Congressional Budget Office
Nonpartisan Analysis for the U.S. Congress

How Increased Use of Gene Therapy Treatment for Sickle Cell Disease Could Affect the Federal Budget

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Summary

Gene therapies replace or modify disease-causing genes in human cells. Those therapies, which are still relatively new, are used to prevent, cure, or treat the symptoms of a particular disease. In this report, the Congressional Budget Office discusses how it would estimate the budgetary effects of policies that sought to increase the use of gene therapy treatment for sickle cell disease (SCD). CBO focuses on SCD because two new gene therapies were recently approved for its treatment, and the first few patients outside clinical trials have been treated with those therapies.[1] Gene therapies in development target a range of diseases, including cancer, heart disease, and inherited genetic diseases.[2]

Gene Therapy for Treatment of Sickle Cell Disease in the United States

SCD is one of the most common inherited blood disorders in the United States, affecting about 100,000 people. More than 90 percent of patients with SCD are non-Hispanic Black or African American. Because it is caused by a single gene mutation, SCD is an ideal candidate for gene therapy. When a person's oxygen levels are low, that gene mutation causes red blood cells to turn into hard, sickle-shaped cells that clump together in blood vessels, blocking blood flow, causing severe pain, and potentially resulting in serious complications. Those episodes are often referred to as pain crises. SCD reduces an individual's life expectancy by about 20 years, and health care costs for people with SCD are much higher than average.

Under the current standard of care, treatment of sickle cell disease consists largely of symptom management and treatment of pain crises. Although a stem cell transplant cures SCD, many patients cannot find a suitable donor. Two recently approved gene therapies—Casgevy and Lyfgenia—have the potential to cure SCD in more patients. Each therapy has a list price of over $2 million and involves a one-time treatment, though that treatment is lengthy and has safety risks. Future health care costs might be averted for patients who are successfully treated with those therapies, but information about the therapies' long-term effects on health, longevity, and health care spending is not yet available.

Assessing the Budgetary Effects of Policies That Would Increase Use of That Treatment

CBO has not estimated the federal budgetary effects of any specific policy that would address the use of gene therapies to treat SCD. Four key categories of budgetary effects are the following:

- Changes in treatment costs, which depend mainly on the number of patients and on the change in the average treatment costs relative to spending under current law;
- Other conventional effects, which are effects on federal spending (such as savings from improved health and lower rates of disability) that do not account for changes in the size of the economy;
- Population-change effects, which include the costs of benefits received and the revenues collected during the time when people would be living longer because of the treatment; and
- Dynamic effects, which include conventional effects, population-change effects, and all other effects on spending and revenues stemming from changes in the size of the economy.

CBO's approach to assessing the budgetary effects of policies to expand gene therapy treatment for SCD would be consistent with the agency's approach to analyzing policies that would increase treatment for hepatitis C, extend Medicare coverage to include anti-obesity medications, and encourage disease prevention.[3]

What Are Gene Therapies?

A person's genes contain instructions for making proteins that are essential for good health. Mutations, or changes in genes, can lead to missing proteins or ones that do not work properly. Mutations can cause a variety of diseases that may be inherited, such as sickle cell disease, cystic fibrosis, and hemophilia.

Gene therapies replace or modify disease-causing genes in human cells to prevent, cure, or treat the symptoms of that disease. Because they target specific genes, those therapies are well-suited for treating inherited diseases that result from a single gene mutation. Depending on the disease, cells that have undergone gene therapy can produce a functional enzyme or protein, enhance a patient's immune system, or target and destroy cancer cells. Unlike traditional therapies (such as surgery or prescription drugs), gene therapies modify a person's genetic makeup and, in many cases, address the underlying cause of a particular disease rather than treating its effects.

How Do Gene Therapies Work?

Gene therapies work in various ways. Some therapies alter a patient's existing DNA by deactivating or "turning off" a particular genetic switch that causes a specific disease (known as gene silencing) or by editing a faulty gene to restore normal function (known as gene editing). The leading technology in gene editing is CRISPR/Cas 9, which selectively modifies genetic material. Other gene therapies replace a particular DNA sequence with new genetic material to restore or improve gene function to slow disease progression. Generally, gene therapy cannot reverse existing symptoms or complications caused by the disease.

Certain gene therapies offer the prospect of a cure for diseases that previously had few, if any, cures. Unlike many traditional therapies, which require ongoing clinical care over a patient's lifetime, gene therapies could in some cases consist of a one-time treatment process—though the course of treatment takes several months to prepare for and administer. Information on long-term clinical outcomes from gene therapy treatment is not yet available, but evidence from people treated in clinical trials suggests that those therapies confer benefits that reduce a patient's future health care use and spending.

How Many Gene Therapies Are in Use or Under Development?

