
Diabetes in the District of Columbia

Government of the District of Columbia
Department of Health
Health Regulation and Licensing Administration

Prepared by
The Milken Institute School of Public Health
The George Washington University

Susan F. Wood, PhD
Joy C. Eckert
Alycia Hogenmiller
Dilipan W. Sundaramoorthy
Sharma Cook
Adriane Fugh-Berman, MD
This report was submitted to the DC Department of Health on September 30, 2016.
# Table of Contents

I. Executive Summary..................................................................................................................5
   Background...............................................................................................................................5
   Comparing AccessRx and Open Payments............................................................................5
   Key Findings............................................................................................................................7

II. Health and Healthcare in the District of Columbia.............................................................9
   Demographic Overview of DC...............................................................................................9
   Healthcare Access and Use......................................................................................................10
   Diabetes in DC.......................................................................................................................12

III. Prescription Drug Analysis.................................................................................................15
   National Prescription Drug Expenditures...........................................................................15
   Analysis of DC Drug Expenditures......................................................................................16

IV. Diabetes Overview.............................................................................................................19
   Types of Diabetes...................................................................................................................20
   Diet and Exercise....................................................................................................................20
   Drug Treatments.....................................................................................................................21
   Insulin....................................................................................................................................23

V. Costs of Diabetes Treatment.................................................................................................25
   Costs to Patients and Payers.................................................................................................26
   Costs to Medicaid....................................................................................................................27
   Analysis of DC Medicaid Spending for Diabetes.................................................................28
   Cost Drivers.............................................................................................................................31
   Less Costly Insulin..................................................................................................................34

VI. Analysis of Drug Promotion for Diabetes..........................................................................35
   Marketing Expenditures in DC.............................................................................................35
   Payments to Physicians..........................................................................................................36
   Importance of In-Person Marketing (Detailing)......................................................................39
   Attributing Promotions of Specific Drugs to Detailing Expenditures....................................39

VII. Recommendations...............................................................................................................41

References..................................................................................................................................43

Appendix A: Glossary of Terms...............................................................................................47
Appendix B: Table of Diabetes Drugs.......................................................................................48
I. Executive Summary

Background

The District of Columbia’s AccessRx Act of 2004 requires pharmaceutical companies to report marketing expenditures to the District of Columbia Department of Health (DC DOH). This information is analyzed by researchers at the George Washington University Milken Institute School of Public Health for DC DOH.

The AccessRx program generates two annual reports. An Expenditures Report documents pharmaceutical marketing expenditures on gifts (to physicians, other healthcare professionals, hospitals, and other organizations), advertising, and the salaries of detailers. The subject of the second report, Impacts of Pharmaceutical Marketing on Healthcare in the District of Columbia, investigates how pharmaceutical marketing may affect health and healthcare in the District of Columbia.

Previous reports include:

- Focus on Gifts to Organizations and Influential Physicians (2014)
- Focus on Use of Antipsychotics in Seniors (2013)

This 2016 Impacts of Pharmaceutical Marketing on Healthcare in the District of Columbia report focuses on how diabetes care and the cost of diabetes treatment are affected by marketing and promotion practices.

Comparing AccessRx and Open Payments

AccessRx data provides a wealth of information, unique in the nation, that enables analyses no other jurisdiction can do. The Physician Payments Sunshine Act of 2010 established the national Open Payments system that requires all pharmaceutical and medical device manufacturers to report payments to physicians and teaching hospitals to the Centers for Medicare and Medicaid Services (CMS). The Open Payments data are publicly available and searchable online. CMS began collecting the data in August 2013, but 2014 represents the first full year of reported data.

AccessRx and Open Payments serve similar purposes but capture different sets of data. Open Payments only requires companies to report on gifts to physicians and teaching hospitals. The DC DOH AccessRx program is far more comprehensive, requiring reporting for all other licensed healthcare providers (e.g. nurses, nurse practitioners, physician assistants, and pharmacists), non-teaching hospitals, healthcare staff, and organizations. Only AccessRx picks up gifts
received by nurse-practitioners (NPs), nurse midwives, nurse anesthetists, physician assistants (PAs), podiatrists, and optometrists. The number of prescriptions written by NPs and PAs has more than doubled over the past five years; in 2015, NPs and PAs wrote 676 million of 4.4 billion prescriptions in the U.S. (IMS 2015).

In addition, only AccessRx tracks salaries and other payments for any detailers and other personnel (employees and contractors) involved in marketing pharmaceuticals in the District. In DC in 2014, this spending category, called Aggregate Expenses, was the largest, with more than $60 million in detailing expenditures reported. AccessRx also tracks expenditures on local advertising, including District-specific print, television and other advertisements. Another advantage AccessRx has over Open Payments is that AccessRx data go back to 2007, enabling analysis of changes over time.

An advantage Open Payments has over AccessRx is that data, including physician names, are publicly available. Payments to physicians and teaching hospitals are searchable online through Open Payments, allowing researchers to track patterns in gifts. Additionally, individual patients can see whether their physicians have accepted gifts from pharmaceutical companies. Although AccessRx reports are publicly available, details of individual expenditures, such as name and payment amounts, cannot be reported. According to the AccessRx Act, reported information at the individual or organizational level is confidential and available in detail only to DC DOH.
Key Findings

Diabetes drives up individual healthcare costs and costs to healthcare systems. In the District of Columbia, one in eleven (9.1%) residents has diabetes. In 2013, diabetes was the ninth leading cause of hospitalization in DC, with 1,572 visits (BRFSS 2015). Although the prevalence of diabetes in DC increased by 15.7% from 2010 to 2014, DC Medicaid spending on diabetes drugs grew by 350% in the same five year period (Health, United States 2016). The cost of pharmaceutical treatments for diabetes made up 10% of the $151.9 million in DC Medicaid drug reimbursement in 2014. Of the 21 drugs with over one million dollars in DC Medicaid drug spending, four were diabetic treatments. These four treatments accounted for 8% of all Medicaid reimbursements in 2014.

Drug Promotion in DC

In 2014, pharmaceutical and device manufacturers reported spending $91.2 million on marketing in the District of Columbia to AccessRx and Open Payments.

- $60.7 million for Aggregate Expenses (salaries and other expenditures on drug reps, other pharmaceutical company employees and contractors engaged in marketing)
- $22.6 million for Gift Expenses
- $7.9 million for Advertising Expenses

Diabetes Drug Promotion

We identified 42 brand-name diabetes drugs with more than $360,000 in the Open Payments reporting system that were associated with payments in DC in 2014. The diabetes drug associated with the most physician payments was Invokana (canagliflozin) with $154,000 in associated gifts. Endocrinologists received 70% of all physician gifts associated with diabetes medications. Seventy-seven endocrinologists, including pediatric endocrinologists, accepted $639,000 worth of gifts and payments from pharmaceutical companies.

In-person marketing can have long-term effects on physicians’ prescribing habits. The marketing category with the highest reported spending was salaries and expenses of drug reps, other pharmaceutical company employees and contractors engaged in marketing.

We developed a methodology to estimate the proportion of expenditures on salary and other expenses for sales and marketing staff that can be attributed to marketing a particular drug. This may be a marker for how extensively specific drugs are being marketed in the District. We estimated that ten companies spent $3.8 million in salary and other expenses for sales and marketing staff to promote diabetes drugs in the District of Columbia. The newly approved SGLT-2 inhibitor and GLP-1 analogue drug classes had the highest estimated detailing amounts, each totaling more than $1.2 million. While DC Medicaid spent little on these drug classes in 2014, high expenditures on drug promotion for SGLT-2 inhibitors and GLP-1 analogues may precede increased prescribing rates for these costly medications.
II. Health and Healthcare in the District of Columbia

Demographic Overview of DC

In 2015, DC’s estimated total population was 672,228, 11% higher than the 2010 population of 601,723 (QuickFacts 2016). The District includes eight Wards, each comprising 12-13% of the population. About 50% of DC’s children (0-17 years old) reside in Wards 4, 7, and 8, while about 50% of older adults (65+ years old) reside in Wards 3, 4 and 5 (Merrill 2016).

DC’s ethnic composition is 47% African-American, 36% White, 11% Latino, and 4% Asian. Ward 3 has a White population greater than 75%; Wards 7 and 8 have populations more than 90% African-American. Latinos are the largest growing racial demographic, with a 33% increase since 2010 (Merrill 2016).

Unemployment in DC in 2014 was 7.8%, compared to the 2014 national average of 5.6% (District of Columbia 2016). Unemployment rates varied widely: while Wards 7 and 8 had unemployment rates of 22% and 23% respectively, the rate of unemployment in Ward 3 was 4% (Merrill 2016).

In 2014, 19% of residents in the city lived in poverty, about the same as the DC poverty rate in 2010. Wards 7 and 8 had poverty rates of 25% and 29%, compared to Ward 3 at 2% in 2014. About 27.6% of African-American residents lived in poverty compared to only 8.3% of White residents. Over 40% of African-American children lived in poverty compared to only 4.9% of White children (Merrill 2016).

Figure 1: Number of Families Living Below the Poverty Line in 2015

Source: Merrill 2016
Healthcare Access and Use

When asked to rate their health, 12.8% of DC adults reported their health as fair or poor in 2013, compared to 16.7% nationally. The elderly, those making less than $25,000 a year, and African-Americans all had over 20% of respondents rating their health as only fair or poor. Nearly 30% of Ward 8 residents reported fair or poor health, compared to about 17% in Wards 4, 5, and 7 (BRFSS 2015).

In 2013, over 92% of DC residents had health insurance, about 9 percentage points above the national average. About 50% of residents are covered by employer-issued insurance, while 25% are covered by Medicaid/CHIP, 8% are covered by Medicare, 11% are non-group insured, and 6.4% are uninsured. Latinos were the least likely to be insured, 17.7% were uninsured, compared to 12.8% of African-American residents and 3.2% of White residents (BRFSS 2015).

Despite relatively high rates of insurance coverage, about 24% of residents report not having a consistent health care provider (BRFSS 2015). In 2013, about 10% of the total population delayed or did not receive care due to high medical costs, slightly higher than the national average of 9.1% (Health, United States 2016). As chronic conditions, including diabetes and asthma, rise in the District, it becomes more important for residents to have a consistent healthcare provider. One study found that patients with chronic diseases who moderately improved their continuity of care experienced dramatically reduced complications and adverse events and also incurred less costs (Hussey 2014).

