies to be valuable in improving adherence to chronic disease medications.<sup>19</sup>

In this analysis, a higher proportion of commercially insured individuals filling their diabetes drugs using TRC-HD, or a mix of TRC-HD and retail, were adherent to oral diabetes drugs compared to those using only retail pharmacies (dispensing both 30- and 90-day supplies). Only about half of individuals treated for diabetes using retail as the only channel to fill their medications were adherent to oral diabetes drugs.

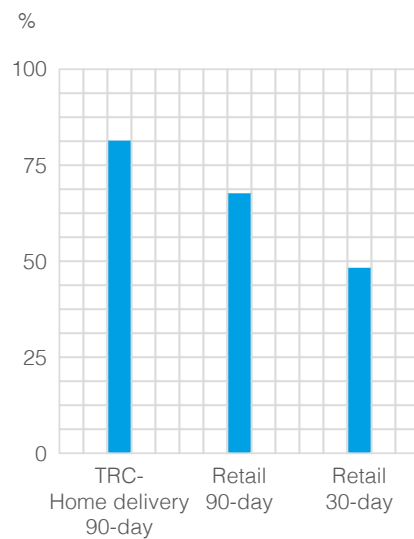


## Percent of patients adherent to oral diabetes medications

BY CHANNEL, 2016



BY CHANNEL AND SUPPLY AMOUNT, 2016



Express Scripts TRC-home delivery offers patients specialized diabetes support and the convenience of 90-day supplies that leads to better adherence. While the TRC-HD model drives the highest adherence, filling 90-day prescriptions at retail leads to better adherence than filling multiple 30-day prescriptions for chronic maintenance medications, such as those for diabetes. Data showed that a higher proportion of diabetes patients who filled 90-day supplies using TRC-HD or retail pharmacies were adherent to their oral diabetes medications than those who filled only 30-day supplies at retail.

With improved patient adherence to oral diabetes medications, plans could potentially avoid more than **\$210M** in healthcare costs

### Cost of nonadherence to oral diabetes medications

Previous research has found that nonadherence to diabetes medications results in increased downstream healthcare costs and inpatient and ER visits.<sup>16,17</sup> Our data showed that diabetes patients who were not adherent to their oral diabetes drugs had 1.3 times higher medical costs compared to those who were adherent. Nonadherent diabetes patients had 1.5 times higher ER visit costs and 1.6 times higher inpatient costs than adherent individuals.

Even adding pharmacy costs, which tend to be higher among adherent patients, total healthcare costs for nonadherent diabetes patients was more than 4% higher than for those who were adherent. For commercially insured members, this difference of nearly \$493 per person amounted to more than \$210 million in potentially avoidable costs resulting from improved adherence.

### Plan costs by adherence to oral diabetes drugs

PER PATIENT, 2016

	Adherent	Nonadherent
Inpatient hospitalizations	\$1,935.58	\$3,118.01
ER visits	\$323.34	\$497.19
Total medical	\$6,680.65	\$8,436.46
Total pharmacy	\$4,001.88	\$2,739.01
Total healthcare	\$10,682.53	\$11,175.47

Adherence to diabetes medications is critical not only for preventing the catastrophic consequences of the disease, but also for lowering total healthcare costs. Among people with diabetes along with any complications, those adherent to their oral diabetes medications averaged 9.4% lower total healthcare costs than those who were not adherent.

Plan costs by adherence to oral diabetes drugs,  
for patients with complications

PER PATIENT, 2016

	Adherent	Nonadherent
Medical	\$8,011.08	\$10,380.67
Pharmacy	\$4,214.76	\$2,992.25
Total healthcare	\$12,225.84	\$13,372.91

Note: Not all patients with diabetes and complications qualify for adherence calculations by meeting all inclusion criteria for the adherence estimation, such as having continuous eligibility and having two or more claims for oral diabetes drugs.

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**25% of people  
treated for  
diabetes used  
insulin in 2016**

# Insulins

## Insulin types and usage

We examined the most recent data available to identify trends in insulin use among Americans of different ages, genders and geographic locations.

One in four individuals treated for diabetes used insulin, with one in 10 using *only* insulin in 2016. As expected, usage of insulin is greatest among younger patients, where type 1 diabetes is more prevalent. In fact, among people treated for diabetes, 67.5% of children 12 years of age and under used insulin in 2016, compared to only 23.6% of adults aged 45 to 64.