As of November 2024, the Food and Drug Administration (FDA) has approved 23 gene therapies to treat multiple myeloma, lymphoma, other cancers, inherited blood disorders (including beta thalassemia and sickle cell disease), as well as several rare childhood neurological diseases.[4] According to one analysis, global spending on cell and gene therapies was $5.9 billion in 2023, and 62 percent (or $3.7 billion) of that spending was in the United States.[5] (Cell therapies involve transferring genetically modified cells with necessary functions into patients. Gene therapies, in contrast, transfer genetic material into a patient for take-up by the patient's own cells.) Over 600 cell and gene therapies were in clinical trials at the end of 2020, and one estimate suggests that the FDA will approve 66 new gene therapies by 2032.[6]

Sickle Cell Disease in the United States

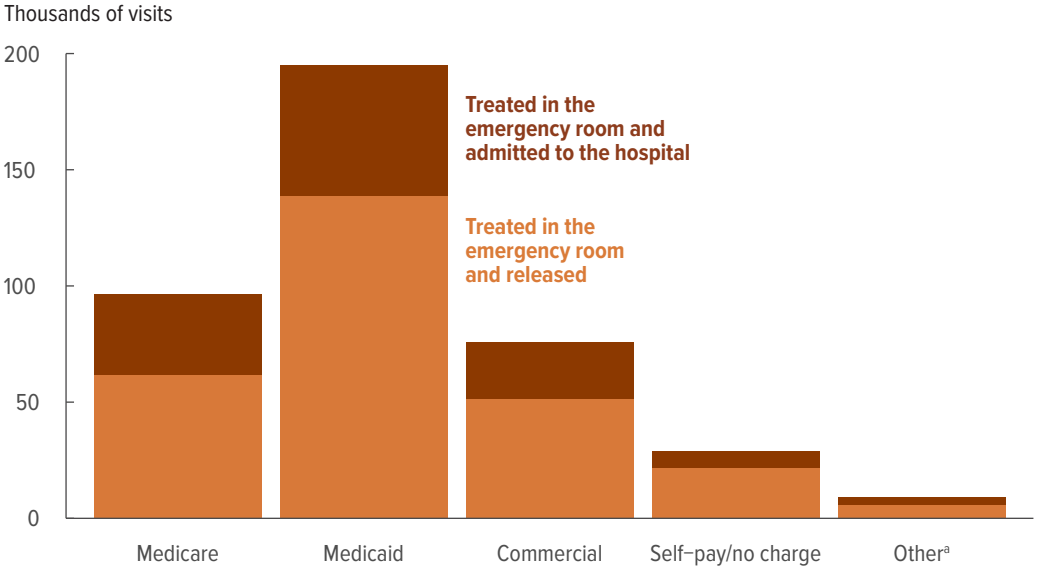
Sickle cell disease is a group of inherited blood disorders caused by a gene mutation that makes red blood cells brittle, hard, and sickle-shaped during times of low oxygen exposure. Red blood cells are typically circular and flexible and can slide easily through blood vessels. In patients with SCD, sickled cells get stuck in blood vessels and block blood flow, causing extreme pain and, in some cases, major adverse outcomes such as stroke or heart attack. Other complications of SCD include vitamin deficiencies, delayed growth and puberty because of anemia, blood clots, problems with pregnancy, and chronic or long-term pain. Estimates suggest that SCD reduces a person's life expectancy by about 20 years. SCD affects about 100,000 people in the United States, more than 90 percent of whom are non-Hispanic Black or African American.[7] Newborn screening for SCD occurs in every state, enabling early detection and treatment.[8]

How Is SCD Treated Under the Current Standard of Care?

Some newborns diagnosed with SCD begin experiencing symptoms when they are only three months old, and medications to manage the disease may be prescribed before a child reaches age one. As they get older, people with SCD may experience different and more serious medical problems—stroke or damage to the lungs, kidneys, spleen, and liver—that occur when organ tissues do not get enough oxygen.[9] For most patients with SCD, treatment consists of symptom management, including blood transfusions and medications. In addition to medications to manage pain, there are medications that help prevent pain crises, but they do not offer a cure and must be taken on an ongoing basis.[10] Use of those medications has been low because of safety concerns about long-term

Figure 1.

Number of SCD-Related Emergency Room Visits, by Type and Payer, 2021



Individuals visiting an emergency room may be admitted to the hospital or treated on site and then released. Among SCD-related emergency room visits by Medicare enrollees in 2021, 36 percent resulted in a hospital admission, compared with 29 percent of visits among Medicaid enrollees and 32 percent of visits among individuals with commercial health insurance.

Data source: Weighted national estimates come from HCUP Nationwide Emergency Department Sample (NEDS), 2021, Agency for Healthcare Research and Quality (AHRQ), and are based on data collected by individual state partners and provided to AHRQ. See www.cbo.gov/publication/60775#data.

SCD = sickle cell disease.

a. Includes workers' compensation, TRICARE/CHAMPUS, CHAMPVA, Title V, and other government programs.

exposure and other factors, such as variation in effectiveness among patients.[11]

About 10 percent to 15 percent of patients with SCD are eligible for a stem cell transplant, the only cure under the current standard of care.[12] To be eligible to receive a transplant, patients must have a matched blood-relative donor and a severe enough case to justify the substantial risks that accompany transplants, including life-threatening complications (such as infections and organ damage). The total cost of a stem cell transplant is about $400,000 but can vary greatly depending on the hospital's location, the patient's length of stay, and other relevant factors.[13]

Only a subset of eligible patients receive a transplant. That is because of the potential safety risks, the challenges in determining the optimal timing for transplants, and the cost of the procedure. Data on the number of patients receiving transplants are limited, but one estimate suggests that, as of 2014, only about 1,200 people with SCD had received a stem cell transplant.[14] For most patients with SCD, no cure is available.

