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ASSISTANT SECRETARY FOR PLANNING AND EVALUATION

REPORT TO CONGRESS

Report on the Affordability of Insulin

Required by the William M. (Mac) Thornberry National Defense Authorization Act for Fiscal Year 2021

U.S. Department of Health and Human Services
Office of the Assistant Secretary for Planning and Evaluation

December 16, 2022

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Executive Summary

Executive Summary

An estimated 37 million Americans, who represent approximately 11.3 percent of the U.S. population or 1 in 9 people, have diabetes.[1] Of these, about 28.5 million people are diagnosed with diabetes and 8.5 million are undiagnosed. Diabetes is more frequently diagnosed among American Indian, Alaska Native, Black, Hispanic, and Asian American individuals, compared to White individuals.[2] Diabetes is also associated with lower incomes and lower levels of education.[3]

According to the CDC, diabetes is the most expensive chronic condition in the United States.[4] Insulin is the mainstay of therapy to treat type 1 diabetes and a common treatment for type 2 diabetes as well.[5] More than 7 million individuals with diabetes, including all with type 1 diabetes and substantial numbers of those with type 2 diabetes or other conditions, need to use insulin daily to achieve glycemic control.[6] However, insulin affordability remains a key concern for many reasons, including high out-of-pocket health care costs.

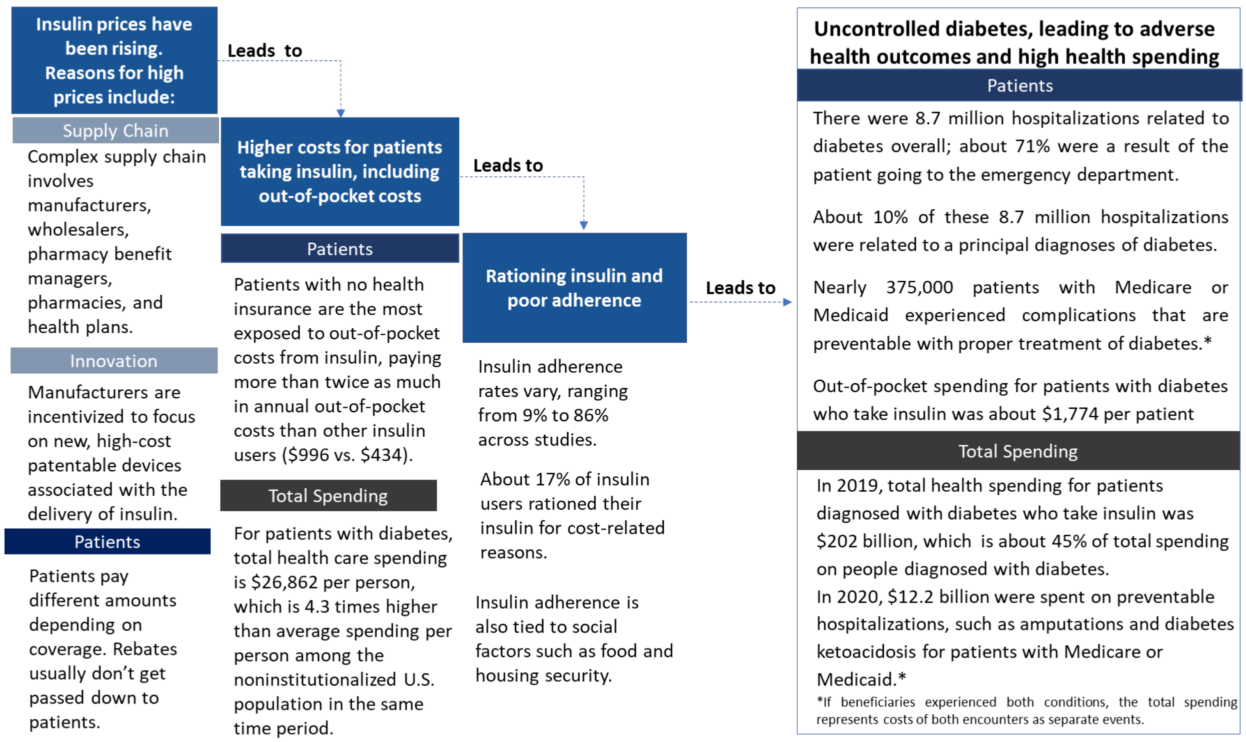
Recognizing insulin affordability as a problem, Congress directed the Secretary of Health and Human Services (HHS) to examine the affordability of insulin, including analyzing adherence to insulin prescriptions, rates of diabetic ketoacidosis, downstream impacts of insulin adherence, spending by Federal health programs on acute episodes that could have been averted by adhering to an insulin prescription, and other factors that may be affected by insulin affordability.[*] [7] In this Report to Congress, we examine these topics and describe ongoing policy efforts to improve affordability of and access to insulin, including several provisions in the Inflation Reduction Act of 2022.

I. Overview

When patients cannot afford insulin, it has cascading health and health care consequences. In 2021, survey findings indicated that about 17 percent of patients using insulin reported rationing their insulin, with the highest rate of rationing occurring among people who are uninsured (29 percent), followed by people with private insurance (18.8 percent).[8] Figure ES-1 below describes the potential pathways through which high costs of insulin affects health and health care spending, and includes key findings based on our review of the literature and analyses of survey and administrative health care data.

[*] Section 10004 of the William M. (Mac) Thornberry National Defense Authorization Act for Fiscal Year 2021, which became law on January 1, 2021, directs ASPE to examine insulin affordability in the United States.

Figure ES-1. Insulin Affordability and Potential Downstream Health Consequences



Notes: Figure includes data from analyses presented in the full Insulin Affordability Report to Congress, using the Medicare Expenditure Panel Survey, Medicare and Medicaid health care claims data, and the Health Care Cost and Utilization Project National Inpatient Sample. In addition, some findings are based on literature cited in the full Report to Congress.

II. Causes of High Insulin Prices

Insulin is a biological product that is produced from living cells and, when provided in a delivery device (e.g., pre-filled syringe or pre-filled pen), is a combination biologic-device product. Typically, biological products and biosimilars* are more expensive to produce than small-molecule drugs, which are chemically derived.

The insulin supply chain is complex and comprised of drug and device manufacturers, wholesalers, pharmacy benefit managers (PBMs), pharmacies, and health plans.[9] The market for insulin is dominated by three pharmaceutical companies – Novo Nordisk, Eli Lilly, and Sanofi – who set the initial price of insulin. These three companies are the sole suppliers of insulin in the United States and make up approximately 90 percent of the global market.[10] Thus, lack of competition is one major contributor to high insulin prices.

* A biological product that is highly similar to and has no clinically meaningful differences from an existing FDA-approved reference product.

New competitors do not enter the market for multiple reasons, including high production and commercialization costs for follow-on and interchangeable biosimilars, incentives that encourage a focus on developing new, patentable devices associated with the delivery of insulin, extensive patent litigation for biological products, and use of market power to gain favorable placement on formularies that minimizes competition.[11] Once insulin is produced, wholesalers, PBMs, pharmacies, and health plans each negotiate prices for their sector of the market. As a result, patients pay different amounts depending on negotiated rates, rebates, and other factors. Uninsured patients typically pay the most for insulin.

There is variation in list prices for insulin, depending on the type of insurer, age of patients using insulin, type of insulin being used, and other factors. However, a review of the existing literature demonstrates that the list price of insulin is high and has grown substantially over the past few decades.[12] To date, there are two approved "interchangeable" biosimilars – Semglee (2020) and Rezvoglar (2021) – and two follow-on insulin products – Basaglar (2015) and Admelog (2017), which were originally approved through a different regulatory pathway. Competition between biosimilars and reference biological products should drive down insulin prices, reducing medical spending on diabetes care. However, the magnitude of these potential savings depends on the development of a competitive environment for each insulin product, including how quickly and how many biosimilar competitors enter each insulin market.

A recent study finds that an increase in the number of biosimilar products would lead to an estimated $4.1 billion in savings on insulin over five years as a direct result of biosimilar entry for a variety of stakeholders (payers, patients, and third parties).[13]

III. Health Care Spending for Patients who Use Insulin

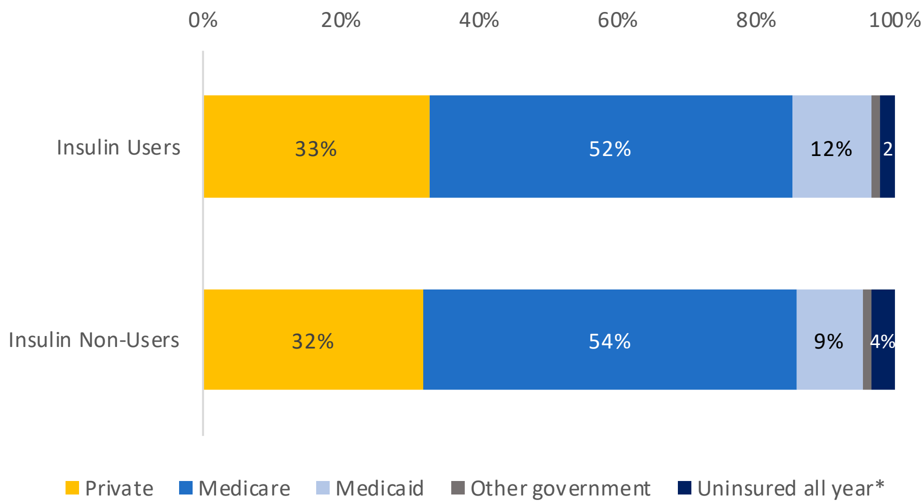
We used survey and claims data to examine health care costs of diabetes and insulin from the perspective of stakeholders most affected by insulin prices – patients, payers, and taxpayers.

Among people who take insulin, which is about 27 percent of the population of patients with diabetes in the Medical Expenditure Panel Survey (MEPS), about 52 percent have Medicare.[*] Many Medicare beneficiaries will be helped by the Inflation Reduction Act (IRA) which has provisions to lower drug spending and cap out-of-pocket costs for insulin.

About 33 percent of patients using insulin are privately insured, 12 percent are Medicaid beneficiaries, and about 2 percent are uninsured. Uninsured patients are the most exposed to out-of-pocket costs, followed by patients with private insurance who have high-deductible plans. Figure ES-2 presents the share of patients with diabetes who take insulin and those who do not take insulin, by type of health coverage.

[*] Medicare beneficiaries include both beneficiaries who receive the low-income subsidy (LIS) and those who do not receive LIS.

Figure ES-2. Insulin Use and Type of Coverage, 2019



Source: Medical Expenditure Panel Survey (MEPS), 2019. Civilian noninstitutionalized population.

Notes: The insurance categories are hierarchical: Medicare (with or without Part D drug coverage, including Medicare only, Medicare and Medicaid, and Medicare and private insurance), private insurance (including private insurance only and Marketplace any time during the year), Medicaid (includes Medicaid only or Medicaid and other government programs), other government programs only, and uninsured (lacked insurance from any source for the entire calendar year)

* Other ways of measuring health coverage suggest larger numbers of insulin users were without health insurance coverage at some point in the year: about 542,000 (7.2 percent) were uninsured in at least one month of that year (data not shown).

Total health care spending for people diagnosed with diabetes, including other conditions, was estimated to be about $446 billion in 2019 across 27.6 million people with diabetes based on the MEPS data.

Total health care spending for people who take insulin is estimated to be about $202 billion in 2019, which is 45 percent of total spending on people diagnosed with diabetes, even though patients who take insulin account for only 27 percent of the population with diabetes. This translates to about $26,861 per person in total health expenditures for patients who take insulin, which is 4.3 times higher than the average health care spending per person in the United States for the noninstitutionalized civilian population in 2019 ($6,252).[14]

Of the $202 billion total health care spending for those taking insulin, about $41 billion or 20 percent was spent on insulin itself. Medicare and privately insured patients had the highest total spending per patient ($29,479 and $26,233, respectively). Table ES-1 shows the total and per patient health care spending for patients who are taking insulin and of this total, the amount spent on insulin. About 64 percent of the spending on insulin is for patients covered by Medicare or Medicaid.

Table ES-1. Total Health Care, Prescribed Medicines, and Insulin Expenditures for Insulin Users, by Type of Coverage, 2019

Type of Coverage	Total Health Expenditures (in millions)	%	Mean health expenditure per person	Total Insulin Expenditures (in millions)	%	Mean Insulin expenditures per person
Overall	$202,138	100%	$26,861	$40,587	100%	$5,393
Private	$65,662	32%	$26,633	$13,998	34%	$5,678
Medicare	$115,892	57%	$29,479	$22,283	55%	$5,668
Medicaid	$15,630	8%	$17,716	$3,613	9%	$4,096
Uninsured[a]	$2,521	1%	$10,263	$714	2%	$2,811

Source: Medical Expenditure Panel Survey (MEPS), 2019. Civilian noninstitutionalized population.

Notes: Expenditures shown are based on gross drug costs without adjustment for the value of rebates that insulin manufacturers may pay to the government or health plan sponsors. See note in Report on the hierarchical structure of the insurance categories. "Overall" also includes adults who had insurance through other government programs.

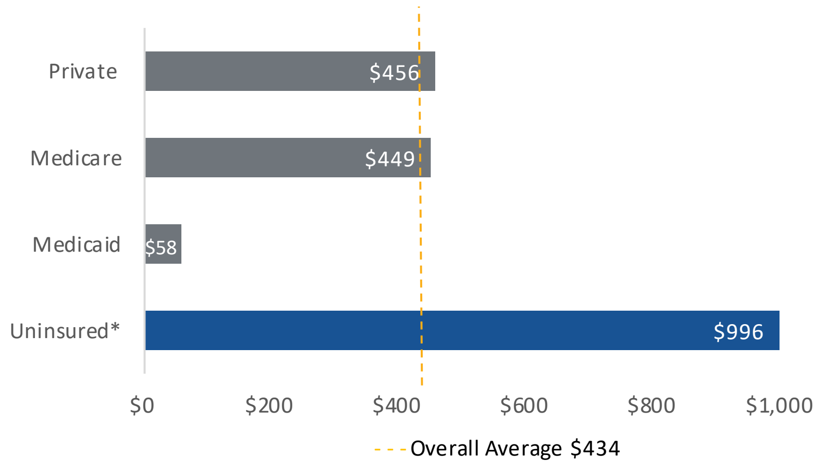
[a] For the uninsured population, annual average estimates are from the MEPS, 2014-19. Expenditures for 2014 to 2018 are inflated to 2019 dollars using the Personal Health Care Expenditure deflator to adjust total health care expenditures, by the Consumer Price Index (CPI) for medical care to adjust out-of-pocket health care expenditures for people with diagnosed diabetes and insulin users, and by the CPI for prescription drugs to adjust expenditures on prescribed medicines and insulin.

Out-of-Pocket Spending on Insulin

For out-of-pocket spending on total health care, patients paid about $1,774 overall in 2019, with patients who are uninsured or those who have private insurance having the highest out-of-pocket annual spending ($2,776 or $2,232, respectively).

Patients who use insulin spent an average of $434 annually on insulin (see Figure ES-3), with more than half of those enrolled in Medicare or private insurance (employer-sponsored or individual market) spending more than $35 on at least one monthly fill. Insulin users who were uninsured for an entire year spent an annual average of $996 on their insulin fills, about double the average amount paid by all patients (see Figure ES-3). The average annual out-of-pocket cost for insulin for patients with private insurance was $456 per person.

Figure ES-3. Average Annual Out-of-Pocket Costs for Insulin Among Insulin Users, by Type of Insurance Coverage, 2019



Source: Medical Expenditure Panel Survey (MEPS), 2019. Civilian noninstitutionalized population.

Notes: See Note 1 on Figure ES-1 for an explanation on the hierarchical insurance categories.

* For the uninsured population, annual average estimates are from the MEPS, 2014-19. Out-of-pocket expenditures on insulin for 2014 to 2018 are inflated to 2019 dollars using the Consumer Price Index for prescription drugs.

Other ways of measuring health coverage suggest larger numbers of insulin users were without health insurance coverage at some point in the year: about 542,000 (7.2 percent) were uninsured in at least one month of that year (data not shown). We estimate that 5 – 7 percent of patients have a spell of insurance for a month or more during the year.

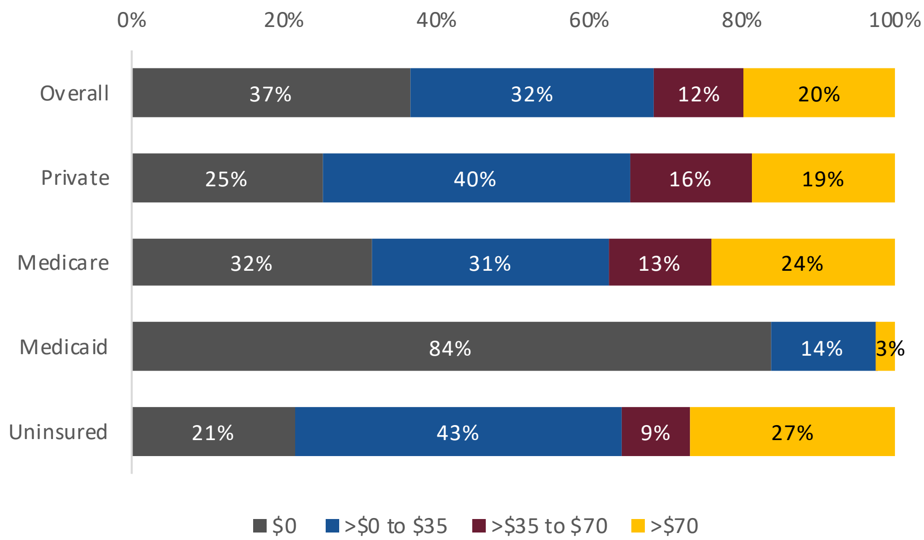
While the average annual out-of-pocket cost for insulin in 2019 was $434, half of insulin users paid $120 or less out-of-pocket, and 19.4 percent of insulin users paid nothing.

Out-of-Pocket Spending Per Insulin Fill

Medicare enrollees and privately insured patients both paid an average of $63 per insulin fill in 2019. People with no insurance paid an average of $123 per insulin fill. Importantly, more than three-quarters of monthly fills for privately insured patients required some cost-sharing, with more than one-third having cost-sharing exceeding $35, and nearly one-fifth have cost-sharing exceeding $70 (Figure ES-4).

Among the prescriptions with reported days supplied, 30 days was the mode and median days supplied so fills represent an approximate 30-day supply of insulin. While 30 days was the most common prescription length in the dataset, some prescriptions lack information on the number of days supplied, and smaller numbers of prescriptions may represent more or less than a 30-day supply; these factors introduce some uncertainty into estimates of the proportion of insulin users paying more than $35 per 30-day supply.

Figure ES-4. Share of Insulin Prescription Fills with Cost Sharing Per Fill, by Type of Coverage, 2019



Source: Medical Expenditure Panel Survey (MEPS), 2019. Civilian noninstitutionalized population.

Notes: The insurance categories are hierarchical. "Overall" also include adults who had insurance through other government programs. For the uninsured population, annual average estimates are from the MEPS, 2014-19. Out-of-pocket expenditures on insulin for 2014 to 2018 are inflated to 2019 dollars using the Consumer Price Index for prescription drugs.

These findings suggest that health care costs for diabetes are substantial, particularly out-of-pocket insulin costs for patients who are uninsured and patients with private insurance. Analyses from the Kaiser Family Foundation shows that nearly 30 percent of workers with employer-based insurance coverage have a high-deductible health plan.[15] For the subset of patients with private insurance who have high-deductible health plans and require insulin, the out-of-pocket costs for insulin may be especially burdensome. Moreover, insulin costs are not the only costs associated with managing diabetes; there are additional costs to treat diabetes, including other health-related expenditures. Thus, the ability to afford insulin is also influenced by other health care expenses incurred by patients.

IV. The Link Between Insulin Adherence and Affordability

Medication adherence to insulin is critical to limit short-term and long-term consequences from poorly controlled diabetes, all of which affect health care expenditures, use, and patients' quality of life. Adherence rates vary widely across populations, with rates as low as 8 percent and as high as 86 percent across different studies and populations.[16] Patient out-of-pocket cost is one of many factors contributing to adherence to insulin, and non-adherence can worsen the rates of diabetes-related complications.[17] Moreover, proper use of insulin requires other resources such as adequate and stable housing and nutritious food. Analysis using MEPS (2016 – 2017) data showed that the share of adult insulin users with low or very low food security (14 percent) was six percentage points higher than for adults overall (8.4

percent). Patients who do not have sufficient financial resources may have to make tradeoffs between following their prescribed insulin regimen and other living expenses, such as adequate and stable housing and food.[18]

V. Downstream Health Effects of Uncontrolled Diabetes

If patients do not adhere to appropriate diabetes treatment, including taking insulin if it is prescribed, it can lead to severe health consequences. Uncontrolled diabetes results in reduced quality of life and increased health care spending and use. Diabetes-related complications can arise due to medication nonadherence as well as other factors that reduce the body's ability to control blood sugar, such as poor nutrition (often a result of food insecurity), infection, obesity, and inflammation.[19] For patients that require insulin to manage diabetes, the risk of complications is particularly serious because insulin regimens help manage large fluctuations in one's blood glucose and require careful attention to prescribed dose, timing, and nutrition.

Based on analyses of the Agency for Healthcare Research and Quality's Healthcare Cost and Utilization Project National Inpatient Sample data, in 2019:

- There were 8.7 million hospitalizations related to diabetes overall. About 71 percent of those hospitalizations started in the emergency department. Of these 8.7 million hospitalizations, 10 percent were hospitalizations where the principal diagnoses were diabetes, which means that diabetes was the main reason for the hospitalization.
- On average, the length of a hospital stay for diabetes is nearly five days. Among the hospitalizations for diabetes with selected complications, hospitalizations for diabetes with end stage renal disease (ESRD) had the longest length of stay (7.4 days) and hospitalizations for diabetic ketoacidosis had the shortest length of stay (3.3 days). The average cost for a hospitalization ranged from a low of $8,426 for diabetic ketoacidosis to a high of $23,359 for ESRD.
- About 83 percent of hospitalizations for diabetes occurred among patients living in communities in the bottom 50 percent of U.S. income, calculated using the-median household income of the patient's zip code of residence, underscoring the need for affordable access to treatment for diabetes.

