

The Value of Investment in Health Care

Better Care, Better Lives

Full Report

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Executive Summary

Over the past few decades, significant advances in the U.S. health care system have helped people live longer and better lives. In fact, both mortality and disability rates have fallen consistently since the 1970s.

This period has also seen substantial increases in health spending. All too often, health care discussions seem to center on the substantial increase in per person spending on health care during this period (Figure 1), rather than the benefits of improved health care that the spending brought. A focus on costs merely as a problem overlooks the value that patients and society in general derive from improved health. While costs are undoubtedly an important part of the health care debate, they should be considered in the context of the benefits achieved.

The Value of Investment in Health Care attempts to spur such a discussion by focusing on overall improvements in health as well as taking a specific look at four conditions (heart attack, type 2 diabetes, stroke, and breast cancer) that are among the most common causes of death and disability (Figure 2). The study suggests that the value of improved health in the U.S. population over the past 20 years ***significantly outweighs*** the additional health care expenditures that accompanied the improvements. In this report, we seek to answer a basic question that frequently goes unaddressed in the current debate: Is our increased health care spending worth it? The findings of this study show that the answer clearly is "Yes."

Summary of Findings

Overall Health

Our analysis suggests that, in the past 20 years, each additional dollar spent on health care services has produced health gains valued at $2.40 to $3.00.

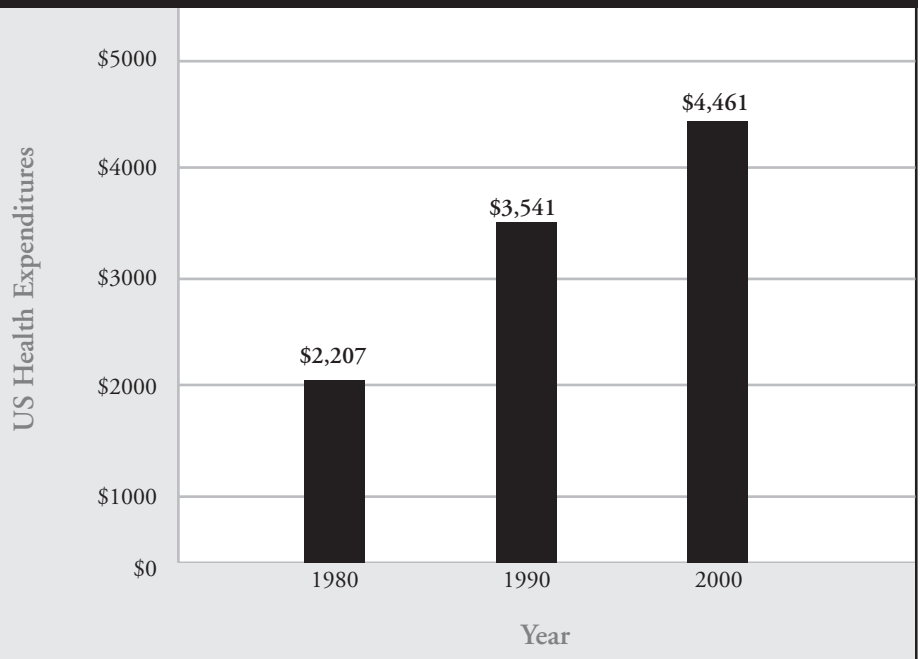
Annual age-adjusted per person health care costs between 1980 and 2000 increased by $2,254 (102%), but this was accompanied by significant health gains, including:

- Annual death rates declined from 1,039.1 to 872 per 100,000 persons (16%), as shown in Figure 3.
- Life expectancy from birth increased by 3.2 years (4%), as shown in Figure 4.
- Disability rates for people over 65 years declined from 26.2 to 19.7 per 100 persons (25%), as shown in Figure 5.
- Number of days in the hospital, a measure of population health, fell from 129.7 to 56.6 per 100 persons (56%).
- Death rates in three of the diseases discussed in this report have fallen in the past 20 years. Death rates for type 2 diabetes have risen throughout the 1990s, coupled with an increase in the incidence of obesity.

