



GAO

Accountability * Integrity * Reliability

United States Government Accountability Office
Washington, DC 20548

January 31, 2012

The Honorable Orrin G. Hatch
Ranking Member
Committee on Finance
United States Senate

Subject: *Drug Pricing: Research on Savings from Generic Drug Use*

Dear Senator Hatch:

Prescription drug spending in the United States reached \$307 billion in 2010—an increase of \$135 billion since 2001¹—and comprised approximately 12 percent of all health care spending in the country. Until the early 2000s, drug spending was one of the fastest growing components of health care spending. However, since that time, the rate of increase has generally declined each year, attributable in part to the greater use of generic drugs, which are copies of approved brand-name drugs.² Generic versions of brand-name drugs become available to consumers when brand-name drugs' patents and periods of market exclusivity expire and generic manufacturers obtain approval to market their drug.³ The competition that brand-name drugs face from generic equivalents is associated with lower overall drug prices, particularly as the number of generic manufacturers grows and price competition among them increases.⁴ On average, the retail price of a generic drug is 75 percent lower than the retail price of a brand-name drug.⁵

¹See IMS Institute for Healthcare Informatics, *The Use of Medicines in the United States: Review of 2010* (Parsippany, N.J.: April 2011). For the purposes of this report, we use the terms prescription drugs and drugs interchangeably.

²A brand-name drug is a drug marketed under a proprietary, trademark-protected name. For the purposes of this report, we use the terms generic drug and generic interchangeably. We also use the terms brand-name drug and brand interchangeably.

³Patents are issued by the U.S. Patent and Trademark Office, generally for a term of 20 years from the date of filing. A patent grants its owner the right to exclude others from making, using, selling, offering to sell, or importing the patented invention into the United States. See 35 U.S.C. § 154(a)(2). In the case of drugs, the patent protects the investment in the drug's development by giving the manufacturer the sole right to sell the drug while the patent is in effect.

⁴While research has shown that generic drug prices decrease relative to the number of generic manufacturers that enter the market, research is less clear regarding the overall effect of generic entry on brand prices. While some studies have found that the price of a brand-name drug increases following generic entry, others have found that generic entry exerts a downward pressure on brand prices. In the latter case, while brand-name prices typically increase over time, with generic entry they do not increase as much as they would have otherwise.

⁵Congressional Budget Office (CBO), *Effects of Using Generic Drugs on Medicare's Prescription Drug Spending* (Washington, D.C.: September 2010).

Increased use of generic drugs can partly be attributed to the regulatory framework that was established in the Drug Price Competition and Patent Term Restoration Act of 1984, commonly known as the Hatch-Waxman Act.⁶ The Hatch-Waxman Act facilitated earlier, and less costly, market entry of generic drugs, while protecting the patent rights of brand-name drug manufacturers, to encourage continued investment in research and development. When the act was enacted in 1984, the generic utilization rate—which is the share of all drugs dispensed that are generic—was about 19 percent. Today it is about 78 percent for drugs dispensed in retail settings, such as independent, chain, and mail-order pharmacies, as well as in long-term care facilities.⁷ The generic utilization rate is expected to continue to grow over the next few years as a number of blockbuster drugs⁸ come off patent through 2015.

While the Hatch-Waxman Act has helped to increase the number of generic alternatives to brand-name drugs, other factors influence whether providers and consumers use generic drugs. For example, third-party payers—including private health insurance plans and public programs such as Medicare—⁹use strategies such as tiered copayments to encourage the use of less expensive drugs within a therapeutic class, which are often generics.¹⁰ Also, perceptions of the safety and efficacy of generic drugs may affect their use. Thus, use of generic drugs—and the savings realized—can vary by payer as well as across therapeutic classes. You asked us to identify research completed on estimates of cost savings from the use of generic drugs in the United States. This report summarizes the findings of peer-reviewed articles, government reports, and studies by national organizations, including trade and nonprofit organizations, on this topic.¹¹

To identify research completed on estimates of cost savings from the use of generic drugs in the United States, we conducted a structured literature review, which resulted in 30 articles we determined to be relevant to our objective (see the enclosure for a list of the articles we identified). To conduct this review, we searched

⁶Pub. L. No. 98-417, 98 Stat. 1585 (1984).

⁷In addition to long-term care facilities, prescription drugs can be dispensed in other institutional settings, such as hospitals and clinics. Complete data on the 2010 generic utilization rate were not publicly available for drugs dispensed in institutional settings. However, drugs dispensed in retail settings and long-term care facilities comprise approximately 76 percent of all prescription drug spending in the United States, with drugs dispensed in retail settings accounting for almost all of these drugs.

⁸Blockbuster drugs are drugs that generate at least \$1 billion in revenue per year for the company that manufactures them. From 2012 through 2015, 13 blockbuster drugs that account for about \$78 billion in drug sales are expected to come off patent, including Plavix (an anti-platelet medication), Seroquel (an antipsychotic), and Singulair (an asthma medication).

⁹Medicare is the federally financed health insurance program for persons aged 65 or over, certain individuals with disabilities, and individuals with end-stage renal disease. Medicare covers drugs dispensed in hospital inpatient settings or skilled nursing facilities through Part A and outpatient prescription drugs either through Medicare Part B or Part D. Part B covers physician-administered drugs. Part D, which went into effect in 2006, provides a voluntary outpatient prescription drug benefit for the Medicare program.

¹⁰Third-party payers may use a variety of copayment structures. For example, in a common three tier copayment structure, enrollees pay a low copayment for generic drugs (the first tier), a higher one for preferred brand-name drugs (the second tier), and the highest copayment for nonpreferred brand-name drugs (the third tier). A therapeutic class is defined as a group of drugs that are similar in chemical structure, pharmacological effect, or clinical use.

¹¹For the purposes of this report, we use the terms articles, reports, and studies interchangeably.

seven reference databases that included peer-reviewed journal articles and other periodicals to capture articles published on or between January 2000 and October 24, 2011.¹² We used a combination of search terms related to cost savings from the use of generic drugs, including synonyms for generic drugs, monetary terms, and modifiers (see the enclosure for a complete list of the search terms). We determined whether an article was relevant to our objective based on whether it included an empirical analysis that produced estimates of cost savings from the use of generic drugs. We excluded articles that: (1) were not focused on the United States; (2) were news articles, opinion pieces, or PowerPoint presentations; or (3) did not describe a methodology for calculating the savings estimates. We also excluded articles that: (1) included estimates of cost savings involving the use of generic drugs, but it was unclear whether other factors also contributed to the savings;¹³ (2) analyzed differences in the prices of brand and generic drugs, but did not look at cost savings for a given population; or (3) focused on estimates of cost savings from generic versions of biologics.¹⁴ To supplement this information, we searched government websites, such as the Department of Health and Human Services' website, for studies that met our criteria. We also searched the websites of national organizations, including those of trade groups, such as the Generic Pharmaceutical Association (GPhA), and nonprofits, such as the Kaiser Family Foundation. In addition, we searched the Nexis database for trade articles discussing cost savings from generic drugs using the same search terms as our review of reference databases. To help ensure our searches captured relevant articles, we reviewed the bibliographies of the studies we identified as relevant to identify other potentially relevant articles. We also interviewed officials at the Congressional Budget Office (CBO), GPhA, and IMS Health¹⁵ about prior work on estimates of cost savings from the use of generic drugs, and included any additional reports the officials identified if they met our criteria. We analyzed the 30 articles identified through our literature review to group them by topic covered and summarized key methodological similarities and differences within and among the groups. However, we did not independently assess the methodologies of the articles, including the reliability of data used.