Lack of consistent primary care and preventative care tends to shift healthcare delivery to more costly settings such as hospitals and emergency departments (EDs). Because primary and preventative care reduce hospitalizations and emergency department visits, high hospital utilization rates indicate barriers to accessing effective primary and preventive care. The DC Community Health Needs Assessment (DC CHNA) analyzed records from four federally qualified health centers and nine community health centers (note: Wards 4 and 7 have no hospitals). DC CHNA found that 71% of hospital discharges were for African-American patients, compared to only 15% for White patients. Wards 7 and 8 accounted for the highest percentage of hospital usage at 18% each, while Ward 3 and Ward 2 accounted for only 6% and 7% respectively. Medicaid beneficiaries accounted for 35% of hospital discharges compared to 31% using Medicare, and 32% using commercial insurance (Merrill 2016).
Access to pharmacies presents another disparity issue (Figure 4). In particular, Wards 7 and 8 combined have only six pharmacies despite the wards’ higher rates of chronic conditions like diabetes. Ward 2 alone has 42 pharmacies, and Ward 3 has 21 pharmacies (District of Columbia 2016).

**Figure 4: Map of Pharmacies Licensed to Administer Vaccines in DC**

![Map of Pharmacies Licensed to Administer Vaccines in DC](source: Pharmacies Licensed to Administer Vaccinations 2016)
Diabetes in DC

In 2014, one in eleven (9.1%) District residents had diabetes. In 2013, diabetes was the ninth leading cause of hospitalization in DC, with 1,572 visits. Diabetes was also the fifth leading cause of death with 144 deaths, more than chronic lower respiratory diseases, Alzheimer’s disease, HIV/AIDS, or homicides. Wards 4, 5, 7 and 8 experienced the highest number of diabetes deaths (more than 25 deaths), while Ward 3 experienced only 1 death (BRFSS 2015).

Diabetes was the fifth leading cause of death with 144 deaths, more than chronic lower respiratory diseases, Alzheimer’s disease, HIV/AIDS, or homicides.

Risk factors for diabetes include obesity, low activity levels, and experiencing food insecurity. The 2016 DC Community Health Needs Assessment concluded that poor access to healthy, affordable nutrition, including fruits and vegetables, “is a challenge for many DC residents”. “Food deserts,” areas without easy access to groceries, are endemic in DC; Wards 7 and 8, where about 25% of the city’s population live, together have just three grocery stores and three farmers markets (Merrill 2016).

DC has a citywide childhood obesity rate of 35%, and 71.9% of children reported not being physically active (defined as at least 60 minutes of physical activity per day at least five times a week). Adult obesity rates were 22.8% citywide, with a high of 42.8% in Ward 8 and a low of 12% in Ward 3. Ward 5 and 7 had adult obesity rates of 32.1% and 35%, respectively. Almost one in three (31%) adults were overweight, with similar rates across the city. Latinos in DC had a higher rate (39%) of overweight adults than any other ethnic group. About half (54%) of all DC residents are either obese or overweight, and in Wards 5, 7 and 8 this number jumps to 70% (Merrill 2016).

In 2013, about 20% of DC adults reported not performing any physical activity in the past month. One in three (34.5%) adults in Ward 8 reported no physical activity in the last 30 days, compared to one in ten (10.5%) in Ward 3. African-American adults had a much higher rate of inactivity (36.4%) than any other ethnic group (Merrill 2016).
An analysis of ED records found that up to 30% of visits for diabetes, asthma, and other chronic conditions were potentially preventable with better access to effective primary and preventive care. For diabetes, rates of ED visits for African-Americans in DC were over 6 times higher than for Whites (Figure 2). Wards 5 and 7 had over five times higher rates of ED visits due to diabetes compared to Ward 3 (Figure 3) (Merrill 2016).

**Figure 2: ED Visit Rate for Diabetes by Race, 2010-2014**

![Figure 2: ED Visit Rate for Diabetes by Race, 2010-2014](source.png)

Source: Merrill 2016

**Figure 3: ED Visits for Diabetes by Ward, 2010-2014**

![Figure 3: ED Visits for Diabetes by Ward, 2010-2014](source.png)

Source: Merrill 2016
III. Prescription Drug Analysis

National Prescription Drug Expenditures
In 2014, prescription drugs made up $297.7 billion, or 11.6% of all national personal healthcare expenditures. Of these costs, customers paid 15.0% ($44.7 billion) out-of-pocket; private insurance covered 42.8% ($127.3 billion); Medicare covered 29.0% ($86.4 billion), and Medicaid covered 9.2% ($27.3 billion). Nationally, prescription drug expenditures in 2014 amounted to $935 per capita (Health, United States 2016). Between 2013 and 2014, the rate of growth in prescription drug spending jumped from 2.4% to 12.2%, in large part due to new specialty drugs for hepatitis C, cancer, and multiple sclerosis. For comparison, total spending in 2014 only grew 4.4% (Martin 2016).

Increases in prescription drug prices have serious ramifications for both Medicaid beneficiaries and Medicaid programs. According to 2014 CMS data, 11.6% of Medicaid beneficiaries reported delays in receiving care or prescription drugs, or not receiving care or drugs altogether, due to high costs (Health, United States 2016). According to a national Kaiser Family Foundation national analysis, five major drug groups constituted 36 of the 50 most costly outpatient drugs covered by Medicaid (Young 2016):

- Antivirals (10 drugs)
- Antiasthmatics and Bronchodilators (8 drugs)
- ADHD/Anti-Narcolepsy/Anti-Obesity/Anorexiants (7 drugs)
- Antipsychotics/Antimanic Drugs (6 drugs)
- Antidiabetics (5 drugs)
Analysis of DC Drug Expenditures

According to our analysis (Table 1), D.C.’s Medicaid prescription drug program cost $153 million in 2014, of which Medicaid reimbursed $151.9 million. About 39.9% of this reimbursement went towards just 21 drugs, each of which cost DC Medicaid over $1 million. In 2014, the amount spent on these 21 drugs increased 37% due to recent price increases; per prescription costs increased 28%.

Table 1: Drugs with Greater Than $1 Million in DC Medicaid Spending in 2014

<table>
<thead>
<tr>
<th>Brand Name</th>
<th>Generic Name</th>
<th>Cost to Medicaid</th>
<th>Number of Prescriptions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abilify</td>
<td>aripiprazole</td>
<td>$9,559,589</td>
<td>10,882</td>
</tr>
<tr>
<td>Lantus</td>
<td>insulin glargine</td>
<td>$6,306,260</td>
<td>20,267</td>
</tr>
<tr>
<td>Sovaldi</td>
<td>sofosbuvir</td>
<td>$6,299,863</td>
<td>223</td>
</tr>
<tr>
<td>Advair</td>
<td>fluticasone/salmeterol</td>
<td>$4,480,699</td>
<td>14,223</td>
</tr>
<tr>
<td>Flovent</td>
<td>fluticasone propionate</td>
<td>$4,422,804</td>
<td>24,631</td>
</tr>
<tr>
<td>Invega</td>
<td>paliperidone</td>
<td>$3,487,884</td>
<td>2,723</td>
</tr>
<tr>
<td>Novolog</td>
<td>insulin aspart</td>
<td>$3,223,267</td>
<td>10,365</td>
</tr>
<tr>
<td>Suboxone</td>
<td>buprenorphine/naloxone</td>
<td>$2,603,176</td>
<td>6,046</td>
</tr>
<tr>
<td>Nexium</td>
<td>esomeprazole</td>
<td>$2,113,994</td>
<td>8,061</td>
</tr>
<tr>
<td>Ventolin</td>
<td>salbutamol</td>
<td>$1,968,485</td>
<td>43,242</td>
</tr>
<tr>
<td>Spiriva</td>
<td>tiotropium bromide</td>
<td>$1,896,750</td>
<td>6,440</td>
</tr>
<tr>
<td>Leveim</td>
<td>insulin detemir</td>
<td>$1,684,117</td>
<td>5,162</td>
</tr>
<tr>
<td>ProAir</td>
<td>salbutamol</td>
<td>$1,666,813</td>
<td>30,078</td>
</tr>
<tr>
<td>Januvia</td>
<td>sitagliptin</td>
<td>$1,557,121</td>
<td>5,195</td>
</tr>
<tr>
<td>Humira</td>
<td>adalimumab</td>
<td>$1,551,819</td>
<td>535</td>
</tr>
<tr>
<td>Olysio</td>
<td>simeprevir</td>
<td>$1,456,305</td>
<td>65</td>
</tr>
<tr>
<td>Remodulin</td>
<td>treprostinil</td>
<td>$1,354,332</td>
<td>74</td>
</tr>
<tr>
<td>Synagis</td>
<td>palivizumab</td>
<td>$1,320,830</td>
<td>567</td>
</tr>
<tr>
<td>-</td>
<td>methylphenidate</td>
<td>$1,316,633</td>
<td>9,371</td>
</tr>
<tr>
<td>Lyrica</td>
<td>pregabalin</td>
<td>$1,248,529</td>
<td>4,622</td>
</tr>
<tr>
<td>-</td>
<td>budesonide</td>
<td>$1,056,542</td>
<td>2,701</td>
</tr>
</tbody>
</table>
Eight drugs were not on this list prior to 2014: Humira, Novolog, Levemir, Januvia, Lyrica, Sovaldi, Olysio, and Remodulin. Two of these drugs, the hepatitis C treatments Sovaldi and Olysio, gained FDA approval in 2013, and jumped to over $7.75 million in spending in a little over a year. These and other specialty hepatitis C drugs have driven higher-than-normal growth in prescription drug expenditures nationally. The two antipsychotics (Abilify and Invega) made up $13 million in Medicaid reimbursements. Spending in the antipsychotic category has been stable since 2011.

This list also includes four diabetes drugs: Januvia, Lantus, Levemir, and Novolog. Three of these drugs – Lantus, Levemir, and Novolog – are injectable insulin analogues. Each costs more than $300 per prescription in 2014, up from about $240 in 2013 and $160 in 2010. The fourth diabetes drug, Januvia, is an oral medication that increased in price from $263 per prescription in 2013 to $300 per prescription in 2014.

