

# Diabetes and Pharmaceutical Spending: New Treatments, New Solutions

## Overview

With rising health care costs gaining more attention, some have pointed to increased spending on prescription drugs as part of the problem. Yet this perspective overlooks the real reasons that spending on pharmaceuticals has grown in recent years, as well as the value that new medicines provide to patients and the economy by treating diseases more effectively and helping curb overall health care spending.

Spending on pharmaceuticals represents just 10% of overall health care spending. Yet for some of the most serious diseases and conditions, this spending has risen considerably over the past 10 years.

This paper examines one increasingly prevalent disease—diabetes—and focuses on why spending on pharmaceuticals to treat it has grown and continues to rise. Several clear reasons emerge:

- the number of people diagnosed with diabetes over the last decade has risen by 50% and continues to rise;
- five new classes of medicines have emerged to treat type 2 diabetes and are being adopted by physicians as key tools in the fight against this disease;
- current standards of diabetes care increasingly emphasize drug therapy in addition to diet and exercise strategies; and
- disease management strategies have emphasized use of pharmaceuticals to treat diabetes because they can yield better health outcomes and lower overall cost.

This paper is the first in a continuing series by the Pharmaceutical Research and Manufacturers of America (PhRMA) on the expanding use of medicines in healthcare and the clinical and economic impact of this trend on treating disease.

## The Cost of Treating Diabetes Has Risen Dramatically—and Continues to Grow

In 1992, Americans spent \$664.3 million on oral diabetes drugs and \$646.5 million on insulins, for a total of \$1.3 billion in spending on diabetes medicines. Over the next 10 years, spending on medicines to treat diabetes increased to \$7.3 billion—\$1.9 billion on insulins and \$5.4 billion on oral diabetes drugs. In addition to the dramatic increase in the number of people with diabetes, increased pharmaceutical spending also is due to

*“Diabetic patients make up 6% of our population but consume 15% of our healthcare dollar. The main cost of diabetes is in the treatment of its complications and not in the day-to-day treatment of the disease itself. The millions of dollars we spend on treatment for patients once they develop heart disease, stroke and kidney failure could be significantly decreased if we instead helped patients manage their diabetes with pharmaceuticals. These new medicines provide powerful tools to prevent complications down the road and can help save the health care system money in the long run. As someone once said, if you think that it is expensive to treat diabetes, try not treating it.”*

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the emergence of important new medicines to treat the diseases and a growing recognition of their value in controlling diabetes and its costs.<sup>1</sup>

Although spending on medicines to treat diabetes has increased, it remains a small part of the total cost of diabetes care and of increased costs for diabetes care over time. Since 1992, the *direct* cost of diabetes care has more than doubled—from \$45.2 billion in 1992 to \$91.8 billion in 2002. [Figure 1] Direct medical expenditures comprised \$23.2 billion for diabetes care, \$24.6 billion for chronic complications attributable to diabetes, and \$44.1 billion for excess prevalence of general medical conditions. *Indirect* expenditures resulting from lost workdays, restricted activity days, mortality, and permanent disability due to diabetes totaled \$39.8 billion. In addition, when adjusting for differences in age, sex, and race/ethnicity between the population with and without diabetes, people with diabetes had medical expenditures that were 2.4 times higher than expenditures that would be incurred by the same group in the absence of diabetes.<sup>2</sup> If diabetes prevalence rates remained constant over time, the projected increase in the number of people with diabetes