Simply put, without the above improvements in health and the associated investment, the U.S. would have spent $634 billion less on health care in 2000, but we would have experienced:

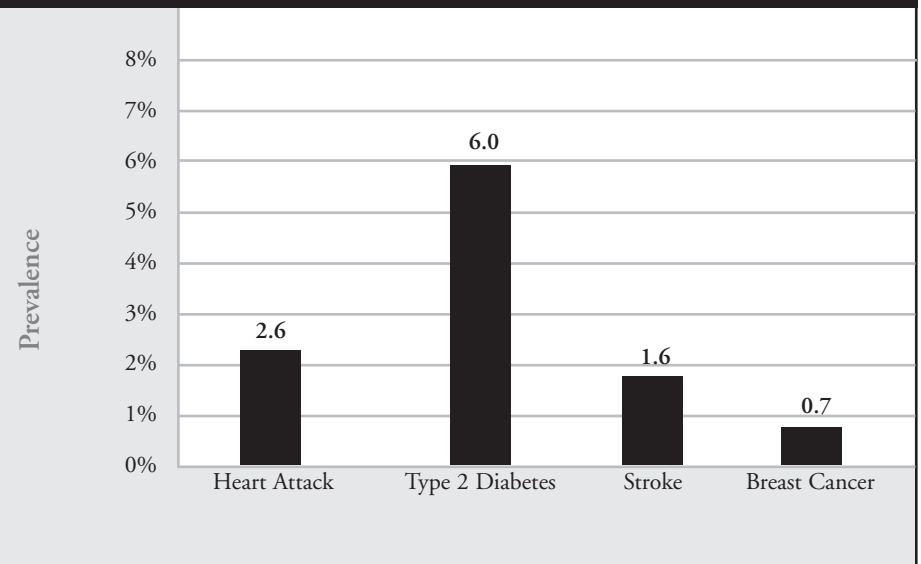
- 470,000 more deaths,
- 2.3 million more people with disabilities, and
- 206 million more days spent in the hospital.

Figure 1 ■ U.S. Health Care Expenditures per Person (2000 U.S. $)



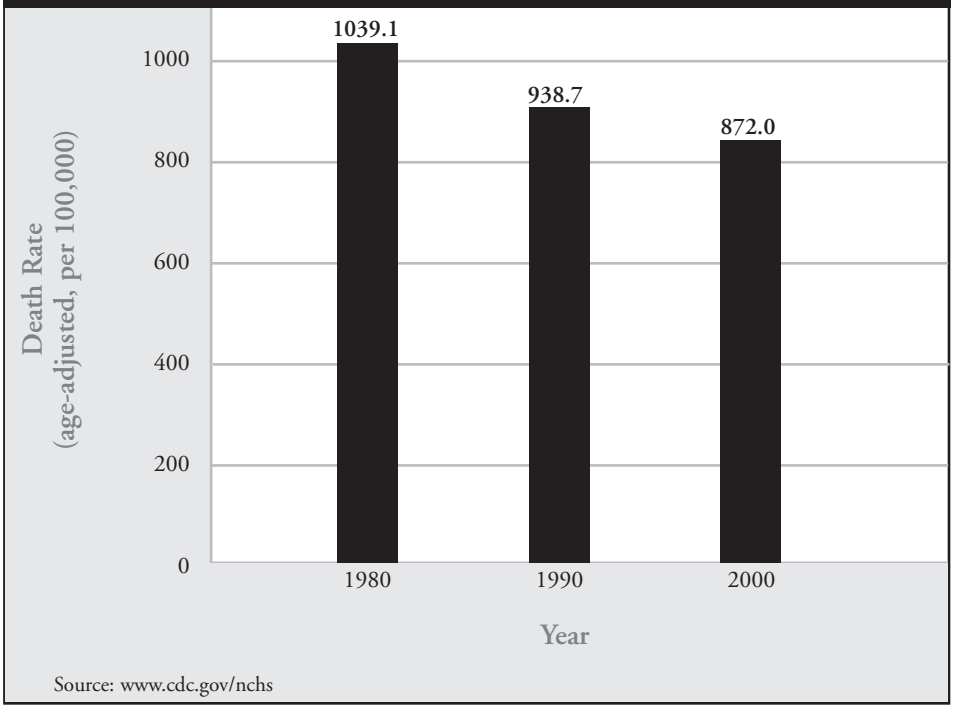
Source: Health United States 2002; Consumer Price Index (All Items)