Insurance Coverage and Health Care Spending Among SCD Patients

SCD patients are disproportionately covered by government health insurance. As with many chronic diseases, SCD requires intensive health care that results in high costs. Information on the health insurance coverage of people with SCD is limited, but estimates suggest that Medicaid covers about half of SCD patients, and 11 percent are covered by Medicare; some patients are covered by both programs.[15] (Medicaid is a joint federal and state program that provides health insurance for qualifying people with limited income and resources. Medicare is a federal insurance program that covers qualifying people age 65 or older and people under 65 with certain disabilities.)

Data from emergency room visits by people with SCD are consistent with those coverage estimates. In 2021, people with SCD visited an emergency room approximately 405,000 times, and just over 30 percent of those visits resulted in a hospital admission. Nearly half of those patients (195,080) were insured by Medicaid, an additional one-fourth (96,417) were insured by Medicare, and nearly one-fifth (75,741) had commercial health insurance (see Figure 1). The remaining roughly 5 percent were covered by other government programs, including

worker's compensation, TRICARE/CHAMPUS, CHAMPVA, and Title V, or they paid out of pocket. Patients with SCD are hospitalized or have an emergency room visit two to three times per year, on average, and rates are highest among 18- to 30-year-olds covered by Medicaid or Medicare.[16] Higher health care use results in higher health care costs among people with SCD compared with those without the disease. A recent systematic review of costs associated with SCD found that people with the disease had higher inpatient, emergency room, and home health costs than people without SCD.[17]

Among Medicaid enrollees in 2021, those with SCD had average annual total spending of $22,600, more than double the average spending among all Medicaid enrollees ($9,175). For Medicaid enrollees with the most severe cases of SCD, who would make up a large portion of those eligible for gene therapy, costs were up to $200,000 per year, driven by multiple hospitalizations and an average of 25 emergency room visits.[18] Costs of managing SCD increase over time as patients with the disease age.[19] In addition to incurring high health care costs, many people with SCD have a reduced ability to work. The need for regular hospitalizations and blood transfusions leaves many people with SCD, as well as their caregivers, unable to work or less productive at work.[20]

Gene Therapies for Treating Sickle Cell Disease

On December 8, 2023, the FDA approved the first two gene therapies for SCD, Lyfgenia and Casgevy, for treatment of patients age 12 or older with a history of pain crises. To date, use of those therapies has been largely confined to clinical trials. Unlike with stem cell transplants, no matched donor is required for gene therapy, so that treatment could be available to a broader set of patients.

Approved Gene Therapies for SCD

Treatment with Lyfgenia and Casgevy involves several steps, including multiple hospital stays. First, a patient's stem cells are collected, then they are modified, and finally they are transplanted into the patient through a single infusion using a process similar to that for a stem cell transplant.

Stem cell collection involves roughly 90 days of preparation with monthly blood transfusions and six to eight weeks of several rounds of stem cell collection. Each round requires a hospital stay of one to three days. Once the stem cells are collected, they are modified in a laboratory over several months.

Once modification is complete, patients undergo a four- to six-week hospital stay that includes "conditioning" chemotherapy to eliminate the stem cells with the sickle trait and make room for the modified cells. That process is followed by reintroduction of the modified cells and follow-up monitoring.[21] Complications from the chemotherapy or the Lyfgenia or Casgevy infusion can prolong the course of treatment. Follow-up evaluations are expected to continue for up to 15 years.[22] Both therapies are intended to be one-time treatments. Data about safety and longer-term outcomes are not yet available, but patients who are successfully treated as adolescents could avoid serious and costly pain crises throughout their lifetime.

Lyfgenia and Casgevy modify the stem cells in different ways:

- Lyfgenia uses a bioengineered virus—referred to as a viral vector—to deliver a working copy of the hemoglobin gene to a patient's stem cells. After being transplanted back into the patient, the modified stem cells produce healthy hemoglobin, which results in normal red blood cells and prevents SCD complications.
- Casgevy is the first FDA-approved therapy that uses the CRISPR/Cas9 gene editing technology. That technology is used to edit the faulty hemoglobin gene in a patient's stem cells so that the modified stem cells produce healthy red blood cells when transplanted back into the patient.[23]

Use of Gene Therapies for SCD

According to the manufacturers of the two products—Bluebird Bio (Lyfgenia) and Vertex (Casgevy)—the first few patients received the treatments outside of clinical trials in fall 2024.[24] The take-up rate will be affected by the costs of treatment, the length and complexity of treatment, and evidence on treatments' long-term outcomes. The capacity of providers to offer the treatment and their experience with the treatment will also influence the use of those therapies. Only certain hospitals are authorized to provide gene therapy for SCD; currently, there are close to 50 qualified treatment centers for Lyfgenia and over 35 authorized treatment centers for Casgevy in the United States.[25]

In clinical trials, both therapies resulted in the elimination of pain crises for most patients. In the case of Lyfgenia, 28 of 32 patients achieved complete resolution of pain crises between 6 and 18 months after infusion.[26] In the case of Casgevy, 29 of 31 patients treated in clinical trials achieved freedom from severe pain crises for at least 12 consecutive months during a 24-month follow-up period. Complications of the therapy and associated treatments (such as chemotherapy) were observed in clinical trials, including blood cancers and infertility.