## What is Diabetes?

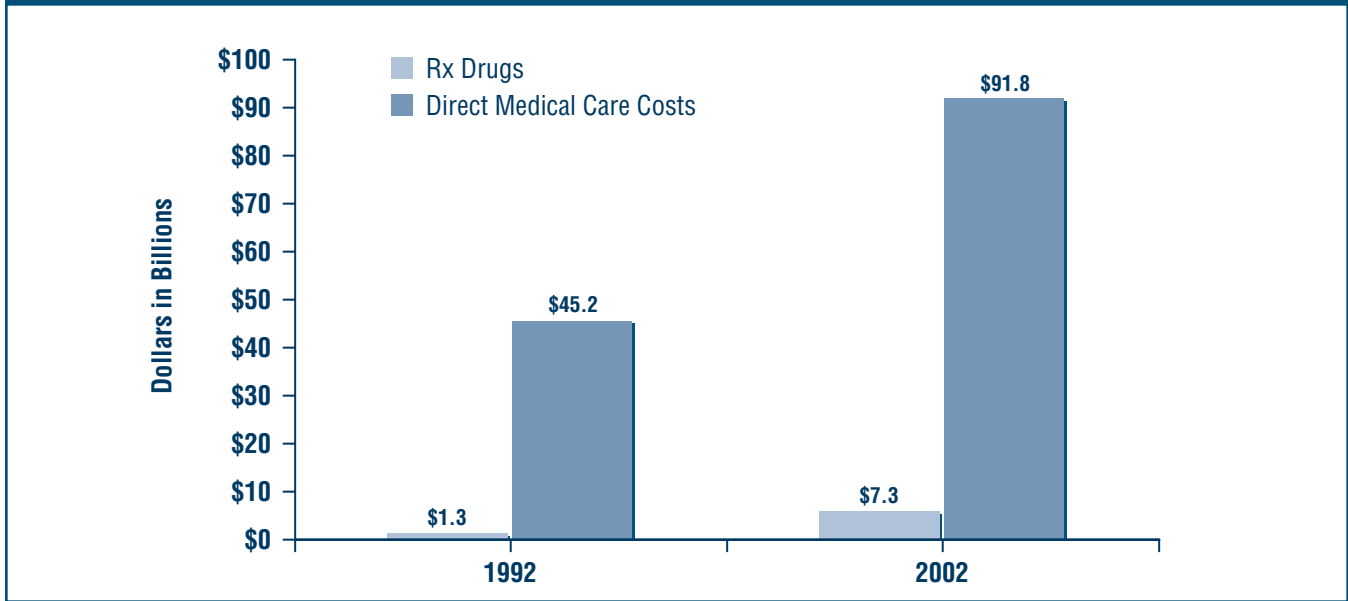
Diabetes is a group of chronic diseases characterized by elevated levels of blood sugar, or glucose, due to problems in the way the body produces and uses insulin. Diabetes has two major forms:

- **Type 1 diabetes** “is an autoimmune disease in which the body attacks and ultimately destroys the insulin-producing cells of the pancreas.”<sup>3</sup> Insulin is a hormone that transports glucose from the blood to storage in tissues such as the liver and muscles. If the body’s natural supply of insulin is cut off, blood sugar levels rise. The disease can develop at any age, although onset is most common during childhood. Type 1 diabetes accounts for 5 to 10 percent of all diagnosed cases of diabetes.
- **Type 2 diabetes** is a complex disorder in which the body is unable to produce enough insulin or properly use its own insulin to control blood sugar levels. “Type 2 diabetes is the most common form of diabetes, representing 90 to 95 percent of all cases of diagnosed diabetes.”<sup>4</sup> This form of diabetes generally develops during adulthood, and is often associated with obesity and hypertension.

The primary goal of treating both type 1 and type 2 diabetes is controlling blood sugar so that levels do not go too high or too low. Good control of blood sugar levels slows the progression of the disease and reduces the occurrence of complications. Without adequate treatment, diabetes leads to many serious and often fatal health conditions, in large part through vascular disorders leading to organ failure. For example, diabetes is the main cause of kidney failure, new cases of blindness, and lower limb amputations, and is a major risk factor for heart disease and stroke.<sup>5</sup> Large clinical studies have shown that “early and aggressive treatment of diabetes may delay or even prevent many of the complications associated with diabetes, leading to improved quality of life and reduced expenditures in patients with type 2 diabetes.”<sup>6</sup> In patients with type 2 diabetes, co-existing conditions such as hypertension and abnormal lipid levels must also be treated, further adding to the cost of treatment.

would cost an estimated \$156 billion by 2010 and \$192 billion by 2020.

**Figure 1: Retail Spending on Diabetes Medications and Direct Medical Care Costs Attributable to Diabetes, 1992 and 2002**



Sources: Rx Drug Spending Data: IMS Health, based on custom analysis of *Retail and Provider Perspective*™, 3/2003.; 1992 Medical Care Cost Data: American Diabetes Association: *Direct and Indirect Costs of Diabetes in the United States in 1992* (Alexandria, VA: ADA, 1993); 2002 Medical Care Data: American Diabetes Association, “Economic Costs of Diabetes in the U.S. in 2002”; *Diabetes Care* 26 (March 2003): 3.

## Why Has Spending on Diabetes Drugs Increased?

Some are asking why spending on medicines is increasing. Examining this question in the context of specific diseases, such as diabetes, rather than simply citing national-level spending figures, helps answer this question.