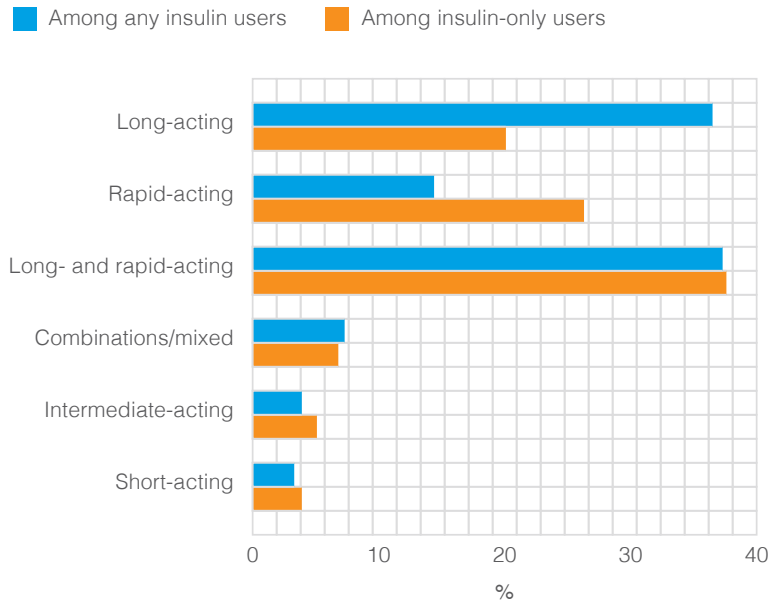
In the US, four types of insulin with differing action profiles are approved to lower blood glucose levels and help improve the body's ability to use glucose. Rapid-acting and long-acting insulin analogues have essentially displaced the mixed, short-acting and intermediate-acting recombinant insulins that were introduced in the 1980s. Rapid-acting forms, also known as prandial (mealtime) insulins, counteract blood glucose spikes after meals. They begin working within about 20 minutes, peak in just an hour or so and remain effective for two to four hours. Long-acting (basal) insulins have a delayed onset of action to maintain a constant insulin level in the body for 24 hours or longer.

In 2016, over 37% of patients had concomitant use of both long- and rapid-acting insulins for treatment.

In 2016, more than **37% of patients used both long- and rapid-acting insulins for treatment**

Prevalence of use of among insulin users

BY INSULIN TYPE, 2016



Our analysis also revealed variation in the kinds of insulin by age. A greater proportion of children aged 12 years or younger (42.6%) were using rapid-acting insulins for diabetes treatment. Comparatively, for adults aged 45 and older, more people were using both long-acting and rapid-acting insulins for diabetes treatment.

Prevalence of use among insulin users

BY INSULIN TYPE AND AGE GROUP, 2016

	0-12	13-19	20-44	45-64	65+
Long-acting	5.8%	4.1%	9.5%	18.2%	24.6%
Rapid-acting	42.6%	41.6%	37.1%	23.3%	10.4%
Long- and rapid-acting	41.6%	44.6%	37.2%	37.8%	35.9%
Combinations/mixed	0.2%	1.6%	3.0%	7.7%	13.0%
Intermediate-acting	1.4%	1.5%	7.0%	4.2%	5.4%
Short-acting	0.4%	0.7%	3.0%	4.5%	4.7%

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**77% of people**  
treated for  
diabetes use  
glucose test strips

## Devices and supplies

### Device and supply types and usage

People with diabetes use several types of devices and supplies for monitoring blood glucose and/or administering insulin. Adjusting meals, physical activity and treatment according to blood glucose levels is crucial to assuring the best control, particularly for those with type 1 diabetes. Most major guidelines recommend that blood glucose be checked several times a day, depending on the type and severity of diabetes and the needs of the patient.<sup>18</sup>

Devices and supplies such as glucose test strips, glucose meters and control solutions for calibrating the meters are typically used for blood glucose monitoring, while lancets and lancing devices are used specifically to draw blood for glucose monitoring. Supplies such as syringes, pen needles and pumps are used to administer insulin. About 35% of all people treated for diabetes used devices associated with blood glucose monitoring, while nearly 19% used insulin-delivery devices in 2016.