Insurance Coverage of Gene Therapies for SCD

Lyfgenia and Casgevy are just beginning to be used outside of clinical trials. Coverage policies have yet to be determined and will probably vary among public and private payers.

Coverage in Medicaid. Medicaid covers gene therapy for SCD, but states may decide to limit eligibility for the treatment. By law, state Medicaid programs are required to cover all approved drugs for which the manufacturer agrees to provide rebates through the Medicaid Drug Rebate Program (MDRP). Treatments such as Lyfgenia and Casgevy, which are administered in an inpatient setting, are considered covered outpatient drugs in the Medicaid program and are therefore subject to Medicaid rebates.[27] Under the MDRP, Medicaid's net prices for those therapies are lower than the list prices because of rebates and Medicaid's best price policy, which allows the program to pay the lowest price available to commercial insurers.[28]

It is unknown whether state Medicaid programs would impose drug utilization controls—policies such as prior authorization, step therapy, or eligibility requirements—to manage the high costs of gene therapies for SCD. For older cell and gene therapies, Medicaid's coverage is more restrictive than the FDA indication in some states because Medicaid patients must meet additional requirements to be eligible for covered treatment.[29]

In addition to standard coverage requirements in Medicaid, the Centers for Medicare & Medicaid Services' (CMS') Innovation Center established a voluntary model—the Cell and Gene Therapy Access Model—for states and manufacturers to use outcome-based arrangements to finance the provision of gene therapy to Medicaid enrollees. The first therapy of focus under that model is gene therapy for sickle cell disease. Other diseases may follow.[30] Under the model, CMS and manufacturers negotiate prices and supplemental rebates for gene therapies; payments are tied to specific outcome measures, such as reductions in pain crises. State Medicaid programs agree to a standard access policy that is the same across all states. States are allowed to enroll in the model beginning in January 2025.

Coverage in Medicare. Medicare covers gene therapy for SCD. Under current law, Medicare covers new medical technologies that are deemed reasonable and necessary, that are not excluded by law, and that fall within one of its defined benefit categories. When new technologies do not fit within Medicare's existing payment codes, Medicare creates a payment code to cover the therapy. Medicare can grant additional payments for a new technology that confers substantial clinical improvements over existing therapies and that involves substantial costs. In October 2024, Medicare approved both Lyfgenia and Casgevy for new technology add-on payments of a maximum of $2,325,000 for Lyfgenia and $1,650,000 for Casgevy in fiscal year 2025.[31]

Coverage in Commercial Insurance. Private insurers cover gene therapy for SCD in some cases. CBO examined current coverage policies for Lyfgenia and Casgevy among the five health insurance companies with the highest enrollment in the United States.[32] Those policies suggest that commercial insurers are establishing coverage criteria for the two gene therapies that are more restrictive than the FDA indication.[33]

Before the insurers approve coverage of a gene therapy for SCD, several conditions must be met. For example, all five insurers require patients to have a documented history of at least two pain crises per year for the previous two years, and three of the five insurers require patients to be eligible for a stem cell transplant but unable to find a matched donor. Four of the five also require patients to have tried and failed at least one medication treatment.

Because of the high cost but potentially curative nature of gene therapies, various parties (payers, researchers, and others) have suggested that payment for gene therapies going forward could be tied to a treated patient's outcomes under one of several models. (These payment models are illustrative and apply only to commercial insurance; other models have been proposed.)[34] Under a warranty model, for instance, a payer would cover the full cost of treatment up front. The manufacturer would pay a premium to a third-party insurer, who would reimburse the payer if the treatment failed. The

warranty could cover the cost of the drug or the health care costs that were caused by the treatment's failure.[35] In an outcome-based payment model, a payer would tie payment for a treatment to patient outcomes. The payer could make payments to the manufacturer if the treatment worked or receive refunds if the treatment failed.[36]

Policy Approaches to Increase Gene Therapy Treatment

Policymakers could facilitate the adoption of new gene therapies for SCD by changing coverage or payment policies. Given the high share of patients with SCD who have Medicaid coverage, policy efforts might focus on that program. Approaches in Medicaid could include increasing the federal role in the coverage of and payment for gene therapies and adjusting payment policy to promote value-based payments. (That type of system links payments to health outcomes such as treatment efficacy and lack of side effects.) Policymakers could also change Medicare policies that would affect the provision of gene therapy, and some changes in coverage or payment in public programs could be extended to commercial insurers.

Increasing the Federal Role in Gene Therapy Coverage and Payment in Medicaid

Under current law, gene therapies in Medicaid are covered as outpatient drugs subject to rebates under the Medicaid Drug Rebate Program. That policy could be changed in several ways that would influence how Medicaid paid for or covered those treatments. One approach, which has been suggested by the Medicaid and CHIP Payment and Access Commission, would be to remove gene therapies from the structure of the MDRP and create a new benefit for cell and gene therapies. That benefit, which would be administered at the federal level, would standardize coverage and payment across states and plans.[37] A new benefit for cell and gene therapies could also be applied to commercial insurers. If standardized coverage under that benefit was less restrictive than it would be under current law, that change would increase eligibility for the treatment because there would be fewer utilization controls.

Another suggestion, which comes from some drug manufacturers, is to have the federal government facilitate the take-up of gene therapies for SCD by changing the share that it pays. One such approach would boost Medicaid's payments to states by enhancing the federal medical assistance percentage (or FMAP) for those therapies.[38] If states spent less (relative to spending under current law) because of higher federal matching and therefore loosened their utilization controls, more patients would become eligible to receive gene therapy.