¹²The databases we searched included those with a medical or economic focus as well as those including articles across multiple disciplines. They were: MEDLINE, EMBASE, EMCare, EconLit, NTIS, SciSearch, and Social SciSearch. While we restricted our search to articles published on or between January 2000 and October 24, 2011, some articles identified were based on data prior to this time period.

¹³Examples of such articles are those that discussed pharmacy benefit design changes to encourage generic use, such as the initiation of a three tier copayment structure. In these cases, the articles were excluded because they did not distinguish whether cost savings estimates resulted from generic drug use or other factors, such as the use of lower-cost brand-name drugs.

¹⁴Biologics are products, such as vaccines, derived from living sources, such as humans, animals, and microorganisms. See 42 U.S.C. § 262(i). Biosimilars—or follow-on versions of biologics—are not subject to the Hatch-Waxman Act, and there has historically been limited market penetration of these products. In order to encourage a market for biosimilars, the Patient Protection and Affordable Care Act (PPACA) established a pathway for approval of biosimilars analogous to the Hatch-Waxman Act, and the Food and Drug Administration is currently developing regulations to implement the provisions. See Pub. L. No. 111-148, § 7002, 124 Stat. 119, 804-21 (2010).

¹⁵IMS Health is an international company that supplies the pharmaceutical and health care industries with market information.

We conducted our work from October 2011 to January 2012 in accordance with all sections of GAO's Quality Assurance Framework that are relevant to our objectives. The framework requires that we plan and perform the engagement to obtain sufficient and appropriate evidence to meet our stated objectives and to discuss any limitations in our work. We believe that the information and data obtained, and the analysis conducted, provide a reasonable basis for any findings and conclusions in this product. Because we did not evaluate the policies or operations of any federal agency to develop the information presented in this report, we did not seek comments from any agency.

Results in Brief

Our review identified articles that used varying approaches to estimate the savings associated with generic drug use in the United States. One group of studies estimated the savings in reduced drug costs that have accrued from the use of generics. For example, a series of studies estimated the total savings that have accrued to the U.S. health care system from substituting generic drugs for their brand-name counterparts, and found that from 1999 through 2010 doing so saved more than \$1 trillion. A second group of studies estimated the potential to save more on drugs through greater use of generics. For example, one study assessed the potential for additional savings within the Medicare Part D program—which provides outpatient prescription drug coverage for Medicare—and found that if generic drugs had always been substituted for the brand-name drugs studied, about \$900 million would have been saved in 2007. A third group of studies estimated the effect on health care costs of using generic versions of certain types of drugs where questions had generally been raised about whether substituting generic drugs for brand-name drugs was medically appropriate. Unlike the other two groups which focused on savings on drugs only, these studies compared savings from the lower cost of generic drugs to other health care costs that could accrue from their use, such as increased hospitalizations. The studies had mixed results regarding the effect of using these generics in that some found they raised health care costs, while others found they led to cost savings.

Background

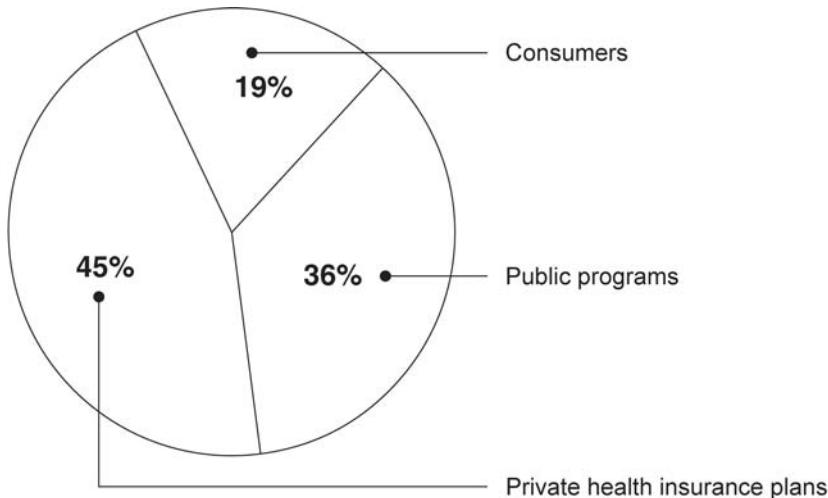
In order to be approved by the U.S. Food and Drug Administration (FDA), generic drugs must be the same as their brand-name counterparts in the following ways: they must have the same active ingredient(s); the same route of administration, for example, a drug that is taken orally versus by injection; the same dosage form, for example, a pill versus a syrup; the same strength; and the same intended use.¹⁶ Generic drugs also must meet FDA manufacturing standards and be bioequivalent, meaning that the rate and extent of absorption of generic drugs into the bloodstream do not show a statistically significant difference from their brand-name counterparts. However, bioequivalence standards set by FDA allow for variation between brand and generic drugs that is considered small enough for the drugs to still be considered interchangeable. Such variation may occur because, for example, generic drugs may have different inactive ingredients, such as binding materials, dyes, preservatives, or flavoring agents compared to brand-name drugs.

¹⁶Active ingredients include any component of a drug that is intended to provide pharmacological activity or other direct effect in the diagnosis, cure, mitigation, treatment, or prevention of disease. See 21 C.F.R. § 210.3(b)(7).

Spending on Prescription Drugs

Prescription drug spending consists of payments from third-party payers, including private health insurance plans and public programs, and of consumers' out-of-pocket costs.¹⁷ Most—approximately 76 percent—of drug spending in the United States is for drugs dispensed in retail settings and long-term care facilities, with drugs dispensed in retail settings accounting for almost all of these drugs. In 2010, private health insurance plans paid \$117 billion or 45.2 percent of the \$259.1 billion spent on retail prescription drugs.¹⁸ Public programs paid \$93.3 billion, accounting for 36 percent, and consumers paid \$48.8 billion out of pocket, accounting for 18.8 percent of the spending (see fig. 1).

Figure 1: Spending on Prescription Drugs in Retail Settings by Payer Type, 2010



Source: GAO analysis of the Centers for Medicare & Medicaid Services' National Health Expenditure Accounts.

Note: Prescription drugs can be dispensed in retail settings, such as independent, chain, and mail-order pharmacies, as well as in institutional settings, such as long-term-care facilities, hospitals, and clinics. Data on drug spending by payer type were not publicly available for drugs dispensed in institutional settings. However, drugs dispensed in retail settings and long-term care facilities comprise approximately 76 percent of all prescription drug spending in the United States, with drugs dispensed in retail settings accounting for almost all of these drugs.

Within public programs, federal programs accounted for 90 percent of all spending on prescription drugs in retail settings, with state and local spending on programs such as Medicaid accounting for the rest.¹⁹ Medicare was by far the biggest federal payer, representing 70.8 percent of all federal spending on prescription drugs. (See table 1 for more information on federal spending on prescription drugs.)

¹⁷Consumers' out-of-pocket costs generally include direct spending by consumers for drugs not covered by third-party payers and cost-sharing, including copayments and deductibles, for drugs covered by these payers. For the purposes of this report, out-of-pocket costs do not include consumers' premium payments for health insurance plans.