Four diabetes drugs made up 8% of all DC Medicaid drug spending in 2014, and all diabetes drugs made up about 10% of DC Medicaid drug spending.
IV. Diabetes Overview

Worldwide, there are 415 million Type-2 diabetic patients; by 2040 there are expected to be 642 million (Singh 2016). The CDC reported that in 2014, 22.0 million Americans had diagnosed diabetes, with 1.4 million new cases occurring in 2014. Diabetes primarily affects older adults; 21.5% of Americans between 65 and 74 and 19.2% of Americans 75 years and older have diabetes. By comparison, only 1.5% of those ages 0-45 have diabetes (Diabetes Data and Statistics 2016). Whites had an age-adjusted prevalence rate of 5.8% while African-Americans had an age-adjusted rate of 9.5%.

Diabetes mellitus (DM), known commonly as diabetes, is a chronic disorder of the pancreas resulting in defects in insulin secretion, a defect in the effect of insulin on specific organs, or both. A normal pancreas maintains the body’s blood sugar levels within a certain range. Insulin helps remove glucose, a simple sugar, from the blood. Inadequate levels of insulin can lead to high blood sugar concentrations.

High blood sugar (hyperglycemia) damages cells and organs over time (Palmer 2016). Chronic damage to large blood vessels from high blood sugar (macrovascular disease) increases the risk of heart attacks and strokes. Damage to small blood vessels (microvascular disease) increases the risk of kidney disease (including kidney failure), retinopathy (including blindness), and amputations. Other complications include neuropathy, increased risk of some infections (Singh 2016) and increased cancer risk (Way 2016). Diabetic ketoacidosis is a life-threatening condition caused by very high blood sugar that can lead to seizures, coma and death (Tiwari 2015). Because Type-1 diabetics produce little to no insulin on their own, they are at risk of developing ketoacidosis; this condition is far less common in Type-2 diabetics (Prescrire International 2016).

Hypoglycemia, or low blood sugar, is caused by antidiabetic drugs. All drugs used to treat diabetes can cause hypoglycemia, but insulin is the most likely to cause this problem, compared to oral antidiabetic medications. Hypoglycemia may be mild or severe. Being aware of hypoglycemic symptoms that indicate decreased blood-glucose levels is called hypoglycemia awareness, which is important in preventing mild hypoglycemia from becoming severe hypoglycemia. Mild hypoglycemia may cause hunger, shakiness, weakness, sweating, pallor, confusion, and headache. Severe hypoglycemia can cause unconsciousness and seizures (Yeh 2016).

Symptoms associated with hypoglycemia can be addressed by eating or drinking something high in glucose, such as apple juice, a candy bar, or a spoonful of peanut butter. Hypoglycemia is a leading cause of emergency room visits (Tseng 2014) and is a risk factor for cardiovascular events and death (Yeh 2016).
Types of Diabetes

The two main types of diabetes are Type-1 diabetes mellitus (T1DM), formerly known as juvenile diabetes, and Type-2 diabetes mellitus (T2DM), formerly known as adult-onset diabetes.

Type-1 diabetes results from an autoimmune destruction of the pancreatic beta cells that make insulin. Type-1 diabetes, which is typically diagnosed before the age of 20, accounts for 5–10% of people with diabetes in the U.S. (Tiwari 2015). Over time, Type-1 diabetic patients become unable to produce any insulin on their own, and depend on insulin injections for survival. Insulin is the only diabetic treatment that reduces mortality in Type-1 diabetics (Prescrire International 2016).

Type-2 diabetes mellitus (T2DM) accounts for about 90% of people with diabetes; it is associated with age, obesity, and diet (Tsujino 2015). Excessive amounts of glucose in the blood can cause fat, muscle, and liver cells to become resistant to insulin. Decreasing the amount of glucose consumed will directly decrease the amount of sugar in the blood, thus reducing the progression of T2DM (Way 2016).

Pre-diabetes, or impaired glucose tolerance (IGT), is a risk factor for developing T2DM; it occurs when blood glucose levels are high but within normal range. Gestational diabetes is a temporary condition that occurs only during pregnancy and typically resolves after birth; it is a risk factor for developing T2DM later in life.

Blood sugar level is assessed through blood tests. A random or fasting blood sugar test gives a snapshot of a blood sugar level, but the best way to assess blood sugar control in diabetics is through a hemoglobin A1C (HbA1c) blood test. HbA1c is a form of hemoglobin, a pigment in red blood cells, to which glucose is attached. An HbA1c level provides an estimate of blood sugar levels over the lifespan of the red blood cells, which is about 120 days.

Diet and Exercise

Diet and exercise are an effective treatment for T2DM and can be an effective add-on treatment to insulin in T1DM. For Type-2 diabetics, diet modification and increased physical activity are the recommended first line therapy (Way 2016). Maintaining a healthy body weight, increasing dietary fiber, and reducing total and saturated fat intake are also helpful (Lindstrom 2010). All patients with diabetes, whether or not they are on medication, can better control their diabetes by reducing their carbohydrate intake (Bell 2014; Krebs 2016; Tiwari 2015). Unlike diabetes drugs, decreasing carbohydrate intake is not associated with any adverse effects (Krebs 2016).
Besides treating diabetes, diet modifications and increased physical activity have a pivotal role in preventing T2DM – regardless of the patient’s risk factors (Stevens 2015). For preventing diabetes, exercise was better than drug treatment. Additionally, exercise helps to delay the progression of T2DM (Lindstrom 2010; Way 2016; Krebs 2016). Diabetes onset and progression can be delayed by as much as four years through lifestyle interventions and delayed by two years with metformin treatment in both high-risk patients and patients diagnosed with Type-2 diabetes. The effects of lifestyle intervention or metformin in preventing or delaying diabetes can persist for at least ten years (Knowler 2009).

**Drug Treatments**

Approved antidiabetic drugs include seven classes of oral drugs (sulfonylureas, meglitinides, alpha glucosidase inhibitors, thiazolidine/PPAR inhibitor glinides, DPP4 inhibitors, SGLT-2 inhibitors, and a biguanide), and three classes of subcutaneously injected drugs (insulin, amylin analogues, and GLP-1 analogues). All diabetes drugs decrease glucose in the blood, although they have different mechanisms of action.

**Metformin**

Metformin, a biguanide, is an old, inexpensive, highly effective drug available in generic form. An oral therapy approved by the FDA in 1994, metformin has been available in Europe since the 1950s (Setter 2003). Metformin should be first-line therapy for all Type-2 diabetic patients (DeGeeter 2014; Palmer 2016). It also benefits Type-1 and high-risk patients. Metformin reduces the amount of glucose that is produced by the liver, and decreases the intestinal absorption of glucose (Harrigan 2001). Metformin has also shown to increase insulin sensitivity in Type-1 diabetics. Metformin reduces the progression of T2DM (Dardando 2014), and, in prediabetics, helps prevent diabetes (Lindstrom 2016).

For T2DM, it is not clear that adding other drugs to metformin adds any benefit. A systematic review that included 176 trials and 25 observational studies comparing metformin alone versus a combination drug that included metformin found no advantage of combination drugs over metformin alone (Maruthur 2016). Combining metformin and a sulfonylurea may increase risk of cardiovascular mortality in patients (Prescrire International 2014).

Metformin is even useful in Type-1 diabetics, increasing insulin sensitivity, and reducing total daily insulin without additional risk of hypoglycemia (DeGeeter 2016).

When combined with insulin in Type-1 diabetics, metformin mitigates the weight gain induced by insulin (DeGeeter 2016). The combination of insulin and metformin decreases insulin sensitivity within three months (Moon 2007).
Metformin therapy also reduces the incidence of Type-2 diabetes mellitus in high-risk patients and delays the incidence of diabetes mellitus by two years (Knowler 2009). Thus, metformin therapy has been proven beneficial in pre-diabetics, Type-1, and Type-2 diabetics (Knowler 2009; Setter 2003; DeGeeter 2016).

**Other Antidiabetic Drugs**

Besides metformin, other oral antidiabetic drugs include sulfonylureas, meglitinides (also called glinides), alpha-glucosidase inhibitors, thiazolidinediones (glitazones), DPP-4 inhibitors (gliptins), GLP-1 analogues and SGLT-2 inhibitors (gliflozins). Most oral therapies reduce HbA1c to a similar extent, except for DPP-4 inhibitors, which have smaller effects. (Maruthur 2016) Metformin and GLP-1 receptor agonists cause more nausea, vomiting and diarrhea than other drugs. Serious adverse effects differ by drug class.

Sulfonylureas, such as glipizide, glyburide, and glimepiride, decrease HbA1c by about 1.5%; only glyburide appears to be effective for preventing complications of diabetes. Sulfonylureas cause weight gain and dose-related hypoglycemia. They are the most likely oral drug to cause hypoglycemia.

Meglitinides, or glinides, include repaglinide (Prandin) and nateglinide (Starlix). These lower HbA1c by about 1.3%. These drugs cause hypoglycemia to the same extent as sulfonylureas and also cause weight gain and sometimes liver damage. Drug interactions are a problem.

Alpha-glucosidase inhibitors, such as acarbose, lower HbA1c modestly, by about 0.7%. They do not cause weight gain and do not generally cause hypoglycemia. However, they are associated with unpleasant gastrointestinal effects, including diarrhea, flatulence, and abdominal pain.

Glitazones, or thiazolidinediones, include rosiglitazone (Avandia) and pioglitazones (Actos). They decrease HbA1c by about 1%. These drugs cause weight gain, bone fractures, vision problems, liver damage, and increase the risk of heart failure. They have no advantages over other drugs.

DPP-4 inhibitors, or gliptins, lower HbA1c about 0.7%. They include sitagliptin (Januvia), saxagliptin (Onglyza), and linagliptin (Tradjenta). They do not cause weight gain and do not generally cause hypoglycemia. These drugs are associated with serious allergic reactions, including anaphylaxis. Gliptins increase the risk of infections, and can cause depression, headaches, and kidney dysfunction. Several are associated with cardiac problems and liver damage. Gliptins increase the risk of pancreatitis and may increase pancreatic cancer.