Facilitating Value-Based Payments in Medicaid Through the Best Price Policy

Another way to reduce utilization controls for gene therapy in Medicaid—and therefore increase eligibility for the treatments—would be to facilitate value-based payments for those therapies by modifying the program's best price policy. The value-based payment structure offers lower initial payments, with further payments dependent on outcomes.

Before 2020, commercial insurers were concerned that the best price policy in Medicaid would limit the willingness of manufacturers to engage in value-based payments because doing so would lock manufacturers into lower prices in Medicaid.[39] But under the 2020 final rule that gave states, commercial payers, and manufacturers more flexibility to enter into value-based payments for prescription drugs, CMS allowed manufacturers to report multiple best prices for value-based purchasing arrangements if manufacturers made the arrangements available to all state Medicaid programs.[40]

To get the lowest commercial price available, however, state Medicaid programs have to administer the value-based arrangements, and they may not have the resources to do that. Some academics and advocates have suggested that rather than requiring Medicaid programs to administer value-based purchasing arrangements, the best price policy could be revised to allow state Medicaid plans to participate in commercial contracts offered by manufacturers where reimbursement for a treatment is tied to future health outcomes.[41] If states spent less under that approach (relative to spending under current law) and therefore put in place less utilization management than they would have otherwise, more patients would become eligible to receive gene therapy.

Modifying Payment Policies for Gene Therapy in Medicare

In the Medicare program, policymakers could encourage take-up of gene therapies for SCD by increasing the add-on payment above current amounts, by adjusting outlier payments—additional payments for cases that are extremely costly relative to the average case—or by establishing bundled payments for those therapies.[42] If hospitals received higher payments (through outlier or bundled payments) than they receive under current law,

they might be more likely to offer the treatment, thus increasing the number of people treated.

How CBO Would Estimate the Budgetary Effects of Increased Use of Gene Therapy Treatment for Sickle Cell Disease

CBO would start with the number of people receiving the treatment as a building block for its estimate of the budgetary effects of a policy to increase gene therapy treatment of SCD. From there, CBO would trace through the effects on outlays and revenues.

Estimating the Use of Gene Therapies for SCD

To identify the number of people with SCD who would receive gene therapy treatment under a given policy, CBO would first identify the target population. In the case of the recently approved gene therapies for SCD, both Lyfgenia and Casgevy are indicated for the treatment of patients 12 years of age or older with SCD and a history of pain crises. CBO would use available evidence in the literature or its own data analysis to estimate the size of that eligible population.

After identifying the eligible population, CBO would estimate the number of people who would receive gene therapy under the specific policy. That estimate would start with the universe of eligible individuals and evaluate potential take-up on the basis of factors that are likely to affect a patient's access to or willingness to receive gene therapy. Such factors might include expected insurance coverage and out-of-pocket costs, the expected clinical benefits of the therapy, the risk of adverse effects, and the number and location of providers authorized to administer the therapy.

To inform its estimates of the use of new therapies for SCD, CBO would consider available evidence on the current use of similar medical services. For example, the agency could examine the take-up of other cell or gene therapies, such as CAR-T (a cell therapy used to treat various cancers) to inform its expectations about the use of gene therapy for SCD. Those examples may not translate well to the context of SCD gene therapy, however, given differences in the eligible populations, treatment costs, and other factors, such as the riskiness of the procedure and evidence on the duration of effects.

Effects on Federal Outlays and Revenues

CBO would estimate changes to outlays and revenues for each year of the 10-year projection period. If requested and as practicable, CBO could use present-value estimates to assess budgetary effects beyond the 10-year period (see Box 1).[43] Using the number of people receiving treatment, CBO would then consider the costs of the treatment, other conventional budgetary effects, population-change effects, and dynamic effects.

Conventional cost estimates generally reflect the expectation that the size of the economy remains unchanged under a legislative proposal. In particular, by long-standing convention, nominal gross domestic product (GDP), nominal gross national product (measuring output by residents regardless of location), and total income remain roughly unchanged. In most cases, other macroeconomic variables also remain unchanged.

Population-change effects on the budget focus on benefits provided to and taxes paid by people because of a change in the gross population of the United States—for example, people's living longer because they receive gene therapy treatment. When practicable, CBO derives such budgetary estimates primarily from the direct effects on labor income and from eligibility for benefits.

Dynamic effects on the budget reflect changes in all macroeconomic variables. If the legislation would have a major effect on GDP, such as when provisions related to SCD gene therapy are part of a large set of policies, then CBO would undertake this more complex analysis as required by the Congress and when practicable. CBO would also consider and describe sources of uncertainty in estimating the budgetary effects of any policy.

Costs of Treatment. Once CBO estimated the number of people who would receive gene therapy for SCD and their type of insurance coverage, the agency would project the cost of the treatment, which would depend on the policy's specifications. A policy that established an enhanced federal matching rate for gene therapy for SCD (meaning that the federal government paid a larger share of that treatment cost for Medicaid enrollees) would have a different per unit treatment cost than a policy that established a value-based payment approach for gene therapies, for instance.