¹⁸Data on prescription drug spending by payer type were not publicly available for drugs dispensed in institutional settings.

¹⁹Medicaid is a joint federal-state program that finances health care for certain categories of low-income individuals. Medicaid programs vary from state to state. Federal spending on prescription drugs includes the federal share of the cost of prescription drugs for Medicaid beneficiaries.

Table 1: Federal Spending on Prescription Drugs in Retail Settings, 2010

Payer	Total spending (in billions)	Percent of federal
Medicare	\$59.5	70.8%
Medicaid ^a	14.8	17.6
Department of Defense	6.1	7.3
Department of Veterans Affairs	2.6	3.1
Other federal spending ^b	1.0	1.2
Total	\$84	100%

Source: GAO analysis of the Centers for Medicare & Medicaid Services' National Health Expenditure Accounts.

Note: Prescription drugs can be dispensed in retail settings, such as independent, chain, and mail-order pharmacies, as well as in institutional settings, such as long-term-care facilities, hospitals, and clinics. Data on drug spending by payer type were not publicly available for drugs dispensed in institutional settings. However, drugs dispensed in retail settings and long-term care facilities comprise approximately 76 percent of all prescription drug spending in the United States, with drugs dispensed in retail settings accounting for almost all of these drugs.

^aIncludes federal spending through Medicaid and the Children's Health Insurance Program.

^bIncludes federal spending by the Indian Health Service and through the Maternal and Child Health program. Also, includes spending through workers compensation programs, which are paid for with federal, state, and local funds.

While private health insurance plans accounted for the largest share of retail drug spending in 2010, the share paid for by public programs has grown in recent years—increasing nearly 10 percent since 2005. The increase in public programs' share of spending can largely be attributed to the implementation of Medicare Part D in 2006. Going forward, a number of factors may affect the growth of prescription drug spending and the distribution of this spending across payers. The implementation of various provisions of the Patient Protection and Affordable Care Act, as amended (PPACA), may affect prescription drug coverage, use, and prices.²⁰ Additionally, market factors, such as the upcoming loss of patent protection for certain blockbuster drugs, as well as the cost of new brand-name drugs entering the market, could also affect spending.

Factors that Affect Generic Drug Use

According to a report by the Department of Health and Human Services, the availability of generic drugs is the most important factor affecting generic drug use.²¹ FDA approval is required before drugs can be marketed for sale in the United States, though this process differs for brand-name and generic drugs. To obtain FDA's approval for a new, brand-name drug,²² manufacturers must submit a new drug application (NDA) containing data on the safety and effectiveness of the drug as determined through clinical trials and other studies.²³ Prior to enactment of the

²⁰For example, PPACA requires that uninsured individuals obtain health insurance coverage. Specifically, beginning in January 2014, most individuals must maintain coverage for themselves and their dependents, which includes employer-sponsored health plans, individual plans, and government-sponsored plans. Pub. L. No. 111-148, §§ 1501(b), 10106(b), 124 Stat. 119, 244-49, 909-10 (2010), as amended by the Health Care and Education Reconciliation Act of 2010, Pub. L. No. 111-152, §§ 1002, 1004, 124 Stat. 1029, 1032-34 (2010) (to be codified at 26 U.S.C. § 5000A).

²¹See Office of the Assistant Secretary for Planning and Evaluation, U.S. Department of Health and Human Services, *Expanding the Use of Generic Drugs* (Washington, D.C.: Dec. 1, 2010).

²²A new drug is a new chemical formula or an approved drug prescribed for use in a new way.

²³See 21 U.S.C. § 355(b). The entity that submits an application to market a drug is referred to as a sponsor. We use manufacturer here because the sponsor of an application is usually a manufacturer.

Hatch-Waxman Act, the same types of studies were required for generic drugs as for brand-name drugs. However, to facilitate generic entry into the market, the act established changes to the FDA approval process for generic drugs.²⁴ Specifically, it included provisions by which manufacturers of generic drugs may submit an abbreviated new drug application (ANDA) to FDA.²⁵ The ANDA process does not require manufacturers to conduct, or provide evidence from, the clinical trials that are required of manufacturers of brand-name drugs. Rather, generic drug manufacturers must demonstrate that a generic drug is bioequivalent to an approved brand-name drug. As a result, the ANDA process is less time consuming and less costly than the NDA process.

The Hatch-Waxman Act contained additional provisions to facilitate the entry of generics onto the market. First, the act accelerated the approval process for generic drugs by allowing generic manufacturers to collect data needed for an ANDA before the patent on the brand-name drug expires.²⁶ Second, the act encouraged generic drug manufacturers to challenge a patent associated with an approved brand-name drug prior to its expiration by making the first generic manufacturer to do so eligible for a 180-day market exclusivity period.²⁷ For 180 days after first marketing the drug, the generic manufacturer does not have competition from other generic manufacturers.²⁸ The Hatch-Waxman Act has been helpful in encouraging the development of generic versions of brand-name drugs, as evidenced by the fact that

²⁴The Hatch-Waxman Act also made changes for brand-name drugs, for example, by establishing patent-term extensions to encourage drug manufacturers to invest in research and development. Because manufacturers of such drugs apply for and are granted patents from the Patent and Trademark Office before they seek approval from FDA, part of their time under patent is spent conducting the clinical trials necessary for FDA approval and going through the FDA approval process—which combined could take about 10-15 years of the 20-year patent term. The patent extensions were intended to offset part of the patent term that elapsed prior to the drug being marketed.

²⁵See 21 U.S.C. § 355(j).

²⁶While the Hatch-Waxman Act accelerated the generic drug approval process, FDA's ability to review ANDAs in a timely fashion may delay generic drugs' entry to the market. We have previously examined FDA's review of ANDAs, and found that from 2004 to 2008, FDA increased the number of ANDAs it reviewed by 42 percent; however over the same period, FDA also received a greater number of applications each year than it was able to review, resulting in 1,441 pending ANDAs in 2008—a 123 percent increase since 2004. See GAO, *Food and Drug Administration: FDA Faces Challenges Meeting Its Growing Medical Product Responsibilities and Should Develop Complete Estimates of Its Resource Needs*, [GAO-09-581](#) (Washington, D.C.: June 19, 2009). By the end of 2011, FDA reported that it had a backlog of about 2,500 ANDAs.

²⁷One example of a patent challenge is when a generic drug manufacturer asserts that the brand-name patent is invalid. For example, a generic manufacturer may argue that a patent is invalid because the patent was duplicative and therefore improperly granted. When a patent is challenged, the brand-name manufacturer has the right to bring the generic manufacturer to court where the challenge is decided through either a court decision or a settlement; if the brand-name manufacturer does not bring a lawsuit, the generic manufacturer may immediately begin marketing the drug after receiving FDA approval. The Federal Trade Commission has alleged that there have been anticompetitive patent agreements between brand-name and generic drug manufacturers. In particular, it has raised issue with "pay-for-delay" agreements in which a brand-name manufacturer agrees to pay a potential generic competitor to delay marketing the generic drug.