In addition, uncontrolled diabetes occurred in 108,165 adult non-maternal hospitalizations, which is about 1 percent of all diabetes-related hospitalizations. Most of these hospitalizations occurred among adults with Type 2 diabetes (87 percent). The most common diabetes complications evident among these hospitalizations were hyperglycemia (62 percent) and chronic kidney disease (38 percent).

One severe diabetes complication is a lower extremity amputation, which occurred in 87,270 adult non-maternal hospitalizations in 2019, about 1.0 percent of all adult diabetes-related hospitalizations. Most of these individuals had Type 2 diabetes (95 percent).

Other severe complications that are not included in our analyses include blindness, life-threatening infections, and death.

Potentially Avoidable Hospitalizations for Medicare and Medicaid Beneficiaries

We also examined potentially avoidable hospitalization costs for Medicare and Medicaid beneficiaries with diabetes, specifically examining the costs for patients with amputations and ketoacidosis. Total health care costs for these services were $12.2 billion dollars, with about $10.5 billion for Medicare patients, of which Medicare paid about 90 percent, and $1.7 billion for Medicaid enrollees, which would be shared by both State and Federal governments based on applicable Federal Medical Assistance Percentage (FMAP).

VI. Initiatives to Curb Out-of-Pocket Spending

Federal initiatives to reduce out-of-pocket spending on insulin include recent passage of the Inflation Reduction Act (IRA), which includes provisions that aim to lower out-of-pocket costs for people enrolled in a Medicare Part D prescription drug plan and provisions to limit coinsurance for insulin for people with Part B coverage. Estimates suggest that Medicare beneficiaries who use insulin would have saved $734 million in Part D if the IRA's out-of-pocket copayment cap of $35 per month supply of covered insulin had been in effect in 2020.

States are also working on initiatives to limit out-of-pocket spending on insulin. There are currently 23 states (as of September 2022) that have insulin caps, ranging from $25 (3 states) to $100 (5 states) per 30-day prescription or per month. Notably, however, state laws are not able to regulate self-insured plans due to ERISA. Self-insured plans comprise 64 percent of the total employer-based insurance market.[20] Several states have insulin affordability programs for the uninsured and underinsured. In addition, there are private/state-run patient assistance programs, however, it is unclear to what extent these improve accessibility to insulin. For patient assistance programs run by drug manufacturers, there have been complaints that these programs are not transparent about their eligibility requirements, make it hard to apply and renew, and can limit patients to a specific brand and treatment.

Other stakeholders, including insurers, PBMs, manufacturers, and nonprofits are also implementing initiatives to increase accessibility of insulin, underscoring widespread recognition that insulin affordability is a critical problem that needs to be addressed. However, additional policy action is needed to assist patients without health insurance and those with private insurance who have high-deductible plans and can face significant cost-sharing to access insulin on a regular basis.

VII. Conclusion

Among individuals who use insulin, our estimates suggest that insulin spending represents 27 to 28 percent of total out-of-pocket spending on all health care services overall and represents a similar share among those with private insurance or Medicare. For the 27 percent of patients with diabetes who need insulin, insulin is an added expense in an otherwise already expensive health care system. Insulin costs are particularly high for patients who are uninsured or those who have private insurance. If insulin is required, non-adherence to insulin can have severe consequences. The health consequences of diabetes, if not properly managed, can significantly reduce patients' quality of life, ability to work, and overall lifespan.

As discussed in this Report, affordability may improve for some insulin users in the coming years for several reasons: 1) Biosimilars of some but not all insulin products have slowly increased competition; 2) IRA limits out-of-pocket costs in Medicare Part D to $35 per month for each covered insulin product and has other provisions such as a Part B coinsurance cap that will help to reduce spending on prescribed medications for users under Medicare; 3) some states have enacted monthly insulin caps for individuals with other types of coverage or provided subsidized insulin for the uninsured and underinsured. These efforts all attempt to address this issue of insulin affordability; yet further action is needed to lower the cost of insulin for people without health insurance as well as those with private insurance, both to improve patient adherence and health outcomes as well as lower overall health care spending.

Report

Chapter 1. Introduction

An estimated 37 million Americans, 11.3 percent of the US population, have diabetes.[21] Diabetes prevalence among adults increases with age and is 29.2 percent among those aged 65 and above.[22] Diabetes is more frequently diagnosed among American Indian, Alaska Native, Black, Hispanic, and Asian American individuals, compared to White individuals.[23] Diabetes is also associated with lower income and lower levels of education.[24]

More than 7 million individuals with diabetes, including all with type 1 diabetes and substantial numbers of those with type 2 diabetes or other conditions, need to use insulin daily to achieve glycemic control.[25] Insulin is expensive, particularly for those who do not have health coverage or whose health coverage requires them to pay a large proportion of prescription drug costs out-of-pocket. Lack of affordability can lead to insulin nonadherence, and lack of insulin can lead to higher risk of heart attack, stroke, and other complications (e.g., ketoacidosis, kidney disease, and others). These complications may lead to hospitalizations, amputations, and death.[26]

Recognizing insulin affordability as a problem, Congress enacted Section 10004 of the William M. (Mac) Thornberry National Defense Authorization Act for Fiscal Year 2021, which became law on January 1, 2021. Section 10004 requires the Secretary of Health and Human Services (HHS) to examine the affordability of insulin, including analyzing adherence to insulin prescriptions, rates of diabetic ketoacidosis, downstream impacts of insulin adherence, spending by Federal health programs on acute episodes that could have been averted by adhering to an insulin prescription, and other factors that may be affected by insulin affordability, for each type of diabetes, including type 1 diabetes, type 2 diabetes, gestational diabetes, and other conditions that rely on insulin. The legislation requires HHS to report on the results of this study. The full text of this provision is in Appendix A:[27]

This Report responds to the charge from Congress in Section 10004. Specifically, we examine the following topical areas, organized by chapter:

Clinical Background and Context of Diabetes and Insulin Use in the United States

- Chapter 1: Outlines the motivation for this Report and provides an overview of each chapter
- Chapter 2: Provides clinical background on diabetes, the prevalence of diabetes in the United States, the role of insulin in treatment of diabetes, and other conditions that are treated with insulin
- Chapter 3: Examines the supply chain for insulin, the market for insulin, and insulin affordability, specifically examining how the market shapes insulin prices. This chapter also presents estimates of potential future savings from biosimilars for insulin

Impacts of Diabetes and Insulin on Health Care Spending and Use

- Chapter 4: Examines the impact of diabetes on patients and the health care system. It includes analyses of health care spending and total out-of-pocket spending for diabetes and insulin, as well spending for an insulin fill by public and private sources of insurance coverage
- Chapter 5: Explores the role insulin affordability has on adherence and examines other factors that impact insulin adherence
- Chapter 6: Examines the frequency and the potentially avoidable federal costs of diabetic ketoacidosis, amputations, and other conditions that can result from lack of access or adherence to insulin
- Chapter 7: Examines how the federal government and states have addressed insulin affordability, including out-of-pocket limits, Inflation Reduction Act (IRA) provisions that impact insulin affordability, and state caps on insulin prices

Conclusion and Implications

- Chapter 8: Presents the conclusion and policy implications of this Report

We note three primary limitations of our analyses. First, the survey data on which some of our analyses rely does not allow us to distinguish between types of diabetes; however, we are able to distinguish among type of diabetes in the administrative data on health care expenditures. Second, neither the survey data nor the administrative data we analyze cover sufficient periods to capture all the long-term health and cost consequences of lack of insulin affordability. Third, we are not able to causally link all health expenditures to lack of insulin affordability.

We address these limitations by measuring the out-of-pocket costs of insulin for individuals with different types of coverage, drawing on the research literature to understand the impact of affordability on adherence, and analyzing the hospitalizations and deaths that can result from nonadherence; however, we are not able to demonstrate that all of the adverse effects of nonadherence are the direct consequence of affordability challenges, nor are we able to capture all long-term health effects that arise when insulin is unaffordable and insulin adherence is low.

Since passage of the National Defense Authorization Act requiring this Report, Congress has taken additional action to improve insulin affordability. As we discuss in Chapter 5, the Inflation Reduction Act (IRA), signed by President Biden on August 16, 2022, places a $35 cap on monthly spending per insulin product in Medicare Part D and Medicare Part B starting in 2023.[28] Insulin users may also benefit from the IRA's inflation rebates in Part D (through smaller price increases than would have occurred in the absence of the rebates) and Part B (through either smaller price increases or direct rebates to patients); from its mechanism for spreading high monthly out-of-pocket costs across the Part D plan year; and, given the many comorbidities of people with diabetes, from its $2,000 annual cap on out-of-pocket spending in Part D. This report provides information that may be useful to policymakers regarding proposals to improve the affordability of insulin.

Chapter 2. Diabetes

In this chapter, we provide an overview of the condition and describe screening recommendations. We also present the prevalence of diabetes in the United States to understand the magnitude of the problem and describe the associated comorbid conditions. We conclude by describing the role of insulin in the treatment of diabetes.

Key Findings from this Chapter include:

- Type 2 diabetes is the predominant form of diabetes in the United States, with 90 - 95 percent of people with diabetes presenting with this type.
- The prevalence of diabetes is rising, and it currently impacts 11 percent of all Americans (37 million), including those who have the condition but have not yet been diagnosed. The prevalence of gestational diabetes, an important sub-type of diabetes that impacts pregnant women, is also rising.
- Insulin is the first-line therapy to treat type 1 diabetes. For type 2 diabetes, lifestyle modification is the first step of treatment and oral medications (typically Metformin) are the first-line medication therapy. Insulin is a subsequent therapy option for type 2 diabetes if blood sugar is difficult to control on oral medications alone.
- CDC diabetes surveillance data shows that in 2020 about 1 in 3 (33%) adults with diabetes required insulin therapy. More than 7 million individuals with diabetes, including all with type 1 diabetes and substantial numbers of those with type 2 diabetes or other conditions, need to use insulin daily to achieve glycemic control.
- There are two primary types of insulin: basal insulin and prandial or meal-time insulin. Among these types of insulin, there are differences in how quickly they become maximally active (peak), and how long they last, which impacts the complexity of the regimen for patients.

I. Clinical Background: What is Diabetes?

Diabetes is a chronic disease that is characterized by insulin dysfunction that occurs when the pancreas does not produce enough insulin (type 1 diabetes), or when the body does not respond to insulin properly and/or have enough insulin production to overcome this deficit (type 2 diabetes).[29,30] Insulin dysfunction can either come from defective insulin production or resistance to insulin function or a combination of both.[31] Diabetes requires regular monitoring and treatment to improve quality of life and prevent the long-term sequelae associated with uncontrolled disease.

Optimizing the function of insulin, a hormone naturally produced by specialized cells in the pancreas, helps glucose (carbohydrates) from food absorbed from the intestines be used by cells as a source of energy. If insulin production or function is disrupted, it can lead to diabetes. Below, we describe each main type of diabetes and general treatment approach:

- Type 1 diabetes is an autoimmune disease that occurs when the body does not make insulin (or only makes a small amount) and usually presents in children. Type 1 diabetes is related to the immune system destroying the insulin-producing cells in the pancreas. It includes a strong genetic component. Type 1 diabetes treatment consists primarily of life-long insulin replacement therapy.
- Type 2 diabetes occurs when the body becomes resistant to insulin's function leading to a lack of utilization of insulin naturally produced by an individual's pancreas. The causes of type 2 diabetes are more numerous and complex, with disease usually arising in adults over the age of 40 – though with increasing incidence in recent decades among younger adults and even adolescents. Obesity is one of the strongest risk factors; other risk factors include diet and activity levels, in addition to inherited genetic components.[32] Structural inequities such as food and nutrition insecurity, lack of adequate opportunities for safe exercise, and lack of adequate access to health care contribute to substantial disparities in diabetes rates.[33] Type 2 diabetes treatment consists of lifestyle modification, oral medications and, if uncontrolled on these two alone, insulin therapy and/or non-insulin injectable medications.[34]
- Gestational diabetes is a sub-type of diabetes characterized by insulin resistance during pregnancy and is often discovered on routine screening during prenatal visits with an obstetrics provider. Gestational diabetes affects 2-10 percent of all pregnancies in the United States and is associated with negative health outcomes in the mother as well as the infant.[35] Similar to type 2 diabetes, gestational diabetes is managed with lifestyle modification and first-line oral medications (i.e., Metformin), followed by insulin if it remains uncontrolled. If gestational diabetes persists after pregnancy, it is considered type 2 diabetes.

The number of people with diabetes is rising in the United States, which we describe in more detail below.[36] Most people with diabetes have type 2 diabetes (90-95 percent), followed by type 1 diabetes (5-10 percent).[37] In 2020, the rate of gestational diabetes was 7.8 percent, which is an increase of 30 percent from 2016.[38] There are other forms of diabetes, which are relatively rare.[*]

II. Diagnosis: Screening and Monitoring Diabetes

The U.S. Preventive Services Task Force (USPSTF) recommends screening for diabetes for overweight or obese adults beginning at the age of 35 for type 2 diabetes, or at younger ages if signs and symptoms are present.[39] Screening for diabetes consists of a basic fasting blood glucose level or a screening hemoglobin A1C test. Along with other screenings (e.g., cholesterol screening), diabetes screening can inform medical advice for early lifestyle modification and determine the potential need for medications. Screening is particularly important for patient populations at higher risk for developing diabetes. This includes people with a family history of diabetes, those showing signs of pre-diabetes or obesity, and pregnant women who can be at risk for gestational diabetes during pregnancy.[40]

[*] Other etiologies that can cause diabetes are genetic defects of B-cells function, genetic defect in insulin action, diseases of the exocrine pancreas, endocrine system disorders, infections, drug or chemical induced, and other genetic syndromes associated with diabetes.

Early screening can also identify patients at risk for diabetes. This stage is often referred to as pre-diabetes. Early preventive intervention at this stage can avoid the need for costly medical interventions in the future. Pre-diabetes treatment consists predominately of lifestyle modification through diet, exercise, and weight loss, and in some cases, medication (typically Metformin)[41]

If diagnosed with diabetes, glucose monitoring is critical to ensure blood sugars are adequately controlled under a patient's therapy regimen or lifestyle plan; this can take the form of periodic laboratory assessments of hemoglobin A1C, home glucose testing, or both, depending on the patient's clinical situation. Controlling blood sugar can mitigate the long-term health impacts of high blood glucose and prevent costly health complications. Regular physical exams, routine access to primary care, and access to treatment and blood glucose monitoring are also critical to prevent diabetes-related complications for patients.[42]

III. Prevalence of Diabetes

The number of people with diabetes in the United States is estimated using two large-scale epidemiological surveys: the National Health and Nutrition Examination Survey (NHANES) and the National Health Interview Survey (NHIS).[43,44]

Analyses from the Centers for Disease Control and Prevention (CDC) using NHANES and NHIS data indicate that as of 2019, about 37 million people have diabetes. This represents about 11 percent of the total U.S. population (330 million in 2019) or 1 in 9 Americans who suffer from diabetes. Estimates of the U.S. population diagnosed and undiagnosed with diabetes is presented in Table 2-1 below, which also provides the prevalence of diabetes by demographic characteristics.

Of the total number of people with diabetes (about 37 million), about 8.5 million are undiagnosed (23 percent)[*] and 28.5 million (77 percent) have been diagnosed with diabetes.

Most diagnosed cases are among the 65 and older age group (84 percent diagnosed cases) and the majority of undiagnosed cases are among the 18-44 age group (about 38 percent). In addition, more women have undiagnosed diabetes (27 percent) relative to men (19 percent). Among racial and ethnic groups, Asian (33 percent), Black (non-Hispanic) (28 percent), and Hispanics (28 percent) have higher percentage of undiagnosed diabetes relative to whites, whose rates of undiagnosed diabetes are about 19 percent. Although, the American Indian/Alaska Native (AI/AN) population is not included in Table 2-1, existing research shows AI/AN patients are 3 times more likely to be diagnosed and 2.3 times more likely to die from diabetes compared to non-Hispanic whites.[45]

[*] 2020 CDC National Diabetes Statistics Report: Undiagnosed diabetes was estimated using the NHANES survey responses for individuals who did not have a diabetes diagnosis but had fasting blood glucose or hemoglobin A1C levels consistent with a diagnosis of diabetes.

Table 2-1. Diabetes Prevalence in the United States by Demographic Characteristics, 2019

Demographic Characteristics	Classification of Diabetes Population: Diagnosed diabetes (millions)	Diagnosed diabetes (%)	Undiagnosed diabetes (millions)	Undiagnosed diabetes (%)	Total Diabetes (millions)	Total Diabetes (%)
Age in years						
18-44	3.5	62.5%	2.1	37.5%	5.6	100%
45-64	11.8	76.1%	3.8	24.5%	15.5	100%
≥ 65	13.3	83.7%	2.6	16.4%	15.9	100%
Sex						
Male	15.4	80.6%	3.6	18.9%	19.1	100%
Female	13.1	72.8%	4.9	27.2%	18	100%
Race and Ethnicity						
White (non-Hispanic)	17.8	80.2%	4.3	19.4%	22.2	100%
Black (non-Hispanic)	3.9	72.2%	1.5	27.8%	5.4	100%
Asian (non-Hispanic)	1.8	66.7%	0.9	33.3%	2.7	100%
Hispanic	4.7	72.3%	1.8	27.7%	6.5	100%
Total	**28.5**	**76.9%**	**8.5**	**22.9%**	**37.1**	**100%**

Data sources: 2017-March 2020 National Health and Nutrition Examination Survey; estimated numbers for 2019 were derived from percentages for 2017–March 2020 applied to July 1, 2019 U.S. resident population estimates from the US Census Bureau 2019 US Census Bureau data. Undiagnosed diabetes was based on fasting plasma glucose and A1C levels among people self-reporting no diabetes.

Notes: Percentages are relative to a given category based on the row totals. For example, 76.9% of the 37.1 million individuals diagnosed with diabetes have diagnosed diabetes

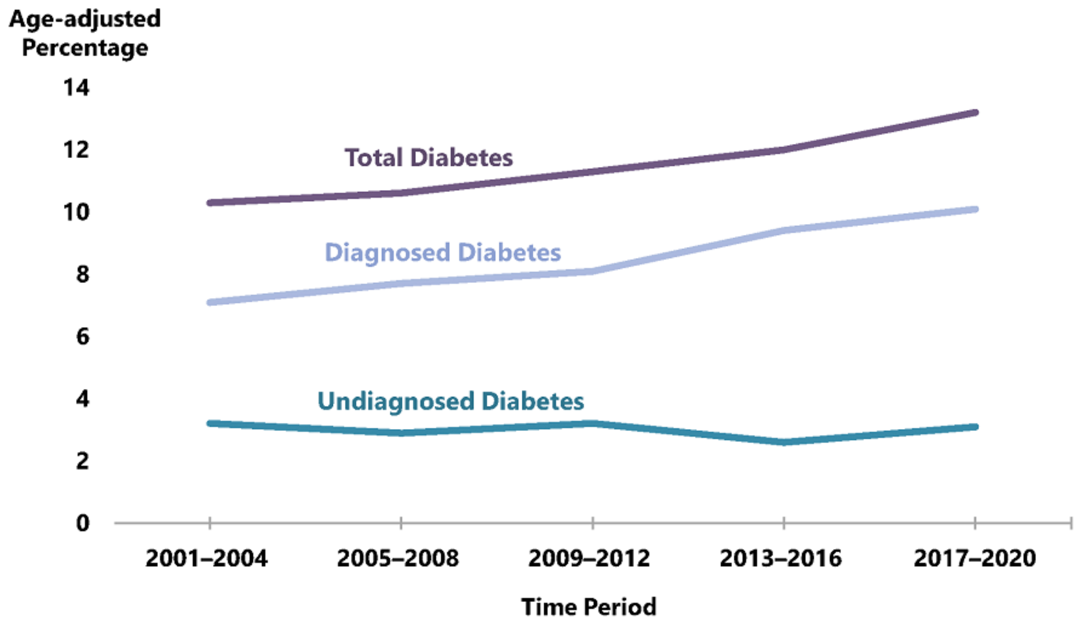
Table adapted from: CDC diabetes statistics-report

For patients younger than the age of 20 (data not shown), about 283,000 Americans are diagnosed with diabetes, which is equal to 0.35% of the US population.[46]

Diabetes Trends Over Time

Data analyzed by the CDC shows that the prevalence of diabetes steadily increased from 2001-2004 to 2017-2020, with rates of diagnosed diabetes increasing from about 10 percent to over 12 percent of the total U.S. population during this period. Rates of diagnosed diabetes follow a similar trend, indicating a higher detection rate for diabetes as a share of the total (Figure 2-1).

Figure 2-1. Prevalence of Diabetes Over Time, 2001-2020



Data source: 2001-March 2020 National Health and Nutrition Examination Surveys.

Figure source: CDC Diabetes Home; Data and Statistics; Prevalence of Both Diagnosed and Undiagnosed Diabetes.

The significant increase in prevalence of diabetes is likely due to the rapid increase in obesity prevalence during this period.[47] Due to the complex causes of type 2 diabetes, obesity plays a significant role in the development of type 2 diabetes, and this relationship varies greatly by race and ethnicity.[48] During the year 2015-2016, about one-third of U.S. adults were obese based on body mass index, with African Americans (41.7 percent) and Hispanics (34.9 percent) more likely to be obese compared to Whites (30.7 percent) and Asians (8.4 percent).[28]

Other factors contributing to the increase in diabetes prevalence include improved survival of patients with type 1 diabetes, overall aging of the U.S. population, dietary and exercise habits, and increased access to screening, especially after the passage of the Affordable Care Act (ACA).[*] [49] Rates for gestational diabetes (not shown) have also increased over time, likely related to the rising rates of obesity generally in the US population. A decade ago, the prevalence of gestational diabetes was over 1 in 20 births in the US,[50] but the CDC now estimates this condition effects 1 in 10 births.[51]

Based on CDC Surveillance data (not shown), about 5.7 percent of all diabetes cases, or 1.6 million adults (20 years of age or older), are individuals with type 1 diabetes and require insulin to manage their

[*] Prediabetes has also increased in prevalence over time. In 2018, it is estimated that 88 million adults over the age of 18 years of age have prediabetes. Of all U.S. adults over the age of 18, about 35 percent have prediabetes based on blood sugar metrics based on CDC surveillance data. Please see appendix for more details.

condition. The remaining 90-95 percent have type 2 diabetes. Among all adult patients diagnosed with diabetes, using surveillance data, it is estimated that approximately 33 percent require a therapy regimen that includes insulin.[52]

IV. Comorbidities

Patients with diabetes often have comorbid conditions that impact their health, health care use, and spending. These include obesity, poor cholesterol, and high blood pressure.[*]

As discussed above, obesity plays a significant role in the development of diabetes. Poor cholesterol also often goes hand in hand with obesity, both of which increase the risk of serious acute health events (e.g., heart attack and stroke), especially in combination with diabetes.[28] In addition to obesity, hypertension or high blood-pressure is another comorbidity associated with diabetes and is a condition that carries many complications.[18] Diabetes is the most common cause and hypertension is the next leading cause of chronic kidney disease and kidney failure. Thus, having both diabetes and hypertension is particularly harmful and may cause long-standing kidney damage that can result in a patient entering end-stage renal disease (ESRD). ESRD requires expensive and time-intensive therapies such as dialysis. The progression to ESRD is a common cause of patients younger than age 65 to qualify for Medicare.[53] Finally, hypertension increases the risk of heart attack and stroke, both of which are also more common among patients with diabetes compared to those not diagnosed with diabetes.