Figure 2 ■ Percent (%) of U.S. Population in 2003 Affected by Conditions Studied



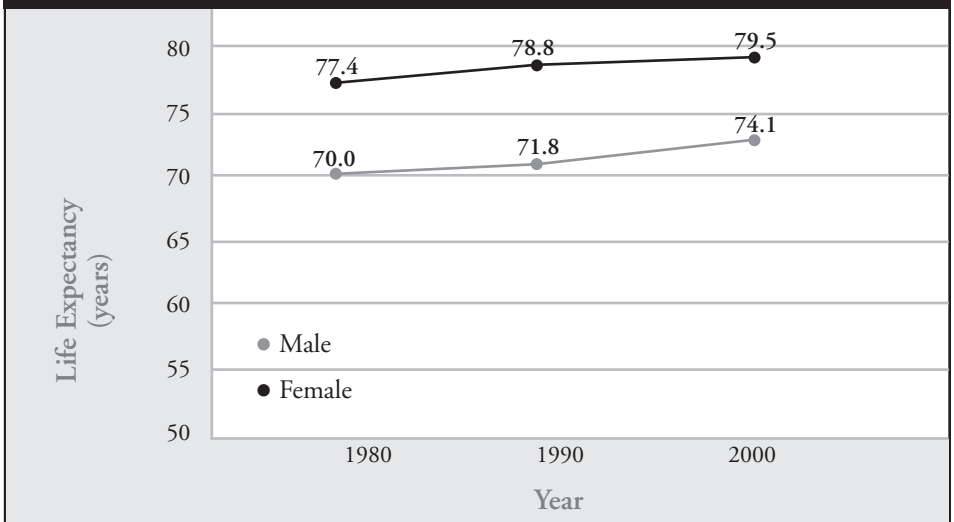
Source: American Heart Association; www.diabetes.org; www.cdc.gov/nchs

Figure 3 ■ Decline in Death Rates, 1980-2000



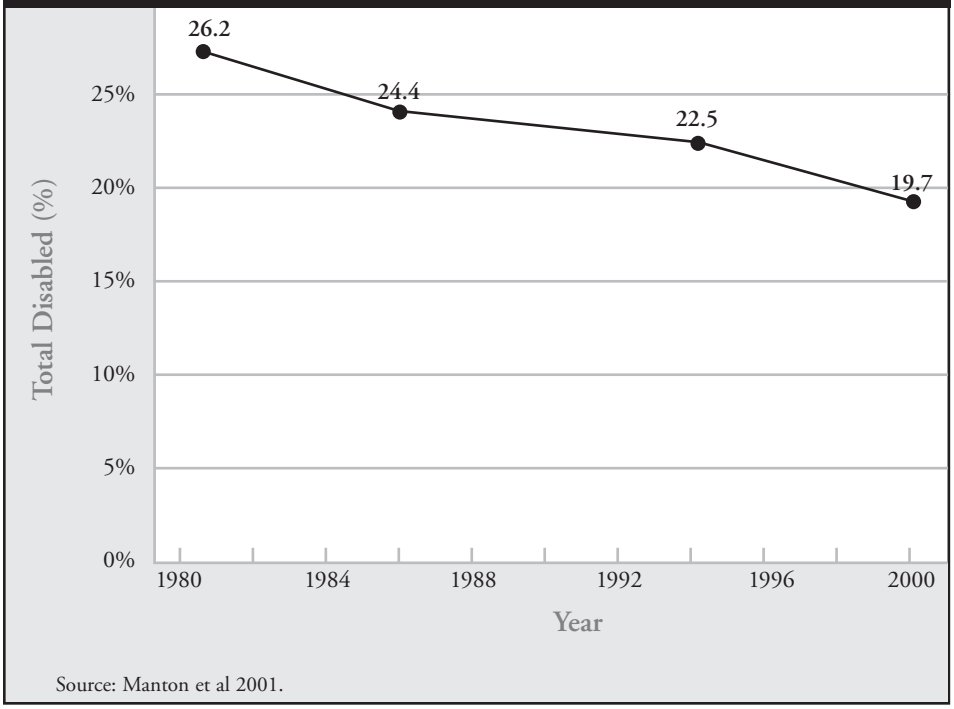
Source: www.cdc.gov/nchs

Figure 4 ■ Increase in Life Expectancy from Birth, 1980-2000



Source: Health United States, 2002

Figure 5 ■ Decline in Disability Rates for People Aged Over 65 Years, 1982-2000



Source: Manton et al 2001.