CBO would compare estimated treatment costs for a given policy with treatment costs under current law. The agency also would incorporate the additional costs of receiving gene therapies, such as the cost of hospitalization. CBO would then assess how those costs would change over time under both current law and under the policy.

Box 1.

Evaluating the Timing of Federal Budgetary Effects of Gene Therapies Compared With Other Health Interventions

Health interventions that impose up-front costs can, in some cases, reduce a patient's need for medical care in the future. In such cases, reductions in future health care spending can offset all or part of the initial cost of treatment. Offsetting savings from curative or preventive therapies, if they occur, are often realized much later, as the need for ongoing care is averted. The timing of up-front costs and future offsetting savings has implications for the Congressional Budget Office's assessment of the budgetary effects of health interventions, especially if costs occur within the 10-year projection period but savings are realized after that period ends.

For instance, consider the following health interventions:

- **Gene therapies to treat sickle cell disease (SCD).** Lyfgenia and Casgevy are both intended to be one-time treatments that could cure SCD while patients are still adolescents. The treatments impose up-front list prices of over $2 million but have the potential to reduce spending over the long term compared with older modes of treatment. Without a cure, patients with SCD accumulate substantial costs over a shorter-than-average lifespan, including the costs of managing acute pain crises and the costs of ongoing medical therapy. If one-time gene therapies proved to be a cure, patients' and insurers' initial costs would be high, but savings would accrue over time (including after the standard 10-year budget period) because of reduced use of medical care. Those savings could offset some or all of the up-front cost. CBO has not assessed the budgetary effects of any specific proposal to increase gene therapy treatment among people with SCD.
- **Direct-acting antivirals to treat hepatitis C.** Like gene therapies for SCD, these treatments are one-time cures. In CBO's assessment, as of 2020, the cost of those treatments varies from $11,500 to $17,000, depending on the specific medication. Without that treatment, patients with hepatitis C incur substantial costs over their lifetime as the disease progresses. In CBO's assessment, the accumulated savings from averted health care costs within the 10-year period after treatment of hepatitis C would exceed the direct costs of treatment in two illustrative scenarios in which treatment increased among people enrolled in Medicaid. Because costly complications from hepatitis C often take 20 to 30 years to emerge, additional savings from early intervention would show up well outside the 10-year period.[1]
- **Anti-obesity medications.** Unlike gene therapies and direct-acting antivirals, anti-obesity medications are not

1. Congressional Budget Office, *Budgetary Effects of Policies That Would Increase Hepatitis C Treatment* (June 2024), www.cbo.gov/publication/60237.

Continued

Other Conventional Effects on Federal Spending. CBO's estimates of the effects of gene therapy treatment on health care spending would incorporate any savings from improved health on the basis of any existing evidence. For instance, a share of any reductions in spending stemming from improvements in health among Medicaid beneficiaries would accrue to the federal government.

To estimate savings from averted health care costs, CBO would evaluate the available evidence and data. The agency would estimate average health care spending associated with SCD treatment under the current standard of care (including spending to treat complications from the disease) and the likely effect of gene therapy on that spending. The estimated reduction in spending from gene therapy would incorporate the expected effectiveness of that therapy, including the costs of addressing any adverse side effects.

How CBO assessed the budgetary effects of changes in health care spending for SCD-related therapies would depend on the programs affected by the policy. Changes in health care spending arising from a policy that affected people enrolled in Medicaid would be borne by the federal and state governments based on the FMAP, which determines the share of Medicaid costs paid by the federal government. Changes arising from a policy that affected people enrolled in Medicare would be borne in part by the federal government and in part by beneficiaries, through out-of-pocket payments and premiums. Because some Medicare beneficiaries have supplemental insurance, some of the cost increases they experienced would be borne by third-party payers.

Box 1. Continued

Evaluating the Timing of Federal Budgetary Effects of Gene Therapies Compared With Other Health Interventions

curative and must be taken continuously to be effective. The medications are expected to cost, on average, $5,600 per person per year in 2026 (the first year of the projection period) and to vary thereafter; those costs would occur throughout the projection period and beyond. In CBO's assessment, use of those medications would improve beneficiaries' health, mainly by reducing the incidence of obesity-related chronic diseases, such as diabetes and cardiovascular conditions. For a person who took the drug continuously for 10 years, CBO's analysis showed no savings in the first year but some offsetting savings in subsequent years. Still, those savings would be small compared with the costs of the medications.[2]

- **Preventive care services aimed at improving health.** Preventive care services (such as cancer screenings) differ from the treatments listed above because they are provided to a broad population (for example, all women above age 40 in the case of mammograms), many of whom will never suffer from the disease. Therefore, the costs of screening apply to everyone who receives the service, but savings will be realized for only a fraction of recipients. (Treatments for SCD, hepatitis C, and obesity are targeted at patients who meet more specific criteria and thus are more likely to directly benefit.) The amount and timing of expected savings following preventive care would depend on the specific intervention.[3]

Even though those interventions differ greatly in terms of the timing of their therapeutic costs, offsetting savings from health improvements, and other effects, CBO's basic approach to assessing the budgetary effects is consistent in all cases. The net budgetary effect of any medical intervention would depend on the total federal share of costs for that intervention, any savings for patients who are treated successfully, and any changes in revenues or spending stemming from people living longer. To calculate savings (or costs) that would occur outside the projection period, the agency would use present-value estimates. Those estimates summarize the long-term effects of federal health care policies, showing what share of the up-front federal costs of such policies might be offset by federal savings from improved health over the long run.[4]

2. Congressional Budget Office, *How Would Authorizing Medicare to Cover Anti-Obesity Medications Affect the Federal Budget?* (October 2024), www.cbo.gov/publication/60441.