²⁸Multiple generic manufacturers may qualify for the 180-day market exclusivity if several ANDA applicants file a substantially complete application on the same day.

in the early 1980s, 35 percent of top-selling drugs with expired patents had generic versions available, but by the late 1990s almost all had generics available.²⁹

Once generic drugs are approved by FDA, providers and consumers may substitute them for their bioequivalent, brand-name counterparts; we refer to this process as generic substitution. They also may substitute generic drugs for brand-name drugs that are not bioequivalent, but are within the same therapeutic class, which we refer to as therapeutic substitution. While generic substitution is generally considered medically appropriate,³⁰ there are a number of circumstances under which therapeutic substitution may not be appropriate. For example, some drugs in a therapeutic class either may be more effective than others for certain individuals or may not be safe for people with complicating health conditions. Taken together, generic and therapeutic substitution make up the generic utilization rate (that is, the share of all drugs dispensed that are generic), which may be affected by a number of factors, including:

- State generic substitution laws: States are responsible for regulating the practice of pharmacy. Consequently, there is variation among state requirements with respect to dispensing generics. For example, some states require pharmacists to practice generic substitution, unless the prescribing physician indicates that only the brand-name drug may be dispensed. Other states allow, but do not require, pharmacists to substitute generic drugs if the prescriber does not specify brand-name only. Additionally, some states require pharmacists to notify or get consent from consumers prior to substituting generic drugs, while others do not.³¹ In the case of therapeutic substitution, a pharmacist cannot substitute between drugs; rather a physician must make the decision to prescribe a generic.
- Pharmacy benefit management: Federal programs and private health insurance plans have implemented strategies to help encourage the use of generic drugs by their beneficiaries or members. Their strategies include tiered copayments, where generic drugs have a lower copayment than brand-name drugs; step-therapy, where consumers are required to try the most cost-effective drug in a therapeutic class first, usually a generic; generic-only coverage; offering free samples of generic medications; financial incentives for physicians and pharmacists to choose generics; and educational efforts to describe the benefits of using generic drugs, which may be targeted at both physicians and consumers.
- Perceptions of generic drugs' safety and efficacy: Physicians, pharmacists, and consumers may have perceptions about the safety and efficacy of generic drugs compared to brand-name drugs, which in turn affect what drugs they choose to use. These perceptions are based on a number of factors, including prior

²⁹CBO, *How Increased Competition from Generic Drugs has Affected Prices and Returns in the Pharmaceutical Industry* (Washington, D.C.: July 1998).

³⁰While rare, there are circumstances in which consumers may medically require the brand-name version of a drug, such as if they are allergic to an inactive ingredient found in the generic version.

³¹See Office of the Assistant Secretary for Planning and Evaluation, 2010 (citing [Epilepsy.com/Professionals](http://professionals.epilepsy.com/Professionals). State Law or Statutes Governing Generic Substitution by Pharmacists, Apr. 25, 2007, at http://professionals.epilepsy.com/page/statutes_by_pharmacists.html.)

experience, results of relevant studies, or advertising. Negative perceptions of generic drugs may be more common where questions have been raised about the medical appropriateness of generic or therapeutic substitution. For example, there is controversy within the health care community about whether generic substitution is appropriate for drugs for which there are relatively small differences between the therapeutic dose and doses that could lead to serious treatment failure or serious adverse drug reactions. These drugs are referred to as having a narrow therapeutic index (NTI) and are commonly understood to include anti-epileptic drugs, thyroid drugs, and immunosuppressant drugs.³²

While the overall generic utilization rate was 78 percent in 2010 for drugs dispensed in retail settings and long-term care facilities, the rate at which generic drugs were substituted for brand-name drugs when a generic equivalent was available was 93 percent.³³ Thus, additional savings from generic drugs are likely to come mostly from an increase in therapeutic substitution, in which a generic is substituted for a brand-name drug that is not bioequivalent. Savings could also come from an increase in the percentage of the prescription drug market that is available for generic substitution, that is from more brand-name drugs gaining generic counterparts. In 2010, 26 percent of drugs dispensed in retail settings and long-term care facilities consisted of brand-name drugs that did not have generic counterparts.³⁴

Research Used Varying Approaches to Estimate the Savings Associated with Generic Drug Use

Our review found that research used varying approaches to estimate the savings associated with generic drug use in the United States. One group of studies estimated the savings in reduced drug costs that have accrued from the use of generics, while a second group of studies estimated the potential to save more on drugs through greater generic use. Additionally, we identified a third group of studies that estimated the effect of using generic versions of certain types of drugs on health care costs.

Cost Savings Accrued from the Use of Generic Drugs

We identified a group of studies that estimated the savings in reduced drug costs that have accrued from the use of generics. The estimates of cost savings varied, in part because the studies ranged in scope. For example, some looked only at generic substitution, while others focused on both generic and therapeutic substitution. Additionally, the period of observation varied among the studies as did the population of interest. While we identified a series of studies that examined savings to the U.S. health care system as a whole, most other studies focused on savings accrued from the implementation of a program to encourage generic drug use or for

³²FDA does not currently designate specific drugs as NTI drugs and, in approving ANDAs, FDA uses the same bioequivalence standards for drugs with a wide therapeutic index and NTI drugs. FDA has historically stated that different standards were not needed; however, the agency has recently decided to revisit this issue. See, FDA, *Summary Minutes of the Advisory Committee for Pharmaceutical Science and Clinical Pharmacology* (Silver Spring, Md.: July 26, 2011).

³³IMS Institute for Healthcare Informatics, 2011.

³⁴IMS Institute for Healthcare Informatics, 2011.

a specific population. The studies also calculated savings in different ways. Methods included estimating the difference between the total amount paid for generic drugs over a specified time period with the amount that would have been paid if brand-name drugs had been used instead and comparing differences in drug costs with and without the implementation of a program to encourage generic use. Examples of studies that looked at cost savings accrued include the following:

- A series of studies conducted for GPhA by IMS Health estimated the total savings generic substitution provided to the overall U.S. health care system for the 12-year period 1999 through 2010.³⁵ The reports found that during this period, generic substitution has saved the U.S. health care system more than \$1 trillion. In 2010 alone, generic substitution generated more than \$157 billion in savings.³⁶ These reports are the most current and comprehensive analyses of cost savings accrued from generic drugs.³⁷ The analyses estimated differences in the total amount paid for generic and brand-name drugs for the U.S. retail and institutional prescription drug market. In calculating savings, the price of brand-name drugs before generic entry into the market was used. An IMS official we interviewed explained that IMS used this approach because generic entry can affect brand prices.³⁸
- A 2010 CBO study examined savings as a result of generic substitution in the Medicare Part D Program.³⁹ Using Part D claims data, the study found that dispensing generic drugs rather than their brand-name counterparts reduced total Part D prescription drug costs in 2007 by about \$33 billion.⁴⁰ The study noted the difficulty associated with establishing the exact share of savings that accrued to the Part D program versus its enrollees. Thus, CBO estimated the proportion of savings accrued to each as being the same proportion as their total

³⁵GPhA, *Savings: An Economic Analysis of Generic Drug Usage in the U.S.* (September 2011); GPhA, *Savings Achieved through the Use of Generic Pharmaceuticals, 2000-2009* (July 2010); GPhA, *Economic Analysis: Generic Pharmaceuticals 1999-2008—\$734 Billion in Health Care Savings* (May 2009).

³⁶GPhA, 2011.