Prevalence of use for glucose test strips was highest at nearly 77%; however, use declined slightly from nearly 80% in 2014. On the other hand, among people using devices, more than a third used pen needles for administering insulin, with usage increasing between 2014 and 2016.

### Prevalence of use for diabetes devices and supplies

2014 TO 2016

		2014	2015	2016
Glucose monitoring	Glucose test strips	79.7%	78.4%	76.7%
	Glucose meters	13.0%	10.8%	11.0%
	Control solution	1.5%	1.3%	0.6%
Drawing blood for glucose monitoring	Lancets	40.0%	38.6%	39.0%
	Lancing devices	1.1%	1.4%	1.6%
Insulin administration	Pen needles	31.5%	32.1%	34.1%
	Syringes	12.2%	11.5%	10.6%
	Insulin pumps	1.1%	1.4%	1.6%

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# Glossary

## Type 1 diabetes

Type 1 diabetes was formerly known as insulin-dependent diabetes mellitus or juvenile-onset diabetes. Primarily, it develops early in life when the pancreas cells that produce the hormone insulin, which regulates blood glucose, are destroyed by the body's immune system. Consequently, all people with type 1 diabetes require insulin replacement to stay alive.

Insulin classifications are based on the time to reach the bloodstream from the site of injection, the time to reach peak effectiveness and the amount of time the insulin continues to remain effective.

1. **Rapid-acting insulins**, such as Humalog® (insulin lispro), reach the bloodstream about 15 to 30 minutes after injection, reach maximum strength in about one hour and continue to work for two to four hours.
2. **Regular or short-acting insulins**, such as Novolin® R (Regular, Human Insulin [rDNA origin]) usually start working within 30 minutes after injection, peak from two to three hours after injection and continue to work for approximately three to six hours.
3. **Intermediate-acting insulins**, such as Humulin® N (NPH) take effect in about two to four hours after injection, peak four to 12 hours later and remain effective for about 12 to 18 hours.
4. **Long-acting insulins**, such as Lantus® (insulin glargine), reach the bloodstream several hours after injection and maintain relatively constant basal (baseline) blood glucose levels over a 24-hour period.
5. **Mixed/combo insulins**, such as Humalog® Mix 75/25 or NovoLog® 70/30, combine shorter duration and longer duration insulins into one single dosage form for convenience.

**Devices and supplies** for glucose monitoring and insulin administration are also frequently used by diabetes patients. Glucose test strips, meters, lancets and lancing devices are used to monitor blood glucose levels. Traditionally, using insulin involved drawing it from vials and injecting it into the body using syringes. Now, alternatives such as refillable pen-like injection devices and prefilled disposable insulin pens are more common.

## Type 2 diabetes

Type 2 diabetes was formerly known as non-insulin-dependent or adult-onset diabetes. It results from resistance to insulin's effects, insufficient insulin production or both. Type 2 diabetes is by far the most common, estimated to account for 90% to 95% of all diagnosed diabetes cases among adults in U.S.<sup>2</sup> Obesity, unhealthy diet and lack of exercise are risk factors for developing type 2 diabetes.

In addition to lifestyle modification recommendations, people with type 2 diabetes are usually treated with oral medications.<sup>19</sup> Insulin and/or other non-insulin injectable diabetes drugs may be added to regimens for type 2 diabetes patients whose blood glucose is not controlled sufficiently by oral medications.

### The oral medication classes are:

1. **Sulfonylureas**, such as Amaryl® (glimepiride) and Glucotrol® (glipizide), are the oldest oral diabetes drug class still in use. Sulfonylureas stimulate the beta cells of the pancreas to release more insulin.
2. **Meglitinides**, such as Prandin® (repaglinide) are similar in action to sulfonylureas. Low blood sugar is a possible side effect of meglitinides and sulfonylureas.
3. **Biguanides**, such as metformin (Glumetza®), form the cornerstone of the diabetes oral drug therapy. Metformin is recommended as the first-line therapy prescribed to people newly diagnosed with type 2 diabetes. They lower blood glucose levels primarily by decreasing the amount of glucose produced by the liver.
4. **Thiazolidinediones**, such as Avandia® (rosiglitazone), act as insulin sensitizers and also reduce production of glucose in the liver.
5. **Dipeptidyl peptidase 4 (DPP-4) inhibitors**, such as Januvia® (sitagliptin), prevent the breakdown of glucagon-like peptide 1 (GLP), thereby increasing insulin secretion and reducing blood glucose levels in the body.