### *The Prevalence and Diagnosis of Diabetes Has Increased*

The number of Americans diagnosed with diabetes jumped 49% from 1990 to 2000.<sup>7</sup> About 17 million Americans now suffer from this disease—an estimated 11.1 million have been diagnosed, and an estimated 5.9 million people (or one-third) are unaware that they have the disease.<sup>8</sup>

According to the American Diabetes Association, “the prevalence of diabetes increases with age and is higher

among certain racial and ethnic minority populations. The growth, aging, and increasing racial and ethnic diversity of the U.S. population portends a substantial increase in the size of the population with diabetes.”<sup>9</sup> Although rates of diabetes are similar for men and women, the rates for non-Hispanic blacks and Mexican-Americans are higher than those for non-Hispanic whites. For example, Type 2 diabetes among African Americans aged 40 to 74 has doubled in just 12 years, from 8.9% to 18.2%. More than 10% of all Mexican Americans aged 20 or older have diabetes. This percentage more than doubles—to 24%—among Mexican Americans aged 45 to 74. Approximately 50% of Arizona’s Pima Indians between the ages of 30 and 64 have diabetes.<sup>10</sup>

The increase in prevalence of diabetes is a big contributor to increased prescription medicine costs and even more important to total health care costs because the annual healthcare costs of treating a person with diabetes is more than 2.4 times that of treating a person without diabetes (\$13,243 versus \$5,642).<sup>11</sup> Moreover,

this increase is likely to continue because the Centers for Disease Control and Prevention (CDC) “conservatively estimates that diabetes in the U.S. will increase 165% by 2050.”<sup>12</sup>

### More, and Better, Medications are Now Available to Treat Diabetes

Before the discovery of insulin in 1921, everyone with type 1 diabetes died within 6 months to 2 years after diagnosis.<sup>13</sup> In 1921, Canadian researchers isolated a substance from a dog’s pancreas, which they called “insulin.” The first insulin used to treat people with diabetes was made from crudely purified pancreas glands from pigs and cattle. Over the years, insulin preparations steadily improved. In 1982, **human insulin** produced in a laboratory through recombinant DNA technology entered the market. Human insulin has largely taken the place of the earlier insulin.

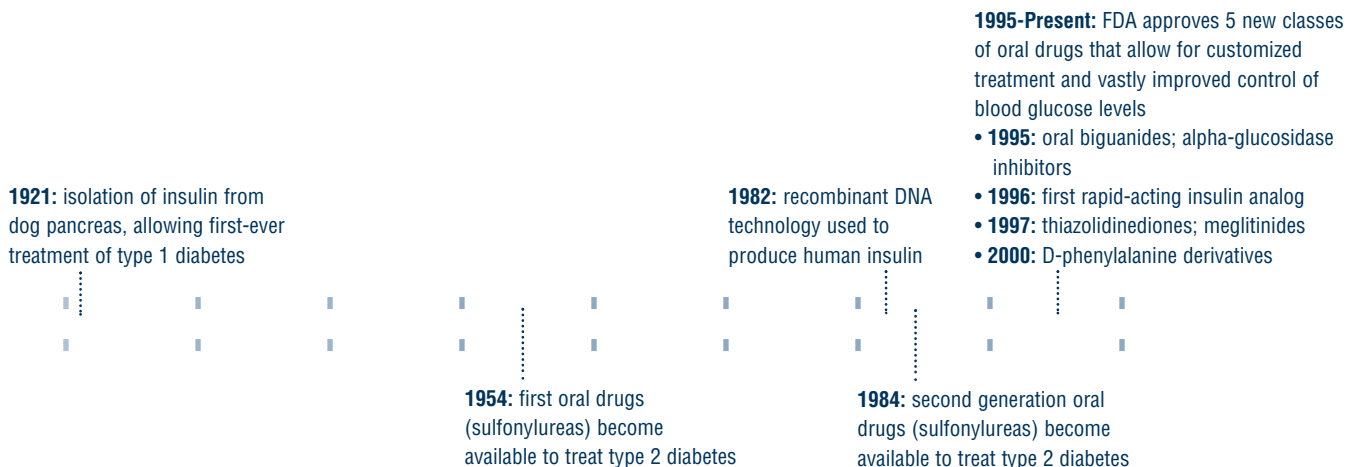
Human insulin is available in several different forms, each for a specific use according to the needs of the patient. Historically, regular insulin, which was the fastest-acting insulin available until recently, had to be given 30-45 minutes before a meal to allow insulin action to begin. Further, regular insulin persisted in the bloodstream for several hours, increasing the risk of low blood sugar for many patients. This action profile of regular insulin sometimes meant that if a person took the insulin too close to a meal, he or she would

be likely to have high blood sugar (hyperglycemia) an hour or two after eating, and low blood sugar (hypoglycemia) 3 to 6 hours after eating. Hypoglycemia can cause a person to become nervous, shaky, confused, and dizzy. Judgment can be impaired if blood sugar becomes too low, and a person can faint. Seizures, coma, and possible neurological damage are also possible with hypoglycemia.