---

* Information for this section was sourced from Prescrire 2015.
GLP-1 analogues, including liraglutide (Victoza) and dulaglutide (Trulicity), lower HbA1c about 1%. Combining it with metformin enhances the glucose-lowering effect without increasing the risk of hypoglycemia. GLP-1 analogues cause weight loss. They can also cause gastrointestinal problems, kidney failure, and pancreatic disorders.

SGLT-2 inhibitors, or gliflozins, include canagliflozin (Invokana), dapagliflozin (Farxiga), and empagliflozin (Jardiance). They lower HbA1c about 0.7%. They are not generally associated with hypoglycemia and cause weight loss. SGLT-2 inhibitors can cause genital and urinary tract infections, kidney failure, low blood pressure, and may increase bone fracture, hepatitis, cancer and death rates.

**Oral Combinations**

When a brand-name drug is nearing the end of its patent life, a company may “evergreen” a drug by combining it with metformin and obtaining a new patent for the combination. Combination drugs may be very expensive, and there may be no advantage over metformin alone. There has been no clinically proven association in the reduction of cardiovascular mortality or all-cause mortality when using combination drugs (Palmer 2016).

**Insulin**

Insulin is required for Type-1 diabetics, but is rarely appropriate for Type-2 diabetics. For T2DM, insulin therapy shows no benefit (Prescrire International 2014). Insulins are divided into two major groups: NPH insulin and insulin analogues. Insulins are typically categorized by onset (time until insulin lowers blood glucose levels), peak-time (time range when insulin has maximum effect on blood glucose) and duration (time range that insulin continues to lower blood glucose).

- **NPH insulins** (Humulin R and Novolin R) are short-acting, beginning to work within 1-2 hours and typically lasting for 3 to 6 hours.
- **Rapid-acting insulin analogues** (including Apidra, Humalog, and Novolog) begin to work as quickly as 15 minutes after injection, peak shortly after, and last for 2 to 4 hours.
- **Long-acting insulin analogues** begin working within 2-5 hours and have durations of around 24 hours (American Diabetes Association 2015). Insulin analogues are generally newer and much more expensive than NPH insulins.

Type-1 diabetics, however, are dependent on injected insulin to survive. Long-acting insulins (active for more than 12 hours) may cost twice as much as the intermediate-acting insulins (active for 8 – 10 hours) and rapid-acting insulins (active for less than one hour). Two long-acting insulins, insulin glargine and insulin detemir, are the most costly insulins. Additionally,
long-acting insulins are more likely to result in serious hypoglycemic events that increase both inpatient and outpatient expenses (Wang 2003).

**Animal versus Human Insulin**

Insulin can be extracted from animal pancreases. Animal insulins, which may have some advantages, are unavailable in the US, although they are available in Canada and elsewhere. Today, insulins available in the U.S. are recombinant products bioengineered from human genes.

A systematic review reported that some T1DM patients have better metabolic and symptomatic control on animal insulin (Klein 2014). Some patients prefer animal insulin, which may be associated with greater hypoglycemia awareness, so patients can recognize the symptoms and eat something to reverse it (Meneilly 1995). A systematic review of 45 randomized control trials that included over 2,000 participants reported that there were not any clinically relevant differences in benefits or harms between animal and human insulin (Richter 2002). Hypurin Pork Regular (porcine-R) and Neutral Protamine Hagedorn (bovine-NPH) are available in Canada but not in the U.S (Klein 2014).

**Administration of Insulin**

Until the last decade, insulin was sold exclusively in glass vials. Patients would measure out and inject the insulin using a separate syringe. Recently, pharmaceutical companies have developed auto-injecting syringes. These devices, also referred to as “pens”, come prefilled with insulin and use a numbered dial to measure out insulin as a patient needs. Patients inject the insulin using a new disposable syringe needle sold separately from the pen for each injection, and the device has a simple button the patient presses to administer the injection. The patient hears an audible “click” when the injection has been completed. When the device runs out of insulin, the pen is thrown away.

Companies sell insulin in both vial and injectable pen forms. For example, Sanofi markets insulin glargine as Lantus, sold in a vial, and Lantus SoloSTAR, sold as a prefilled injectable pen. A study that received financial support from Sanofi showed no difference in insulin usage, blood sugar control, or HbA1c levels between patients that used Lantus in vial form and Lantus Solostar in the injectable pen form (Xie 2013).

Our analysis of DC Medicaid data showed that the Lantus Solostar pens cost about $60 more per prescription than Lantus sold in a vial. This does not include the additional cost of the special needles needed for pens, which are more expensive than syringes.
V. Costs of Diabetes Treatment

National health expenditures totaled $2.8 trillion in 2012, of which $1.3 trillion are major cost components (i.e. institutional care, outpatient care, and outpatient medication/supplies) according to a nationwide analysis. The investigators found that diabetic patients incurred about $306 billion of these major cost components. Of the $306 billion in medical costs, $176 billion were directly tied to patients’ diabetes medical care. In other words, “for the cost components analyzed, more than 1 in every 10 health care dollars is attributed to diabetes” (American Diabetes Association 2013).

**Figure 5: Economic Costs Due to Diabetes (in billions)**

![Diagram showing economic costs due to diabetes]

Source: American Diabetes Association 2013

The three largest components of direct medical costs were hospital inpatient care (43% of direct medical costs), prescription medications to treat complications from diabetes (18%), and antidiabetic medications and diabetic supplies (12%) (American Diabetes Association 2013).

Diabetes-associated costs directly accounted for 15.7% of national hospital inpatient care costs and 17.5% of national medication costs in 2012. Diabetes directly accounted for almost half of an individual’s “physician office visits, emergency department visits, hospital outpatient visits, and medication prescriptions (excluding insulin and other antidiabetic agents).” Most (62.4%) direct costs are borne by government insurance, but uninsured diabetics also consume state and Federal funds by, for example, visiting the emergency room 55% more often (American Diabetes Association 2013).
In addition to direct costs, indirect costs (absenteeism, lost productivity, earlier mortality, etc.) account for an additional $69 billion, bringing the total 2012 attributable cost of diabetes to $245 billion, up from $174 billion in 2007 (American Diabetes Association 2013).

These costs do not include the estimated 6.3 million American adults with undiagnosed diabetes, nor does it include higher costs for dental and optometric care associated with complications of diabetes, or costs associated with amputations. Diabetes research, intervention programs, and productivity lost due to care for a diabetic family member, or healthcare administration costs attributed to diabetes are also not included (American Diabetes Association 2013).

In 2012, the District of Columbia incurred $440 million in costs attributable to diabetes (American Diabetes Association 2013). This estimate used a much lower diabetes prevalence (5.3%) than reported by the CDC in 2012 (8.9%); thus, the true overall cost to DC may be much higher (Diabetes Data and Statistics 2016).

### Costs to Patients and Payers

A 2013 American Diabetes Association study concluded that the annual total health expenditures for an individual with diabetes in 2012 was 2.3 times higher than for someone without diabetes. This equates to an additional $7,888 each year in medical expenses attributed to diabetes. Women had higher additional per-year costs ($8,331) than men ($7,458); African-Americans had the highest costs ($9,540) compared to lower costs for White Americans ($8,331) and Hispanics ($5,930) (American Diabetes Association 2013).

In 2013, privately insured individuals with diabetes had $1,184 more in out-of-pocket costs per-year compared to those without diabetes. Children (Ages 0-18) had the second highest per-capita health expenditures of any groups as well as the highest increases in spending between 2011 and 2013. Costs for insured children spiked by $1,361 from 2012 to 2013, nearly double the increase of any other age group in the same period. Adults aged 55-64 had the highest expenditure, while adults aged 19-54 had lower, nearly uniform per-year expenditures (Shakiba 2015).

A study utilizing 2009-2010 data found excess medical costs for T2DM no matter what age the patient was diagnosed (Table 6). The age-weighted and gender-weighted average lifetime medical costs due to diabetes was $85,200 per patient, with 53% of these costs due to diabetic complications (Zhuo 2013). Total lifetime excess costs directly related to Type-2 diabetes increased as the age of diagnosis decreased.
Costs to Medicaid

Nationally, costs of insulin and non-insulin medications have risen dramatically in recent years, with much of this cost being passed on to Medicaid. In 1991, Medicaid paid between $2.36-$4.43 per unit of insulin and insulin analogues. In 2014, Medicaid reimbursed pharmacies $9.64 per unit of short-acting insulin analogues, $9.22 per unit of intermediate-acting insulin analogues, and $19.78 per unit of long-acting insulin analogues. Medicaid also paid $14.79 per unit of premixed insulin (a combination of short and long-acting insulin) and $19.78 per unit of rapid-acting insulin (an even faster-acting insulin) (Luo 2015).

Between 2002 and 2013, the mean price of insulin jumped almost 200% (Hua 2016). Prices for DPP-4 inhibitors increased 34% from $6.67 to $8.92 per tablet between 2006 and 2013. In contrast, the prices for metformin, the generic medication most popularly prescribed for Type-2 diabetes, dropped from $1.24 to $0.31 per tablet in the same period (Luo 2015).

The same analysis found that those with insulin prescriptions used 206 ml of insulin in 2013 compared to 173 ml in 2002. Spending on insulin per patient increased by $505 between 2002 and 2013; the same patients spent on average $508 on analogue insulin and just $228 on human insulin in 2013 (Hua 2016).
Analysis of DC Medicaid Spending for Diabetes

According to our analysis of DC Medicaid prescription data from 2014, diabetes medication cost Medicaid more than $17.1 million, a 34.7% increase from $12.6 million in 2013. From 2010 to 2014, DC Medicaid spending on diabetes drugs jumped 350% from $3.7 million to $17.1 million. During the same five year period, the number of diagnosed cases of diabetes in the District grew from 39,592 to 45,809, a 15.7% increase (Figure 7). The increase in the price of diabetes drugs has far outpaced the growth in both individual drug utilization and the prevalence of diabetes.