V. Treatment with Insulin

Insulin Therapy for Type 1 and Type 2 Diabetes

As noted above, insulin is the primary treatment of type 1 diabetes and used for treating type 2 diabetes when more conservative treatment approaches do not work. For patients with type 1 diabetes, the recommendation is to be treated with multiple daily injections of a combination of insulin types or continuous administration with an insulin pump. These regimens include both a long-acting or basal insulin, as well as rapid-acting insulins to reduce risk of hyperglycemia, or increased blood glucose levels, during and after meals.[54]

For patients with type 2 diabetes, the treatment approach focuses on lifestyle modification first and then the first line therapy is an oral medication, typically Metformin, depending on management needs. Many patients with type 2 diabetes may eventually require insulin therapy when lifestyle changes and medications no longer control blood glucose levels within a healthy range.[55] Generally, long-acting, or basal insulins are then added on for patients with type 2 diabetes, and in some cases, meal-time insulin as well.

[*] There are other comorbidities associated with diabetes, such as celiac disease, hyperthyroidism, hemochromatosis, etc.

Types of Insulin

While insulin was first used as a medication in 1922, there has been significant innovation in the molecular structure and the delivery devices used to administer insulin in recent decades. All insulin currently used to treat diabetes is made using recombinant DNA technology, and there are two general types used for developing an insulin therapy regimen: basal insulin and prandial or meal-time insulin. Among these types of insulin, there are differences in how quickly they become maximally active (peak), and how long they last, which impacts the complexity of the regimen for patients. [56,57,58]

Insulin types are listed in Table 2-2 below. Generally, basal insulin is long-acting and gives a low-level of insulin activity for an extended period, often for the entire day. Directions for basal insulins are easier for patients to follow since they are taken usually once a day. Prandial insulin is fast-acting insulin that gives a high-level of insulin activity for a short period of time, often only lasting around an hour or shorter. These insulins are ideal for when blood sugars rise rapidly, which commonly occurs after mealtime. These insulins are taken multiple times a day based on mealtimes and can add complexity to the insulin regimen. Finally, there are also mixed insulins, which consist of both long and short-acting insulins (as well as non-insulin enhancers) with variable durations and potency of action. [59]

Many patients with diabetes requiring insulin therapy have complex insulin regimens. Regimens may include a combination of therapies, including insulin with other oral medications or multiple different types of insulin, to manage diabetes and reduce risk of serious health effects. It is important to note that insulin must be taken as directed in terms of timing and dosage. People with diabetes are at risk of serious health effects, such as hypoglycemia, if insulin is not taken as directed (e.g., incorrect insulin type at the wrong time or if too much insulin is taken).

Table 2-2. Types of Insulin

Type of Insulin	Description
Rapid-acting (insulin analogs)	Starts working within 15 minutes are injection, peaks between one and two hours, and lasts 2-3 hours. This insulin is taken just before or after a meal.
Short-acting (human insulin)	Reaches the bloodstream within 30-60 minutes after injection, peaks at 2-3 hours and it is out of the body after 3-6 hours. This insulin is generally taken 30-45 minutes before meals.
Intermediate-acting (insulin analogs, human insulin)	Begins to work about 2-4 hours after injection, peaks 4-12 hours later and is effective for about 12-18 hours. It is used to control blood sugar between meals and may be used in the morning, at bedtime, or both.
Long-acting (insulin analogs, human insulin)	Starts working within 2-4 hours after injection and can last in the body up to 24 hours.[a] It is usually used in the morning or at bedtime to control blood sugar throughout the day.
Premixed insulin (insulin analogs, human insulin, non-insulin enhancers)	Premixed insulins can include a combination of a short-acting and a longer-acting insulin from the categories above in variable proportions (e.g., 75 percent long acting, 25 percent short-acting), to simplify administration for patients.

Note: Human insulin, also called regular insulin, represents older lines of insulin and has less predictable onset and duration of actions. Newer lines of insulin are typically insulin analogs that have a modified structure to emulate the body's natural pattern of insulin release and sustain a more predictable duration of action compared to human insulin.[60] These varying durations of actions are important clinically because they help providers develop an insulin regimen suited to meet a patient's insulin needs.[61]

[a] The peak time for long-acting insulin is assumed to be twice the onset time, 4-8 hours.

What Happens if Diabetes Goes Untreated?

Diabetes is a chronic condition that can involve multiple organ systems over the disease course. If insulin is required to manage diabetes, it must be taken as prescribed. If diabetes goes untreated, it carries an increased risk for serious health problems, such as heart attack, stroke, blindness/vision loss, kidney dysfunction, nerve damage, poor wound healing, infection, and lower-limb amputations.[62] These can all have significant impacts on an individual's quality of life, ability to work, and overall lifespan.

In 2020, diabetes was the 8th leading cause of death in the U.S., accounting for 31 deaths for every 100,000 people in the U.S. population, and it is a risk factor for other common causes of death such as heart disease and kidney failure.[63] People with diabetes are twice as likely to have heart disease and stroke compared to those without diabetes. Diabetes is also the leading cause of kidney failure, nontraumatic lower-limb amputations, and blindness among adults.[64] Untreated diabetes is also associated with increased direct and indirect health care utilization and spending. We describe the harmful effects of untreated diabetes in Chapters 5 and 6.

Chapter 3. Insulin Market and Prices

In this chapter, we review the literature to outline the insulin supply chain process and present information on the current market for insulin. We discuss the price of insulin and the factors that have contributed to increasing insulin prices. We then examine what would potentially happen to insulin prices if there was an increase in the number of biosimilar insulin products in the market.

Key findings from this Chapter include:

- Understanding the key stakeholders involved in the insulin supply chain and the insulin market is critical for understanding insulin affordability. The insulin supply chain is comprised of biological products and device manufacturers, wholesalers, pharmacy benefit managers (PBMs), pharmacies, and health plans, each of whom is involved in a complex payment system that requires multiple transactions among key stakeholders.
- The market for insulin is dominated by three pharmaceutical companies and they are the sole suppliers of insulin in the United States. New competitors do not enter the market for multiple reasons, including high production costs for biosimilars; incentives that encourage a focus on developing new, patentable devices associated with the delivery of insulin; extensive litigation for biological products; and the use of market power to gain favorable formulary placement that minimizes competition.
- Insulin manufacturers set the initial price of insulin. Once insulin is produced, wholesalers, PBMs, pharmacies, and health plans each negotiate prices for their sector of the market. Patients pay different amounts depending on negotiated rates, rebates, and other factors. Uninsured patients typically pay the most for insulin.
- There is variation in list prices (that, is before rebates) for insulin, depending on the type of insurer, age of insurance enrollees, type of insulin being used, and other factors. Rebates are a large share of list prices for insulin based on data submissions from pharmaceutical manufacturers.[65] However, a review of literature demonstrates that net prices of insulin (even after rebates) are high and have grown substantially over time. One recent study estimated that rebates for insulin products are three-quarters of their list prices.[66]
- Competition between biosimilars and reference biological product should drive down insulin prices, reducing medical spending on diabetes care. However, the magnitude of these potential savings depends on the development of a competitive environment for each insulin product, including how quickly and how many biosimilar competitors enter each insulin market. A recent study finds that an increase in the number of biosimilar products would lead to an estimated $4.1 billion in savings on insulin over 5 years as a direct result of biosimilar entry for a variety of stakeholders (payers, patients, and third parties).

I. Insulin Supply Chain

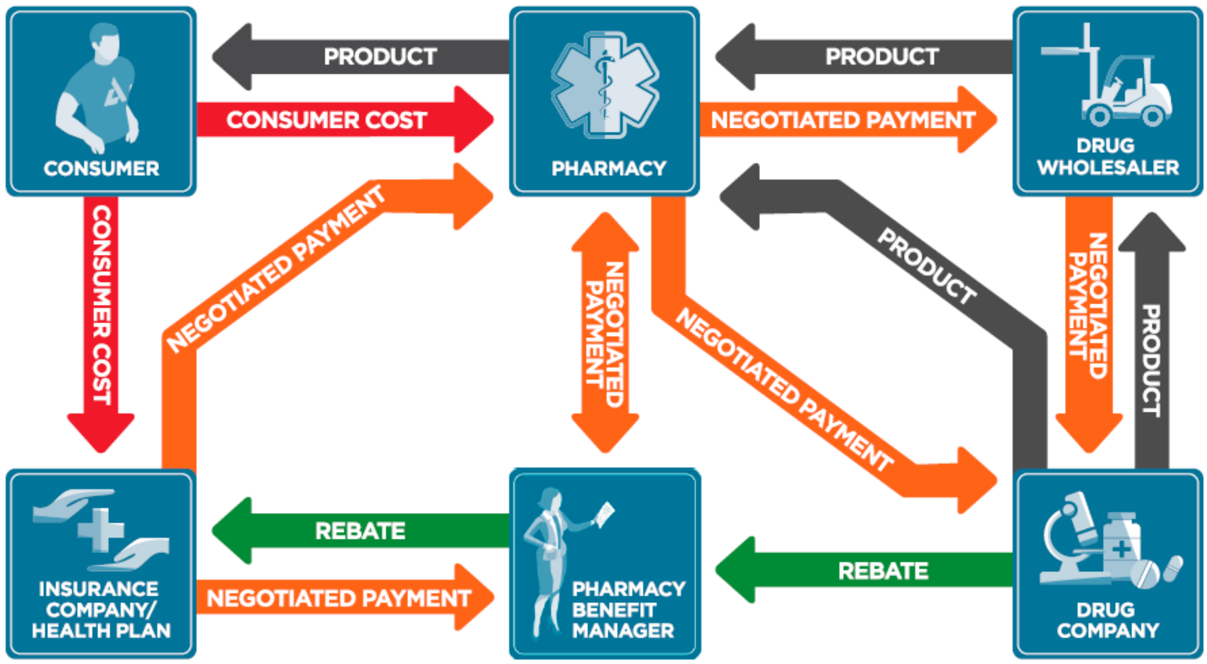
The availability of essential medicines is required for managing diabetes.[67] Understanding the complexity and dynamics of the insulin supply chain, how it can make markets vulnerable to shortages, and how it affects the price patients pay for insulin used in the treatment of diabetes is critical for understanding insulin affordability.

Figure 3-1 below illustrates the insulin supply chain and its key players. The insulin supply chain is complex and similar to that of other prescription drugs.[68,69] Figure 3-1 shows that the insulin supply chain is comprised of manufacturers, wholesalers, PBMs, pharmacies, and health plan. Each stakeholder in the supply chain is involved in a complex payment system that requires multiple transactions among key stakeholders.

When pharmacies dispense an insulin product to patients, they collect a share of the insulin cost required by the patient's health plan (if insured). Patients pay either a co-payment (a fixed amount) or co-insurance (a fixed percentage of the total cost of insulin). Pharmacies in turn bill PBMs for a share of the cost of insulin, including a base price and a markup for services, such as dispensing fee. Uninsured patients are more likely to pay the full price of insulin,[70] although certain companies have launched patient assistance programs to help pay for the cost of insulin for eligible patients, including those without insurance.[71]

PBMs have relationships with manufacturers, health plans, and pharmacies. Health plans contract with PBMs to manage their drug benefits on behalf of the plan and develop policies for covered drugs. PBMs represent health plans by negotiating prices with the manufacturers, which can result in manufacturers providing rebates, discounts, and fees to PBMs in exchange for placement on PBM formularies. In general, the price that patients pay is a function of the prices, rebates, and fees negotiated among the stakeholders.[72] Similarly, the net price manufacturers receive is the list price minus the 1) fees paid to wholesalers, 2) discounts to pharmacies, and 3) rebates paid to PBMs or health plans for including their insulin in the formulary. Importantly, savings from rebates do not generally reduce spending for patients.

Figure 3-1. Insulin Supply Chain: A Complex System



Source: Figure 3 in Cefalu et al [73]

In addition to the insulin supply chain, insulin affordability is also impacted by the complex medical device supply chain because using insulin requires use of medical devices and technology, such as blood sugar monitors (glucometers), test strips, syringes, and needles.

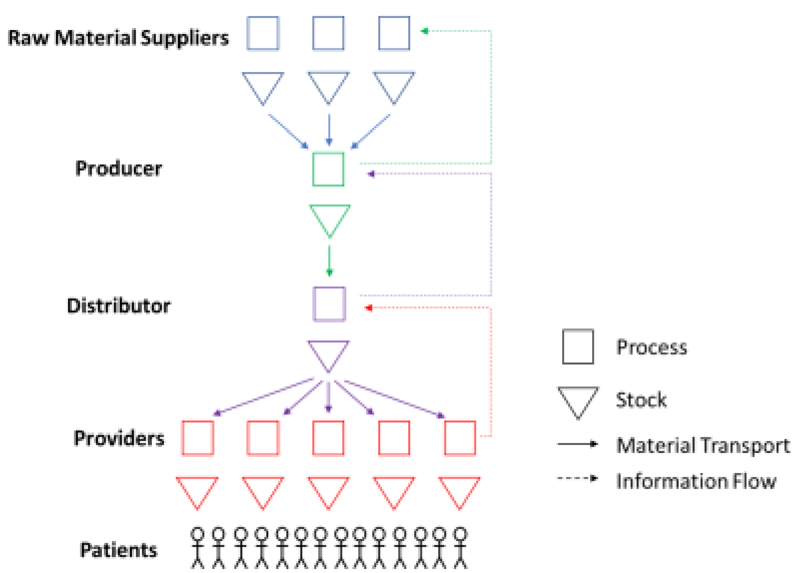
Medical Device Supply Chain

Insulin is a biological product and, when provided in a delivery device (e.g., pre-filled syringe or pre-filled pen), is a combination biologic-device product. These insulin delivery devices make it easier for patients to adhere to complex insulin regimens and reduce risk of serious health effects but are typically more expensive.[74] Insulin typically is provided in two general ways. Insulin may be delivered via a pre-filled syringe or pre-filled pen (device) that contains insulin (biological product), which is more expensive but also easier to use for patients because it contains the correct dose amount and makes the injection process simpler. Insulin can also be delivered via a traditional vial and syringe administration where the patient has to draw the insulin into a syringe from a vial. The latter approach is less expensive, but also more difficult for patients and may result in variable dosing.

Figure 3-2 presents a general illustration of the supply chain for medical devices. The process begins with raw material suppliers. A medical device can have many different parts and as a result, there may be many suppliers of raw material and components, who can be located around the world, often referred to in tiers based on their relationship to the manufacturer. For example, Tier 1 suppliers sell goods to the manufacturer directly, Tier 2 suppliers sell to Tier 1 suppliers and are thus one step further removed from the manufacturers, Tier 3 suppliers sell to Tier 2 suppliers, and so on.[75]

Producers may sell their medical devices directly to providers, which include retail pharmacies and hospitals, or through distributors. Medical devices, such as glucometers and test strips, may be purchased directly by patients without a prescription (over the counter) from retail pharmacies or patients can have these prescribed to them. However, a large health care delivery system may also purchase insulin pumps from the manufacturer or distributor to provide insulin therapy during hospital stays. Distributors, such as McKesson, Cardinal Health and AmeriSource Bergen, negotiate with manufacturers, store the products, and sell the products to end users. Group purchasing organizations that negotiate contracts with manufacturers and distributors on behalf of their hospital members may also be involved. When hospitals provide health care services, patients pay for coverage through premiums and a share of the cost of care. Similarly, the health insurance plan sponsor (or payer) pays for its share of the cost of care.

Figure 3-2. Medical Device Supply Chain



Notes: *Providers may be retail pharmacies, or hospitals.*

Source: Adapted from Figure 1 in NASEM (2022)[76]

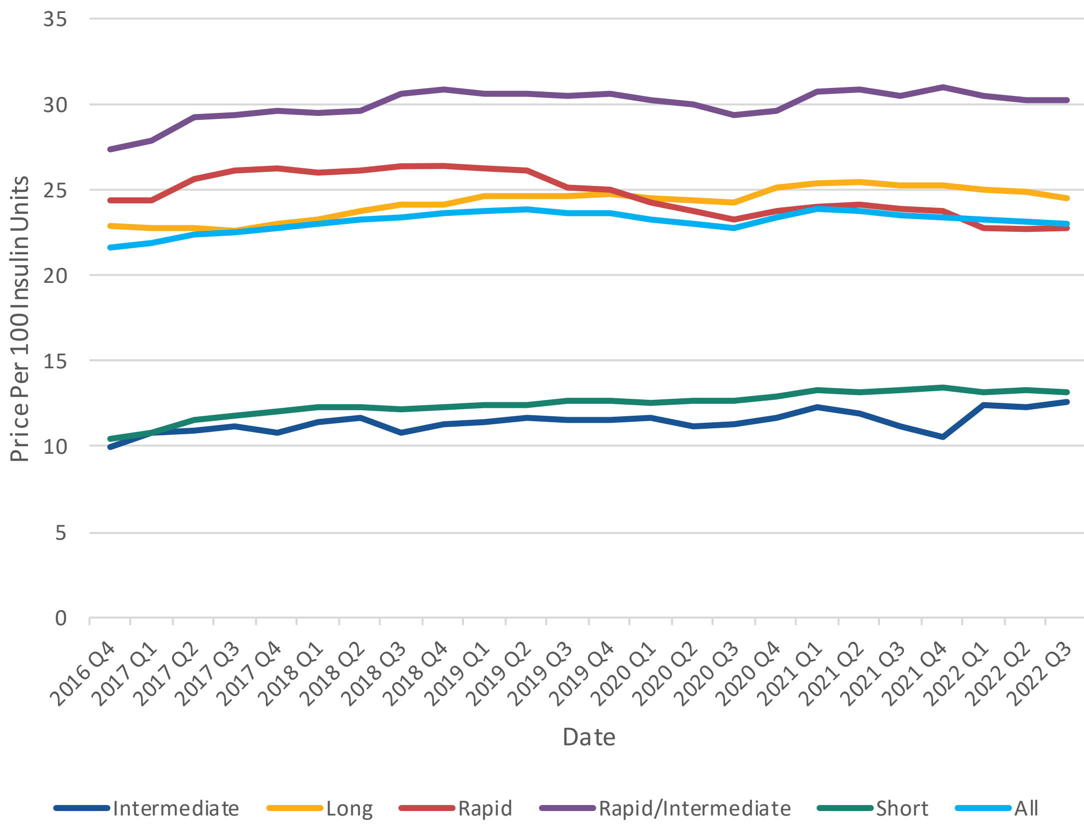
II. Insulin Market, Pricing, and Affordability

Insulin was first developed in 1921 with patents sold to the University of Toronto for $1 because the researchers that developed insulin wanted it to be accessible and inexpensive.[77] Over time, average prices for insulin have increased significantly (about double over the 2012-2016 period), increasing the financial burdens for Americans who use insulin and inhibiting access to this life saving medicine—particularly those who are uninsured or have high out-of-pocket costs for needed medicines, as we describe in

Chapter 4. For example, the price of Humalog, a commonly used fast acting insulin, increased from $21 in 1999 to $332 in 2019.[78] Moreover, prices for insulin analogs cost 10 times more in the United States than any other developed country.[79]

Gross prices for all types of insulin increased rapidly between 2012 and 2016.[80] Figure 3-3 shows that invoice prices for insulin products across duration types have been more stable since that period. Invoice prices for rapid/intermediate-acting, rapid-acting, and long-acting insulins have been higher than invoice prices for short-acting or intermediate-acting insulins. But invoice prices for each type have increased slightly (long-acting, rapid/intermediate-acting, and short-acting), decreased slightly (rapid-acting), or remained about the same (intermediate-acting and overall average across duration types).

Figure 3-3. Quarterly Insulin Invoice Price Trends by Duration Type, October 2016-September 2022



Source: ASPE analysis of IQVIA National Sales Perspective data.

Notes: Pens and vials only. Excludes long-incretin mimetic mixes and Myxredlin. Different insulin durations have different average strengths per mL, with short-acting insulin products, for example, having the highest average strength. Estimates for each type of insulin and for all insulin products overall are averages weighted by adjusted strength.

Prices vary between pens and vials based on the line of insulin. However, for rapid-acting insulins, pens may be 40 percent more expensive than insulin purchased in vial form.[81]

Market for Insulin

The global market for insulin is dominated by three primary pharmaceutical companies – Novo Nordisk, Eli Lilly, and Sanofi. These three companies are the sole suppliers of insulin in the United States and make up approximately 90 percent of the global market. There are four primary reasons why no other competitors have remained on the market: insulin is a biological product and making a "biosimilar" version is difficult and expensive, there has been incremental innovation on devices associated with the delivery of insulin allowing for new patents, there is extensive patent litigation for biological products, and companies can use their market power to gain favorable formulary placement that minimizes competition.