In 1996, the U.S. Food and Drug Administration (FDA) approved the first rapid-acting insulin analog, and a second such insulin was recently approved. Rapid-action insulins work more like the body’s own insulin because of their quick action and ability to decrease blood sugar levels after meals. The rapid-acting insulins are designed to be taken just before, or immediately after, a meal. Rapid-acting insulins begin working almost immediately—within 10 to 15 minutes—to help the body metabolize sugars in carbohydrates. It peaks from 1 to 3 hours after injection, and essentially is gone from the body in roughly 4 hours. This quick action means that the insulin is less likely to cause low blood sugar problems hours later. In 2001, a long-acting analog of insulin with activity up to 24 hours was introduced. This long-acting insulin is intended to provide a baseline amount of insulin throughout the day.

Until 1995, only one category of oral medicines was available to patients with type 2 diabetes. This category of drugs, the **sulfonylureas** (SU), was a major advance

### The Accelerating Pace of Discovery in Diabetes Drug Treatments



in treatment for type 2 diabetes because it was the first oral medicine that could be used to treat the disease. Available in the United States since 1954, SU drugs stimulate the pancreas of a patient with type 2 diabetes to produce more insulin and remains an important part of diabetes treatment today.<sup>14</sup> Second generation SU drugs with fewer side effects have been developed and are used as “monotherapy” or as part of “combination therapy” with other types of diabetes pills and/or insulin.

Since 1995, five new classes of medicines have been introduced to treat diabetes. These new classes (biguanides, alpha-glucosidase inhibitors, thiazolidinediones, meglitinides, and D-phenylalanine derivatives) allow physicians to customize treatments and help individuals better manage and control their disease. Keeping blood sugar levels as close to normal as possible is important in both type 1 and type 2 diabetes because, by preventing or slowing the progression of devastating complications, such as eye, kidney, and nerve damage, they result in improved clinical outcomes. Having a variety of medications that treat diabetes in different ways gives individuals greater opportunities to control their disease and achieve better outcomes, including better quality of life.

- **Biguanides, approved by the FDA in 1995** for use in the United States, lower blood sugar levels by keeping the liver from making too much glucose, increasing glucose removal from the bloodstream by enhancing the sensitivity of muscle cells to insulin, and decreasing intestinal absorption of glucose. Unlike the SU drugs, the biguanides do not directly increase insulin levels; therefore they cannot cause hypoglycemia. Nor do these medicines promote obesity, high blood pressure, and abnormal blood lipid levels, all of which are often observed in patients with insulin resistance. Also, because biguanides have a different mechanism of action than SU drugs, medicines of this type can be used in combination with SUs to better control a person’s blood sugar levels, and thus avoid or delay the progression of diabetes and its complications.
- **Alpha-glucosidase inhibitors, approved by the FDA in 1995**, help to control blood sugar levels by

blocking the enzyme that digests starches into carbohydrates in the small intestine. Slowing starch digestion makes it easier to avoid high levels of blood sugar after a meal. These medicines can be used in combination with SUs to better control a person’s blood sugar levels—the ultimate treatment goal in diabetes.

- **Thiazolidinediones, approved by the FDA in 1997**, reduce the resistance to the actions of insulin in the muscle and other cells of patients with type 2 diabetes. Making a person’s cells more sensitive to insulin enables these cells to remove sugar from the blood more efficiently and to use it as a source of energy in cell function.<sup>15</sup> These medicines can be used in combination with SUs or biguanides because they work through a different mechanism of action.
- **Meglitinides, the first of which was approved by the FDA in 1997, and D-phenylalanine derivatives, the first of which was approved by the FDA in 2000**, are sometimes classified together as “glitinides” or “non-SU secretagogues.” They act in a manner similar to the SU medicines in that they help the pancreas make more insulin in response to a meal. However, unlike the SU medicines, they act very quickly and their peak insulin production effects occur about 1 hour after the pill is taken. Thus the person’s insulin levels peak with his or her blood glucose levels after a meal. Medicines in these classes are structurally different than the SU medicines, so they can be taken by patients who are allergic to sulfa medicines. They can also taken with a biguanide medicine to improve control of blood sugar levels.