³⁷A previous analysis of cost savings accrued from generic drugs to the overall U.S. health care system was conducted by CBO, but was based on data from 1994 when fewer generic drugs were used. The CBO report, entitled “How Increased Competition from Generic Drugs Has Affected Prices and Returns in the Pharmaceutical Industry,” used data from approximately 70 percent of prescription sales through U.S. retail pharmacies and estimated that generic substitution saved approximately \$8 billion to \$10 billion.

³⁸The IMS official explained that they used the brand-name price prior to generic entry, as sometimes brand manufacturers increase their prices when generics enter the market. One explanation for this practice is that if some, less price-sensitive consumers perceive the quality of brand-name drugs to be better than their generic competitors, they will purchase the brand-name drugs even at higher prices. Thus, the official stated that using brand prices before generic entry provides a more reliable way of estimating the savings associated with generics, because the analysis is not affected by these price changes.

³⁹CBO, 2010.

⁴⁰Health care claims generally refer to charges submitted by physicians, hospitals, pharmacies, or other providers for the sale of drugs, among other services, to private health insurance plans or public programs. In the case of Medicare Part D, private health insurance plans typically contract with the Centers for Medicare and Medicaid Services to provide coverage for beneficiaries and submit claims to the Part D program.

payments to Part D plans and pharmacies in that year. As a result, CBO estimated that approximately 72 percent (\$24 billion) of savings accrued to the Part D program and 28 percent (\$9 billion) to enrollees. In contrast to the GPhA reports, CBO calculated cost savings assuming that generic entry is not likely to have a substantial effect on the price of the brand-name drug and used the prices of brand drugs in 2007 in conducting its analysis. CBO officials we interviewed explained that they made this assumption because there is conflicting evidence as to the effect of generic entry on brand-name drug prices.

- A third article looked at cost savings accrued from the implementation of a program to promote increased use of generic drugs in a large managed care organization.⁴¹ Using claims data, the study compared those physicians who participated in the program in 2005 and 2006 to those who did not and found that the program produced drug cost savings through an increase in both generic and therapeutic substitution. After program expenses, the program saved the organization \$397,486 in 2005 and \$453,545 in 2006.⁴²
- A fourth study looked at cost savings accrued from the implementation of a policy to promote the use of a generic antidepressant over its brand-name counterpart in a Department of Veterans Affairs (VA) hospital.⁴³ Using VA data and estimating differences in the total amount paid for the generic and brand-name versions of the drug, the study found that from March 2002-August 2004, the policy resulted in a total of \$2.5 million in savings.

Potential Cost Savings from Greater Generic Drug Use

We identified a second group of studies that estimated the potential to save more on drugs through greater use of generics. Similar to research on cost savings accrued, while the research found that additional savings opportunities exist, the extent of the savings varied by study scope. Most of the studies identified focused on the potential cost savings from increasing generic substitution within a given population. However, studies also estimated the potential cost savings from greater therapeutic substitution or policies to encourage generic drug use, as well as the costs associated with delayed entry of generic drugs into the marketplace. Articles in this group also differed in population of interest and the number of drugs studied. Studies generally calculated potential savings by estimating the difference between the total amount paid for brand-name drugs over a specified time period with the amount that would have been paid if generic drugs had been used instead. Additionally, while most studies assumed a 100 percent substitution rate in conducting these calculations, others assumed varying levels of substitution. Studies that used a 100 percent substitution rate may have overestimated savings potential, as reaching

⁴¹A managed care organization is a health care organization that emphasizes standardized treatment protocols, case management, and controlled access to care.

⁴²A.B. Scott, E.J. Culley, and J. O'Donnel, "Effects of a Physician Office Generic Drug Sampling System on Generic Dispensing Ratios and Drug Costs in a Large Managed Care Organization," *Journal of Managed Care Pharmacy*, vol. 13, no. 5 (2007), 412-419.

⁴³S.K. Dobscha, L.M. Winterbottom, and L.S. Snodgrass, "Reducing Drug Costs at a Veterans Affairs Hospital by Increasing Market-share of Generic Fluoxetine," *Community Mental Health Journal*, vol. 43, no. 1 (February 2007), 75-84.

this level of substitution is likely unrealistic and, particularly in the case of therapeutic substitution, not always medically appropriate. Examples of studies that looked at potential cost savings include the following:

- One study estimated that potential national savings from increasing generic substitution from about 61 percent to 100 percent would have been approximately \$9 billion for adults in 2000.⁴⁴ The estimate was based on patient-reported estimates of drug prices using a nationally representative sample from the Medical Expenditures Panel Survey Household Component and included all payer types.⁴⁵
- Another study estimated that Medicaid’s potential cost savings from increasing generic substitution from 81 percent to 100 percent for 20 popular brand drugs was \$329 million in 2009.⁴⁶ The study was based on Medicaid drug utilization data and incorporated the price impact of drug manufacturer rebates to state Medicaid programs into its calculations.⁴⁷
- The 2010 CBO study, in addition to estimating cost savings accrued in the Medicare Part D program, assessed the potential for additional savings from generic and therapeutic substitution, and found that if substitution rates had been 100 percent, about \$900 million would have been saved from generic substitution and \$4 billion from therapeutic substitution in 2007.⁴⁸ Potential cost savings calculations from therapeutic substitution were for seven therapeutic classes and incorporated rebate data.⁴⁹

⁴⁴J.S. Haas, K.A. Phillips, E.P. Gerstenberger, and A.C. Seger, “Potential Savings from Substituting Generic Drugs for Brand-Name Drugs: Medical Expenditure Panel Survey, 1997-2000,” *Annals of Internal Medicine*, vol. 142, no. 11 (June 2005), 891-897.

⁴⁵The Medical Expenditure Panel Survey Household Component collects data, including prescriptions filled, from individual households and their members and is supplemented by data from their medical providers.

⁴⁶A. Brill, “Overspending on Multi-Source Drugs in Medicaid,” *American Enterprise Institute for Public Policy Research* (March 2011).

⁴⁷In general, in order to have their drugs covered by Medicaid, manufacturers are required to pay states rebates, calculated based on a statutorily defined formula, on outpatient drugs that are dispensed to the states’ Medicaid patients. As of January 1, 2010, PPACA increased the rebate percentage for this formula from 15.1 percent to 23.1 percent of the average manufacturer price (AMP) for most brand-name drugs and from 11 percent to 13 percent of the AMP for generic drugs. Pub. L. No. 111-148, § 2501, 124 Stat. 119, 306-10 (2010) (codified at 42 U.S.C. § 1396r-8). However, as this study was based on 2009 data, the rebate percentages in place prior to PPACA applied. While this study incorporated the price impact of drug manufacturer rebates on state Medicaid programs in its calculations, some studies that looked at savings to the Medicaid program did not.

⁴⁸CBO, 2010. Actual generic and therapeutic substitution rates for 2007 were not included in the report.

⁴⁹The seven therapeutic classes that CBO examined accounted for only 17 percent of total prescription drug costs in 2007. Thus, potential savings from therapeutic substitution could have been higher to the extent that other classes also present opportunities for therapeutic substitution. However, the authors also noted that savings could have been lower, because in many cases it would not have been medically appropriate to switch a prescription. The authors took rebate data into account only in calculating savings from therapeutic substitution, stating that outside of the Medicaid program, rebates are generally only given for brand-name drugs that do have generic counterparts.