One way to increase competition and potentially reduce the cost of insulin is to incentivize the use of biosimilar products. Insulin is a "biological product" —a class of drugs that "can be composed of sugars, proteins, or nucleic acids or complex combinations of these substances, or may be living entities such as cells and tissues"[82] – that are generally difficult to precisely replicate, making the common generic entry pathway infeasible. The Food and Drug Administration (FDA) was granted authority to establish a pathway for "biosimilars," follow-on competitive entrants to biological reference products, by the Biologics Price Competition and Innovation Act of 2009 (BPCIA), passed into law as part of the ACA in 2010. BPCIA defines a biosimilar as a biological product demonstrated to be "highly similar to and [that] has no clinically meaningful differences from an existing FDA-approved reference product."[83] As biological products become an increasingly large share of medical spending, biosimilars have become a key component of the national strategy to tackle high and growing spending on prescription drugs.[84] However, the United States has been slower in establishing a streamlined regulatory pathway for biosimilar products. For example, the European Medicines Agency established its biosimilars approval pathway in 2005, which led to its first biosimilar approval in 2006. As of December 31, 2021, the European Medicines Agency had approved biosimilar competitors for 18 reference drugs, including biosimilars for three different insulin reference products (insulin aspart, insulin glargine, and insulin lispro).[85] In contrast, the first U.S. biosimilar approval was in 2015, and as of December 31, 2021, there are only nine biological reference products that faced biosimilar competition.[86] Specifically for U.S. insulin markets, there are only two biosimilar insulins, both of which received FDA approval in 2021 and are in reference to the same reference product, insulin glargine. The biosimilars are Rezvoglar and Semglee, both of which have been approved as an "interchangeable biosimilar," meaning it may be substituted for the reference product directly by pharmacists, subject to state pharmacy law.[87]

The second reason there has been limited competition in the market for insulin is innovation of the device that delivers insulin. Insulin was first used in patients in 1922, a century ago, meaning that there are no active patents on the *drug*. However, insulin makers have continued to innovate on the *devices* used to deliver insulin. This is often referred to as "diabetes technology." Diabetes technologies include devices involved in insulin delivery (such as insulin pens and insulin pumps), devices used to monitor glucose levels or determine insulin dosage (glucose monitors, test strips), and software ("apps") that are used in combination with devices to manage diabetes. While the use of diabetes technology can improve the management of diabetes, the complexity and rapid change of the technology can also be a barrier in the management of diabetes, and in some cases may be used as a method for extending the life of a patent or supporting higher prices.[88] Currently, the most common delivery device for insulin is a pen injector. The advantage of these new technologies is that patients have a less intrusive mechanism for receiving their insulin with less pain and fewer side effects, however, drug companies can layer patents for their device innovations thereby discouraging competition, because potential biosimilar product companies cannot enter the market with up-to-date technology or must navigate higher legal costs to do so.[89] This, in turn, leads to increasing prices for insulin products from the brand companies.

The third reason there has been limited competition in the insulin market is extensive patent litigation for biological products that delays market entry of competitors. Across all biosimilars in the United States, patent infringement cases have been common and can impact biosimilar market entry, thereby resulting in higher development costs and less potential profit because much of the exclusivity period is already exhausted by the time patent litigation is resolved.

The final reason for lack of competition in the market for insulin is the use of market power by the dominant companies to negotiate for favorable placement on formularies due to the use of high rebates from manufacturers to PBMs.[90] One recent study estimated that rebates for insulin products are three-quarters of their list prices.[91] In exchange, the branded insulin company has preferred access to a formulary, guaranteeing a large swathe of patients take their drug. Use of rebates gives a competitive edge to the originator company, because the biosimilar product company would need to lower their prices significantly in order to be placed on a formulary, oftentimes discouraging entry into this market.

Affordability: List and Net Prices

There is substantial variation in the estimates for list prices of insulin depending on the type of insurer, age of insurance enrollees, type of insulin being used and studied, and the time that a research study was conducted. However, across all the literature on insulin prices, the primary takeaway is that prices for insulin are high by any standard, and often 5 to 10 times higher in the United States relative to other countries, and prices have grown substantially over the past few decades.[92] Below is a snapshot of some of the evidence on list prices for insulin (the prices before any discounts are considered).

- One of the most recent, comprehensive assessments of insulin prices is a 2022 study that examined spending on insulin from the MEPS from 2008 through 2017 by payer type. The authors found that between 2008 and 2017, list prices for insulin per beneficiary increased 184 percent for commercial payers for a total of $5,962 in 2017; increased 276 percent for Medicare for a total of $6,267 in 2017; and increased 141 percent in Medicaid to $4,108 in 2017.[93]
- Another study using SSR Health drug pricing data from 2007 through June 2018 focused specifically on four types of biological products: three non-insulin products (filgrastim, pegfilgrastim, and infliximab), and insulin glargine**.** These biological products were selected because they had biosimilar competitors on the market and thus were likely to be a lower bound for the cost. The annual increase for insulin glargine was 14.7 percent increase per year, which plateaued around $6,000 when the first follow-on biosimilar was introduced in 2018. Competition helped to mitigate price increases even though the final price for insulin glargine remained high for a drug with competition from a potentially cheaper competitor.
- An ASPE report examining IQVIA data from 2018 found the average gross manufacturer price for a standard unit of insulin in the United States was $98.70, which was more than ten times the price in a sample of 32 foreign countries, where the average price was $8.81.[94] Insulin products are also among the most heavily rebated prescription drugs, with net prices (gross prices minus manufacturer rebates to PBMs) estimated as about one-quarter of gross prices.[95] Even if we adjust the ratio of US to international insulin prices by this estimate, and assume no rebates to insulin prices in comparator countries, US net insulin prices would still be about twice

international prices. These findings demonstrate that extremely high prices for insulin are particular to the US health care system.

The largest concern with growing list prices – even as rebates grow as well – is that patients do not benefit because rebates are not passed on to beneficiaries, meaning their out-of-pocket spending remains pegged to the very high list prices. The Inflation Reduction Act is attempting to make out-of-pocket costs for prescribed drugs more affordable, but that only impacts the Medicare population. We explore this in Chapter 7.

Potential Future Savings from Biosimilars

Theoretically, competition between biosimilars and reference biological products should drive down insulin prices, reducing medical spending on diabetes care. However, the magnitude of these potential savings depends on the development of a competitive environment for each insulin product, including how quickly and how many biosimilar competitors enter each insulin market. As seen with the entry of the follow-on insulin glargine product, Basaglar, that entered the insulin market in 2016, and more recently with other insulin products that have been approved as interchangeable biosimilars, the effects of biosimilars on competition can be muted and often delayed through patent litigation from brand manufacturers.

An approximate estimate of potential savings resulting from biosimilar entry can be adapted from Mulcahy et al., (2022),[96] which estimated that U.S. savings between 2021 and 2025 under three different scenarios depending on the number of biosimilar competitors that enter the market relative to the fourth quarter of 2020 (Table 3-1). The authors projected $4.1 billion in savings (about 2 percent of current insulin spending, shared among payers, patients, and third parties) over the period 2021-2025 as a direct result of biosimilar entry. The authors also conducted sensitivity analyses that consider the effects of higher probabilities of future biosimilar entry, more rapid biosimilar market-share capture, and more intense price-competition between biosimilars and reference products. Taken together, savings on insulin could amount to as much as $13.9 billion, about 7 percent of gross U.S. insulin spending over this period.

Focusing specifically on different types of insulin products, insulin glargine, insulin lispro, and insulin aspart represent over 95 percent of the projected total savings. U.S. biosimilar markets are still in the nascent stages of development; however, as time passes, a greater number of biosimilar products for insulin are expected to enter the market, intensifying price competition and lowering prices further. As mentioned in "The Comprehensive Plan for Addressing High Drug Prices,"[97] biosimilar development and uptake could be facilitated by legislation that reduces the period of exclusivity for reference biological products, incentivizes clinicians to prescribe biosimilars, or lowers out-of-pocket costs for biosimilar products relative to the reference biological product.[98]

Table 3-1. Projected 5-Year Savings on Insulin Products From Biosimilar Competition

	2021 - 2025 Savings (in Millions of Dollars) Decomposed by Source:		
	(1)	(2)	(3)
Insulin Product	Lower Biosimilar Prices ($)	Lower Reference Product Prices ($)	Total Savings ($)
Insulin Glargine	596.4	1,533.7	2,130.1
Insulin Lispro	237.5	670.6	908.1
Insulin Aspart	236.3	667.6	903.9
Insulin Aspart/Insulin Aspart Protamine	11.8	34.2	46.0
Insulin Human Base	8.5	25.2	33.7
Insulin Detemir	7.3	21.8	29.1
Insulin Human Base/Insulin Human	3.2	9.5	12.6
Insulin Human Isophane	3.0	9.0	12.0
Insulin Lispro/Insulin Lispro Protamine	2.0	5.9	7.9
Insulin Glulisine	0.0	0.0	0.0
Total	1,106.0	2,977.5	4,083.4

Notes: Calculations in this table are adapted from Section VII of the eAppendix within Mulcahy et al., 2022.[99]

Despite the promise of biosimilars and efforts to encourage their use, the three companies that dominate insulin sales have the ability to adjust prices as needed to price out competitors. In one study, there were examples of new competitors entering the market, after which the dominant three companies all lowered their prices until the competitors were priced out of the market.[100] Because biosimilar products are expensive to develop, undercutting potential profits has a significant impact on the potential profitability of competitors and therefore deters market entrance. However, these prices are not nearly as low as a truly competitive market would be. Increased utilization of biosimilars would also have to overcome the use of market power to gain favorable placement on a formulary due to the use of high rebates as discussed above.

Chapter 4. Spending on Diabetes and Insulin

In this chapter, we examine the impact of diabetes and insulin on health care spending from the perspective of downstream stakeholders most affected by insulin prices – patients, payers, and taxpayers. Using existing survey and health expenditure data, we examine health insurance coverage, total health care spending, and out-of-pocket spending among people with diabetes (including those who are taking insulin) to identify the patients and payers that are the most impacted by health care costs associated with diabetes and insulin.

Key findings from this Chapter include:

- Based on the Medicare Expenditure Panel Survey (MEPS), in 2019, about 27 percent of patients (about 7.5 million of 27.6 million) with diabetes took insulin.
- About 52 percent of patients using insulin are Medicare beneficiaries who may benefit from the Inflation Reduction Act provisions, which aim to make insulin more affordable by, for example, capping out-of-pocket spending to $35 per insulin product.
- About 33 percent of patients using insulin are privately insured, 12 percent are Medicaid beneficiaries, and about 2 percent are uninsured. Uninsured patients are the most exposed to out-of-pocket costs, followed by patients with private insurance.
- Total health care spending for the 27.6 million people diagnosed with diabetes, including spending for other conditions, was estimated to be about $446 billion in 2019 based on the MEPS survey. Total health care spending for the 7.5 million people diagnosed with diabetes who take insulin is estimated to be about $202 billion, which is nearly half (45 percent) of total spending on people diagnosed with diabetes.
- While the average annual out-of-pocket cost for insulin in 2019 was $434, half of insulin users paid $120 or less out-of-pocket, and 19.4 percent of insulin users paid nothing. On average, uninsured insulin users paid more than twice as much out-of-pocket, $996 per year, than the overall average of all insulin users. The average annual out-of-pocket cost for insulin for patients with private insurance was $456 per person.
- Medicare enrollees and privately insured patients both paid an average of $63 per insulin fill in 2019. People without insurance paid an average of $123. More than three-quarters of monthly fills for privately insured patients required some cost-sharing, with more than one-third paying more than $35, and nearly one-fifth paying more than $70.

I. Health Insurance Coverage Among Insulin Users

Based on analysis of 2019 data from the Medical Expenditure Panel Survey (MEPS), there were 27.6 million total patients with diabetes, and of these, about 27 percent were taking insulin (Table 4-1).

Patient responsibility for insulin costs varies by type of health insurance coverage. More than half of U.S. insulin users are Medicare beneficiaries. These Medicare beneficiaries may benefit from the Inflation Reduction Act provisions that take effect in 2023, which aim to reduce out-of-pocket spending for Part D and Part B enrollees through a number of provisions, such as capping monthly cost-sharing at $35 per insulin product and excluding insulin products from the Medicare deductible, in which beneficiaries pay 100 percent of gross drug costs.[*]

About 12 percent of insulin users have Medicaid, which offers the most protection from out-of-pocket costs. About one-third of insulin users have private coverage, from employers or in the individual market including the Marketplace, and protections from out-of-pocket spending may not be sufficient. Based on the 2022 Commonwealth Fund's biennial survey on health insurance, nearly 30 percent of working-aged adults with employer coverage were underinsured.[101,102] Moreover, patients with private insurance may have high premium and deductible costs, leading them to ration care, which we discuss more fully in the next Chapter.

Table 4-1. People with Diabetes, by Insulin Use and Type of Health Coverage, 2019

	Insulin Users		Insulin Non-Users		Total	
Type of Coverage	Number (thousands)	Share (%)	Number (thousands)	Share (%)	Number (thousands)	Share (%)
Privately Insured	2,465	32.8%	6,390	31.9%	8,855	32%
Medicare	3,931	52.2%	10,801	53.9%	14,732	53%
Medicaid	882	11.7%	1,883	9.4%	2,764	10%
Uninsured all year	246*	2.2%	721	3.6%	833	3%
Total	7,525	100.0%	20,033	100.0%	27,558	100%

Source: Medical Expenditure Panel Survey (MEPS), 2019. Civilian noninstitutionalized population.

Notes: The insurance categories are hierarchical: Medicare (with or without Part D drug coverage, including Medicare only, Medicare and Medicaid, and Medicare and private insurance), private insurance (including private insurance only and Marketplace any time during the year), Medicaid (includes Medicaid only or Medicaid and other government programs), other government programs only, and uninsured (lacked insurance from any source for the entire calendar year). "Overall" also includes adults who had insurance through other government programs.

* For uninsured insulin users, annual average estimate is from the MEPS, 2014-19.

People without health insurance are the most exposed to out-of-pocket costs. On average, from 2014 through 2019, 246,000 insulin users (2.2 percent) were uninsured for the entire year. This is the only health coverage category in which insulin users were significantly different than people with diabetes who did not use insulin ($p<.05$). Other ways of measuring health coverage suggest larger numbers of insulin users were without health insurance coverage at some point in the year: about 5.7 percent were uninsured at their first interview in 2019, and about 7.2 percent (542,000) were uninsured in at least one month of that year (data not shown).

[*] Other provisions in the IRA that will impact out-of-pocket spending for Part B and D Medicare enrollees include inflation rebates, ability of Medicare to negotiate the cost of high-priced drugs, and a $2,000 out-of-pocket annual cap on Part D spending.

II. Health Care, Prescribed Medicines, and Insulin Spending for People with Diabetes

Using 2019 MEPS data, we examined health care spending for two populations: 1) all patients diagnosed with diabetes and 2) all patients taking insulin. The former group is important because they allow for a more comprehensive understanding of the burden of diabetes on patients and payers. For this group, the sample includes patients with diabetes managed through lifestyle modification as well as diabetes that requires medication therapy and/or insulin therapy. For the latter group, the sample is likely comprised of patients who generally have more severe disease.

For both groups, we examined three types of spending: total health spending, spending on prescribed medications, and spending specifically for insulin. We begin with total health spending because patients with diabetes and patients taking insulin have additional health care expenditures beyond insulin, and any examination of patient and payer burden should consider all health expenditures incurred by patients and payers.

Health Care Expenditures for All People Diagnosed with Diabetes

Health Care Expenditures

Total health care spending for people diagnosed with diabetes was estimated to be about $446 billion in 2019 based on the MEPS survey. This estimate includes spending for the treatment of diabetes, treatment for diabetes-associated complications and comorbid conditions, treatment unrelated to diabetes, and preventive care. Estimates show that 32 percent of the $446 billion, or about $142 billion in 2019, spent on health care for patients with diabetes is for prescribed medicines, which includes, but is not limited to insulin.[*]

Differences in expenditures across types of insurance reflect differences in the number of people with diagnosed diabetes, diabetes severity in the covered populations, the prices paid by each payer, and any differences in the intensity of treatment.

Expenditures for Insulin Users

Expenditures for insulin users, who may have more severe diabetes than those whose diabetes can be treated with diet, exercise, or other medications, were $202 billion, or nearly half (46 percent) of expenditures for people with diagnosed diabetes (Table 4-2). This translates to about $26,861 per person in total health care expenditures for patients who take insulin, which is 4.3 times higher than the average health care spending per person in the United States for the noninstitutionalized civilian population in 2019 ($6,252). Health care expenditures for Medicare and Medicaid beneficiaries who were insulin users were $116 billion and $16 billion, respectively or 57 percent and 8 percent of expenditures, respectively.

[*] These estimates are based on transaction prices paid to pharmacies and do not reflect manufacturer rebates, which can be substantial for insulin.

Table 4-2. Total and Out-of-Pocket Health Care, Prescribed Medicines, and Insulin Expenditures for Insulin Users, by Type of Coverage

	Total Health Expenditures			Prescribed Medicines Expenditures			Insulin Expenditures		
Type of Coverage	Total (millions)	%	Mean per person	Total (millions)	%	Mean per person	Total (millions)	%	Mean per person
Total									
Overall	$202,138	100%	$26,861	$78,290	100%	$10,404	$40,587	100%	$5,393
Private	$65,662	32%	$26,633	$24,985	32%	$10,134	$13,998	34%	$5,678
Medicare	$115,892	57%	$29,479	$43,823	56%	$11,147	$22,283	55%	$5,668
Medicaid	$15,630	8%	$17,716	$8,099	10%	$9,180	$3,613	9%	$4,096
Uninsured[a]	$2,521	1%	$10,263	$1,457	2%	$5,767	$714	2%	$2,811
OOP									
Overall	$13,346	100%	$1,774	$6,705	100%	$891	$3,262	100%	$434
Private	$5,502	41%	$2,232	$2,443	36%	$991	$1,123	34%	$456
Medicare	$6,972	52%	$1,773	$3,589	54%	$913	$1,765	54%	$449
Medicaid	$227	2%[b]	$257	$103	2%[b]	$117	[c]	[c]	[c]
Uninsured[a]	$708	5%	$2,776	$499	7%	$2,001	$250	8%	$996

Source: Medical Expenditure Panel Survey (MEPS), 2019. Civilian noninstitutionalized population.

Notes: Expenditures shown are based on gross drug costs without adjustment for the value of rebates that insulin manufacturers may pay to the government or health plan sponsors. See note in Table 4-1 on the hierarchical structure of the insurance categories. “Overall” also includes adults who had insurance through other government programs.

[a] For the uninsured population, annual average estimates are from the MEPS, 2014-19. Expenditures for 2014 to 2018 are inflated to 2019 dollars using the Personal Health Care Expenditure deflator to adjust total health care expenditures, by the Consumer Price Index (CPI) for medical care to adjust out-of-pocket health care expenditures for people with diagnosed diabetes and insulin users, and by the CPI for prescription drugs to adjust expenditures on prescribed medicines and insulin.

[b] Estimates are imprecise due to small sample sizes.

[c] Estimates are not shown due to imprecision arising from small sample sizes.

An additional $66 billion and $3 billion, respectively, were spent on privately insured and uninsured insulin users. Among insulin users, $78 billion was spent on all prescribed medicines, including $41 billion on insulin. Insulin accounted for a fifth of $202 billion in total health care expenditures among insulin users.

Out-of-pocket expenditures on insulin totaled $3.3 billion, accounting for about half of the $6.7 billion out-of-pocket spending by insulin users on prescribed medicines. Medicare beneficiaries spent $1.8 billion out-of-pocket for insulin. Estimates of out-of-pocket spending by Medicaid beneficiaries who used insulin are imprecise because regulations limit cost sharing for Medicaid beneficiaries, and the totals are comparatively low.

The privately insured spent $1.1 billion out-of-pocket on insulin. Uninsured people spent $250 million out-of-pocket on insulin, only part of the $714 million total expenditures on insulin for them. Other payers for patients who are uninsured include charities, safety net providers, and programs that have limited benefits. The other payers do not include coupons and manufacturer programs, which are treated like other discounts and are not counted as expenditures. Among insulin users, insulin accounted for 27 to 28 percent of out-of-pocket spending on all health care overall as well as for the privately insured and Medicare beneficiaries (Table 4-3). Insulin is a significantly lower proportion of out-of-pocket spending for Medicaid beneficiaries than for insulin users overall.

Table 4-3. Mean Out-of-Pocket Spending on Insulin as a Percentage of Out-of-Pocket Health Care Expenditures on Health Care Among Insulin Users in 2019, by Type of Coverage

Type of Coverage	Mean Percentage
Overall	26.7%
Private	27.4%
Medicare	28.3%
Medicaid	14.5%**
Uninsured[a]	32.2%

Source: Medical Expenditure Panel Survey (MEPS), 2019. Civilian noninstitutionalized population.

Notes: The insurance categories are hierarchical: Medicare (with or without Part D drug coverage, including Medicare only, Medicare and Medicaid, and Medicare and private insurance), private insurance (including private insurance only and Medicaid any time during the year), Medicaid (includes Medicaid only or Medicaid and other government programs), other government programs only (not shown), and uninsured (lacked insurance from any source for the entire calendar year). "Overall" also include adults who had insurance through other government programs. For people with zero out-of-pocket expenditures on health care, the percentage was set to zero.

[a] For the uninsured population, annual average estimates are from the MEPS, 2014-19. Expenditures for 2014 to 2018 are inflated to 2019 dollars using the Consumer Price Index (CPI) for medical care to adjust out-of-pocket health care expenditures and the CPI for prescription drugs to adjust expenditures on insulin.

** Statistically significantly different from overall at the .01 level.

These estimates suggest that even though lowering cost sharing for insulin is likely to reduce out-of-pocket costs, insulin users will continue to be responsible for out-of-pocket spending on health services and on other drugs. Insulin accounted for a significantly smaller share of out-of-pocket costs among Medicaid beneficiaries.

We summed out-of-pocket costs across each person's insulin fills to obtain annual out-of-pocket expenditures per insulin user (Table 4-4), which varied widely. While the average annual out-of-pocket cost for insulin in 2019 was $434, half of insulin users paid $120 or less out-of-pocket, and 19.4 percent of insulin users paid nothing. On average, uninsured insulin users paid more than twice as much out-of-pocket, $996 per year, than the overall average. Among Medicaid beneficiaries, 64.3 percent had no out-of-pocket costs for insulin during the year.

Table 4-4. Annual Out-of-Pocket Expenses for Insulin, by Type of Coverage

Type of Coverage	Median Annual OOP Per Person	Mean Annual OOP Per Person	Share with No Out-of-Pocket Spending
Overall	$120	$434	19.4%
Private	$171	$456	14.4%
Medicare	$150	$449	12.8% **
Medicaid	$0 **[a]	$58 **[a]	64.3% **[a]
Uninsured[b]	$170	$996 **	8.2% **

Source: Medical Expenditure Panel Survey (MEPS), 2019. Civilian noninstitutionalized population.