Because these classes of medications have different mechanisms of action and side effects, combination therapy (using more than one type of medicine to treat the condition) can prevent patients from becoming hypoglycemic, as well as prevent the long-term effects of diabetes, such as cardiovascular problems, blindness, amputations, and kidney failure. To facilitate this strategy, one diabetes medication already available combines an SU with a biguanide.

## ***Evolving Standards of Medical Care Emphasize Earlier and More Aggressive Treatment***

Research has revealed much about the basic science and underlying mechanisms of diabetes, including the role of the liver and pancreas in glucose metabolism, issues of insulin resistance, and the effect of diabetes on multiple body systems. As a result, medical standards for diagnosing, treating, and monitoring diabetes have changed significantly, with a resulting increase in spending for diabetes and related medications.

For example, in the late 1990s, the level of fasting blood glucose used for diagnosing diabetes was lowered from 140 mg/dl to 126 mg/dl because studies showed that patients with the higher fasting blood sugar levels were already developing the complications of diabetes when they were diagnosed.<sup>16</sup> Diagnosing patients earlier and providing them with appropriate medications can help regulate blood sugar levels and prevent or delay these complications.

The concept of early and aggressive action clearly applies to treatment as well as diagnosis. During the 1990s, several key studies demonstrated that lowering blood glucose levels in patients with diabetes significantly reduced the incidence of microvascular complications, such as eye disease and kidney failure. For example, in the UK Prospective Diabetes Study (UKPDS), whose results were published in 1998, the rate of microvascular complications were decreased by 25% in patients with type 2 diabetes who were treated intensively with a sulfonylurea, metformin, or insulin compared with patients on conventional diet therapy.<sup>17,18</sup> As this study concluded, “Until recently, many patients have fallen short of these treatment goals because of a variety of factors, including ...lack of adherence and understanding of both patients and physicians. New therapeutic options are now available, and aggressive intervention may prevent or delay the onset of microvascular and macrovascular complications, including coronary heart disease, stroke, and peripheral vascular disease among others.”<sup>19</sup> Although the intensive management of diabetes, which is neces-

sary to achieve tighter blood glucose control, is associated with higher “up front” costs, the investment has been shown to be effective in reducing morbidity and mortality, as well as minimizing later expenditures for the most costly long-term complications.<sup>20</sup>

In addition to controlling blood sugar levels, ways to reduce the risk of type 2 diabetes complications include controlling cholesterol level and blood pressure through diet and/or medication, smoking cessation, maintaining an appropriate weight, and exercising regularly. Diet and exercise also have been shown to reduce the risk of developing type 2 diabetes in people with “impaired glucose tolerance.” An oral medicine from the biguanide class has been found to help reduce the risk of developing type 2 diabetes.<sup>21</sup>

Science has also improved our methods for monitoring diabetes in patients, allowing for adjustment of medications when necessary. For example, a blood test developed in the 1970s measures the percentage of a patient’s hemoglobin that has glucose attached to it (glycosylated hemoglobin or HbA1c). This test has been shown to track a person’s long-term blood sugar levels and, more importantly, the potential risk of developing diabetes complications. Thus, the HbA1c level is very useful in assessing the adequacy of a patient’s treatment program and as a tool for adjusting medication dosages. The goal for a person with diabetes is to have an HbA1c level of less than 6.5–7%. Any level about 7% indicates that changes in the patient’s treatment should be considered. These changes can include increasing the dosage of medicines, changing medicine, or adding additional medicines in addition to revisiting the weight, diet and exercise components of the patient’s treatment plan.

## ***Treating Co-existing Illnesses is a Growing Component of Diabetes Care***

Researchers and physicians have come to appreciate the importance of controlling other chronic conditions, principally high blood pressure and high lipid levels, that often occur in tandem with diabetes as an integral

## Institute of Medicine Report Supports Early, Aggressive Diabetes Treatment

The health consequences of not treating diabetes early are grave. According to the American Diabetes Association, “undiagnosed and untreated diabetes can lead to many serious and often fatal health conditions. Diabetes is the main cause of kidney failure, new cases of blindness, and lower limb amputations, and is a major risk factor for heart disease and stroke.”