6. **Sodium-glucose transporter 2 (SGLT2) inhibitors**, such as Invokana® (canagliflozin), are the newest class of oral diabetes drugs, with the first one approved in 2013. They inhibit the compound that is responsible for reabsorbing glucose in the kidney, causing excess glucose to be eliminated through urination.
7. **Alpha-glucosidase inhibitors, such as Precose® (acarbose)**, prevent the breakdown of starch and sugar from food in the intestine.
8. **Oral combination drugs, such as Janumet® (sitagliptin/metformin)**, are fixed-dose combinations (FDCs) of two or more classes listed above. Most FDCs include metformin as one of the drug components

**Non-insulin injectable diabetes medications**, such as Bydureon® (exenatide), are GLP-1 receptor agonists that trigger insulin production and suppress the liver's glucose output. They are used mainly to treat type 2 diabetes.

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From a sample size of more than 26 million commercially insured individuals, including retirees with private health insurance, this research examined the de-identified pharmacy claims of more than 1.4 million individuals who filled at least one prescription for the management of diabetes in 2016. Beneficiaries of a government-sponsored benefit, such as Medicare, Medicaid or public health insurance exchange, were not included in this analysis.

In addition, this research examined medical claims data for a section of the commercially insured members whose prescription drug benefits are managed by Express Scripts. The integrated medical and pharmacy claims data for over 9 million commercially insured individuals available from our RationalMed® solution were used to examine the medical-related research measures. For all medical data analyses, we identified people with chronic conditions, including diabetes, using the ICD-9 and ICD-10 CM coding system. The plan sponsors providing the pharmacy benefit paid at least some portion of the cost for the diabetes prescriptions dispensed to their members, providing what is known as a funded benefit.

Measures estimated during a three-year period were calculated for the period from Jan. 1, 2014 to Dec. 31, 2016. Measures for 2016 were calculated for the period from Jan. 1, 2016 to Dec. 31, 2016. Our analysis only included commercially insured plans and privately insured retiree plans that were continuously enrolled in the Express Scripts book of business for all three years.

People with diabetes are defined as members having one or more claims for a diabetes therapy class or a diabetes-related device. All diabetes drugs, including oral medications, insulin and non-insulin injectable drugs are included in the data. Additionally, claims for devices/supplies used by people with diabetes and billed under the pharmacy benefit are included in the data.

People without diabetes are defined as members with a prescription claim that is not associated with diabetes (drug or device). Non-prescription medications (except for diabetic supplies billed under the pharmacy benefit) and prescriptions that were dispensed in

hospitals, long-term care facilities and other institutional settings were excluded.

Prevalence of use is calculated by dividing the sum of people with diabetes by the sum of all members. Market share of drugs is calculated by dividing the sum of prescription claims of interest by total sum of all prescription claims for that metric (e.g. sum of all prescription claims for oral fixed-dose combinations/sum of all oral prescription claims). Prescription drug plan costs include ingredient costs, taxes, dispensing fees and administrative fees net of rebates.

Medical costs included the dollar amount paid for any medical claims that are covered under the medical benefit. Total medical costs included costs for all medical services, including inpatient hospitalizations and emergency room visits, which are covered under the medical benefit and paid for by plan sponsors. Total healthcare costs include the sum of all costs under both pharmacy and medical benefits.

Adherence was calculated using the medication possession ratio (MPR), which is the sum of the days' supply for all fills of a given oral diabetes drug in a particular period, divided by the number of days in the period for a diabetes patient having two or more fills of the oral diabetes drug during the period. Patients with a MPR of less than 0.8 or 80% were considered nonadherent.

New to diabetes therapy patients were defined as individuals who did not have any prescription for diabetes medication filled in the previous 180 days from the time of their first diabetes drug or device claim in a particular year.

Data examined in this report was limited to Express Scripts commercially insured plan sponsors with no contractual limitations for data use.

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