Notes: See note on hierarchical structure of MEPS data in Table 4-1. "Overall" also include adults who had insurance through other government programs. For the uninsured population, annual average estimates are from the MEPS, 2014-19. Out-of-pocket expenditures on insulin for 2014 to 2018 are inflated to 2019 dollars using the Consumer Price Index for prescription drugs.

[a] Estimates are imprecise due to small sample sizes.

* Statistically significantly different from overall at the .05 level.

** Statistically significantly different from overall at the .01 level.

III. Out-of-Pocket Costs Per Fill

We also used MEPS to examine out-of-pocket cost per insulin fill. Among the prescriptions with reported days supplied, 30 days was the mode and median days supplied so fills represent an approximate 30-day supply of insulin.[*]

The estimates in Table 4-5 suggest wide variation in the amounts people paid out-of-pocket for insulin obtained from retail, mail, and online pharmacies in 2019. The median overall out-of-pocket payments was $9, indicating half the fills were for that amount or less. The mean (average) out-of-pocket payment was $58 per fill, but among people uninsured the entire year, the average out-of-pocket cost per fill was $123, more than double the overall average. Out-of-pocket costs for uninsured patients would likely have been greater if not for charities, safety net providers, programs with limited benefits, and manufacturer programs and coupons.[†]

The mean out-of-pocket costs in Table 4-5 may be more than one-twelfth the annual spending shown in Table 4-4 above because some insulin users have fewer than twelve fills for the year. In the course of the year, some individuals with diabetes will start insulin treatment, while others, such as patients with limited life expectancy, may receive clinical guidance to discontinue or reduce treatment with insulin.[103] And some may not adhere to their prescribed treatment, either stretching their fills over longer periods than

[*] In the MEPS data provided by pharmacies, 32 percent of insulin fills lacked the days supplied. Among the fills with reported days supplied, 30 days was the mode and median.

[†] As in Table 4-3, manufacturer programs and coupons are treated like other discounts and are not counted as expenditures by the patient or other payers.

advised by their doctors or not filling their insulin prescriptions, due to cost or for other reasons (see chapter 5 for discussion on adherence).

Table 4-5. Median and Mean Out-of-Pocket Cost Per Insulin Fill, by Type of Coverage, 2019

Type of Coverage	Median		Mean	
Overall	$9		$58	
Private	$25	**	$63	
Medicare	$10	a	$63	
Medicaid	$0	**b	$6	**b
Uninsured[a]	$12		$123	**

Source: Medical Expenditure Panel Survey (MEPS), 2019. Civilian noninstitutionalized population.

Notes: See note on hierarchical structure of MEPS data in Table 4-1. For the uninsured population, annual average estimates are from the MEPS, 2014-19. Out-of-pocket expenditures on insulin for 2014 to 2018 are inflated to 2019 dollars using the Consumer Price Index for prescription drugs.

* Statistically significantly different from overall at the .05 level.

** Statistically significantly different from overall at the .01 level.

[a] Estimate is imprecise.

[b] Estimates are imprecise due to small sample sizes.

Table 4-6 presents the shares of insulin fills, by type of coverage, for which there was any out-of-pocket spending. Overall, 63.5 percent of insulin fills required some cost-sharing, with 31.5 percent of fills requiring more than $35, and 19.8 percent requiring more than $70. Fills for privately insured and uninsured patients were significantly more likely to require cost-sharing than overall, while fills for Medicaid beneficiaries were significantly less likely to have any cost-sharing, cost-sharing above $35, or cost-sharing above $70. The most likely reason a small proportion of Medicaid beneficiaries had high out-of-pocket costs for insulin fills was that they also had periods without coverage.

While 30 days was the most common prescription length in the dataset, some prescriptions lack information on the number of days supplied, and smaller numbers of prescriptions may represent more or less than a 30-day supply; these factors introduce some uncertainty into our estimates of the proportion of insulin users paying more than $35 per 30-day supply.

Table 4-6. Share of Fills with Cost-Sharing Per Fill Above $0, $35, and $70, by Type of Coverage, 2019

Type of Coverage	Greater than $0		Greater than $35		Greater than $70	
Overall	63.5%		31.5%		19.8%	
Private	75.1%	**	34.8%		18.8%	
Medicare	68.5%		37.5%		24.2%	
Medicaid	16.4%	**	2.7%	**[b]	2.5%	**[b]
Uninsured[a]	78.6%	**	35.8%		26.8%	

Source: Medical Expenditure Panel Survey (MEPS), 2019. Civilian noninstitutionalized population.

Notes: See note on hierarchical structure of MEPS data in Table 4-1.

[a] For the uninsured population, annual average estimates are from the MEPS, 2014-19. Out-of-pocket expenditures on insulin for 2014 to 2018 are inflated to 2019 dollars using the Consumer Price Index for prescription drugs.

[b] Estimates are imprecise due to small sample sizes.

* Statistically significantly different from overall at the .05 level.

** Statistically significantly different from overall at the .01 level.

Chapter 5. Insulin Adherence

In this chapter, we focus on the importance of taking insulin as prescribed and present adherence rates for insulin. We then explore how adherence rates are linked to insulin affordability and the affordability of housing and food.

At baseline, proper insulin usage is critical for controlling diabetes and reducing the long-term and damaging implications of uncontrolled diabetes on overall patient health. To understand how patients manage proper insulin utilization as prescribed, we examine medication adherence, which is an approach to measure how closely patients can follow their treatment regimen as prescribed by a provider. While many factors contribute to adherence, we focus specifically on discussing the relationship between out-of-pocket health care expenditures and medication adherence. This is particularly true for diabetes because the insulin treatment regime can be complicated and without appropriate insulin use as prescribed, costs of care can be high and health complications significant.

Key findings for this chapter include:

- Medication adherence to insulin is critical to limit short-term and long-term consequences from poorly controlled diabetes, all of which impact patients' quality of life, health care use, and expenditures.
- Adherence rates vary widely across populations because insulin adherence is difficult to measure, with rates as low as 9 percent and as high as 86 percent across different studies and populations.
- Insulin adherence is tied to affordability of insulin, particularly out-of-pocket spending on insulin. Our review of the literature suggests that patient out-of-pocket cost is one of many factors contributing to adherence, and non-adherence can worsen the rates of diabetes-related complications.
- Proper use of insulin requires other resources such as adequate and stable housing and consistent access to nutritious food. Analysis using the Medicare Expenditure Panel Survey (2016 – 2017) show that the share of adult insulin users with low or very low food security (14 percent) was higher than for adults overall (8.4 percent).
- Patients who do not have sufficient financial resources may have to make tradeoffs between following their prescribed insulin regimen and other living expenses such as adequate and stable housing and food.

I. Medication Adherence for Diabetes

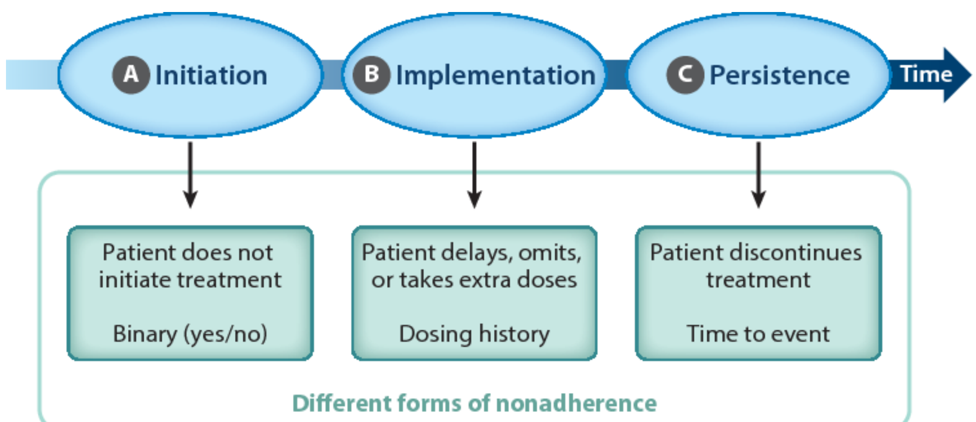
Adherence is broadly defined by the World Health Organization (WHO) as "the extent to which the patient follows medical instructions."[104] According to the CDC diabetes surveillance system, about 33 percent of patients who are diagnosed with diabetes in the United States depend upon insulin. For these patients, medication adherence is critical for optimal care and disease management.[105]

A plethora of existing research shows that poor medication adherence, including forgoing medications, taking less than needed, or delaying prescribed medications, affects how well a disease, including diabetes, can be controlled.[106,107] Poor adherence contributes to high rates of disease complications. Conversely, following medication therapy as prescribed is associated with a range of health improvements and reduced health care expenditures.[108] In a systematic review by Evans et al., improved insulin adherence among individuals with type 2 diabetes resulted in better health outcomes (e.g., fewer inpatient hospitalizations, reduced length of stay in the hospital, fewer emergency department visits, etc.) and lower health care cost and utilization.[109] Other studies have used claims data to examine health care expenditures for patients with diabetes, finding that higher insulin adherence was associated with lower total health care costs, improved blood sugar control, and decreased emergency department visits.[110,111]

Conceptualizing and Measuring Adherence

There is no gold standard for measuring adherence. In the taxonomy of adherence, medication adherence is split into three phases: initiation, implementation, and persistence, which are described in Figure 5-1.[112]

Figure 5-1. Taxonomy for the Phases of Medication Adherence and Non-Adherence



Notes: Figure is referenced from a study published in 2019 Annual review of pharmacology and toxicology.[113]

For diabetes, treatment regimens can be complex and expensive, especially for patients with multiple medications and multiple health conditions. All of the phases of adherence are friction points, or points where action is needed to better adhere to prescribed medications. These friction points pose a particular challenge for patients requiring insulin therapy for many reasons, including but not limited to the complexity of treatment regimens, the challenges associated with the mode of insulin administration (e.g., self-injection), the presence of risks due to hypoglycemia if insulin is not used at appropriate time intervals and as directed, and the high out-of-pocket costs associated with insulin, especially for certain populations as discussed in Chapter 4.

II. Adherence Rates for Insulin Use to Manage Diabetes

Existing research demonstrates that there is wide variation in insulin adherence rates, depending on the population examined and the way adherence is measured. A recent study conducted a systematic review of adherence and estimated that self-reported adherence rates range from 43 to 86 percent for patients perfectly following their insulin regimen as prescribed. [114, 115] These rates are typically lower in marginalized populations and those in less stable social environments. [116] Another systematic review of 71 studies found that overall estimates of diabetes-related treatment adherence ranges between 9.4 percent and 84.3 percent, with a median of 51.2 percent among patients with type 2 diabetes, but this includes adherence of insulin with other treatments. [117] Another study used self-reported measures of adherence and found adherence rates at 71 percent for insulin treatment among patients with type 2 diabetes in the U.S (2021). [118]

Disparities in insulin adherence have been identified among people of color, who are disproportionately affected by poor health outcomes and experience greater challenges in accessing health care. [119] A study using the U.S. National Health and Wellness Survey dataset (2012) found that medication adherence, including insulin, was lowest among Hispanic (31.9 percent), Asian (33.6 percent), and non-Hispanic Black (38.5 percent) individuals, compared to non-Hispanic white (50.3 percent), and American Indian (45.2 percent) individuals. [120] In a study using a diabetes self-management survey, non-Hispanic white patients had the highest self-reported insulin adherence compared to other racial and ethnic groups, while Black patients had the lowest adherence. [121] Structural inequities such as food and nutrition insecurity, lack of adequate opportunities for safe exercise, language and cultural differences, historical mistrust of the health care system, implicit bias and provider discrimination, and lack of adequate access to health care may all contribute to these disparities. [122]

III. The Relationship between Insulin Spending and Insulin Adherence

Although there are multiple factors that influence adherence, the cost of insulin has emerged as a key reason why patients may not take their insulin as prescribed.[*] Insulin rationing occurs when a patient forgoes doses of insulin because they are unable to afford the costs of their insulin prescription, leading to medication non-adherence. Using data from the NHIS, researchers used a weighted sample, representing about 6 million patients with diabetes who use insulin, to examine rationing behavior. Results showed that an estimated 1.3 million (of these 6 million) or 17 percent of American insulin user rationed their insulin in 2021 for cost-related reasons. [123] The most common form of rationing among all insulin users was delaying purchase (14.2 percent). Among patients with type 1 diabetes, the most common form of rationing was taking less than needed (16.5 percent). The highest rate of rationing was among patients with no health insurance (29.2 percent), followed by patients with private insurance (18.8 percent), Medicare beneficiaries (13.5 percent) and Medicaid beneficiaries (11.6 percent). [124]

Research finds a number of factors associated with non-adherence due to cost of medication. An analysis of the NHIS using data from 2013–2018 found that cost-related medication non-adherence among adults with diabetes was associated with financial hardship due to medical bills, having no health insurance,

[*] Adherence is driven by multiple factors, including sociodemographic factors, medication-specific factors such as medication cost, medication use complexity (inhalers vs pills), regimen complexity (number of medications in therapy regimen), access to health care, and patient-specific factors such as health literacy, fear of side effects/injections, psychosocial factors, cognitive baseline, pill/dose fatigue, income, and insurance status.

being low income, having multiple comorbidities, or being female, regardless of age. However, compared to those younger than 65 years old, those 65 or older had higher odds of cost-related medication non-adherence if they were uninsured, had a longer diabetes duration, or had other health factors or risk factors (for example, hypertension, hypercholesterolemia, and smoking).[125] In another NHIS analysis of commercially insured adults with diabetes, adults with high-deductible health insurance plans reported cost-related medication nonadherence and had more skipped or delayed diabetes medication refills and lower doses compared to adults with other health insurance plans.[126]

As evidenced above, affordability of medications in general, and for insulin specifically, remains a particularly important concern for patients with diabetes. When out-of-pocket costs are high, patients may be more likely to forego insulin, which can exacerbate the rates of uncontrolled diabetes and the subsequent complications.

IV. The Relationship Between Insulin Adherence and Affordability

Rising out-of-pocket costs for insulin may lead to challenges affording insulin, and in turn, affect insulin adherence.[127] In addition to out-of-pocket costs associated with insulin, rising housing and food prices may also affect insulin adherence. Over the past year, housing and rental prices have increased about 18 percent and food prices have increased 11 percent in the past year.[128,129,130] These increases may have implications for insulin use and medication adherence in several ways. First, the affordability of insulin is related to having adequate housing and food security, which is a major priority for multiple federal agencies, including HHS and the US Department of Agriculture (USDA).[131] Because insulin is a biologic medication, it requires special storage in a cool environment (i.e., refrigerator) to ensure the medication's molecular quality is upheld. Patients experiencing housing instability, housing inadequacy, or challenges paying utilities, may struggle to ensure their medication quality is not compromised.[*] [132] Second, patients taking insulin have specific dietary needs, and many insulin regimens require following specific food intake requirements – most notably consistent intake every day, without large fluctuations in timing or quantities of food.[133] Food insecurity is defined as limited or uncertain access to enough food for an active, healthy life, and it is associated with harmful health consequences for patients with diabetes.[134,135]

Previous research found 19 percent of nonelderly adult insulin users were food insecure.[136] To further explore this issue, we used Medical Expenditure Panel Survey (MEPS) data to examine the level of food security for all adults, including the elderly, and identify differences in food security between all adults and insulin users (Table 5-1). The MEPS survey instrument and our analysis follow the constructs developed by the U.S. Department of Agriculture, Economic Research Service, which defines food security as "access by all people at all times to enough food for an active, healthy life."[137] Based on the number of survey responses indicating lack of such access, households are characterized as food-secure or food-insecure. Those who are food-secure are further characterized as having high or moderate food security, while the food-insecure are characterized as having low or very low food security.

[*] Housing inadequacy includes physical inadequacies related to plumbing, heating, electricity, and upkeep. Source: Department of Housing and Urban Development.

On average in 2016-17,[*] 77.2 percent of adult insulin users had "high" food security, compared to 85.6 percent of adults overall. The share of adult insulin users with "low" or "very low" food security was higher than for adults overall: 9.8 percent of insulin users had "low" food security compared to 5.8 percent of all adults, and 4.2 percent of insulin users had "very low" food security compared to 2.6 percent of all adults.

The prevalence of food security differed by insurance status. Among insulin users, 83.4 percent of the privately insured had "high" food security, while less than half of Medicaid beneficiaries had "high" food security. Among Medicaid beneficiaries who used insulin, 11.4 percent had "very low" food security, more than double the rate among all insulin users, 4.2 percent. These disparities in food security across insurance groups likely reflect differences in income and other social factors discussed earlier.

Table 5-1. Food Security among All Adults and Adult Insulin Users, by Type of Coverage

Type of Coverage	High		Moderate		Low		Very Low	
All Adults								
Overall	85.5%		6.0%		5.8%		2.6%	
Private	90.2%	**	4.7%	**	3.8%	**	1.3%	**
Medicare	87.5%	**	4.9%	**	5.0%	*	2.7%	
Medicaid	64.2%	**	12.6%	**	15.6%	**	7.6%	**
Uninsured	72.0%	**	11.3%	**	11.3%	**	5.5%	**
Adult Insulin Users								
Overall	77.2%	††	8.8%	††	9.8%	††	4.2%	††
Private	83.4%	**††	6.8%		6.8%	†	3.1%	†
Medicare	79.5%	††	8.2%	††	8.8%	††	3.5%	
Medicaid	47.6%	**††	16.4%	*	24.6%	**†	11.4%	*
Uninsured	62.8%		17.9%		11.7%	[a]		[b]

Source: Annual average estimates from the Medical Expenditure Panel Survey, 2016-2017 for adults ages 18 and older in the civilian noninstitutionalized population.

Notes: Food security based on a validated instrument developed by the U.S. Department of Agriculture. See Note in Table 4-1 for an explanation of the insurance categories. "All Adults," "Adults with Diagnosed Diabetes," and "Insulin Users" also include adults who had insurance through other government programs.

* Statistically significantly different from overall at the .05 level.

** Statistically significantly different from overall at the .01 level.

† Statistically significantly different from all adults with the same insurance status or overall at the .05 level.

†† Statistically significantly different from all adults with the same insurance status or overall at the .01 level.

[a] Estimates are imprecise due to small sample sizes.

[b] Estimates are not shown due to imprecision arising from small sample sizes.

[*] The MEPS Food Security questionnaire was not administered in 2018 or 2019. The 2020 MEPS Food Security data were released in September 2022, and could not be incorporated into this Report.

The findings presented above used data from 2016 and 2017 to examine rates of food security among insulin users relative to the general population of adults. The recent increase in prices for food and may further exacerbate food insecurity and housing instability and inadequacy. For people who struggle to afford basic living expenses, patients may miss doses of their diabetes therapy to afford other basic living expenses such as housing and food.

Chapter 6. Downstream Impacts of Serious Diabetes-Related Complications on Health Care Use

Uncontrolled diabetes (i.e., long-term high blood sugar levels) results in severe health complications and increased health care spending and use. Diabetes-related complications can arise due to medication nonadherence as well as other factors that reduce the body's ability to control blood sugar such as infection, obesity, and inflammation. For patients that require insulin to manage diabetes, the risk of complications is particularly serious because insulin regimens help manage large fluctuations in one's blood glucose and require careful attention to prescribed dose, timing, and nutrition. If insulin is not taken as prescribed, there is an increased risk of acute complications (e.g., diabetic ketoacidosis).[*] Acute complications often present as medical emergencies, requiring emergency room visits and inpatient care.

In previous chapters, we described how out-of-pocket spending is linked to adherence to insulin regimens, which, in turn is linked to the ability to afford insulin. We also noted that adherence rates vary widely and are particularly concerning for underserved populations. In this chapter, we focus specifically on health care use that occurs as a result of diabetes-related complications, which can occur when patients are unable to adhere to prescribed medications, including insulin.

Key findings from this chapter include:

- In 2019, there were 8.7 million hospitalizations related to diabetes overall. About 71 percent were a result of the patient going to the emergency department. Ten percent of the 8.7 million hospitalizations had a principal diagnosis of diabetes.
- On average, the length of a hospital stay for diabetes was nearly five days. Among the hospitalizations for diabetes with selected complications, hospitalizations for diabetes with end stage renal disease (ESRD) had the longest length of stay (7.4 days) and the hospitalizations for diabetes with ketoacidosis had the shortest length of stay (3.3 days). The average cost for a hospitalization ranged from a low of $8,426 for diabetes ketoacidosis to a high of $23,359 for ESRD.
- About 83 percent of hospitalizations occurred among patients living in communities in the bottom 50 percent of U.S. income, measured using median household income of the patient's zip code, underscoring the need for affordable access to treatment for diabetes.
- We also examined potentially avoidable hospitalization costs for Medicare and Medicaid beneficiaries with diabetes, specifically examining the costs for patients with amputations and ketoacidosis. Among Medicare in 2020, total costs were $3.8 billion for amputations, $5.6 billion for ketoacidosis, and another $1.0 billion for patients with both. Medicare paid more than 90 percent of overall costs, covering $3.5 billion for amputations, $5.2 billion for ketoacidosis, and $936 million for hospitalizations involving both.

[*] The impacts of chronically high blood sugar also carry damaging long-term impacts such as end-organ damage (kidneys, eyes, nervous system, and cardiovascular system).

- Total costs in 2020 for Medicaid beneficiaries (shared between the federal government and the states) were $370 million for amputations and $1.3 billion for ketoacidosis. Overall average spending per hospitalized beneficiary was $14,448 for amputations and $19,437 for ketoacidosis.
- Although we cannot attribute these potentially avoidable hospitalizations only to insulin affordability problems, the potential reduction in hospitalizations from diabetes-related complications from improved insulin affordability suggests that some of the costs of improving insulin affordability could be offset by reducing the $11.3 billion in annual government costs from these hospitalizations. These government costs include $9.6 billion in Medicare, all borne by the federal government, and $1.7 billion in Medicaid, shared between the federal government and the states according to the applicable Federal Medical Assistance Percentage (FMAP). Additional costs for these potentially avoidable hospitalizations fall on patients and third parties.