**Figure 7: Diabetes Cost to DC Medicaid and Number of DC Diabetes Cases from 2010-2014**

*From 2010 to 2014, DC Medicaid spending on diabetes drugs jumped 350% from $3.7 million to $17.1 million.*
The largest increases in spending were among insulins and DPP-4 inhibitors (gliptins). In 2014, DC Medicaid spent $13.4 million on seven insulin products (Lantus, Novolog, Leveimir, Apidra, Humalog, Novolin, and Humulin), up from $10 million in 2013. In 2014, DC Medicaid spent $2.6 million on six DPP-4 inhibitors (Januvia, Janumet, Onglyza, Tradjenta, Jentadueto, and Oseni), an increase of 54.5% from $1.7 million in 2013.

Table 2: Cost per Prescription of Insulins to DC Medicaid 2014

<table>
<thead>
<tr>
<th>Brand Name</th>
<th>Established Name</th>
<th>Cost per Prescription</th>
<th>Medicaid Spending</th>
<th>Number of Prescriptions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Levemir</td>
<td>insulin detemir</td>
<td>$326</td>
<td>$1,684,117</td>
<td>$5,162</td>
</tr>
<tr>
<td>Apidra</td>
<td>insulin glulisine</td>
<td>$316</td>
<td>$715,941</td>
<td>$2,263</td>
</tr>
<tr>
<td>Lantus</td>
<td>insulin glargine</td>
<td>$311</td>
<td>$6,306,260</td>
<td>$20,267</td>
</tr>
<tr>
<td>Novolog</td>
<td>insulin aspart</td>
<td>$311</td>
<td>$3,223,267</td>
<td>$10,365</td>
</tr>
<tr>
<td>Humalog</td>
<td>insulin lispro</td>
<td>$278</td>
<td>$711,220</td>
<td>$2,560</td>
</tr>
<tr>
<td>Humulin</td>
<td>insulin</td>
<td>$175</td>
<td>$364,056</td>
<td>$2,081</td>
</tr>
<tr>
<td>Novolin</td>
<td>insulin</td>
<td>$169</td>
<td>$366,129</td>
<td>$2,165</td>
</tr>
</tbody>
</table>

The average DC Medicaid cost per prescription for all types of insulin doubled in five years, up from $150 in 2010 to $300 in 2014. The new insulin analogues have higher costs per prescription compared to older insulins (Table 2). Medicaid spending on Lantus, one of these newer insulin analogues, exceeded all other diabetes drugs in DC as well as nationally. In 2014, DC Medicaid spent $6.3 million, second highest expenditures among all drugs, on 20,267 prescriptions of Lantus at approximately $311 per prescription. Other types of insulins also have a high Medicaid cost per prescription (Table 2), ranging from $169 to $326.

The average DC Medicaid cost per prescription for all types of insulin doubled in 5 years, up from $150 in 2010 to $300 in 2014.

Among antihyperglycemics (Table 3), GLP1 analogues had the highest DC Medicaid cost per prescription, ranging from $404 - $489 in 2014. Victoza (liraglutide) cost $489 per prescription the highest among all diabetes drugs.
Table 3: Cost per Prescription of Antidiabetics to DC Medicaid 2014

<table>
<thead>
<tr>
<th>Brand Name</th>
<th>Generic Name</th>
<th>Cost per Prescription</th>
<th>Medicaid Spending</th>
<th>Number of Prescriptions</th>
<th>Class of Drug</th>
</tr>
</thead>
<tbody>
<tr>
<td>Victoza</td>
<td>liraglutide</td>
<td>$489</td>
<td>$183,873</td>
<td>376</td>
<td>GLP-1 analogue</td>
</tr>
<tr>
<td>Prandin</td>
<td>repaglinide</td>
<td>$413</td>
<td>$38,855</td>
<td>94</td>
<td>Meglitinide</td>
</tr>
<tr>
<td>Bydureon</td>
<td>exenatide XR</td>
<td>$410</td>
<td>$2,052</td>
<td>5</td>
<td>GLP-1 analogue</td>
</tr>
<tr>
<td>Byetta</td>
<td>exenatide</td>
<td>$404</td>
<td>$31,105</td>
<td>77</td>
<td>GLP-1 analogue</td>
</tr>
<tr>
<td>Farxiga</td>
<td>dapaglifozin</td>
<td>$301</td>
<td>$603</td>
<td>2</td>
<td>SGLT-2 Inhibitor</td>
</tr>
<tr>
<td>Jentadueto</td>
<td>linagliptin/metformin</td>
<td>$300</td>
<td>$4,505</td>
<td>15</td>
<td>DPP-4 Inhibitor</td>
</tr>
<tr>
<td>Januvia\‡</td>
<td>sitagliptin</td>
<td>$300</td>
<td>$1,557,121</td>
<td>5,195</td>
<td>DPP-4 inhibitor</td>
</tr>
<tr>
<td>Oseni</td>
<td>alogliptin/pioglitazone</td>
<td>$296</td>
<td>$3,551</td>
<td>12</td>
<td>DPP-4 Inhibitor</td>
</tr>
<tr>
<td>Tradjenta</td>
<td>linagliptin</td>
<td>$295</td>
<td>$70,463</td>
<td>239</td>
<td>DPP-4 Inhibitor</td>
</tr>
<tr>
<td>Onglyza</td>
<td>saxagliptin</td>
<td>$293</td>
<td>$195,849</td>
<td>669</td>
<td>DPP-4 inhibitor</td>
</tr>
<tr>
<td>Janumet</td>
<td>sitagliptin/metformin</td>
<td>$285</td>
<td>$750,619</td>
<td>2,634</td>
<td>DPP-4 inhibitor</td>
</tr>
<tr>
<td>Kombiglyze</td>
<td>saxagliptin/metformin</td>
<td>$282</td>
<td>$97,208</td>
<td>345</td>
<td>DPP-4 inhibitor</td>
</tr>
<tr>
<td>Invokana</td>
<td>canagliflozin</td>
<td>$271</td>
<td>$8,930</td>
<td>33</td>
<td>SGLT-2 Inhibitor</td>
</tr>
<tr>
<td>- nateglinide</td>
<td>$80</td>
<td>$4,080</td>
<td>51</td>
<td></td>
<td>Meglitinide</td>
</tr>
<tr>
<td>- repaglinide</td>
<td>$75</td>
<td>$9,353</td>
<td>125</td>
<td></td>
<td>Meglitinide</td>
</tr>
<tr>
<td>- acarbose</td>
<td>$36</td>
<td>$2,597</td>
<td>73</td>
<td></td>
<td>Alpha-Glucosidase Inhibitor</td>
</tr>
<tr>
<td>- glyburide</td>
<td>$15</td>
<td>$54,173</td>
<td>3,861</td>
<td></td>
<td>Sulfonylurea</td>
</tr>
<tr>
<td>- glipizide</td>
<td>$10</td>
<td>$167,235</td>
<td>17,240</td>
<td></td>
<td>Sulfonylurea</td>
</tr>
<tr>
<td>- metformin\‡</td>
<td>$8</td>
<td>$452,089</td>
<td>53,293</td>
<td></td>
<td>Biguanide</td>
</tr>
<tr>
<td>- glimepiride</td>
<td>$8</td>
<td>$11,877</td>
<td>1,500</td>
<td></td>
<td>Sulfonylurea</td>
</tr>
</tbody>
</table>

Metformin, the first line pharmaceutical treatment for Type-2 diabetes, was prescribed more often than any other diabetes drugs; in 2014, DC Medicaid paid for 53,293 prescriptions of metformin. Metformin is the most inexpensive diabetes drug. DC Medicaid paid out $452,089 in reimbursements for metformin in 2014, a cost of $8 per prescription. Glipizide, a generic sulfonylurea, had 17,240 prescriptions in 2014, with a Medicaid cost per prescription of $10. Overall, generic oral medications had the lowest costs per prescription. No generics exist for insulin, but older products are less expensive than newer products.

\‡ Januvia (sitagliptin) was the non-insulin antidiabetic drug with the highest DC Medicaid spending in 2014
\‡ Metformin was the antidiabetic drug with the highest number of prescriptions
Cost Drivers

The healthcare industry determines drug prices through a complicated and confusing series of negotiations, rebates, and deductions. Drug manufacturers set an initial list price for a new product that is determined by analyzing a number of factors including: current costs of treatment for the disease, competitors’ prices, number of patients with the disease, cost of production, and what the market will bear. Pharmacy benefit managers (PBMs), including CVS and Express Scripts, and other healthcare entities individually attempt to negotiate a lower price for their members. Insurance providers then determine how much they are willing to pay, with the remaining cost borne by consumers.

Figure 8: Flow of Funds for Single-Source Brand-Name Drugs Purchased at a Retail Pharmacy and Managed by a Pharmacy Benefit Manager for an Employer Health Plan

Source: Congressional Budget Office 2007
Express Scripts, the country’s largest PBM, demonstrated in their 2015 *Drug Trends Report* that prices for diabetes medication have increased both for PBMs and for consumers. For members of ExpressScripts insured by Medicaid, diabetes had the highest out-of-pocket costs of any non-specialty therapy class. Looking at ExpressScripts data from Washington, DC and 24 states, the company found that in 2014, out-of-pocket costs for diabetes medication for all members increased 14.0%, the highest growth of all traditional therapy classes. Medicaid beneficiaries (excluding dual-enrolled members) experienced an even greater 21.7% increase in out-of-pocket costs. Only 4.1% could be attributed to greater drug use on a per-member basis; the remaining 17.6% was attributed to an increase in unit costs (Express Scripts 2016).

According to ExpressScripts, brand inflation for Lantus and Humalog was a “key cost driver” for rising diabetes medication costs. Insulin analogues Lantus and Humalog are, respectively, the most expensive and third most expensive non-specialty medications Express Scripts provides for members. Lantus’s unit costs increased 10.7% and Humalog’s unit costs increased 20.4% for Express Scripts members in 2014. Express Scripts expects diabetes drug costs for Medicaid-insured members to increase 23.9% in 2015, 22.4% in 2017, and 21.8% in 2018. The ExpressScripts analysis shows that even after negotiations between PBMs and drug companies, and after offering discounts, many consumers pay higher out-of-pocket costs when pharmaceutical companies raise list prices (Express Scripts 2016).

Express Scripts expects diabetes drug costs for Medicaid-insured members to increase 23.9% in 2015, 22.4% in 2017, and 21.8% in 2018.