On January 7, 2003, the Institute of Medicine (IOM) issued a report urging the Department of Health and Human Services and other public and private stakeholders to focus on 20 priority areas to improve health-care quality and delivery for all Americans.<sup>22</sup> One of the 20 priority areas identified by the IOM was appropriate treatment of diabetes. According to the IOM report, the aim is to “prevent the progression of diabetes through vigilant, systematic management of patients who are newly diagnosed or at a stage in their disease prior to the development of major complications.”<sup>23</sup>

According to the IOM report, outcomes from the Diabetes Control and Complications Trial confirmed that lowering blood glucose levels slows or prevents complications arising from type 1 diabetes. Individuals in the group receiving intensive therapy with three or more insulin injections per day (or who used an insulin pump), and who monitored their blood glucose levels four or more times a day, experienced approximately a 60% reduction in risk for eye disease, kidney disease, and neurological disease as compared with standard treatment group. The lifetime benefit of such intensive therapy could result in approximately 8 years of additional sight, 6 years free from end-stage renal disease, and 6 years deferral of lower-extremity amputation relative to conventional therapy.<sup>24</sup>

component of diabetes management.<sup>25</sup> These conditions are frequently managed with medications. Home glucose monitoring and newer drugs for type 2 diabetes and associated conditions are now allowing many patients to achieve and maintain acceptable blood sugar levels, blood pressure, and lipid levels, which

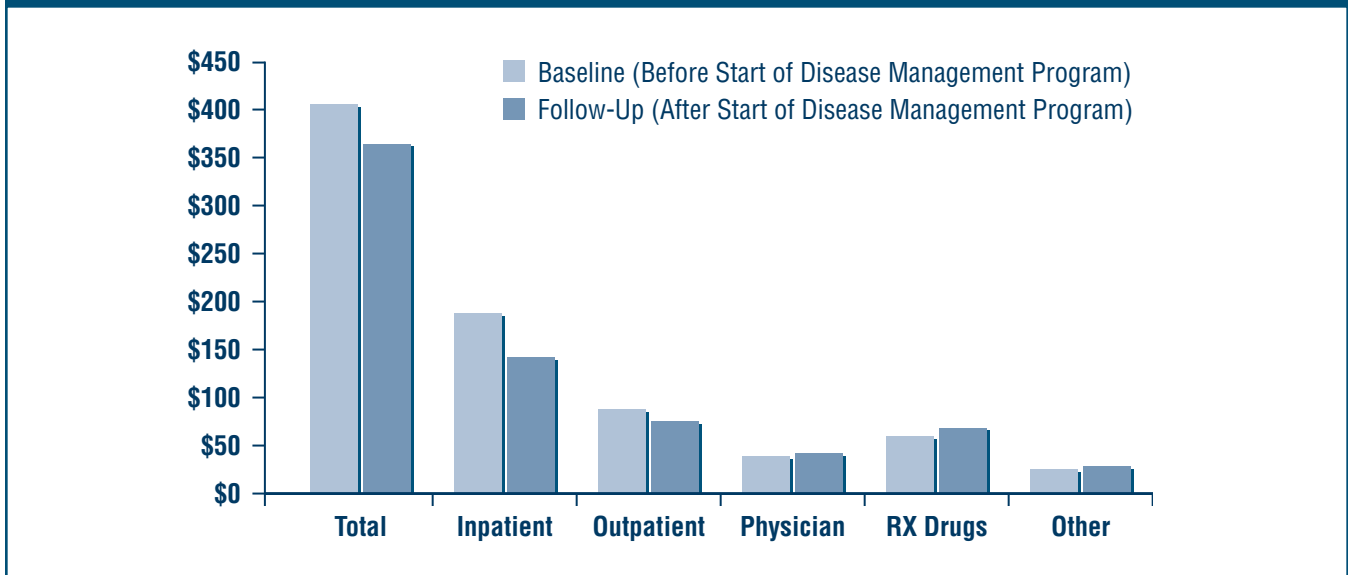
should significantly decrease risk for both microvascular and macrovascular complications.<sup>26</sup> Of course, medicines also are available to treat a variety of diabetes complications when they occur, such as neuropathy (diabetic nerve disease), kidney disease, and erectile dysfunction.

## *Cost Management and Outreach Strategies Increase Short-term Costs But Yield Better Results for Patients and Lower Overall Costs*

Disease management has played an important role in early diabetes treatment, and these programs continue to gain in popularity as providers try to contain health care costs.<sup>27</sup> For example, a comprehensive disease management program for approximately 7,000 diabetes patients in seven managed care organizations produced savings of \$50 per diabetic member per month (12.3%). [Figure 2] Although pharmaceutical costs increased under the program, total health care spending declined. The largest decrease in costs for people with diabetes was attributable to the reduction in inpatient hospitalizations and bed days. Hospital admissions per 1,000 diabetic member years decreased by 18% and bed days fell by 21%.<sup>28</sup> Thus, cost management strategies may contribute to increased spending on medicines for patients with diabetes, but they result in decreased overall health-care spending.