- An industry report conducted by Express Scripts, a pharmacy benefit manager, also estimated the potential savings from increasing generic and therapeutic substitution among its members and found it to be over \$20 billion in 2005; however the study did not separate the savings associated with each type of substitution.⁵⁰ The potential savings estimate was for six therapeutic classes and used company claims data from 48 states.⁵¹ The savings opportunity for each of the 48 states was estimated by therapeutic class as the difference in actual total costs given each state's 2005 generic utilization rate and what costs would have been if the state were able to reach the generic utilization targets for that class.⁵²
- Another study examined the effect of states' generic substitution laws on Medicaid spending.⁵³ The study estimated that for one cholesterol-lowering drug, the program could have saved approximately \$20 million in the 15 months following patent expiration if all states that had a generic substitution policy requiring patient consent eliminated the policy. To calculate potential savings, the study used 2006-2007 Medicaid drug utilization data and compared actual generic savings between states that did not require patient consent and those that did.
- A sixth study examined the cost to Medicaid of delayed generic drug entry to market of three case study drugs.⁵⁴ This study used Medicaid drug utilization data and calculated that if generic drugs had been available and fully substituted at their lowest cost upon the expiration of patent protection, Medicaid could have saved more than \$1.5 billion from 2000 to 2004 for these three drugs.⁵⁵

⁵⁰E. Cox, A. Behnm, and D. Mager, "2005 Generic Drug Usage Report," Express Scripts (2005). Pharmacy benefit managers administer the prescription drug benefits of health insurance plans on behalf of plan sponsors. Their services can include negotiating with manufacturers to lower the price that plans pay for prescription drugs and developing and managing preferred drug lists. Express Scripts is one of the largest pharmacy benefit managers in the United States with at least 3 million members at the time this study was conducted.

⁵¹The six therapeutic classes represented 40 percent of all drug spending for the study population.

⁵²The generic utilization targets were estimated by Express Scripts' clinical pharmacists by evaluating the clinical efficacy and market dynamics of branded and generic medications across the six therapeutic classes selected for the study. Among the six therapeutic classes, generic utilization targets in 2005 ranged from 70 percent for anti-hyperlipidemics to 95 percent for gastrointestinals, calcium channel blockers, and non-steroidal anti-inflammatory drugs.

⁵³W.H. Shrank, N.K. Choudhry, J. Agnew-Blais, A.D. Federman, J.N. Liberman, J. Liu, A.S. Kesselheim, M.A. Brookhart, and M.A. Fischer, "State Generic Substitution Laws Can Lower Drug Outlays Under Medicaid," *Health Affairs*, vol. 29, no.7 (July 2010), 1383-1390.

⁵⁴A.S. Kesselheim, M.A. Fischer, and J. Avorn, "Extensions of Intellectual Property Rights and Delayed Adoption of Generic Drugs: Effects on Medicaid Spending," *Health Affairs*, vol. 25, no.6 (November/December 2006), 1637-1647.

⁵⁵The study noted that generic drugs can be delayed from reaching the U.S. market if, for example, manufacturers obtain patents on changes to the existing brand-name drug, including modified forms of the same drug, new delivery systems for the drug, and new uses of the drug.

Effect of Using Generic Versions of Certain Types of Drugs on Health Care Costs

We identified a third group of studies that estimated the effect on health care costs of using generic versions of certain types of drugs where questions had generally been raised about whether substituting generic drugs for brand-name drugs was medically appropriate; the research found mixed results about whether generic drugs lowered health care costs in these circumstances. Unlike the research discussed above, which focused on savings on drugs only, this research compared savings from the lower cost of generics to other health care costs that might accrue from their use, such as increased hospitalizations, emergency department visits, or physician visits. These studies were generally limited to particular types of drugs where the medical appropriateness of generic or therapeutic substitution has been debated. Studies that looked at generic substitution focused on NTI drugs, whereas studies that looked at therapeutic substitution did not focus on NTI drugs. For example, studies that looked at therapeutic substitution examined selective serotonin reuptake inhibitors (SSRIs), which are currently among the most widely prescribed antidepressants in the United States.⁵⁶ Most studies used a regression analysis for the estimate to account for the potential impact of confounding variables, such as comorbidities on health care costs.⁵⁷ In addition to drugs studied, the articles varied by a number of factors, including period of observation, health care costs measured, selection of confounding variables, and whether patients initiated therapy with a generic drug or switched from a brand drug to a generic drug midtreatment. Examples of studies that looked at the effect of using generic versions of certain types of drugs on health care costs include the following:

- One study examined claims data between 1996 and 2004 for renal transplant patients in eight private health insurance plans to examine the effect of generic substitution of an NTI immunosuppressant drug on health care costs.⁵⁸ The study found that total health care costs 12 months after transplantation were higher for those initiating therapy with the generic immunosuppressant drug at \$36,482 versus the brand version of the drug at \$32,171. This study did not find a difference in hospitalization or physician costs. Rather, the study found that the main reason for the difference in health care costs was the cost associated with needing higher doses of the generic drug or additional immunosuppressants needed to maintain the transplanted kidney in patients using the generic.

⁵⁶SSRIs are not NTI drugs. However, concerns have been raised about therapeutic substitution of these drugs due to some studies suggesting that there are therapeutic differences between SSRIs.

⁵⁷In general, regression analyses measure the relationship between independent variables, which in this case includes drug type, and the dependent variable, which in this case is health care costs. In measuring the relationship between an independent variable and a dependent variable, regression analyses account for other variables that could affect the relationship between the two, also known as confounding variables. Comorbidities are the presence of one or more diseases or conditions in addition to a primary disease or condition.

⁵⁸J.H. Helderman, N. Kang, A.P. Legorreta, and J.Y. Chen, "Healthcare Costs in Renal Transplant Recipients Using Branded versus Generic Ciclosporin," *Applied Health Economics and Health Policy*, vol. 8, no. 1 (2010), 61-68.

- A second study used claims data from 1998 for approximately 2,300 privately insured patients to determine the effect of generic substitution of an NTI anticoagulant drug when a switch occurred midtreatment.⁵⁹ The study compared treatment costs associated with using the brand and generic version of the drug and found that, based on data from 90 days before and the 90 days after the switch, the difference in total costs associated with the brand and generic anticoagulant drug was \$3,128 less per 100 patient years for the generic.
- Another study used claims data from about 45 private health insurance plans from 2003 to 2007 to compare health care costs over 6 months in patients using brand and generic SSRIs when therapeutic substitution occurred midtreatment.⁶⁰ The study found that, on average, compared with patients who remained on brand-name drugs, patients who switched to generic drugs experienced an increase of \$881 in total health care costs. Among other factors leading to the increased costs, patients who switched from brand-name drugs to generic drugs had higher rates of hospitalizations and emergency department visits than did patients who remained on the brand-name drug.
- A fourth study reached a different conclusion about the effect of using generic SSRIs, when patients began treatment with a generic drug.⁶¹ This study used claims data from 2005 to 2007 and compared health care costs for a 6-month period in patients in about 100 private health insurance plans. The study concluded that the total health care costs of patients using generic antidepressants were significantly lower than costs of patients using brand antidepressants, with an average of \$3,660 and \$4,587 respectively.