It is difficult to ascertain the exact cause of these price increases due to the opaque nature of drug pricing and the peculiarities of the pharmaceutical industry itself. For example, increased competition in the form of multiple insulin products has not led to lower prices, even when the insulin products are almost identical. A Bloomberg report in 2015 found that the prices of insulin analogues Lantus (produced by Sanofi) and Levemir (produced by Novo Nordisk) rose in near lockstep from 2009 to 2015 (Langreth 2015). The report found 13 instances of this practice, called “shadow pricing”, where one of the drug’s price was increased only to have the other increased to match the other’s price. As shown in Figure 9, prices for Lantus and Levemir vials increased in tandem by 30% in a single year (Langreth 2015).
The same report also found evidence of shadow pricing in the NPH insulin market; from 2013 to 2015, Eli Lilly’s Humalog and Novo Nordisk’s Novolog have matched each other’s price increases three times. Prices for five diabetes treatments’ prices increased by over 20% in the first quarter of 2014. Levemir and Lantus’ average wholesale price (a rough estimate of what an uninsured patient might pay) increased 30% nationally in 2014. Although the companies producing the drug also increased discounts and rebates for the two drugs, the net result for insurers and patients is higher costs (Langreth 2015).
Less Costly Insulin

The modern insulin market has less competition than would be expected for a drug product discovered in 1923. Price increases in these branded medications can occur in part because patients and prescribers don’t have a generic alternative (Greene 2015). Until recently, pharmaceutical companies have kept up their patent protections for insulin through myriad mechanisms, including incremental modifications to a drug (for example, an extended-release product, or a combination product) to extend patent life (an industry practice called “evergreening”). Companies may also “pay-to-delay,” paying a competing company to delay releasing a generic competitor. Today, of the 15 insulin products on the market, only one is still patent-protected. Nonetheless, no generic competitors exist.

The market for a generic insulin (actually called a “biosimilar”) exists, as insulins have consistently been one of the top five selling drugs in America. An introduction of biosimilar competitors might lower market prices. Because insulin is a large molecule to reproduce and biosimilar drugs require stricter clinical evidence of benefit than generic drugs, the actual price may only be reduced by 20-40% (Greene 2015).

Animal insulin from cows or pigs have been proven to be as safe and effective as human and recombinant insulin (Greene 2015). Animal insulins are not available in the US, although they are in other countries. Both biosimilar and animal insulin preparations would be more cost effective (Tamblyn 2001).
VI. Analysis of Drug Promotion for Diabetes

Marketing Expenditures in DC

In 2014, pharmaceutical and device manufacturers reported a total of $91.2 million for gift, advertising, and aggregate expenses in the District of Columbia to AccessRx and Open Payments. These expenses were broken down into the following categories: Aggregate Expenses ($60.7 million), Gift Expenses ($22.6 million), and Advertising Expenses ($7.9 million). Gift recipients were also delineated between Individual and Non-Individual recipients. The largest category of reported spending was Aggregate Expenses, which accounted for $60.7 million, more than two-thirds of all marketing expenses in DC. A special analysis of aggregate expenses was conducted for this report.

The category Gift Expenses was the second largest category of spending with $22.6 million, including $7.6 million in gifts to organizations, healthcare facilities, and other healthcare providers and $14.9 million reported to Open Payments as gifts to physicians and teaching hospitals.

Most gifts were given to physicians, with a total of $11.2 million in gifts. The greatest number of gifts (76.9%) given to physicians took the form of Food or Beverage, but the greatest value of gifts ($5.3 million) were for Speaking and Related Fees.

Advanced Practices Nurses (nurse-practitioners, nurse-midwives, and nurse-anesthetists, all of whom can prescribe drugs) received $298,809 and Registered Nurses received $108,082 in gifts. Physician Assistants (who can prescribe drugs) received $73,377, and Pharmacists received $52,812 in gifts.

Professional Organizations received the greatest total value of gifts for a Non-Individual Recipients, with $4.4 million, which accounted for 40.9% of the gift value. Teaching Hospitals received $3.8 million in gifts and had the highest number of gifts (628 gifts) for Non-Individual Recipients. The other Non-Individual Recipients accounted for 10% of the total value of gifts given in 2014. These recipients were Advocacy Organization, Universities, Continuing Medical Education Organizations, Clinical Organizations and Pharmacies.

Advocacy and Professional organizations regularly accept large sums of money from pharmaceutical companies. In 2012, the American Diabetes Association accepted more than $1 million in gifts from pharmaceutical companies (Borkowski 2014). Non-profit organizations are required to declare the amounts of donations that they receive, but they are not required to report the name of the company.

---

§ Aggregate Expenses comprised the amount spent on salaries and other expenses for employees and contractors, many of them known as “detailers”, involved in marketing activities in the District.
Payments to Physicians

More than $11 million in gifts to District physicians were reported to Open Payments in 2014. It is well-documented that even small gifts, including meals, influence clinicians’ prescribing practices. Physicians who accept gifts are more likely to prescribe branded drugs (DeJong 2016).

We identified a list of 50 diabetes drugs (42 branded and 8 generic drugs) that appeared in either the Medicaid prescription database or the Open Payments database. Payments to physicians in the Open Payments database are linked to the name of an associated drug or device that is being promoted. Payments associated with the 42 branded diabetes drugs totaled over $360,000 in DC in 2014. The drug associated with the most physician payments was Invokana (canagliflozin), a SGLT-2 inhibitor manufactured by Janssen Pharmaceuticals, with $154,000 in associated gifts. Bydureon (exenatide) and Victoza (liraglutide), both incretin mimetics, were associated with gifts to physicians of $65,191 and $44,659 respectively.

Of the $364,765 in gifts associated with diabetes drugs, 70% ($254,860) was given to physicians who were classified in the specialty Endocrinology, Diabetes and Metabolism. Another 18% of the diabetes drug associated gifts were given to Internal Medicine physicians, and 7% went to “Family Medicine” physicians. The remaining 5% of gifts went to other specialties.

Figure 10: Payments Associated with Diabetes Drugs among Specialties

Seventy-seven endocrinologists, including pediatric endocrinologists, accepted $639,000 worth of pharmaceutical gifts and payments in DC. There were 22 endocrinologists (Table 4) who accepted over $1,000 worth of gifts in the District of Columbia; of these, 14 practice within DC while the other 8 practice outside of DC. Several endocrinologists were paid by pharmaceutical
companies to travel to DC to give promotional talks at local hospitals, including Children’s National and Washington Hospital Center. Similarly, some endocrinologists who practice in DC accepted large sums of gifts outside of DC, for lectures, travel, and meals.

**Table 4: Endocrinologists with Highest Amounts of Gifts from Pharmaceutical Companies Reported to Open Payments**

<table>
<thead>
<tr>
<th>Name</th>
<th>Affiliation</th>
<th>Total Payments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Natasa Janicic-Kahric</td>
<td>Georgetown University Hospital</td>
<td>$197,118</td>
</tr>
<tr>
<td>Joseph Verbalis</td>
<td>Georgetown University Hospital</td>
<td>$126,469</td>
</tr>
<tr>
<td>Abbas Motazedi</td>
<td>Providence Hospital, Center for Diabetes</td>
<td>$104,875</td>
</tr>
<tr>
<td>William Howard</td>
<td>Washington Hospital Center</td>
<td>$77,468</td>
</tr>
<tr>
<td>Leonard Wartofsky</td>
<td>Washington Hospital Center</td>
<td>$65,109</td>
</tr>
<tr>
<td>Vishal Datta</td>
<td>Datta Endocrine &amp; Wellness Center</td>
<td>$34,794</td>
</tr>
<tr>
<td>Jerold Share</td>
<td>Foxhall Endocrinology</td>
<td>$29,994</td>
</tr>
<tr>
<td>Meeta Sharma</td>
<td>Washington Hospital Center</td>
<td>$27,514</td>
</tr>
<tr>
<td>Julia Pineda</td>
<td>Private Practice</td>
<td>$16,126</td>
</tr>
<tr>
<td>Joshua Cohen</td>
<td>George Washington Medical Faculty Associates</td>
<td>$13,989</td>
</tr>
<tr>
<td>Michelle Magee</td>
<td>Washington Hospital Center</td>
<td>$5,908</td>
</tr>
<tr>
<td>Rui Lu</td>
<td>Washington Hospital Center</td>
<td>$5,646</td>
</tr>
<tr>
<td>Michele West</td>
<td>Washington Endocrine Clinic</td>
<td>$2,514</td>
</tr>
<tr>
<td>Mark Sklar</td>
<td>Sklar Endocrinology</td>
<td>$2,396</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Name</th>
<th>Affiliation Outside of DC</th>
<th>Payments in DC (∗)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Susan Nunez</td>
<td>Specially for Children (Central Texas)</td>
<td>$18,265</td>
</tr>
<tr>
<td>Jahangir Cyrus</td>
<td>Baptist Medical Associates (St. Matthews, KY)</td>
<td>$11,158</td>
</tr>
<tr>
<td>Kimberly Bourne</td>
<td>Orlando Diabetes and Endocrine Specialists (Orlando, FL)</td>
<td>$5,765</td>
</tr>
<tr>
<td>Kathleen Prendergast</td>
<td>Baltimore Washington Medical Center</td>
<td>$4,093</td>
</tr>
<tr>
<td>Nahrain Al Zubaidi</td>
<td>Virginia Diabetes Obesity &amp; Endocrinology Center</td>
<td>$3,688</td>
</tr>
<tr>
<td>Domenica Rubino</td>
<td>Washington Center for Weight Management &amp; Research</td>
<td>$3,505</td>
</tr>
<tr>
<td>Theresa Fynn</td>
<td>Premier Endocrinology (St. Cloud, FL)</td>
<td>$3,120</td>
</tr>
<tr>
<td>Yasser Ousman</td>
<td>Inova Center for Wellness and Metabolic Health</td>
<td>$3,058</td>
</tr>
</tbody>
</table>

∗ Payments for marketing activities in DC received by physicians whose main affiliation is outside of DC.
Pharmaceutical companies recruit influential physicians called thought leaders, or more commonly, “Key Opinion Leaders” (KOLs). KOLs may be paid thousands of dollars to provide promotional talks as members of a company’s “speaker’s bureau” as well as continuing medical education (CME) talks, which are not regulated as promotion. Drug companies use both promotional and CME talks to affect physicians’ perceptions of specific drugs and to promote off-label use of drugs (Meffert 2009; Fugh-Berman 2008).