I. Diabetes Progression to Severe Illness

The downstream impacts of poor diabetes management include acute emergencies such as diabetic ketoacidosis and hyperosmolar hyperglycemic syndrome, as well as chronic organ damage that can progress to end stage renal disease (ESRD), chronic kidney disease (CKD), diabetes-associated eye disease, heart disease, and stroke. In addition, diabetes can exacerbate the treatment of individuals with some of the most common hospital conditions including septicemia, bacterial infections, HIV infection, hepatitis, and viral infections. Table 6-1 presents a brief description of the main complications of poorly managed diabetes.

Table 6-1. Severe Health Conditions Related to Poorly Managed Diabetes

Condition	Description
Diabetic ketoacidosis (DKA)	Ketoacidosis occurs when the body does not have enough insulin to use glucose, the body's normal source of energy.[138] While rare, it can produce life-threatening metabolic disturbances that can also lead to coma and death.
Hyperosmolar Hyperglycemic Syndrome (HHS)	HHS occurs when the blood becomes overly concentrated (hyper-osmolar) due to an extreme amount of sugar building up in one's blood (over 600mg/dL). This is a complication that occurs in individuals with type 2 diabetes and presents similar to DKA. Patients are at risk for severe dehydration, coma, death, and life-threatening metabolic disturbances.[139]
Chronic hyperglycemia or high blood sugar	Chronic hyperglycemia can lead to serious health problems in the acute setting if blood sugars are extremely high, and in the chronic setting, if high for long stretches of time.[140]
Chronic kidney disease (CKD)	Chronic elevated blood sugars lead to damage and inflammation in the kidneys and deterioration of function (diabetic nephropathy).[141] Regular urine testing for protein and blood monitoring of kidney function are tests for diabetes-related kidney disease.
End-stage renal disease (ESRD)	This is the final stage of CKD in which the kidneys fail and require dialysis treatment or kidney transplantation.[142] This is also a qualifying event for Medicare coverage, regardless of age or disability status.
Diabetic eye-disease (diabetic retinopathy)	Uncontrolled diabetes damages the retina, which is one of the most common causes of impaired vision and vision loss including blindness. Annual eye exams are a requirement for many patients with diabetes.[143]
Diabetic nerve disease (diabetic neuropathy)	Diabetes can lead to long-term and irreversible nerve damage, causing significant pain and functional limitations in distal extremities – most often in the feet and legs. Combined with the blood vessel and immunocompromising effects of diabetes, foot wounds can be damaged and go unnoticed, progressing to life-threatening infections that sometimes may require drastic treatments such as amputation to prevent septic shock. Regular foot examinations are an important aspect of diabetes care.[144]

Note: Table presents severe health conditions related to uncontrolled diabetes but does not include all severe health conditions associated with uncontrolled diabetes (e.g., heart attack and stroke).

II. Hospitalizations Related to Diabetes

Using the 2019 data from the Agency for Healthcare Research and Quality's Healthcare Cost and Utilization Project (HCUP) National Inpatient Sample (NIS), we examined in-patient health care use for patients with diabetes, including the number of hospitalizations, emergency room visits, lengths of stay, and patient level characteristics, overall and by four types of diabetes-related complications (diabetes with ketoacidosis, diabetes with hyperglycemia, diabetes with CKD, diabetes with ESRD) to better understand who is affected and how they are affected.

Hospital and Emergency Department Use by Health-Related Characteristics

Analysis of the HCUP NIS shows that in 2019, there were a total of 8,754,675 hospital discharges for individuals with a diabetes diagnosis. Consistent with existing literature, among these diabetes-related hospitalizations, 91.1 percent were related to type 2 diabetes compared to 4.6 percent related to type 1 diabetes and 3.5 percent related to gestational diabetes. The majority of diabetes-related hospitalizations (71.1 percent) were admitted through the Emergency Department (ED), suggesting that the patient experienced an acute event requiring immediate medical attention.

Table 6-2 presents information about hospitalizations where diabetes was the principal reason for hospitalization, which is a subset of all diabetes-related hospitalizations, about 10 percent of the 8.8 million discharges for individuals with a diabetes diagnosis. We focus on this population because principal diagnoses of diabetes mean diabetes was the main disease responsible for admission. Results indicate that a high proportion of patients (67.9 percent) were admitted through the ED, with a greater proportion of ED admissions occurring among patients who had diabetes with ketoacidosis (88.9 percent), hyperglycemia (81.0 percent), CKD (76.7 percent) and the lowest among those with ESRD (71.9 percent).

On average, patients hospitalized for diabetes spent nearly five days in the hospital, with the longest length of stay for patients who had ESRD (7.4 days). The shortest length of stay, among patients with diabetes and one of the four diabetes-related complications examined, was 3.3 days for those who had diabetes with ketoacidosis. The average cost for inpatient hospitalization ranged from a low of $8,426 for diabetes ketoacidosis to a high of $23,359 for ESRD, which is higher than the average cost of a hospitalization (about $13,434*) in the United States. In hospital mortality was lowest for diabetes with hyperglycemia (0.4 percent) and highest for ESRD (1.9 percent).[145]

With more severe diabetes complications, hospital and ED costs increase and the likelihood that a primary expected payer is Medicare increases. Across all diabetes-related complications, Medicare is the expected payer for about 35.9 hospitalizations, followed by Medicaid and private insurers, which had roughly similar shares (about 27 percent), and the lowest among those who are self-pay (7.2 percent).

* Estimated using HCUPnet using the 2019 NIS.

Table 6-2. Characteristics for Hospitalizations for a Principal Diagnosis of Diabetes and Select Diabetes-Related Complications, 2019

	Cases with Principal Diagnosis Diabetes	Diabetes with Ketoacidosis	Diabetes with Hyperglycemia	Diabetes with CKD	Diabetes with ESRD
Hospitalizations, Patient Characteristics and Outcomes					
# Hospitalizations	853,880	235,830	228,165	223,255	65,840
% Admitted through ED	67.9	88.9	81.0	76.7	71.9
Race/ Ethnicity of Patient					
% Hispanic	15.8	12.6	16.4	14.3	19.7
% White, non-Hispanic	52.9	54.6	51.7	50.6	36.3
% Black, non-Hispanic	21.7	25.7	24.2	27.7	35.2
% Asian or Pacific Islander, non-Hispanic	3.3	1.2	1.7	2.2	3.2
% Other, non-Hispanic	4.2	3.6	4.2	3.5	4.2
Sex					
% Male	47.2	51.2	57.5	59.3	57.8
% Female	52.8	48.8	42.4	40.7	42.2
Age, in years					
% 0-17	3.6	9.7	3.0	0.1	0.0
% 18-44	39.3	52.6	23.2	13.5	19.2
% 45-64	31.4	27.3	45.2	39.5	45.9
% 65 and older	25.7	10.4	28.6	47.0	34.8
Average Length of Stay, days	4.5	3.3	5.4	6.5	7.4
Average cost per hospitalization, $	11,440	8,426	13,132	17,231	23,259
In-hospital mortality, per 100 discharges	0.52	0.44	0.37	1.23	1.89
% in Urban Hospital	90.0	89.0	91.1	92.1	95.3
Hospital Ownership					
% Private, not-for-profit	72.8	73.5	70.8	74.0	73.0
% Private, for-profit	14.9	13.6	16.4	14.7	14.8
% Public	12.3	12.9	12.8	11.3	12.1
% Teaching Hospital	75.7	73.8	75.4	77.1	80.9
Primary Expected Payer					
% Medicare	35.9	20.6	42.5	65.7	72.5
% Medicaid	27.1	35.9	25.0	14.8	13.3
% Private Insurance	27.2	27.9	21.1	14.4	11.6
% Self-pay / No Charge	7.2	12.4	8.9	3.3	1.2
% Other payers	2.5	3.1	2.4	1.8	1.2

Source: Agency for Healthcare Research and Quality (AHRQ), Healthcare Cost and Utilization Project (HCUP), National Inpatient Sample (NIS), 2019.

Abbreviations: CKD, chronic kidney disease; ESRD, end stage renal disease

Notes: Cases with Principal Diagnosis of Diabetes include all cases hospitalized for diabetes, including but not limited to those with ketoacidosis, hyperglycemia, chronic kidney disease, and ESRD. Other, non-Hispanic category includes Native American, Alaskan Native, and mixed-race patients. Other expected payers include Federal and local government programs (e.g., TRICARE, Indian Health Service, Black Lung, Title V) and Worker's Compensation. Patient race/ethnicity was missing for about 2 percent of hospitalizations. All other categories had less than <0.1% missing information. Total hospital charges were converted to costs using HCUP Cost-to-Charge Ratios[146] based on hospital accounting reports from the Centers for Medicare & Medicaid Services (CMS). Costs reflect the actual expenses incurred in the production of hospital services, such as wages, supplies and utility costs.[147]

Hospital and Emergency Department Use by Insurance Coverage and Demographic Characteristics

Table 6-2 also shows differences in hospitalization characteristics for patients with diabetes as a principal diagnosis by demographic characteristics. The majority of individuals hospitalized for diabetes were adults, with 39.3 percent of hospitalizations for patients between ages 18-44, 31.4 percent for ages 45 – 64, and 25.7 percent for ages 65 and older.

The majority of patients hospitalized for diabetes were non-Hispanic White individuals (52.9 percent), followed by non-Hispanic Black individuals (21.7 percent), and Hispanic individuals (15.8 percent). Non-Hispanic Asian or Pacific Islander individuals, and other non-Hispanic (including American Indian and Alaska Native) individuals comprised 3.3 percent and 4.2 percent of hospitalizations for diabetes, respectively.

We also examined diabetes-related hospitalizations by U.S. income distribution (not shown in Table 6-2). Income distribution was calculated using the-median household income of the patient's zip code of residence.[*] Estimates show that hospitalizations for diabetes were disproportionately more likely to be for individuals who live in communities in the bottom half of the U.S. income distribution: 35.4 percent of hospitalizations occurred for patients from the lowest quartile and 47.8 percent of hospitalizations occurred for patients in the second lowest quartile. Taken together, 83 percent of hospitalizations occurred among beneficiaries living in communities in the bottom 50 percent of U.S. income distribution. Diabetes-related hospitalizations were most likely to be for individuals who live in either a large central/fringe metropolitan area, 53.8 percent, or a medium or small metropolitan area, 30.3 percent. Only 15.2 percent of these hospitalizations were for individuals who lived in rural areas. However, 90.9 percent of the cases were treated in hospitals in urban areas.

Preventable Diabetes Complications

In addition to the diabetes-related disease progression, there are several measures of preventable diabetes complications, as specified by the Agency for Healthcare Research and Quality (AHRQ) Prevention and Pediatric Quality Indicators (PQI/PDI).[148] If diabetes is well controlled and patients are regularly seeing their providers for appropriate management and care, these serious preventable disease complications should not happen. These include uncontrolled diabetes and in severe cases, lower-

[*] Quartiles are defined so that the total U.S. population is evenly distributed. Cut-offs for the quartiles are determined annually using ZIP Code demographic data obtained from Claritas, a vendor that produces population estimates and projections based on data from the U.S. Census Bureau. The value ranges for the income quartiles vary by year. The income quartile is missing for patients who are homeless or foreign or have a missing or invalid ZIP Code reported on the record.

extremity amputations. Uncontrolled diabetes is defined as high blood sugar, and it is identified as a diagnosis by the physician.

Our analysis shows that uncontrolled diabetes occurred in 108,165 adult hospitalizations, 1.2 percent of all diabetes-related hospitalizations (see Table 6-3). The majority of these hospitalizations occurred among adults with Type 2 diabetes, 86.6 percent. The most common diabetes complications evident among these hospitalizations were hyperglycemia (61.9 percent) and chronic kidney disease (38.1 percent). While the majority of uncontrolled diabetes hospitalizations were for non-Hispanic White patients (50.7 percent), there were also a considerable number of hospitalizations for non-Hispanic Black patients (28.2 percent) and Hispanic patients (13.6 percent). Similar to hospitalizations for diabetes with long-term complications, 38.1 percent of hospitalizations were for adults who resided in communities in the bottom income quartile, compared to just 13.9 percent in the top income quartile. Finally, more than half of these hospitalizations were expected to be billed to Medicare (57.8 percent), followed by Medicaid (17.9 percent), private insurance (14.8 percent), and billed as self-pay/no charge (7.2 percent). The average cost of the hospitalization was $7,654 with an average length of stay of 3.5 days.

One important and severe diabetes complication is a lower extremity amputation, which occurred in 87,270 adult hospitalizations in 2019, 1.0 percent of all adult diabetes-related hospitalizations, based on our analysis (see Table 6-3). The vast majority of these individuals had Type 2 diabetes, 94.7 percent. In addition to the lower-extremity amputation, these hospitalizations were related to bacterial infections (51.7 percent), chronic kidney disease (47.9 percent), hyperglycemia, (37.7 percent), septicemia (27.7 percent), and ESRD (18.2 percent). The majority of hospitalizations for diabetes with lower-extremity amputation were for non-Hispanic White patients (55.8 percent), followed non-Hispanic Black patients (21.8 percent), and Hispanic patients (15.6 percent). Thirty eight percent of these hospitalizations were for adults from the lowest income areas in the United States. Among these hospitalizations, the primary expected payer was Medicare in 57.6 percent of hospitalizations, Medicaid in 16.7 percent of hospitalizations, private insurance in 18.6 percent of hospitalizations, and self-pay/no charge in 5.1 percent of hospitalizations. The average cost of the hospitalization was $30,032 with an average length of stay of 11.4 days.

Table 6-3. Characteristics of Hospitalizations for Uncontrolled Diabetes and Lower-Extremity Amputation, 2019

	Uncontrolled diabetes among adults (PQI14)		Lower-extremity amputation among adults with diabetes (PQI16)	
	Number of Discharges	% of Discharges	Number of Discharges	% of Discharges
Total number of discharges	108,165	-	87,270	-
Admitted through the ED	100,950	93.3	59,940	68.7
Type of diabetes and Comorbidities				
Type 1 diabetes	14,720	13.6	4,640	5.3
Type 2 diabetes	93,690	86.6	82,685	94.7
Ketoacidosis	635	0.6	2,240	2.6
ESRD	9,085	8.4	15,875	18.2
Chronic kidney disease	41,260	38.1	41,840	47.9
Hyperglycemia	66,945	61.9	32,910	37.7
Patient Race and ethnicity				
White, non-Hispanic	54,790	50.7	48,670	55.8
Black, non-Hispanic	30,515	28.2	19,035	21.8
Hispanic	14,660	13.6	13,625	15.6
Asian or Pacific Islander, Non-Hispanic	2,575	2.4	1,315	1.5
Other non-Hispanic, including Native American/Alaskan Native	3,745	3.5	3,190	3.7
Patient Sex				
Male	55,435	51.3	62,785	71.9
Female	52,730	48.7	24,485	28.1
Patient Age, in years				
18-44	18,665	17.3	7,570	8.7
45-64	38,245	35.4	43,905	50.3
65 and older	51,255	47.4	35,795	41.0
Community-level income of the Patient's Residence				
First quartile (lowest income)	41,195	38.1	33,300	38.2
Middle quartiles	49,680	45.9	41,330	47.4
Fourth quartile (highest income)	15,035	13.9	11,135	12.8
Location of hospital				
Rural	11,400	10.5	6,410	7.3
Urban	96,765	89.5	80,860	92.7
Hospital ownership				

Private, not-for-profit	74,970	69.3	64,540	74.0
Private, for-profit	20,450	18.9	11,955	13.7
Public	12,745	11.8	10,775	12.3
Primary Expected Payer				
Medicare	62,495	57.8	50,225	57.6
Medicaid	19,380	17.9	14,540	16.7
Private	15,995	14.8	16,205	18.6
Self-pay/No charge	7,815	7.2	4,415	5.1
Other	2,365	2.2	1,815	2.1

Source: Agency for Healthcare Research and Quality (AHRQ), Prevention and Quality Indicators.

Abbreviation: PQI, Prevention Quality Indicator

Note: Other race and ethnicity includes mixed race and non-Hispanic Native American and Alaskan Native patients. Other primary expected payer includes other Federal and local government programs (e.g., TRICARE, Indian Health Service, Black Lung, Title V) and Workers' Compensation. About 2 percent of discharges are missing information on patient race and ethnicity and patient community-level income; less than 0.1 percent of discharges are missing information on the primary expected payer.

III. Potentially Avoidable Hospitalizations Related to Amputations and Ketoacidosis for Medicare Beneficiaries with Diabetes

We also analyzed CMS Medicare and Medicaid data, which provides more information on potentially avoidable hospitalization costs for patients with diabetes. Potentially avoidable hospitalizations are those that could have been avoided because the condition could have been prevented or managed in an outpatient setting. For diabetes, this includes beneficiaries who experience amputations and ketoacidosis. If patients have adequate access to treatments (e.g., insulin) to maintain good blood sugar control and see providers for regular check-ups, these severe complications (e.g., ketoacidosis and amputations) are largely avoidable.

Table 6-4 shows the number of beneficiaries hospitalized with amputations, ketoacidosis, and both as shown on Medicare Part A claims and the associated costs by type of diabetes and payer. Overall, about 83,000 patients were hospitalized with amputations, 148,000 with ketoacidosis, and 52,000 with both shown on their claims. Total costs were $3.8 billion for amputations, $5.6 billion for ketoacidosis, and another $1.0 billion for patients with both. Medicare paid more than 90 percent of overall costs, covering $3.5 billion for amputations, $5.2 billion for ketoacidosis, and $936 million for hospitalizations involving both. More than 90 percent of the beneficiaries and costs in each category were for patients with type 2 diabetes.

Table 6-4. Medicare Hospitalizations for Amputations and Ketoacidosis, Among Beneficiaries with Diabetes, by Type of Diabetes and Payer, 2020

Type of Diabetes	Number of Beneficiaries	Medicare Payment (in millions)	Third Party Payment (in millions)	Patient Payment (in millions)	Total Payment (in millions)
Amputation					
All	82,872	$3,535.0	$204.3	$100.6	$3,839.9
Type 1	3,008	$133.8	$8.0	$8.6	$150.3
Type 2	78,479	$3,349.3	$193.4	$90.9	$3,633.6
Gestational/Other	1,385	$51.9	$3.0	$1.1	$56.0
Ketoacidosis					
All	148,070	$5,158.5	$290.0	$195.9	$5,644.5
Type 1	3,011	$128.6	$7.4	$7.8	$143.8
Type 2	142,884	$4,961.0	$278.8	$184.8	$5,424.5
Gestational/Other	2,175	$69.0	$3.9	$3.3	$76.2
Both Amputation and Ketoacidosis					
All	52,239	$936.9	$50.7	$33.0	$1,020.6
Type 1	1,801	$32.3	$2.0	$2.1	$36.4
Type 2	49,898	$896.9	$48.2	$30.6	$975.7
Gestational/Other	540	$7.7	$0.5	$0.3	$8.5
Total	283,181	$9,630.40	$545.00	$329.50	$10,505.00

Source: ASPE analysis of CMS 2020 Medicare data. Amputations and ketoacidosis identified on Part A in-patient hospital claims. Diabetes diagnosis and type identified on Part A or Part B claims.

Costs per hospitalized Medicare beneficiary are shown in Table 6-5. Medicare paid about 92 percent of average total cost per hospitalized beneficiary for an amputation ($42,657 of $46,336), 91 percent of average total cost per hospitalized beneficiary for ketoacidosis ($34,830 of $38,121), and 92 percent for hospitalized beneficiaries whose claims showed both an amputation and ketoacidosis ($17,935 of $19,537)

Hospitalization costs for amputations and for ketoacidosis were highest for beneficiaries with type 1 diabetes than for beneficiaries with other types of diabetes, but hospitalization costs involving both were highest for beneficiaries with type 2 diabetes. Costs for gestational or other types of diabetes (not type 1 or type 2) were lowest for all three categories of hospitalizations. It is important to note that these estimates for Type 1 diabetes underestimate spending on amputations and ketoacidosis as a share of total costs because a higher share of Type I diabetes occurs among people who are younger and more likely to have Medicaid or private insurance.

Table 6-5. Costs per Beneficiary of Medicare Hospitalizations for Amputations and Ketoacidosis, Among Beneficiaries with Diabetes, by Type of Diabetes and Payer, 2020

Type of Diabetes	Number of Beneficiaries	Medicare	Third Party	Patient	Total
	Amputation				
All	82,872	$42,657	$2,466	$1,214	$46,336
Type 1	3,008	$44,467	$2,646	$2,855	$49,968
Type 2	78,479	$42,678	$2,464	$1,158	$46,300
Gestational/Other	1,385	$37,507	$2,154	$797	$40,458
	Ketoacidosis				
All	148,070	$34,839	$1,959	$1,323	$38,121
Type 1	3,011	$42,695	$2,454	$2,595	$47,745
Type 2	142,884	$34,720	$1,951	$1,293	$37,965
Gestational/Other	2,175	$31,731	$1,776	$1,531	$35,039
	Both Amputation and Ketoacidosis				
All	52,239	$17,935	$970	$632	$19,537
Type 1	1,801	$17,923	$1,111	$1,175	$20,209
Type 2	49,898	$17,975	$965	$612	$19,553
Gestational/Other	540	$14,285	$919	$618	$15,823
Total	283,181	$34,008	$1,925	$1,164	$37,097

Source: ASPE analysis of CMS 2020 Medicare data. Amputations and ketoacidosis identified on Part A in-patient hospital claims. Diabetes diagnosis and type identified on Part A or Part B claims.

IV. Potentially Avoidable Hospitalizations Related to Amputations and Ketoacidosis for Medicaid Beneficiaries

We used Transformed Medicaid Statistical Information System (T-MSIS) claims data to examine hospitalizations for Medicaid patients with diabetes because these data provide additional detail on federal costs that could potentially be avoided through improved insulin affordability and adherence. Table 6-6 shows beneficiaries and costs for amputations and ketoacidosis by type of diabetes. Total costs in 2020, shared between the federal government and the states according to the applicable Federal Medical Assistance Percentage (FMAP), were $370 million for amputations and $1.3 billion for ketoacidosis. Overall average spending per hospitalized beneficiary was $14,448 for amputations and $19,437 for ketoacidosis. Patients with type 2 diabetes account for over 90 percent of beneficiaries and costs for both kinds of hospitalizations; they also have the highest cost per beneficiary. Patients with gestational diabetes had lower costs for each type of hospitalization. Across both amputations and ketoacidosis, about 92,000 beneficiaries experienced these conditions, and this translated to $1.7 million in total spending and an average spending of beneficiary of about $18,000. These estimates only capture a subset of a broader set of complications for diabetes so actual costs are higher than shown in Table 6-5.