3. Congressional Budget Office, *How CBO Analyzes Approaches to Improve Health Through Disease Prevention* (June 2020), www.cbo.gov/publication/56345.

4. Congressional Budget Office, *How CBO Uses Discount Rates to Estimate the Present Value of Future Costs or Savings* (October 2024), Box 1, www.cbo.gov/publication/60284.

Premiums also could change if policies to increase the use of gene therapy affected health care spending for people enrolled in employment-based health insurance or nongroup (individual) coverage obtained through the health insurance marketplaces established under the Affordable Care Act. For enrollees with employer-sponsored insurance, for example, an increase in premiums would decrease the share of compensation that took the form of taxable wages and salaries and increase the share provided as nontaxable health benefits, which would lower federal revenues. Changes in premiums for enrollees with nongroup coverage would affect federal revenues and outlays for premium tax credits.

If increased use of gene therapy treatment for SCD led to improved health among patients, policies to increase that treatment could also affect the federal budget in other ways. Improved health might result in fewer disability claims, for instance, which would reduce outlays for Social Security's Disability Insurance program and for the Supplemental Security Income (SSI) program.

Population-Change Effects. Improved longevity would increase revenues through the collection of additional payroll and income taxes and increase outlays for programs such as Social Security and Medicare because more people would collect benefits.

Dynamic Effects. Improved health also could lead to higher labor productivity and greater labor force growth, boosting wages and total income in the economy. Higher income would reduce the federal deficit in two primary

ways: through more payment of income and payroll taxes and through less eligibility for federally supported programs that provide benefits to people with lower income. Higher income would boost interest rates as well, pushing up net interest costs and partially offsetting the increase in revenues.

Uncertainties. CBO would describe the sources of uncertainty in any estimate of the budgetary effects of a given policy to increase gene therapy for SCD. Uncertainty may arise from empirical evidence that is insufficient or not applicable to the population affected by the policy that CBO is analyzing. The lack of empirical evidence is likely to be a major challenge for any assessment of policies involving gene therapy because those therapies are relatively new and evidence of their use, costs, side effects, and effectiveness is limited. Substantial uncertainty also surrounds the costs of gene therapy and the capacity to deliver that therapy in the future; potential innovations could affect the evolution of those treatments.

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4. Food and Drug Administration, "Approved Cellular and Gene Therapy Products" (accessed December 13, 2024), https://tinyurl.com/s4v225tu.

5. IQVIA Institute for Human Data Science, *Strengthening Pathways for Cell and Gene Therapies: Current State and Future Scenarios* (March 2024), https://tinyurl.com/yrfjx2hp.

6. Tufts Medical Center, "Cell and Gene Therapy (CGT) Pipeline Deep Dive" (accessed November 18, 2024), https://tinyurl.com/bdd9dxuz. Colin M. Young, Casey Quinn, and Mark R. Trusheim, "Durable Cell and Gene Therapy Potential Patient and Financial Impact: U.S. Projections of Product Approvals, Patients Treated, and Product Revenues," *Drug Discovery Today*, vol. 27, no. 1 (January 2022), pp. 17–30, https://tinyurl.com/4kvma8ty.

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8. Centers for Disease Control and Prevention, "Newborn Screening Data" (October 28, 2024), https://tinyurl.com/y3fd64cf.

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28. Under the Medicaid Drug Rebate Program's basic rebate, a manufacturer must pay the larger of either a flat rebate amount equal to 23.1 percent of the average manufacturer price (AMP) for brand-name drugs or the difference between the AMP and the best price (the lowest price offered to any private payer, excluding Medicare Part D plans). In other words, if the manufacturer of the brand-name drug offers certain private-sector purchasers a rebate that exceeds 23.1 percent of the AMP, then the basic rebate received by Medicaid is increased to match that larger private-sector rebate. See Congressional Budget Office, *A Comparison of Brand-Name Drug Prices Among Selected Federal Programs* (February 2021), www.cbo.gov/publication/56978.

29. Diane Berry and others, "Assessing the State of Medicaid Coverage for Gene and Cell Therapies," *Molecular Therapy*, vol. 30, no. 9 (September 2022), pp. 2879–2880, https://tinyurl.com/y6znbjt3. Some state Medicaid programs are using bundled payments for gene therapy. See Avalere, "Examining Variation in Gene Therapy Access Across States" (August 27, 2024), https://tinyurl.com/3bcstmf4.

30. Centers for Medicare & Medicaid Services, "Cell and Gene Therapy (CGT) Access Model" (accessed November 20, 2024), https://tinyurl.com/msh49ued.