Several of the physicians in Table 4 received payments for non-accredited, presumably promotional activities related to diabetes medications. Dr. Natasa Janicic-Kahric accepted $80,000 worth of gifts linked to Invokana (canagliflozin) alone. Dr. Abbas Motazedi accepted nearly $50,000 in gifts associated with Invokana (canagliflozin) and more than $30,000 from AstraZeneca for drugs such as Bydureon (exenatide) and Farxiga (dapagliflozin). Dr. Sharma Meeta accepted more than $20,000 for Invokana (canagliflozin) and more than $6,000 for the insulins Lantus and Apidra.

Drs. Lu and Sklar were not paid for speaking activities but accepted large sums of *Food and Beverage* gifts. Dr. Rui Lu accepted over $5,600 in *Food and Beverage* gifts. There were 190 gift transactions for Dr. Lu reported to Open Payments in 2014 alone. Dr. Mark Sklar accepted over $2,300 in *Food and Beverage* gifts.
Importance of In-Person Marketing (Detailing)

Drug companies have sales and marketing teams for their drug portfolios. These teams, whose members are referred to as “detailers” or “drug reps,” meet with physicians, other health care professionals and staff to promote specific drugs. Sales representatives for pharmaceutical companies build and leverage relationships with practitioners through formal marketing meetings and informal face-to-face interactions to influence prescribing choices. In-person marketing can have long-term effects on a physician's prescribing habits. Companies are required to report their detailing expenditures to the District of Columbia’s AccessRx program; this information is not collected by any other jurisdiction in the United States. Aggregate detailing expenditures (the total salaries paid to all staff and contractors engaged in promotional activities) make up more than half of all marketing expenditures reported for the District of Columbia - the amount is more than double the value gifts to physicians, the next largest category.

Understanding where companies focus marketing resources by examining what companies spend on drug reps and other employees may help to predict prescribing trends, drug utilization, and Medicaid drug spending.

Attributing Promotions of Specific Drugs to Detailing Expenditures

The aggregate detailing expenditures reported to the AccessRx program do not specify how much money is spent on individual drugs. In order to better understand how detailing money is apportioned to individual drugs, we created a new metric called “attributed aggregate detailing” combining data from Open Payments and AccessRx.

Companies reporting data to Open Payments must tag each marketing expenditure with the drug name that is being promoted (this information is not required by AccessRx). Gifts are tagged with labels that include Consulting, Travel and Lodging, and Food and Beverage expenses. Of these categories, Food and Beverage and Non-CME Activities represent the best indicators of in-person marketing efforts. Drug reps routinely bring food and drink to medical facilities and conduct their marketing activities during meals. Food and Beverage can be used as a surrogate for the time detailers spend marketing in-person for a specific drug with doctors, other medical professionals, and their staff. Non-CME Activities typically reflect promotional lectures or meetings.

To estimate dollar amount of aggregate detailing spent on each diabetes drug, we have calculated the percent of a company’s total expenditures on Food and Beverage and Non-CME Activities that is targeted toward specific diabetes drugs. Then, we applied that percentage to
their total aggregate detailing expenditures to create an estimate of how much of these costs can be attributed to diabetes drugs promotion.

Ten companies reported marketing payments associated with diabetes drugs in Open Payments. We combined each drug’s *Food and Beverage* and *Non-CME Activities* expenditures, then divided the total for each drug by the company’s total expenditures in the two categories. Payments without an associated drug name were excluded. We then took this percentage of allocated funds for each drug and applied it to the company’s aggregate detailing reported to AccessRx. This resulted in an estimated dollar amount of aggregate detailing spent on each diabetes drug, a measure we refer to as “attributed aggregate detailing expenditure”. This may be a marker for how extensively specific drugs are being marketed in the District.

Under DC law, AccessRx data are confidential, so we cannot disclose the identities of specific companies or drugs. Therefore, estimates for attributed detailing spending were aggregated by drug class for the ten companies examined (Table 5). The diabetes products were broken down into five classes: insulin analogues, DPP-4 inhibitors, DPP-4 inhibitor/metformin combinations, SGLT-2 inhibitors, and GLP-1 analogues.

**Table 5: Estimated Attributed Aggregate Detailing Expenditures by Diabetes Drug Class**

<table>
<thead>
<tr>
<th>Class of Drug</th>
<th>Number of Companies</th>
<th>Estimated Attributed Aggregate Detailing Expenditures</th>
</tr>
</thead>
<tbody>
<tr>
<td>GLP-1 analogues</td>
<td>4</td>
<td>$1,295,681</td>
</tr>
<tr>
<td>SGLT-2 inhibitors</td>
<td>4</td>
<td>$1,227,029</td>
</tr>
<tr>
<td>DPP-4 inhibitors</td>
<td>5</td>
<td>$635,773</td>
</tr>
<tr>
<td>Insulin analogues</td>
<td>3</td>
<td>$523,936</td>
</tr>
<tr>
<td>DPP-4 inhibitor combinations</td>
<td>4</td>
<td>$72,968</td>
</tr>
<tr>
<td></td>
<td></td>
<td>$3,755,387</td>
</tr>
</tbody>
</table>

We estimate that these ten companies spent about $3.8 million in salary for sales staff to promote diabetes drugs in the District of Columbia. We estimate that three companies spent over half a million dollars in salary to market 5 insulin analogues. Five companies are estimated to have spent over $600,000 on salaries to promote DPP-4 inhibitors, including combination products.

The newly approved SGLT-2 inhibitor and GLP-1 analogue drug classes had the highest estimated detailing amounts, totaling more than $1.2 million each. While DC Medicaid spent little on these drug classes in 2014, high expenditures on drug promotion for SGLT-2 inhibitors and GLP-1 analogues may precede increased prescribing rates for these costly medications.
VII. Recommendations


We recommend expanding efforts to reach more prescribers in DC with unbiased educational materials and training opportunities regarding diabetes prevention and treatment. Under the SafeRx Amendment Act of 2008, the District established the DC Center for Rational Prescribing (DCRx) program to provide healthcare professionals with free, noncommercial continuing education. This program and other noncommercial health professional training opportunities should be promoted in the District of Columbia.

2. Monitor changes in prescribing practice toward highly marketed and newly approved drugs.

New medications targeting management of diabetes appear to be highly marketed through both gifts to physicians and through in-person detailing. The high expenditures on drug promotion for the SGLT-2 inhibitors and GLP-1 analogues suggest that prescribing rates may increase over time in response. Changes in prescribing rates should be monitored to ensure high-quality care, and to reduce unnecessary increases in Medicaid costs.


Expand activities and initiatives promoting access to healthy foods and opportunities for safe exercise. As a primary method of both prevention and treatment of both T1DM and T2DM, improved diet and exercise as first line strategy for diabetes management should be a priority.

4. Realign AccessRx reporting to complement and expand upon Open Payments data.

The new Open Payments data system has made payments to physicians and teaching hospitals publicly available, but unfortunately does not include information on payments to other healthcare providers (e.g. nurses and nurse practitioners) and organizations. AccessRx does collect this data in the District.

Aligning AccessRx reporting standards and requirements to the national Open Payments data would allow for more rigorous and beneficial analysis for the District’s consumption. This can be accomplished in two steps:
• **Requiring pharmaceutical companies to identify a specific drug being marketed for expenditures reported to AccessRx**, as is required of the Open Payments system. This change would allow AccessRx to monitor the shift in promotions to physicians and other providers for specific drugs and report more accurately on pharmaceutical marketing trends.

• **Make AccessRx data publicly available.** AccessRx data could be extremely useful for patients and providers who want to know how their healthcare system is being influenced by pharmaceutical marketing. The data should be freely and easily accessible by the public in an online, searchable form, similar to Open Payments. Patients especially have a right to know how marketing is affecting the care being given by nursing staff, physician assistants and medical organizations.

5. **Begin collecting pharmaceutical marketing data from device manufacturers.**

In many cases, inefficient healthcare expenditures are being shifted from pharmaceuticals to medical devices. For example, in researching this report, we found evidence that the market for diabetes monitoring devices is increasing, which could result in higher expenditures for payers and out-of-pocket costs for patients.

Gathering information on device manufacturers would allow for a more complete analysis of pharmaceutical marketing as well, because the two industries complement each other.
References


DeGeeter M, Williamson B. Alternative Agents in Type 1 Diabetes in Addition to Insulin Therapy: Metformin, Alpha-Glucosidase Inhibitors, Pioglitazone, GLP-1 Agonists, DPP-IV Inhibitors, and SGLT-2 Inhibitors. 2016 Journal of Pharmacy Practice. 29(2) 144-159.


Meffert JJ. Key opinion leaders: where they come from and how that affects the drugs you prescribe. Dermatol Ther. 2009 May-Jun;22(3):262-8.


Tsujino D1, Nishimura R2, Onda Y1, Seo C1, Ando K1, Morimoto A3, Utsunomiya K1. The relationship between HbA1c values and the occurrence of hypoglycemia as assessed by continuous glucose monitoring in patients with type 1 diabetes. Diabetology & Metabolic Syndrome. 2016 Jul 29;8:53.