Table 6-6. Medicaid Hospitalizations for Amputations and Ketoacidosis, Among Beneficiaries with Diabetes, by Type of Diabetes

Amputation			
Type of Diabetes	**Number of Beneficiaries**	**Total Spending**	**Spending Per Beneficiary**
All	25,613	$370,058,046	$14,448
Gestational	23	$108,057	$4,698
Other	876	$6,723,069	$7,675
Type 1	1,275	$14,206,723	$11,143
Type 2	23,439	$349,020,197	$14,891
Ketoacidosis			
Type of Diabetes	**Number of Beneficiaries**	**Total Spending**	**Spending Per Beneficiary**
All	66,127	$1,285,312,759	$19,437
Gestational[a]	14	[a]	[a]
Other	1,312	$17,013,641	$12,968
Type 1	2,754	$48,320,553	$17,546
Type 2	62,047	$1,219,882,813	$19,661
Total[b]	91,740	$1,655,370,805	$18,044.16

Source: ASPE analysis of 2020 CMS Transformed Medicaid Statistical Information System (T-MSIS) data.

Note: Totals include Puerto Rico, Virgin Islands, and Pennsylvania CHIP. If beneficiaries experienced both conditions, the total represents both encounters as separate events.

[a]: Gestational diabetes estimates are included in total number of amputations but total spending condition and spending per beneficiary estimates are not shown due to sample sizes less than 15 cases.

[b]: Total may not add due to inclusion of gestational diabetes spending. Spending estimates for gestational diabetes for ketoacidosis are not reported due to low sample sizes.

Table 6-7 shows the same T-MSIS data by state. Spending per hospitalized beneficiary for amputations ranged from $3,714 in Alabama to $61,786 in New York. Spending per hospitalized beneficiary for ketoacidosis ranged from $3,574 in Arkansas to $88,574 in New York. New York spending per hospitalized beneficiary was more than four times the national figure for each type of hospitalization. Oregon spending per hospitalized beneficiary ranked second highest for each category.

Table 6-7. Medicaid Hospitalizations for Amputations and Ketoacidosis, Among Beneficiaries with Diabetes, by State

	Amputation			Ketoacidosis		
State	Number of Beneficiaries	Total Spending	Spending Per Beneficiary	Number of Beneficiaries	Total Spending	Spending Per Beneficiary
All*	25,613	$370,058,046	$14,448	66,127	$1,285,312,759	$19,437
Alabama	160	$594,236	$3,714	411	$2,288,925	$5,569
Alaska	26	$588,157	$22,621	107	$1,986,123	$18,562
Arizona	790	$7,565,644	$9,577	2,107	$23,788,550	$11,290
Arkansas	432	$1,723,829	$3,990	679	$2,426,551	$3,574
California	3,585	$54,723,969	$15,265	8,826	$153,902,702	$17,437
Colorado	338	$2,833,776	$8,384	755	$9,256,616	$12,260
Connecticut	470	$5,025,902	$10,693	1,120	$12,452,569	$11,118
Delaware	64	$655,131	$10,236	159	$2,703,143	$17,001
District of Columbia	106	$2,297,294	$21,673	296	$5,865,710	$19,817
Florida	1,540	$9,234,639	$5,997	3,653	$26,126,780	$7,152
Georgia	785	$7,821,685	$9,964	1,645	$18,742,785	$11,394
Hawaii	127	$1,153,283	$9,081	445	$7,630,759	$17,148
Idaho	134	$641,347	$4,786	368	$3,080,012	$8,370
Illinois	340	$2,010,855	$5,914	1,471	$11,082,394	$7,534
Indiana	653	$6,952,932	$10,648	1,272	$15,441,882	$12,140
Iowa	241	$1,757,912	$7,294	628	$6,466,953	$10,298
Kansas	378	$4,114,916	$10,886	416	$4,931,587	$11,855
Kentucky	505	$4,118,957	$8,156	1,313	$13,512,833	$10,292
Louisiana	744	$6,064,653	$8,151	1,596	$14,814,292	$9,282
Maine	180	$918,357	$5,102	466	$3,028,117	$6,498
Maryland	365	$5,579,615	$15,287	1,000	$18,436,835	$18,437
Massachusetts	639	$4,847,816	$7,587	1,795	$16,930,243	$9,432
Michigan	427	$4,232,746	$9,913	1,504	$17,417,194	$11,581
Minnesota	492	$5,501,481	$11,182	1,197	$15,184,086	$12,685
Mississippi	442	$2,852,727	$6,454	801	$5,056,158	$6,312
Missouri	193	$1,818,440	$9,422	796	$4,402,275	$5,530
Montana	78	$690,039	$8,847	250	$2,124,719	$8,499
Nebraska	82	$411,107	$5,013	258	$1,626,153	$6,303
Nevada	204	$2,114,742	$10,366	684	$8,466,725	$12,378
New Hampshire	53	$392,835	$7,412	183	$899,932	$4,918
New Jersey	597	$4,755,522	$7,966	1,850	$21,724,741	$11,743
New Mexico	225	$3,656,546	$16,251	605	$11,612,666	$19,194
New York	2,282	$140,995,526	$61,786	6,581	$582,905,689	$88,574
North Carolina	1,052	$5,531,688	$5,258	2,201	$12,441,089	$5,652
North Dakota	83	$1,542,820	$18,588	132	$2,826,860	$21,416
Ohio	287	$1,699,644	$5,922	1,738	$11,912,935	$6,854
Oklahoma	454	$2,842,632	$6,261	880	$6,824,538	$7,755
Oregon	279	$8,478,322	$30,388	991	$48,694,527	$49,137
Pennsylvania	1,597	$17,632,036	$11,041	3,070	$40,336,928	$13,139
Rhode Island	33	$212,088	$6,427	114	$1,005,786	$8,823
South Carolina	370	$4,860,243	$13,136	586	$8,313,466	$14,187
South Dakota	46	$389,112	$8,459	161	$1,462,429	$9,083
Tennessee	524	$2,926,637	$5,585	1,235	$8,372,456	$6,779
Texas	1,629	$12,656,545	$7,770	3,817	$38,000,397	$9,956

Utah	81	$1,272,030	$15,704	230	$3,750,982	$16,309
Vermont	69	$262,950	$3,811	177	$836,518	$4,726
Virginia	357	$3,371,751	$9,445	1,352	$16,718,956	$12,366
Washington	327	$3,797,904	$11,614	1,328	$16,640,420	$12,530
West Virginia	277	$1,688,095	$6,094	862	$7,092,811	$8,228
Wisconsin	195	$1,464,212	$7,509	1,157	$9,594,856	$8,293
Wyoming	42	$276,372	$6,580	61	$389,871	$6,391

Total for Amputation and Ketoacidosis**

Number of beneficiaries: 91,740

Total spending: $1,655,370,805

Spending per beneficiary: $18,044.16

Source: ASPE analysis of 2020 CMS Transformed Medicaid Statistical Information System (T-MSIS) data.

* Includes Puerto Rico, Virgin Islands, and Pennsylvania CHIP, not shown separately.

** Beneficiaries who had both amputation and ketoacidosis, and the associated spending, are counted in both categories.

Chapter 7: Initiatives to Reduce Out-of-Pocket Spending on Insulin

Because out-of-pocket spending on insulin can impact patient adherence and lead to cascading health consequences, federal and state efforts have attempted to mitigate the cost of insulin through various initiatives. In this chapter, we explore existing federal and state initiatives to reduce out-of-pocket spending on insulin. Depending on their timing relative to that of our data, the impacts of some of these initiatives may be reflected in the findings on out-of-pocket insulin costs presented in earlier chapters of this Report.

Key findings from this chapter include:

- Federal initiatives to reduce out-of-pocket spending on insulin include the Inflation Reduction Act (IRA), which caps insulin out-of-pocket spending at $35 per month's supply of each covered insulin product in Medicare, includes provisions that aim to lower out-of-pocket payments for Medicare Part D enrollees, and limits out-of-pocket costs for insulin supplied under Part B. Another initiative – the Part D Senior Savings Model – tests whether an insulin cap of $35 per month would reduce health expenditures and improve health outcomes.
- Estimates suggest that Medicare beneficiaries who use insulin would have saved $734 million in Part D.*
- There are currently 23 states (as of September 2022) that have insulin caps to limit cost sharing for individuals with some employer or individual market health coverage (excluding self-insured plans that are governed under the federal ERISA statute and comprise 64 percent of the employer-sponsored coverage market)—ranging from $25 (3 states) to $100 per 30-day prescription or per month (5 states).
- In addition, there are patient assistance programs; however, it is unclear to what extent these are helpful in improving accessibility to insulin due to complaints that these programs are not transparent about their eligibility requirements, make it hard to apply and renew, and can limit patients to a specific brand and treatment.
- Recently, some insurers, PBMs, and manufacturers have begun capping out-of-pocket monthly expenses for patients with insulin, but it is unclear how widespread this practice is and how it is affecting patients' out-of-pocket spending.

* This is prior to the impact of the Part D Senior Savings Model.

I. Federal Initiatives to Reduce Out-of-Pocket Spending on Insulin for Medicare Patients

Inflation Reduction Act (IRA)

The Inflation Reduction Act includes several provisions that limit out-of-pocket spending on insulin for people with Medicare. We highlight these below:

- Effective January 1, 2023, people enrolled in a Medicare Part D prescription drug plan (PDP) or a Medicare Advantage plan with a prescription drug coverage (MA-PD) have no deductible for covered insulin products and have a per covered insulin product copayment cap of $35 per month supply.[149]
- Effective July 1, 2023, Medicare Part B beneficiaries who use an insulin pump furnished via durable medical equipment will no longer have to pay a deductible for insulin supplied for the pump and have a copayment cap of $35 per month supply for their Part B covered insulin.
- Effective January 1, 2024, one year after the $35 cap, eligibility for the Part D Low-Income Subsidy (LIS)[*] will expand. The IRA raises the income limit for the full LIS from 135 percent of the Federal Poverty Level (FPL) to 150 percent of FPL, which will allow additional Medicare beneficiaries to reduce their out-of-pocket costs for insulin and other medications.

We examined how much people with Medicare Part D and Part B would have saved in out-of-pocket costs if the IRA's out-of-pocket insulin cap had been in effect in 2020. The estimates presented in Table 7-1 suggest that 1.5 million Part D enrollees would have saved $734 million if the IRA insulin provisions had been in effect in 2020, prior to availability of the Medicare Part D Senior Savings Model, which is a Model that tests the effects of capping insulin prices for eligible enrollees implemented under the Centers for Medicare and Medicaid Innovation (Innovation Center).[†][‡]

Most of the savings would have accrued to enrollees who do not qualify for the Low-income Subsidy (LIS), which greatly reduces out-of-pocket costs for Part D enrollees who meet income and resource limits.

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[*] For eligible enrollees whose income and resources are limited, the Medicare Prescription Drug, Improvement and Modernization Act of 2003 established extra help (a subsidy) to pay for prescription drugs. Subsidies are paid by the Federal government to drug plans and provide assistance with premiums, deductibles, and co-payments.

[†] Our estimate of 1.5 million Part D enrollees who would have had lower out-of-pocket costs for insulin if the IRA provisions had been in effect in 2020 is based on the number of Medicare Part D enrollees who spent more than $35 in any month of 2020 on insulin in Part D and Part B combined. This calculation produces a slightly larger number than the CMS estimate of 1.4 million (https://www.cms.gov/newsroom/fact-sheets/inflation-reduction-act-lowers-health-care-costs-millions-americans), which is based on Part D insulin claims only. Either estimate represents a subset of the total number of Medicare enrollees who use insulin, estimated as 3.9 million in Table 4-1 above.

[‡] Estimates do not include the additional effect of LIS expansion, which will be implemented in 2024, one year after the $35 cap is effective.

Table 7-1. Estimated Out-of-Pocket Savings in Medicare Part D If Inflation Reduction Act $35 Out-of-Pocket Insulin Cap Had Been in Effect in 2020

Outcome	Part D Non-LIS	Part D LIS	Part D Total
Total IRA Savings ($ millions)	$723.2	$10.8	$734.0
Number of Insulin Users with Savings	1,477,327	76,503	1,517,871
Average Savings per Insulin User with Savings ($)	$490	$141	$484

Source: ASPE Part D Simulation Model, CMS Medicare Part D 2020 Prescription Drug Event (PDE) and Enrollment data.
Notes: LIS = Low-Income Subsidy. The unduplicated Total Number of Insulin Users with Savings is lower than sum of LIS and non-LIS components because some Part D enrollees change LIS status during the year and are counted in both categories.

Table 7-2 shows the distribution of savings by gender, race, ethnicity, and age, which shows substantial numbers of beneficiaries benefiting from the policy across all demographic groups analyzed. The distribution of savings by gender, race and ethnicity, and age is generally similar across the programs with the following exception: Part D LIS enrollees who benefit from the cap are more likely than Part D non-LIS enrollees to be women, Black, or below the age of 65.*

* The age difference indicates eligibility for Medicare on the basis of disability or End-Stage Renal Disease.

Table 7-2. Demographic Characteristics of Medicare Enrollees with Out-of-Pocket Savings If Inflation Reduction Act Insulin Provisions Had Been in Effect in 2020

	Non-LIS		LIS	
Demographic Characteristics	**(n)**	**%**	**(n)**	**%**
Gender				
Female	708,281	47.9%	43,862	57.3%
Male/Unknown	769,046	52.1%	32,641	42.7%
Race and Ethnicity				
White	1,217,545	82.4%	55,424	72.4%
Black	154,311	10.4%	14,093	18.4%
Latino	25,901	1.8%	3,512	4.6%
Asian	19,795	1.3%	1,146	1.5%
AI/AN	6,705	0.5%	525	0.7%
Other	53,070	3.6%	1,803	2.4%
Age				
< 65	115,104	7.8%	20,366	26.6%
65-69	284,559	19.3%	14,413	18.8%
70-74	420,654	28.5%	15,092	19.7%
75-79	319,859	21.7%	11,566	15.1%
80-84	196,240	13.3%	8,281	10.8%
85-89	95,927	6.5%	4,454	5.8%
>= 90	44,984	3.0%	2,331	3.0%

Source: ASPE Part D Simulation Model, CMS Medicare Part D 2020 Prescription Drug Event (PDE) and Enrollment data.
Notes: Part D LIS = Low-Income Subsidy. Some Part D enrollees who changed LIS status during the year are counted in both categories.

Medicare Part D Senior Savings Model

The Medicare Part D Senior Savings (PDSS) Model, which is implemented under the CMS Innovation Center, is a five-year model that began in 2021, with planned implementation until 2025, to test how an insulin cap of $35 per month would reduce health expenditures and improve health outcomes.[150] The way drug manufacturer discounts are calculated is a disincentive for Medicare drug plans to offer cost-sharing reductions in the coverage gap.[*] Under the Model, supplemental coverage is applied after the manufacturer gap discounts, instead of before the gap discounts. Also, in the first two plan years (2021 and 2022), additional risk-corridor protection is available for plan benefit packages with higher enrollment of patients who use insulin. CMS estimated average savings of $446 in annual out-of-pocket costs for insulin. Federal savings are estimated at $250 million over five years with additional drug discounts.[151] The Model is continuing in 2023, when the IRA insulin provisions will be in effect.[152]

[*] A Medicare beneficiary reaches the Part D drug coverage gap (or doughnut hole) of $4,430 of total drug costs for calendar year 2022. In the coverage gap, Medicare beneficiaries pay up to 25 percent of the drug costs. Beyond the coverage gap ($7,050 for 2022), under the catastrophic coverage, cost-sharing is the higher of $3.95 or 5 percent for generic drugs and $9.85 or 5 percent for brand-name drugs. Without the Part D Savings Model, if a Part D plan or Medicare Advantage plan with Part D benefits reduces cost-sharing in the coverage gap, drug manufacturer discounts are reduced and premiums would increase.

In the first year of the PDSS Model starting January 1, 2021, a total of 1,635 Medicare Advantage plans with drug coverage (MA-PDs) and Medicare Part D prescription drug plans (PDPs) participated in all 50 states, the District of Columbia, and Puerto Rico, with 13.8 million enrollees and an estimated 650,000 insulin users.[153] All of the insulin manufacturers agreed to participate in the model.

About one-third (53 percent) of eligible MA-PDs and 56 percent of eligible PDPs offered the insulin caps in the first two years of the Model (2021 and 2022).[154] In 2021, United and Humana participated relatively more in the model than their share of MA-PDs while Aetna, Centene and Blue Cross Blue Shield plans participated relatively less in the model than their shares of MA-PDs.[155] The average monthly premium was $10 less for MA-PD plans participating in the model than those not participating and $23 more for PDPs participating in the Model than for PDPs not participating. More MA-PD plans participating in the model had a zero-premium compared to non-participating MA-PD plans. Those Medicare beneficiaries who didn't use insulin would have paid the higher PDP premiums if they chose a PDP that participated in the model and raised premiums.[156] MA-PDs participating in the model may experience reduced medical and drug costs with better insulin adherence. PDPs would not benefit from reduced medical costs but could benefit from reduced drug costs with better insulin adherence improving health outcomes.[157]

To build on the Medicare Senior Savings Model and other successful CMS Innovation Center projects, on October 14, 2022, President Biden signed an Executive Order announcing that the CMS Innovation Center would identify additional programs to lower prescription drug costs for Americans; 90 days from the signing of the Executive Order, the Secretary of the U.S. Department of Health & Human Services (HHS) will outline forthcoming models in a report to the White House.

II. State Initiatives to Reduce Out-of-Pocket Spending on Insulin

With the rising cost of insulin and increasing attention to the sometimes-fatal consequences for patients, many states have enacted state insulin caps on out-of-pocket payments and implemented state affordability programs.

State Insulin Caps

State insulin caps limit cost-sharing for individuals with some employer or individual market health coverage, excluding self-insured plans that are governed under the federal ERISA statute and comprise 64 percent of the employer-sponsored coverage market.[158]

There are currently 23 states (as of September 2022) that have insulin caps, ranging from $25 (3 states) to $100 per 30-day prescription or per month. Six states index the amount of the monthly cap. Table 7-3 shows more detail for the states with insulin caps. States have jurisdiction over fully insured private insurance plans that are regulated by the state insurance laws, but states cannot regulate self-insured plans (which represent 64% of privately insured individuals).[159] Only the federal government can place limits on out-of-pocket payments for insulin for all insurance enrollees, including those enrolled in self-insured plans. Additionally, insulin caps reduce out-of-pocket payments for some consumers but do not limit the price of insulin to the insurers, which may increase premiums for private health plans who may face a greater share of the cost of insulin.

Table 7-3. State Insulin Caps

State	Monthly Insulin Cap Per Prescription	Insulin Cap Per Month (Total for all Prescriptions)	Index for Insulin Cap Adjustment	Effective Date
Alabama	$100		CPI – Prescription Drug	October 1, 2021
Colorado		$100[a]		January 1, 2022
Connecticut	$25			January 1, 2022
District of Columbia	$30			January 1, 2022
Delaware		$100		January 1, 2021
Illinois	$100		CPI - Medical Care	January 1, 2021
Kentucky	$30			January 1, 2022
Louisiana	$75		CPI – Prescription Care	January 1, 2023
Maine	$35			June 15, 2021
Maryland	$30		CPI – Medical Care	January 1, 2023
New Hampshire	$30			September 14, 2020
New Mexico	$25			January 1, 2021
New York	$100			January 1, 2021
Oklahoma		$30		November 1, 2021
Oregon	$75		CPI	January 1, 2022
Rhode Island	$40			January 1, 2022
Texas	$25			January 1, 2022
Utah	$30		Average Wholesale Price	January 1, 2021
Vermont		$100		January 1, 2021
Virginia	$50			January 1, 2021
Washington	$100			January 1, 2021
Washington	$35[b]			January 1, 2023
West Virginia	$100			March 7, 2020

[a] Colorado previously had a monthly cap per prescription, effective January 1, 2020.

[b] Washington has a temporary one-year cap of $35, effective January 1, 2023.

Sources: Prescription Drug State Bill Tracking Database 2015-Present. National Conference on State Legislatures and some information from state websites.

Several state Marketplaces eliminated cost sharing for at least some insulin products. Maryland's state Marketplace Value Plans have $0 cost sharing for preferred insulin brands of insulin.[160] The District of Columbia's state Marketplace standard plans eliminated cost sharing for insulin and diabetic supplies starting in 2022, and its Marketplace small group plans will do so starting in 2023.[161] Massachusetts eliminated cost sharing for medication for four select chronic conditions disproportionately affecting communities of color, including medication for diabetes, for its state ConnectorCare Marketplace plans starting in 2023.[162] Tier 1 insulins, which must include at least one of each major type of insulin, are covered with no cost sharing.[163]

Examples of State Insulin Affordability Programs

In addition to out-of-pocket caps, some states have also implemented insulin affordability programs, which we describe below.

Minnesota's Alec Smith* Insulin Affordability Act[164], effective July 1, 2020, is available to state residents with continuing need of insulin who have family income less than 400 percent of the Federal Poverty Level and are not enrolled in Medicaid, Department of Veterans Affairs drug coverage, or are enrolled in health plans (including self-insured plans) with out-of-pocket costs above $75 per month for insulin. Part D enrollees are eligible if total insulin out-of-pocket costs exceed $1,000 per year. The drug manufacturers are required to provide insulin under this program for no more than $50 for a 90-day supply for up to 12 months, with an option to renew annually. Patients can use the drug manufacturers' copay programs, if less expensive. More than 1,100 Minnesotans were enrolled in the Insulin Affordability program in 2021 and used more than $6 million worth of insulin.[165]

The three largest insulin manufacturers are required to participate in the Minnesota Insulin Safety Net Program and accept applications from patients for the program. Eli Lilly provides the insulin through community/outpatient pharmacies and sends replacement insulin or reimburses pharmacies for their acquisition cost. Novo Nordisk and Sanofi ship the insulin directly to patients. The Pharmaceutical Research and Manufacturers of America (PhRMA) filed a lawsuit against the State of Minnesota right before the law took effect arguing that the law violated the Fifth Amendment because it did not reimburse insulin manufacturers.[166] A federal district court judge ruled against PhRMA on March 15, 2021. PhRMA's appeal to the Eighth Circuit is pending.[167]

Connecticut partnered with CVS to start an insulin affordability program[168] in April 2021 offering copays of $25 or $120 for Novo Nordisk insulin products for uninsured and patients with high-deductible plans at participating pharmacies. The copays in this program do not count toward any health plan's deductible or out-of-pocket maximums.