A second aspect of this issue is that despite advances in pharmaceutical and clinical care for diabetes, one-third of people in the U.S. with the disease are not currently diagnosed, and 58% of those who are diagnosed are not receiving adequate treatment. Increased outreach to diagnose people with diabetes would likely result in significantly increased spending on prescription medicines. However, it would also clearly improve the quality of their healthcare and of their lives while reducing long-term spending in other components of the healthcare system. People with diabetes who are untreated or undertreated are at risk for more rapid disease progression, and their overall healthcare costs are higher than

**Figure 2: Overall Savings of \$50 Per Diabetic Per Month in Disease Management Program for 7,000 Diabetic Patients in 7 Managed Care Organizations**



Source: R.J. Rubin, K.A. Dietrich, and A.D. Hawk, "Clinical and Economic Impact of Implementing a Comprehensive Diabetes Management Program in Managed Care," *Journal of Clinical Endocrinology and Metabolism* 83 (1998): 8, 2635–2642.

those who receive adequate treatment.<sup>29</sup> A random sample of 733 patients with diabetes showed that more than half (58%) had HbA1c of greater than 7%. Another study of 3,017 type 2 diabetes patients showed that each percentage point of HbA1c over 6% increased medical care costs for these patients, by 4%, 10%, 20%, and 30%.<sup>30</sup>

## Future Options for Treating Diabetes

The ultimate "cure" for diabetes would be to give someone with diabetes a new pancreas – either a biological transplant from a donor (or derived from a patient's own "stem cells") or a mechanical device that would mimic the pancreas' normal release of insulin in response to rising blood sugar levels. Both of these options are being pursued and researchers have recently made some promising advances in transplanting pancreatic cells, but widespread availability of either option is not on the immediate horizon.

Experimental pharmaceutical treatments for diabetes that work through new mechanisms of actions also are being developed. In fact, 24 new medicines are in development for diabetes today.<sup>31</sup> Some of the new experimental pharmaceutical treatments include:

- a compound that mimics the effects of a natural co-hormone by working along with insulin to control blood glucose levels;
- a protein to promote increased insulin secretion when blood glucose levels are high, but not when they are normal;
- inhaled forms of insulin that would not require injections;
- a compound that may modify the metabolism of fat cells and thus help treat diabetes-related obesity;
- dual-acting sensitizers that increase muscle cell uptake of blood sugar and inhibit the liver's production of blood sugars, as well as reduce blood lipid levels; and
- drugs that are designed to lessen diabetic nerve disease and complications involving small blood vessels, such as those in the eye or kidney.

## Conclusion

In sum, we have increased spending on pharmaceuticals to treat diabetes because new medicines offer a real solution to a serious disease. Without the emergence of these new treatments, as well as new technologies to diagnose and monitor diabetes, the disease and its related complications would take a far higher toll on the health of Americans.

As the number of people with diabetes continues to climb, and as physicians increasingly recognize the important role of pharmaceuticals in treating the disease, these trends can be expected to continue.

Recent experiences in disease management point to the role that new medicines will play in meeting the growing challenge of diabetes. The dollars we spend on more aggressive diagnosis, monitoring, and treatment return better outcomes and lower overall costs. Increased investment in new medicines for diabetes is a positive trend that gives people with diabetes longer, better lives and enables us as a society to focus on other important health care needs rather than paying for more kidney transplants, amputations, and services for the blind. ■

## Notes

<sup>1</sup> IMS Health, based on custom analysis of *Retail and Provider Perspective*<sup>TM</sup> data, 3/2003. 1992 data include sales through chain, independent, and food stores, mass merchandisers, non-federal hospitals, clinics, long-term care, federal facilities, and HMO (staff model). 2002 data include, in addition to above, sales through mail service, home health care, and miscellaneous channels.

<sup>2</sup> American Diabetes Association, "Economic Costs of Diabetes in the U.S. in 2002," *Diabetes Care* 26 (March 2003): 3.

<sup>3</sup> American Diabetes Association and the National Pharmaceutical Council, "A Closer Look at Diabetes," <[http://www.npcnow.org/issues\\_productlist/PDF/DiabetesWeb.pdf](http://www.npcnow.org/issues_productlist/PDF/DiabetesWeb.pdf)> (7 March 2003).

<sup>4</sup> Ibid.

<sup>5</sup> Ibid.