Appendix A: Glossary of Terms

AccessRx – The DC program to which pharmaceutical companies report marketing expenditures in the form of gifts, advertising, and aggregate costs as required by law

BMI – Body Mass Index, a ratio of weight and height used to classify a person as underweight, normal weight, overweight, or obese

BRFSS – The Behavioral Risk Factors Surveillance System, administered by the Centers for Disease Control and Prevention

CDC – Centers for Disease Control and Prevention

CMS – Centers for Medicare and Medicaid Services

DC CHNA – The District of Columbia Community Health Needs Assessment

DC DOH – The District of Columbia Department of Health

ED – Emergency Department

HbA1c – Hemoglobin A1c, a measure of blood glucose concentration

Hypoglycemia - blood glucose levels below 70mg/dL (mild) or 40mg/dL (severe)

Hypoglycemia awareness – being conscious of symptoms (sweating, fatigue, confusion, headache) that indicate low blood sugar

Ketoacidosis – life-threatening metabolic disturbance resulting from acidic blood, can be caused by uncontrolled diabetes, among other conditions

Open Payments – The CMS program which publishes gifts from pharmaceutical and device manufacturers to physicians and teaching hospitals

PBM – Pharmacy Benefit Manager, a third-party administrator of prescription drug programs for health plans, responsible for developing and maintaining the formulary and negotiating drug prices

T1DM – Type 1 Diabetes Mellitus (formerly known as juvenile diabetes)

T2DM – Type 2 Diabetes Mellitus (formerly known as adult-onset diabetes)
### Appendix B: Table of Diabetes Drugs

<table>
<thead>
<tr>
<th>Brand Name</th>
<th>Class of Drug</th>
<th>FDA Approval Date</th>
<th>Cost to DC Medicaid 2014</th>
<th>Number of Prescriptions 2014</th>
<th>Reported Open Payments Gifts 2014</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lantus</td>
<td>insulin analog</td>
<td>Apr-00</td>
<td>$3,306,260</td>
<td>20,267</td>
<td>$7,212</td>
</tr>
<tr>
<td>Novolog</td>
<td>insulin aspart</td>
<td>Nov-01</td>
<td>$3,223,267</td>
<td>10,365</td>
<td>$4,458</td>
</tr>
<tr>
<td>Levernir</td>
<td>insulin glargine</td>
<td>Jun-05</td>
<td>$1,684,117</td>
<td>5,162</td>
<td>$6,241</td>
</tr>
<tr>
<td>Janumet</td>
<td>DPP-4 inhibitor</td>
<td>Oct-06</td>
<td>$7,159,121</td>
<td>5,195</td>
<td>$2,540</td>
</tr>
<tr>
<td>Apidra</td>
<td>DPP-4 inhibitor</td>
<td>Mar-07</td>
<td>$756,619</td>
<td>2,634</td>
<td>$3,139</td>
</tr>
<tr>
<td>Humalog</td>
<td>insulin lispro</td>
<td>Feb-04</td>
<td>$1,521,220</td>
<td>2,560</td>
<td>$4,674</td>
</tr>
<tr>
<td>Novolin</td>
<td>metformin</td>
<td>Jun-96</td>
<td>$366,129</td>
<td>2,165</td>
<td>$0</td>
</tr>
<tr>
<td>Humulin</td>
<td>DPP-4 inhibitor</td>
<td>Aug-82</td>
<td>$364,056</td>
<td>2,081</td>
<td>$248</td>
</tr>
<tr>
<td>Onglyza</td>
<td>GLP-1 Analogue</td>
<td>Jul-09</td>
<td>$195,849</td>
<td>659</td>
<td>$305</td>
</tr>
<tr>
<td>Victoza</td>
<td>DPP-4 inhibitor</td>
<td>Nov-10</td>
<td>$183,873</td>
<td>376</td>
<td>$44,659</td>
</tr>
<tr>
<td>Kombiglyze</td>
<td>saxagliptin/metformin</td>
<td>May-11</td>
<td>$167,235</td>
<td>17,240</td>
<td>$12,855</td>
</tr>
<tr>
<td>Tradjenta</td>
<td>glipizide</td>
<td>Feb-12</td>
<td>$97,208</td>
<td>345</td>
<td>$0</td>
</tr>
<tr>
<td>Prandin</td>
<td>glyburide</td>
<td>Apr-05</td>
<td>$54,173</td>
<td>129</td>
<td>$1,242</td>
</tr>
<tr>
<td>Byetta</td>
<td>glucagon</td>
<td>Jun-98</td>
<td>$50,856</td>
<td>94</td>
<td>$0</td>
</tr>
<tr>
<td>Gliquagen</td>
<td>repaglinide</td>
<td>Apr-05</td>
<td>$31,105</td>
<td>77</td>
<td>$0</td>
</tr>
<tr>
<td>Byetta</td>
<td>sulfonylurea</td>
<td>Apr-05</td>
<td>$26,968</td>
<td>317</td>
<td>$0</td>
</tr>
<tr>
<td>Byetta</td>
<td>Meglitinide</td>
<td>Apr-05</td>
<td>$11,877</td>
<td>1,500</td>
<td>$0</td>
</tr>
<tr>
<td>Jentadueto</td>
<td>canagliflozin</td>
<td>Mar-13</td>
<td>$9,353</td>
<td>33</td>
<td>$154,628</td>
</tr>
<tr>
<td>Jentadueto</td>
<td>DPP-4 inhibitor combination</td>
<td>Feb-12</td>
<td>$8,930</td>
<td>343</td>
<td>$4,505</td>
</tr>
<tr>
<td>Jentadueto</td>
<td>sulfonylurea</td>
<td>Feb-12</td>
<td>$4,505</td>
<td>343</td>
<td>$4,505</td>
</tr>
<tr>
<td></td>
<td>Drug Name</td>
<td>Class</td>
<td>Start Date</td>
<td>Price</td>
<td>Percentage</td>
</tr>
<tr>
<td>------------------------</td>
<td>---------------------------</td>
<td>--------------------------------</td>
<td>------------</td>
<td>---------</td>
<td>------------</td>
</tr>
<tr>
<td>- nateglinide</td>
<td>Meglitinide</td>
<td>-</td>
<td>-</td>
<td>$4,080</td>
<td>51</td>
</tr>
<tr>
<td>Oseni</td>
<td>alogliptin/pioglitazone</td>
<td>DPP-4 Inhibitor</td>
<td>Jan-13</td>
<td>$3,551</td>
<td>12</td>
</tr>
<tr>
<td>- acarbose</td>
<td>Alpha-Glucosidase Inhibitor</td>
<td>-</td>
<td>-</td>
<td>$2,597</td>
<td>73</td>
</tr>
<tr>
<td>ACTOplus met</td>
<td>Pioglitazone/metformin</td>
<td>Thiazolidinedione combination</td>
<td>Aug-05</td>
<td>$2,270</td>
<td>10</td>
</tr>
<tr>
<td>Bydureon</td>
<td>exenatide</td>
<td>GLP-1 Analogue</td>
<td>Jan-12</td>
<td>$2,052</td>
<td>5</td>
</tr>
<tr>
<td>Glucophage</td>
<td>metformin</td>
<td>Biguanide</td>
<td>Mar-95</td>
<td>$1,220</td>
<td>23</td>
</tr>
<tr>
<td>Glucotrol</td>
<td>glipizide</td>
<td>Sulfonylurea</td>
<td>May-84</td>
<td>$1,004</td>
<td>16</td>
</tr>
<tr>
<td>Invokamet</td>
<td>canagliflozin/metformin</td>
<td>SGLT2 Inhibitor combination</td>
<td>Aug-14</td>
<td>$630</td>
<td>2</td>
</tr>
<tr>
<td>Farxiga</td>
<td>dапаглифозин</td>
<td>SGLT2 Inhibitor</td>
<td>Jan-14</td>
<td>$603</td>
<td>2</td>
</tr>
<tr>
<td>Riomet</td>
<td>metformin</td>
<td>Biguanide</td>
<td>Sep-03</td>
<td>$563</td>
<td>2</td>
</tr>
<tr>
<td>Glumetza</td>
<td>metformin</td>
<td>Biguanide</td>
<td>Sept-05</td>
<td>$336</td>
<td>1</td>
</tr>
<tr>
<td>ACTOS</td>
<td>Pioglitazone</td>
<td>Thiazolidinedione</td>
<td>Jul-99</td>
<td>$93</td>
<td>2</td>
</tr>
<tr>
<td>PrandiMet</td>
<td>repaglinide, metformin</td>
<td>Meglitinide combination</td>
<td>Jun-08</td>
<td>$0</td>
<td>0</td>
</tr>
<tr>
<td>Duetac</td>
<td>pioglitazone/glimepiride</td>
<td>Sulfonylurea</td>
<td>Jan-13</td>
<td>$0</td>
<td>0</td>
</tr>
<tr>
<td>Juvisync</td>
<td>sitagliptin/simvastatin</td>
<td>DPP-4 inhibitor combination</td>
<td>Oct-12</td>
<td>$0</td>
<td>0</td>
</tr>
<tr>
<td>Kazano</td>
<td>alogliptin/metformin</td>
<td>DPP-4 inhibitor combination</td>
<td>Jan-13</td>
<td>$0</td>
<td>0</td>
</tr>
<tr>
<td>Avandamet</td>
<td>rosiglitazone/metformin</td>
<td>Thiazolidinedione combination</td>
<td>Oct-02</td>
<td>$0</td>
<td>0</td>
</tr>
<tr>
<td>Symlin</td>
<td>pramlintide</td>
<td>Amylin Analog</td>
<td>Mar-05</td>
<td>$0</td>
<td>0</td>
</tr>
<tr>
<td>Metaglip</td>
<td>glipizide/metformin</td>
<td>Sulfonylurea</td>
<td>Oct-02</td>
<td>$0</td>
<td>0</td>
</tr>
<tr>
<td>Starlix</td>
<td>nateglinide</td>
<td>Meglitinide</td>
<td>Dec-00</td>
<td>$0</td>
<td>0</td>
</tr>
<tr>
<td>Afrezza</td>
<td>Inhaled insulin</td>
<td>Insulin analog</td>
<td>Jun-14</td>
<td>$0</td>
<td>0</td>
</tr>
<tr>
<td>Jardiance</td>
<td>empagliflozin</td>
<td>SGLT2 Inhibitor</td>
<td>Aug-14</td>
<td>$0</td>
<td>0</td>
</tr>
<tr>
<td>Nesina</td>
<td>alogliptin</td>
<td>DPP-4 inhibitor</td>
<td>Jan-13</td>
<td>$0</td>
<td>0</td>
</tr>
<tr>
<td>Tanzeum</td>
<td>albiglutide</td>
<td>GLP-1 Analogue</td>
<td>May-14</td>
<td>$0</td>
<td>0</td>
</tr>
<tr>
<td>Trulicity</td>
<td>dulaglutide</td>
<td>GLP-1 Analogue</td>
<td>Sep-14</td>
<td>$0</td>
<td>0</td>
</tr>
</tbody>
</table>