31. That add-on payment is calculated as equal to the lesser of 75 percent of the costs of the technology or 75 percent of the amount by which the costs exceed the payment rate for the standard Medicare Severity Diagnosis Related Group (MS-DRG) that would apply to Lyfgenia or Casgevy administration—probably MS-DRG 016 (Autologous Bone Marrow Transplant with CC/MCC) or 017 (Autologous Bone Marrow Transplant without CC/MCC). MS-DRGs are a system used by Medicare to categorize hospital inpatient stays for payment purposes. See Medicare and Medicaid Programs and the Children's Health Insurance Program; Hospital Inpatient Prospective Payment Systems for Acute Care Hospitals and the Long-Term Care Hospital Prospective Payment System and Policy Changes and Fiscal Year 2025 Rates; Quality Programs Requirements; and Other Policy Changes, 89 Fed. Reg. 68986 (August 28, 2024).

32. CBO assessed the approval requirements of the coverage policies for the five largest commercial insurers and compared them with the FDA indications for Lyfgenia and Casgevy. The agency assessed age restrictions; requirements for the number of pain crises; transplant qualification and lack of matched-donor requirements; failed medication requirements (such as intolerance to hydroxyurea); and other coverage restrictions. Because the FDA indication is broad, additional requirements were considered restrictive.

33. Food and Drug Administration, "Lyfgenia" (July 10, 2024), www.fda.gov/vaccines-blood-biologics/lyfgenia. The FDA indication for Lyfgenia is for "patients 12 years of age or older with sickle cell disease and a history of vaso-occlusive events."

34. Caroline Horrow and Aaron S. Kesselheim, "Confronting High Costs and Clinical Uncertainty: Innovative Payment Models for Gene Therapies," *Health Affairs*, vol. 42, no. 11 (November 2023), pp. 1532–1540, https://doi.org/10.1377/hlthaff.2023.00527.

35. Ibid.

36. Ibid.

37. Medicaid and CHIP Payment and Access Commission, *Report to Congress on Medicaid and CHIP* (June 2021), p. 16, https://tinyurl.com/bdfsr7t3.

38. Jeremy Allen and others, "Medicaid Coverage Practices for Approved Gene and Cell Therapies: Existing Barriers and Proposed Policy Solutions," *Molecular Therapy: Methods & Clinical Development,* vol. 29 (June 2023), pp. 513–521, https://tinyurl.com/2bt7n64e.

39. For example, if a manufacturer offered substantial rebates to a commercial plan in an outcomes-based contract under circumstances in which the drug failed to provide a desired outcome, the manufacturer would have to offer that same rebate to all state Medicaid programs even if the drug produced desired outcomes for Medicaid patients.

40. Centers for Medicare & Medicaid Services, "CMS Issues Final Rule to Empower States, Manufacturers, and Private Payers to Create New Payment Methods for Innovative New Therapies Based on Patient Outcomes" (press release, December 21, 2020), https://tinyurl.com/7yw26knk.

41. Casey Quinn and others, "Medicaid Best Price Reforms to Enable Innovative Payment Models for Cell and Gene Therapies," *Expert Review of Pharmacoeconomics & Outcomes Research*, vol. 23, no. 2 (2023), pp. 191–203, https://doi.org/10.1080/14737167.2023.2159813.

42. In April, the Centers for Medicare & Medicaid Services proposed paying hospitals 75 percent of the estimated cost of the treatment in addition to what it already pays for the therapy. That amount is more than the usual 65 percent add-on payment that hospitals typically receive for using new technologies. See Maya Goldman, "Medicare Floats Incentive for Hospitals to Offer New Sickle Cell Treatments," *Axios* (April 11, 2024), https://tinyurl.com/4tjsbbdx. Some analysts have suggested that the new technology add-on and outlier payments do not cover the full additional price of a new technology. As a result, there are concerns that hospitals administering those treatments may not be able to recoup their costs. See Gregory W. Daniel and others, *Breakthroughs and Barriers: Advancing Value-Based Payment for Transformative Therapies* (Duke-Margolis Center for Health Policy, May 2019), https://tinyurl.com/53ssc257. Bundled payments, in which providers receive a single payment for all services related to a patient's episode of care, are being used by some state Medicaid programs for gene therapy but could be expanded to Medicare. That payment model is intended to improve efficiency and care coordination relative to a payment model that uses separate claims for every service. See Avalere, "Examining Variation in Gene Therapy Access Across States" (August 27, 2024), https://tinyurl.com/3bcstmf4.

43. For a discussion, see Congressional Budget Office, *How CBO Uses Discount Rates to Estimate the Present Value of Future Costs or Savings* (October 2024), www.cbo.gov/publication/60284.

This Congressional Budget Office report was prepared at the request of the Chair of the House Budget Committee Health Care Task Force. In keeping with the agency's mandate to provide objective, impartial analysis, the report makes no recommendations.

Colin Baker, Jared Maeda, and Kaylee Nielson wrote the report with guidance from Aditi Sen. Elizabeth Cove Delisle, Noelia Duchovny, Sean Dunbar, Ann E. Futrell, Tamara Hayford, Noah Meyerson, Asha Saavoss, Emily Stern, and Chapin White provided comments. Grace Lin, a physician and Robert Wood Johnson Foundation health policy fellow who visited CBO and now works for the agency on a contract basis, provided valuable comments and clinical expertise. Anthony Montano and Rajan Topiwala fact-checked the report.

Jeffrey Kling reviewed the report. Christine Bogusz and Brett Kessler edited it, and R. L. Rebach created the graphics and prepared the report for publication. The report is available at www.cbo.gov/publication/60775.

CBO seeks feedback to make its work as useful as possible. Please send comments to communications@cbo.gov.

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