<sup>6</sup> Terrance Killiea, "Long-term consequences of Type 2 Diabetes Mellitus," *The American Journal of Managed Care* 8 (October 2002): 16 (suppl.).

<sup>7</sup> American Diabetes Association and the National Pharmaceutical Council, op cit.

<sup>8</sup> American Diabetes Association, <[www.diabetes.org](http://www.diabetes.org)>.

<sup>9</sup> American Diabetes Association, "Economic Costs," op cit.

<sup>10</sup> National Institute of Diabetes and Digestive and Kidney Diseases, "National Report Says Minorities Hard Hit by Diabetes: National Diabetes Education Program Responds," press release, January 25, 2000.

<sup>11</sup> American Diabetes Association, "Economic Costs," op cit.

<sup>12</sup> American Diabetes Association and the National Pharmaceutical Council, op cit.

<sup>13</sup> National Institute of Diabetes and Digestive and Kidney Diseases, "Diabetes Prevention Program." <<http://www.niddk.nih.gov/health/diabetes/summary/dpp/dpp.htm>> (19 March 2003)

<sup>14</sup> Silvio Inzucchi, "Oral Antihyperglycemic Therapy for Type 2 Diabetes," *Journal of the American Medical Association* 287 (16 January 2002): 3.

<sup>15</sup> National Institute of Diabetes and Digestive and Kidney Diseases, "Medicines for People with Diabetes," <[www.niddk.nih.gov/health/diabetes/pubs/med/specific.htm](http://www.niddk.nih.gov/health/diabetes/pubs/med/specific.htm)> (27 February 2003)

<sup>16</sup> Normal fasting blood glucose levels in non-diabetics is 70-110mg/dl. This measurement is typically taken in the morning before the patient has had anything to eat or drink. Diagnosis of diabetes can be made based upon two fasting blood glucose levels greater than 126mg/dl, two random blood glucose levels of greater than 200mg/dl in a patient who has symptoms indicating diabetes, or a positive glucose tolerance test where a patients blood glucose level is greater than 200mg/dl after swallowing a 75 gram dose of glucose.

<sup>17</sup> UK Prospective Diabetes Study (UKPDS) Group, "Intensive blood-glucose control with sulfonylureas or insulin compared with conventional treatment and risk of complications in patients with type 2 diabetes," *Lancet* 352 (1998):837-853.

<sup>18</sup> UK Prospective Diabetes Study (UKPDS) Group, "Tight blood pressure control and risk of macrovascular and microvascular complications in type 2 diabetes," *British Medical Journal* 17 (1998):703-713.

<sup>19</sup> Ibid.

<sup>20</sup> The American Association of Clinical Endocrinologists, Medical Guidelines for the Management of Diabetes Mellitus: The AACE System of Intensive Diabetes Self-Management, 2002 Update, accessed May 12, 2003 at: [http://www.aace.com/clin/guidelines/diabetes\\_2002.pdf](http://www.aace.com/clin/guidelines/diabetes_2002.pdf)

<sup>21</sup> National Institute of Diabetes and Digestive and Kidney Diseases, "Diabetes Prevention Program," op cit.

<sup>22</sup> Institute of Medicine. "Priority Areas for National Action: Transforming Health Care Quality," (2003) <[www.iom.edu](http://www.iom.edu)> (1 May 2003).

<sup>23</sup> Ibid.

<sup>24</sup> Ibid.

<sup>25</sup> Collins, Francis, M., "Current Treatment Approaches to Type 2 Diabetes Mellitus: Success and Shortcomings," *The American Journal of Managed Care*, 8 (October 2002: 16 (suppl.).

<sup>26</sup> Ibid.

<sup>27</sup> National Pharmaceutical Council, "Disease Management: Balancing Cost and Quality Studies on the Benefits of Disease Management Services for the Treatment of Diabetes," (Reston, VA: NPC, October 2001).

<sup>28</sup> Robert Rubin, Kimberly Dietrich, and Anne Hawk, "Clinical and Economic Impact of Implementing a Comprehensive Diabetes Management Program in Managed Care," *Journal of Clinical Endocrinology and Metabolism* 83 (1998): 2635-2642.

<sup>29</sup> L Takiya and S. Chawla, “Therapeutic Options for the Management of Type 2 Diabetes Mellitus,” *The American Journal of Managed Care* 8 (November 2002): 1009–1023.

<sup>30</sup> Ibid.

<sup>31</sup> Pharmaceutical Research and Manufacturers of America, “New Medicines in Development” <[www.pfdrma.org/newmedicines](http://www.pfdrma.org/newmedicines)> (1 May 2003).



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