As agreed with your office, unless you publicly announce the contents of this report earlier, we plan no further distribution until 30 days from the report date. At that time, we will send copies to other interested parties. In addition, the report will be available at no charge on the GAO website at <http://www.gao.gov>. If you or your staff have

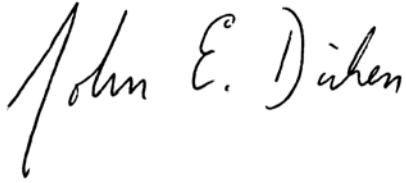
⁵⁹D.M. Witt, D.J. Tillman, C.M. Evans, T.V. Plotkin, and M.A. Sadler, "Evaluation of the Clinical and Economic Impact of a Brand Name-to-Generic Warfarin Sodium Conversion Program," *Pharmacotherapy*, vol. 23, no. 3 (2003), 360-368.

⁶⁰E.Q. Wu, A.P. Yu, V. Lauzon, K. Ramakrishnan, M. Marynchenko, R. Ben-Hamadi, S. Blum, and M.H. Erder, "Economic Impact of Therapeutic Substitution of a Brand Selective Serotonin Reuptake Inhibitor with an Alternative Generic Selective Serotonin Reuptake Inhibitor in Patients with Major Depressive Disorder," *The Annals of Pharmacotherapy*, vol. 45 (April 2011), 441-451.

⁶¹A. Vlahiotis, S.T. Devine, J. Eichholz, and A. Kautzner, "Discontinuation Rates and Health Care Costs in Adult Patients Starting Generic Versus Brand SSRI or SNRI Antidepressants in Commercial Health Plans," *Journal of Managed Care Pharmacy*, vol. 17, no. 2 (March 2011), 123-132.

any questions about this report, please contact me at (202) 512-7114 or dickenj@gao.gov. Contact points for our Offices of Congressional Relations and Public Affairs may be found on the last page of this report. Major contributors to this report were Robert Copeland, Assistant Director; Kathryn Black; Laurie Pachter; and Rachel Svoboda.

Sincerely yours,

A handwritten signature in black ink that reads "John E. Dicken". The signature is written in a cursive style with a large, sweeping initial "J".

John E. Dicken
Director, Health Care

Enclosure

Articles Identified through Literature Review

Through a structured literature review GAO identified 30 articles that included empirical analyses estimating the savings associated with generic drug use. To conduct this review, GAO searched reference databases using a combination of search terms,¹ and supplemented this information by searching government websites, such as the Department of Health and Human Services’ website, and websites of national organizations, including those of trade groups, such as the Generic Pharmaceutical Association, and nonprofits, such as the Kaiser Family Foundation. Articles identified estimated the savings in reduced drug costs that have accrued from the use of generics, the potential to save more on drugs with greater generic use, and the effect of using generic versions of certain types of drugs on health care costs. Table 2 lists the 30 articles by study type.

Table 2: Articles Identified through Literature Review by Study Type

Study type	Study reviewed
Cost savings accrued	Congressional Budget Office, <i>Effects of Using Generic Drugs on Medicare’s Prescription Drug Spending: A CBO Study</i> (Washington, D.C.: September 2010). ^{a,b}
	Dobscha, S.K., L.M. Winterbottom, and L.S. Snodgrass, “Reducing Drug Costs at a Veterans Affairs Hospital by Increasing Market-share of Generic Fluoxetine,” <i>Community Mental Health Journal</i> , vol. 43, no.1 (February 2007), 75-84. ^a
	Generic Pharmaceutical Association, <i>Savings: An Economic Analysis of Generic Drug Usage in the U.S.</i> (September 2011). ^a
	Generic Pharmaceutical Association, <i>Savings Achieved through the Use of Generic Pharmaceuticals, 2000-2009</i> (July 2010). ^a
	Generic Pharmaceutical Association, <i>Economic Analysis: Generic Pharmaceuticals 1999-2008—\$734 Billion in Health Care Savings</i> (May 2009). ^a
	Hong, S.H., and N.F. Canterbury, “Evaluation of the Cost-Saving Potential of a Generic Dispensing Incentive Program,” <i>Drug Benefit Trends</i> , vol. 16 (2004), 515-524.
	Joyce, G.F., J.J. Escarce, M.D. Solomon, and D.P. Goldman, “Employer Drug Benefit Plans and Spending on Prescription Drugs,” <i>Journal of the American Medical Association</i> , vol. 288, no.14 (October 2002), 1733-1739.
	Lieberman, J.N., and M.C. Roebuck, “Prescription Drug Costs and the Generic Dispensing Ratio,” <i>Journal of Managed Care Pharmacy</i> , vol. 16, no. 7 (September 2010), 502-506.
	Scott, A.B., E.J. Culley, and J. O’Donnell, “Effects of a Physician Office Generic Drug Sampling System on Generic Dispensing Ratios and Drug Costs in a Large Managed Care Organization,” <i>Journal of Managed Care Pharmacy</i> , vol. 13, no. 5 (June 2007), 412-419. ^a
	Sy, F.Z., H.M. Choe, D.M. Kennedy, C.J. Standiford, D.M. Parsons, K.D. Bruhnsen, J.G. Stevenson, and S.J. Bernstein, “Moving from A to Z: Successful Implementation of a Statin Switch Program by a Large Physician Group,” <i>American Journal of Managed Care</i> , vol. 15, no. 4 (April 2009), 233-240.

¹We searched the reference databases for article titles, descriptors, and identifiers involving all of the following combinations: “generic drug,” “generic pharmaceutical,” “generic prescription,” “generic medication,” “generic counterpart,” “generic formulation,” “generic version,” “multisource drug,” “multisource pharmaceutical,” “multisource prescription,” “multisource medication;” and “save,” “savings,” “spend,” “cost,” “expenditure,” “expense,” “outlay,” “economic,” “fiscal,” “financial,” “monetary.” We then searched article abstracts using these terms as well as the following modifying terms: “reduce,” “decrease,” “lessen,” “lower,” “minimize,” “curtail,” “moderate,” “increase,” “raise,” “rise,” “maximize,” “add,” “elevate,” “heighten,” “steady,” “level,” “plateau,” “decline,” “surge,” “swell,” “impact,” “effect,” “affect.”