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* The law was named in honor of Alec Smith, a 26-year-old Minnesota man who died in 2017 while rationing insulin he could no longer afford.

Colorado's Insulin Affordability Program,[169] effective January 1, 2022, offers insulin for $50/month up to 12 months for those not eligible or enrolled in Medicaid, Medicare, or a health plan with a monthly insulin cap of $100 or lower. Patients fill out the application form and submit to their pharmacy. The insulin manufacturers are required to replace the insulin given to patients in the program or reimburse the pharmacies the wholesale price.

Washington and Oregon started ArrayRx, a drug discount card program, to use their purchasing power to lower drug costs for uninsured and underinsured individuals, state agencies, labor organizations, and other groups.[170] ArrayRx offers drug discounts to any resident of Washington and Oregon and was expanded to **Nevada** residents in September 2022.[171] Current price for Humalog is $30.81 for a 30-day supply.

Most states have patient assistance programs for the elderly with lower incomes that help pay for drugs, not just insulin.[172] Some state patient assistance programs include patients with lower incomes and non-elderly with or without disabilities. Patient assistance programs can offer drug discount cards or copays. Some patient assistance programs offer free distribution of insulin and diabetic supplies (Delaware and Florida). In Colorado and Minnesota, emergency insulin is available for $35 for a 30-day supply once a year to those without a health plan that limits monthly cost-sharing to $100 (Colorado) or $75 (Minnesota).[173]

III. Patient Assistance Programs

Drug manufacturers, nonprofits, and government organizations have patient assistance programs that offer free medicine or drug discount cards. With patient assistance programs, drug manufacturers gain increased demand (which can help increase prices), public relations benefits, and less pressure to reduce their prices.[174] However, critics argue that patient assistance programs are not transparent about their eligibility requirements, make it hard to apply and renew, and can limit patients to a specific brand and treatment.[175]

Patient assistance programs offered by pharmaceutical manufacturers provide patients who are eligible with access to medications at reduced cost or no cost at all.[176] Several features of these programs, however, may limit their usefulness for patients with diabetes. First, the application processes are generally complex, with reading levels greater than those suggested for patients with low health literacy. This is a concern that is particularly relevant for patients without comprehensive health insurance coverage or who may be underinsured. Second, programs may generally provide medications to the patients' providers' offices instead of directly giving them to the patients, requiring more patient effort to access the medications. Third, most programs focus on only one or two specific medications, and they vary in the benefits they provide and eligibility criteria. There is no standardized application process for patients who may require assistance for multiple medications, and even programs that cover several medications are unlikely to be comprehensive enough to meet the needs of patients with multiple conditions. Further, these programs either only provide patients with a free month or three-month supply, or a year's worth of medication for a reduced price—none of these assistance programs last longer than a year.[177,178]

Although patients frequently rely on clinics that provide care to underserved populations such as Federally Qualified Health Centers and Community Health Centers to apply to patient assistance programs on their behalf, completing these applications can be burdensome for employees at these facilities. As a result, more than 20 percent of these clinics do not use manufacturer sponsored patient assistance programs at all, even though they serve many patients who might benefit from them.[179,180] Further, a study found that most patient assistance programs did not provide assistance for uninsured patients.[181] Patient assistance programs may thus exclude some of the most marginalized diabetic patients.

IV. Insulin Caps by PBMs, Insulin Manufacturers, and Private Insurers

Some pharmacy benefit managers, insulin manufacturers, and private insurers offer insulin caps. In April 2019, Express Scripts, one of the largest pharmacy benefit managers in the country, announced it was launching a "patient assurance program" that will place a $25 per month cap on insulin for patients "no matter what," offered for its plans for Cigna and other insurers.[182] In April 2020, after the COVID-19 pandemic began, Eli Lilly began offering a discount card with $35 copays for most of its insulin products to uninsured patients and patients with commercial insurance.[183] Novo Nordisk offers a discount card with $25 copays per month up to 24 months to patients with private insurance.[184] Sanofi offered its insulin products for $99 per month for uninsured patients[185] and reduced the amount to $35 per month starting July 2022.[186] CVS, which owns Aetna, announced plans to offer employers plans that eliminate cost-sharing for insulin and other diabetes medications on January 29, 2020.[187] Health insurers such as Medica ($25 per month) and Oscar ($3 per month) also have insulin caps.[188] Cigna offers Enhanced Diabetic Care benefits with $0 copays on preferred insulin products for plans on the Marketplace.[189] Additionally, United Healthcare made an announcement to shift cost sharing for insulin products to $0 for eligible patients by July 2022.[190]

Chapter 8. Conclusions and Implications

Over 37 million or 1 in 9 Americans suffer from diabetes and our analyses of MEPS data shows that 7.5 million patients require insulin. These individuals need to access and utilize their insulin products properly on a daily basis in order to control their blood sugars and lead healthy lives.

Patients with diabetes often manage complex treatment regimens that can include oral medications and multiple types of insulin. Insulin accounted for 27 to 28 percent of out-of-pocket spending on all health care overall among insulin users. For patients, insulin is an added expense beyond other health care costs, and it is particularly high for patients who are uninsured or those that have private insurance. Patients covered under Medicaid have the greatest protection from out-of-pocket costs. Medicare Part D enrollees, especially those receiving the low-income subsidy, have greater coverage for insulin spending compared to their counterparts.

The cost barriers to insulin can also have downstream impacts on diabetes management, leading to unnecessarily high rates of nonadherence and insulin rationing. Surveys on insulin affordability have found that 1 in 6 insulin users ration their insulin due to cost-related reasons and this varies based on race, ethnicity, and the type of insurance. Half of all insulin users are in Medicare and, thus, are on fixed incomes that can be easily strained by high-cost items such as insulin. Among patients with private insurance, a recent survey by the Commonwealth Fund finds that 29 percent of people with employer coverage were underinsured, suggesting that for people with private insurance, affording insulin may be challenging.[191] Moreover, for patients who take insulin, good nutrition and adequate housing are critical for proper insulin adherence. Analysis using the Medicare Expenditure Panel Survey (2016 – 2017) show that the share of adult insulin users with low or very low food security (14 percent) was higher than for adults overall (8.4 percent).

These financial costs have downstream implications because insulin nonadherence is associated with worse diabetes control and disease progression. Progression leads to higher rates of diabetes-related complications that often require expensive hospitalizations and include kidney failure (requiring life-long dialysis), blindness, amputations, and much higher rates of mortality. Diabetes is also associated with a higher risk of death by heart-attack and stroke, made worse by the comorbidities of obesity, high cholesterol, and high blood pressure that are strongly associated with the development of type 2 diabetes.

As shown in this Report, affordability will be improving for some insulin users in the coming years. First, biosimilar versions of some but not all insulin products have slowly increased competition, potentially lowering total and out-of-pocket costs. Biosimilars have long-term savings potential, yet they have been slow to disrupt the insulin market that is predominately controlled by the same three manufactures (Eli Lilly, Sanofi Aventis, and Novo Nordisk) that have dominated insulin manufacturing for the past half-century. Second, the IRA limits out-of-pocket costs for people who need insulin and are enrolled in Medicare Part D and B to $35 per month for each covered insulin product. However, these provisions directly benefit only insulin users who are covered under Medicare. The IRA also requires inflation rebates in Part D and Part B, allows enrollees to spread high monthly drug costs across the Part D plan year, expands low-income subsidies for Part D beneficiaries, and caps overall Part D out-of-pocket spending at $2,000 by 2025. The IRA out-of-pocket insulin cap is expected to reduce out-of-pocket spending for Medicare Part D and Part B enrollees, reducing out-of-pocket costs by about $734 million in Part D and $27 million in Part B if the IRA's out-of-pocket insulin cap had been in effect in 2020. However, these provisions do not reduce burdens for other populations who still face high out-of-pocket spending for insulin, such as people without health insurance and people with private insurance. Third, some states have enacted monthly insulin caps for individuals with other types of coverage or provided subsidized insulin for uninsured and underinsured patients. However, these changes are variable across states, and only the federal government can place limits on out-of-pocket payments for insulin for all insurance enrollees, including those enrolled in self-insured plans.[152]

Increasing the availability of biosimilars, IRA provisions to reduce out-of-pocket spending for drugs and insulin, and state cost-sharing caps have all attempted to address this issue of insulin affordability. Yet, significant barriers to affordability remain.

Consequences of uncontrolled diabetes can impact patients' quality of life, ability to work, and overall health spending. For federal programs such as Medicare and Medicaid, as well as private insurance, it is possible that these costs can be partially offset by improving early treatment adherence and preventing downstream consequences. Thus, improving insulin affordability may not only benefit patients but also produce societal and economic benefits by addressing a major upstream barrier in diabetes control. Enhancing patient access to this crucial medication that was discovered nearly a century ago may benefit taxpayers, private payers, and, most of all, American patients and families dependent upon insulin to manage their diabetes.

Appendices

Appendix A. Legislation

William M. (Mac) Thornberry National Defense Authorization Act for Fiscal Year 2021 (Public Law 116-283), January 1, 2021

SEC. 10004. STUDY AND REPORT ON THE AFFORDABILITY OF INSULIN.

The Secretary of Health and Human Services, acting through the Assistant Secretary for Planning and Evaluation, shall—

(1) conduct a study that examines, for each type or classification of diabetes (including type 1 diabetes, type 2 diabetes, gestational diabetes, and other conditions causing reliance on insulin), the effect of the affordability of insulin on—

(A) adherence to insulin prescriptions;

(B) rates of diabetic ketoacidosis;

(C) downstream impacts of insulin adherence, including rates of dialysis treatment and end-stage renal disease;

(D) spending by Federal health programs on acute episodes that could have been averted by adhering to an insulin prescription; and

(E) other factors, as appropriate, to understand the impacts of insulin affordability on health outcomes, Federal Government spending (including under the Medicare program under title XVIII of the Social Security Act (42 U.S.C. 1395 et seq.) and the Medicaid program under title XIX of the Social Security Act (42 U.S.C. 1396 et seq.)), and insured and uninsured individuals with diabetes; and

(2) not later than 2 years after the date of enactment of this Act, submit to Congress a report on the study conducted under paragraph (1).

Appendix B. Prediabetes

Prediabetes is a condition that occurs when blood glucose levels higher than normal but not at the threshold to be diagnosed as diabetes. On laboratory examination, prediabetes occurs when an individual has glycated hemoglobin between 5.7 percent and 6.4 percent, Fasting Plasma Glucose (FPG) level of 100-125 mg/dl, and 2-hour oral glucose tolerance test level of 140-199 mg/dl. Glycated hemoglobin or A1C is the most common measure used to confirm a diabetes or prediabetes diagnosis because it provides a long-term measure of blood sugar rather than alternative tests which measure one's blood sugar at one moment in time. A1C measures the degree to which sugar molecules have collected onto red-blood cells in the bloodstream. A higher percent A1C means that red-blood cells have been exposed to higher degrees of average blood sugars.[192] The A1C test is especially important for providers because it offers a measure of long-term blood sugar control, which gives a better picture of a patient's average blood sugar over the past 2-3 months prior to measurement.[193]

Prediabetes is associated with risk factors such as obesity, hypertension, and dyslipidemia (high triglycerides and low HDL cholesterol). Adults meeting the above criteria are at increased risk of developing type 2 diabetes and adverse cardiovascular outcomes.

Prediabetes is not considered a clinically pathologic condition requiring medication. It is an important condition to track, however, because it is a risk factor for diabetes and cardiovascular disease. Additionally, a diagnosis of prediabetes offers an opportunity to initiate early non-medical and preventative measures such as diet and exercise to reduce disease progression. If lifestyle modification is effective, it can help a patient avoid or delay the need for medications down the line. For adults diagnosed with prediabetes or at risk for prediabetes, the American Diabetes Association (ADA) recommends use of lifestyle modification programs such as Diabetes Prevention Programs (DPP), physical activity, weight loss, diet changes, and metformin therapy (in specific high-risk groups) to reduce risk of developing diabetes and adverse cardiovascular outcomes.[194,195,196]

A systemic review of 16 cohort studies analyzed A1C to predict the progression to diabetes. After the follow-up interval of an average 5.6 years (range 2.8-12 years), individuals with A1C between 5.5 percent and 6.0 percent had increased incidence of diabetes. As A1C rises above these levels, the risk for developing diabetes rises significantly as well as the associated complications.[197]

An estimated 88 million (about 1 in 3) adults had prediabetes in 2018 based on glycated hemoglobin (A1C) or glucose level.[198] Prevalence based on either blood sugar measure was 46.6 percent among adults 65 and above.[199] Prediabetes was more prevalent among men than among women, and the prevalence of prediabetes is higher among racial and ethnic minorities at lower body-mass index measures compared to white non-Hispanic patients.[200] The prevalence rates were particularly high amongst patients of Hawaiians/Pacific Islander, Asian, Black, American Indian/Alaskan Native and Hispanic descent when controlling for obesity class.

According to a study by Andes et al. using NHANES data, about 1 of 5 adolescents (12-18 years of age) and 1 of 4 young adults (19-34 years of age) have prediabetes. The adjusted prevalence of prediabetes is higher among male individuals, and among parents with obesity. These adolescents and young adults with prediabetes carry a similarly increased risk of type 2 diabetes and cardiovascular disease in the future. In this study, non-Hispanic Black adolescents and young adults had higher risk of prediabetes as compared to Hispanics and non-Hispanic White populations. [201] These findings demonstrate the importance early access to health care and the downstream effects of childhood obesity. Children diagnosed with prediabetes require patient-specific counseling as well as parental counseling on healthy diet and exercise habits. Early preventative measure at this stage of disease can lead to benefits for the caretakers as well as the child diagnosed with prediabetes.

Appendix C. Diabetes Prevention

Patients, providers, drug manufacturers, food suppliers, and government all have critical roles in diabetes prevention. To prevent the progression of asymptomatic individuals with prediabetes and diabetes to full-blown disease and complications, it is imperative to screen and diagnose the condition at an earlier stage. In addition, given the multi-organ impacts of uncontrolled diabetes, diabetes prevention also lowers the risk of major causes of morbidity and mortality such as cardiovascular, kidney and eye disease. Finally, healthy diet and exercise habits can improve health and quality of life. The screening recommendations for prediabetes or diabetes varies among organizations.

The U.S. Preventive Services Task Force (USPSTF) recommends that all asymptomatic adults ages 35 to 70 who are overweight or obese be screened for prediabetes or type 2 diabetes.[202] The American Diabetes Association (ADA) offers more detailed screening recommendations for diabetes/prediabetes in asymptomatic adults:[203]

- Testing should be considered in all overweight or obese (BMI >=25 kg/m^2, >=23 kg/m^2 in Asian Americans) individuals who has one or more of the following risk factors:
  - First degree relatives with diabetes
  - High risk race/ethnicity (African American, Alaska Native, American Indian, Asian American, Hispanic/Latino, Native Hawaiian/Pacific Islander ethnicity)
  - Physical inactivity
  - Hypertension (>=140/90 mmHg or on therapy)
  - Dyslipidemia (HDL cholesterol <35 mg/dL, triglycerides > 250 mg/dL)
  - Women with polycystic Ovary Syndrome (PCOS)
  - History of gestational diabetes
  - History of cardiovascular disease (for example, heart disease and stroke)
  - Other clinical conditions associated with insulin resistance (for example, severe obesity or acanthosis nigricans)
  - Adults with prediabetes (HbA1C >=5.7 percent) should be screened yearly.
  - Women diagnosed with Gestational Diabetes Mellitus (GDM) should be lifelong screened at least once every 3 years.
- For individuals considered overweight or obese, testing should start at 35 years. For all else, screening starts at 40 years.
- If results are normal, then testing should be repeated at every 3-year interval, with consideration for more frequent testing depending on initial test results and risk status.

For pediatrics, ADA risk-based screening recommendations for type 2 diabetes/prediabetes among asymptomatic children and adolescents in a clinical setting are as follows:[204]

- Overweight (weight >85th percentile for age and sex, weight for height >85th percentile or weight >120 percent of ideal for height)

- Plus, one or more of the risk factors based on their strength of association with diabetes as indicated by evidence grades:
    - Family history of diabetes in first-degree or second-degree relatives
    - Maternal history of GDM
    - At risk race/ethnicity
    - Signs of insulin resistance or conditions associated with insulin resistance (for example, acanthosis nigricans, hypertension, dyslipidemia, polycystic ovary syndrome, or small-for-gestational-age (SGA) birth weight)

Numerous programs have been introduced across the U.S. to address diabetes prevention for either the general population or specific racial and ethnic groups. The following diabetes prevention programs have been introduced by CDC, the CMS Center for Medicare & Medicaid Innovation, and the Indian Health Service (IHS).

National Diabetes Prevention Program

The National Diabetes Prevention Program (NDPP) is a partnership between public and private organizations that work on preventing or delaying type 2 diabetes. These organizations work with adults with prediabetes and make it easier for them to participate in evidence-based, affordable, and high-quality life-style change programs and over time improve their health. The participating partners/organizations that participate in NDPP are federal agencies, local and state health departments, employers, public and private insurers, businesses focusing on wellness, academic programs, and providers. A key component of this program is lifestyle change which will lead to improved health outcomes. As part of the CDC-recognized program, participants will attend the sessions once weekly for the first six months and then for the next six months they will meet once monthly. The program includes a lifestyle and wellness coach who will motivate participants to start and adhere to the health behaviors.

Effectiveness: The program has demonstrated success in reducing the risk of developing type 2 diabetes. Evaluation findings show that among all participants, the risk of developing diabetes declined by 58 percent and by 71 percent in adults over 60 years old relative to a comparison group that was taking placebo over a three-year period. This was nearly as much of a reduction as among the group taking metformin (31 percent). In a follow up study at ten-year, the incidence of diabetes was about 34 percent less for individuals participating in DPP relative to individuals who took a placebo. The program delayed the onset of disease among those who did develop type two diabetes by four years.[205,206]

Special Diabetes Program for Indians (SDPI)

Congress established the Special Diabetes Program for Indians (SDPI) in 1997 to provide funding for the preventive and treatment services for Indian Health Services (IHS), urban, or tribal Indian health programs across the United States. The current funding for this program is $150 million per year. Currently there are 301 SDPI sites across 35 states including 12 IHS areas. As part of this program, SDPI-directed grantees implement best practices for improvement of diabetes treatment and prevention tactics among community and clinical sites. These best practices include but are not limited to diabetes-related education, nutrition education, antiplatelet therapy, mental health, eye and foot exam, depression screening, and immunization.

Effectiveness: With the help of SDPI, diabetes prevalence decreased in American Indian and Alaska Native communities for the first time, from 15.4 percent in 2013 to 14.6 percent in 2017. The reduction in prevalence is thought to be driven by reduction in number of new cases. Diabetes mortality decreased by 37 percent and diabetes-related kidney failure decreased by 54 percent.[207] The resulting decrease among the AI/AN population in the need for dialysis and kidney transplant, which led to estimated Medicare savings of $525 million over 10 years.[208] The hospitalization rate due to diabetes was reduced by 84 percent along with a reduction in diabetic eye disease among the population, which lowered overall health care costs.[209]

CMMI Medicare Diabetes Prevention Program (DPP)

In 2016, CMS spent $42 billion more on beneficiaries with diabetes as compared to those without diabetes, which included an estimated $1,500 more per beneficiary on Medicare Part D prescription drugs, $3,100 more on hospital and inpatient services, and $2,700 more on physician services as compared to beneficiaries without diabetes in 2016.[210] In response, CMMI developed the Medicare Diabetes Prevention Program (MDPP) Expanded Model, a structured behavioral change model that can prevent the onset of type 2 diabetes in adults with prediabetes. The Model has been in operation since 2018. The intervention consists of a minimum of 16 intensive core sessions of a CDC-approved course implemented over a six-month period. The curriculum includes group-based, classroom teaching of long-term dietary change, increased physical activity, and behavioral changes that can result in long-term sustainable weight control. The goal of the program is five percent weight loss at the end of the intensive session, followed by monthly non-intensive meetings to maintain these healthy behaviors.

Effectiveness: On average, MDPP beneficiaries attended 17 sessions, and lost weight by 5.1 percent as compared to starting weight. Through December 2021, 53 percent of MDPP beneficiaries met the 5 percent weight-loss goal and about a quarter met the 9 percent weight-loss goal. Results on whether MDPP reduces expenditures and improves health outcomes are not yet available.[211]

CMMI Comprehensive ESRD Care (CEC) Model

According to the United States Renal Data system in 2016, ESRD beneficiaries were less than 1 percent of the Medicare population although they accounted for an estimated 7.2 percent of Medicare fee-for-service spending, with a total of $35.4 billion. Diabetic kidney disease is the leading cause of ESRD in the United States.

The Comprehensive ESRD Care (CEC) Model is designed to identify, test, and evaluate new ways to care for Medicare beneficiaries with End Stage Renal Disease (ESRD). Through this model, CMS partners with health care providers and suppliers to assess the new payment and service delivery method for providing high quality comprehensive care to the beneficiaries. The program was initiated in October 2015 and ended March 31, 2021.[212] There are 33 ESRD seamless care organizations (ESCOs) participating in the CEC model. The ESCOs are formed by nephrologists, dialysis clinics and other health care providers. Due to the complexity of their disease and the lack of a comprehensive payment method, the ESRD patients had to visit multiple providers and follow multiple care plans for the condition. The CEC model introduced payment incentives for care coordination with the goals of creating a person-centered, coordinated care experience and improving overall health outcomes in ESRD patients.[213]

Effectiveness: Evaluation of the CEC model from the period of October 2015 to December 2020 found that reductions in spending and utilization and improvements to quality. The CEC model reduced Medicare spending by $217 million (-1.3 percent), however, these results do not consider shared savings payments made to ESCOs. CEC also decreased the number of hospitalizations by 3 percent and increased outpatient dialysis by 0.4 percent. In addition, patients in the Model experienced fewer hospitalizations from ESRD complications. Taken together, the CEC model reduced ESRD related complications, reduced utilization, and resulted in decreases in gross spending.

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