Enclosure

Study type	Study reviewed
Potential cost savings	Bian, B., C.M.L. Kelton, J.J. Guo, and P.R. Wagle, "ACE Inhibitor and ARB Utilization and Expenditures in the Medicaid Fee-For-Service Program From 1991 to 2008," <i>Journal of Managed Care Pharmacy</i> , vol. 16, no. 9 (November/December 2010), 671-679.
	Brill, A., "Overspending on Multi-Source Drugs in Medicaid," <i>American Enterprise Institute for Public Policy Research</i> (March 2011). ^a
	Congressional Budget Office, <i>Effects of Using Generic Drugs on Medicare's Prescription Drug Spending: A CBO Study</i> (Washington, D.C.: September 2010). ^{a,b}
	Cox, E., A. Behm, and D. Mager, <i>2005 Generic Drug Usage Report</i> , a special report prepared at the request of Express Scripts (2005). ^a
	Federal Trade Commission, <i>Pay-for-Delay: How Drug Company Pay-Offs Cost Consumers Billions. An FTC Staff Study</i> (Washington, D.C.: 2010).
	Fischer, M.A., and J. Avorn, "Economic Consequences of Underuse of Generic Drugs: Evidence from Medicaid and Implications for Prescription Drug Benefit Plans," <i>Health Services Research</i> , vol. 38, no. 4 (August 2003), 1051-1064.
	Fischer, M.A., and J. Avorn, "Potential Savings from Increased Use of Generic Drugs in the Elderly: What the Experience of Medicaid and Other Insurance Programs Means for a Medicare Drug Benefit," <i>Pharmacoepidemiology and Drug Safety</i> , vol. 13 (2004), 207-214.
	Haas, J.S., K.A. Phillips, E.P. Gerstenberger, and A.C. Seger, "Potential Savings from Substituting Generic Drugs for Brand-Name Drugs: Medical Expenditure Panel Survey, 1997-2000," <i>Annals of Internal Medicine</i> , vol. 142, no. 11 (June 2005), 891-897. ^a
	Kesselheim, A.S., M.A. Fischer, and J. Avorn, "Extensions of Intellectual Property Rights and Delayed Adoption of Generic Drugs: Effects On Medicaid Spending," <i>Health Affairs</i> , vol. 25, no.6 (November/December 2006), 1637-1647. ^a
	Pharmaceutical Care Management Association, <i>Undermining Generic Drug Substitution: The Cost of Generic Carve-Out Legislation</i> (October 2008).
	Shrank, W.H., N.K. Choudhry, J. Agnew-Blais, A.D. Federman, J.N. Liberman, J. Liu, A. S. Kesselheim, M.A. Brookhart, and M.A. Fischer, "State Generic Substitution Laws Can Lower Drug Outlays Under Medicaid," <i>Health Affairs</i> , vol. 29, no. 7 (July 2010), 1383-1390. ^a
	Shrank, W.H., N.K. Choudhry, J.N. Liberman, and T.A. Brennan, "The Use of Generic Drugs in Prevention of Chronic Disease is Far More Cost-Effective Than Thought, and May Save Money," <i>Health Affairs</i> , vol. 30, no. 7 (July 2011), 1351-1357.
	Shrank, W.H., J.N. Liberman, M.A. Fischer, J. Avorn, E. Kilabuk, A. Chang, A.S. Kesselheim, T.A. Brennan, and N.K. Choudhry, "The Consequences of Requesting 'Dispense as Written'," <i>American Journal of Medicine</i> , vol. 124, no. 4 (April 2011), 309-317.
U.S. Department of Health and Human Services, <i>Report on Prescription Drug Importation</i> (Washington, D.C.: December 2004).	
Effect on health care costs	Billups, S.J., S.L. Plushner, K.L. Olson, T.J. Koehler, and J. Kerzee, "Clinical and Economic Outcomes of Conversion of Simvastatin to Lovastatin in a Group-Model Health Maintenance Organization," <i>Journal of Managed Care Pharmacy</i> , vol.11, no. 8 (October 2005), 681-686.
	Helderman, J.H., N. Kang, A.P. Legorreta, and J.Y. Chen, "Healthcare Costs in Renal Transplant Recipients Using Branded versus Generic Ciclosporin," <i>Applied Health Economics and Health Policy</i> , vol. 8, no. 1 (2010), 61-68. ^a
	Katz, M., J. Scherger, S. Conard, L. Montejano, and S. Chang, "Healthcare Costs Associated with Switching from Brand to Generic Levothyroxine," <i>American Health and Drug Benefits</i> , vol. 3, no. 2 (March/April 2010), 127-134.
	LeLorier, J., M.S. Duh, P.E. Paradis, D. Latremouille-Viau, P. Lefebvre, R. Manjunath, and O. Sheehy, "Economic Impact of Generic Substitution of Lamotrigine: Projected Costs in the U.S. Using Findings in a Canadian Setting," <i>Current Medical Research and Opinion</i> , vol. 24, no. 4 (2008),1069-1081.

Enclosure

Study type	Study reviewed
	Vlahiotis, A., S.T. Devine, J. Eichholz, and A. Kautzner, "Discontinuation Rates and Health Care Costs in Adult Patients Starting Generic versus Brand SSRI or SNRI Antidepressants in Commercial Health Plans," <i>Journal of Managed Care Pharmacy</i> , vol. 17, no. 2 (March 2011), 123-132. ^a
	Witt, D.M., D.J. Tillman, C.M. Evans, T.V. Plotkin, and M.A. Sadler, "Evaluation of the Clinical and Economic Impact of a Brand Name-to-Generic Warfarin Sodium Conversion Program," <i>Pharmacotherapy</i> , vol. 23, no. 3 (2003), 360-368. ^a
	Wu, E.Q., A.P. Yu, V. Lauzon, K. Ramakrishnan, M. Marynchenko, R. Ben-Hamadi, S. Blum, and M.H. Erder, "Economic Impact of Therapeutic Substitution of a Brand Selective Serotonin Reuptake Inhibitor with an Alternative Generic Selective Serotonin Reuptake Inhibitor in Patients with Major Depressive Disorder," <i>Annals of Pharmacotherapy</i> , vol. 45 (April 2011), 441-451. ^a

Source: GAO.

^aArticle discussed in the report.

^bArticle listed under cost savings accrued as well as potential cost savings.

(290984)

This is a work of the U.S. government and is not subject to copyright protection in the United States. The published product may be reproduced and distributed in its entirety without further permission from GAO. However, because this work may contain copyrighted images or other material, permission from the copyright holder may be necessary if you wish to reproduce this material separately.

GAO's Mission

The Government Accountability Office, the audit, evaluation, and investigative arm of Congress, exists to support Congress in meeting its constitutional responsibilities and to help improve the performance and accountability of the federal government for the American people. GAO examines the use of public funds; evaluates federal programs and policies; and provides analyses, recommendations, and other assistance to help Congress make informed oversight, policy, and funding decisions. GAO's commitment to good government is reflected in its core values of accountability, integrity, and reliability.

Obtaining Copies of GAO Reports and Testimony

The fastest and easiest way to obtain copies of GAO documents at no cost is through GAO's website (www.gao.gov). Each weekday afternoon, GAO posts on its website newly released reports, testimony, and correspondence. To have GAO e-mail you a list of newly posted products, go to www.gao.gov and select "E-mail Updates."

Order by Phone

The price of each GAO publication reflects GAO's actual cost of production and distribution and depends on the number of pages in the publication and whether the publication is printed in color or black and white. Pricing and ordering information is posted on GAO's website, <http://www.gao.gov/ordering.htm>.

Place orders by calling (202) 512-6000, toll free (866) 801-7077, or TDD (202) 512-2537.

Orders may be paid for using American Express, Discover Card, MasterCard, Visa, check, or money order. Call for additional information.

Connect with GAO

Connect with GAO on [Facebook](#), [Flickr](#), [Twitter](#), and [YouTube](#). Subscribe to our [RSS Feeds](#) or [E-mail Updates](#). Listen to our [Podcasts](#). Visit GAO on the web at www.gao.gov.

To Report Fraud, Waste, and Abuse in Federal Programs

Contact:

Website: www.gao.gov/fraudnet/fraudnet.htm

E-mail: fraudnet@gao.gov

Automated answering system: (800) 424-5454 or (202) 512-7470

Congressional Relations

Katherine Siggerud, Managing Director, siggerudk@gao.gov, (202) 512-4400, U.S. Government Accountability Office, 441 G Street NW, Room 7125, Washington, DC 20548

Public Affairs

Chuck Young, Managing Director, youngc1@gao.gov, (202) 512-4800 U.S. Government Accountability Office, 441 G Street NW, Room 7149 Washington, DC 20548