Heart Attack

Cardiovascular disease, of which heart attacks are a primary component, continues to be the leading cause of death and disability in the U.S. Each year in the U.S., about 1.5 million people suffer a heart attack, with 2.6% of all people having suffered a heart attack at some point in their lives. Improvements in medical technology, including minimally invasive procedures, and noteworthy progress in thrombolytic therapy immediately following an acute heart attack, have improved survival rates significantly. In addition, breakthrough medicines used to lower blood pressure and reduce cholesterol levels can actually prevent heart attacks.

Based on a study of claims data for Medicare patients who suffered a heart attack, every additional dollar spent on the overall treatment of heart attack has produced health gains valued at $1.10.

Evidence of the value of health gains associated with specific investments in the management of heart attack includes:

- Every additional dollar spent on statin therapy in heart attack survivors (vs. survivors treated with usual care) has produced health gains valued as high as $9.44.
- Every additional dollar spent on the routine use of beta-blockers (vs. under-use) in patients suffering acute heart attacks has produced health gains valued as high as $38.44.

Some of the key innovations in the treatment of heart attacks include:

- Therapy for patients with heart attacks has improved dramatically with the introduction of newer, safer "clot-busting" agents.
- Diagnostic imaging technologies and procedures (e.g., ultrasound and cardiac catheterization) provide critical information on heart functioning and performance, which aids in treatment.
- Percutaneous coronary interventions (PCIs), such as primary and conventional angioplasty with and without stents, improve survival in heart attack patients and provide an alternative to open-heart procedures (e.g., coronary artery bypass graft).
- Intravenous glycoprotein inhibitors are used during PCIs as prevention against clotting of blood.
- Several different therapies are routinely used as maintenance therapy to prevent recurrent heart attacks:
  - Short-term therapy with antiplatelets to prevent blood clots;
  - Antihypertensive agents (e.g., ACE inhibitors, angiotensin receptor blockers, beta-blockers) to control blood pressure; and
  - Statin therapy to lower lipid levels.

Advances in treatment have improved health outcomes for heart attack patients.

- Mortality due to heart attacks has been cut by more than half over the past 20 years, with rates falling from 345.2 to 186.9 per 100,000 persons (Figure 6).
- Early initiation of treatment with statins following an acute heart attack reduces the risk of fatal heart disease or a recurrent heart attack by 24%.
- Implantable cardiac defibrillators, which now can be implanted without open heart surgery, treat life-threatening irregular heart rhythms and reduce the risk of sudden cardiac death.
- Maintenance therapy with beta-blockers in patients who have suffered a heart attack leads to a reduction of 22% in one-year mortality rates.
- The use of glycoprotein inhibitors has been shown to reduce the risk of death, a second heart attack, or need for revascularization by 48% in patients who have suffered a first heart attack.

Type 2 Diabetes

Type 2 diabetes (also known as non-insulin-dependent diabetes mellitus), is the most common form of diabetes, affecting 17 million people in the U.S., or roughly 6% of the population. Unfortunately, poorly managed diabetes can result in long-term complications such as diseases of the eye, kidney, and nervous system, as well as cardiovascular disease. These complications can lead to blindness, nerve damage, kidney failure, heart attack, stroke, and death. In the past few years, substantial progress has been made in understanding the risk factors for diabetes.

Based on a study of claims data for Medicare patients with type 2 diabetes, every additional dollar spent on the overall treatment of type 2 diabetes has produced health gains valued at $1.49.

Evidence of the value of health gains associated with specific investments in management of type 2 diabetes includes:

- Every additional dollar spent on intensive blood glucose control in newly diagnosed type 2 diabetic patients has produced health gains valued at $3.77.
- Every additional dollar spent on statin therapy in type 2 diabetics who also suffer from high cholesterol has produced health gains valued at $3.00.
- Every additional dollar spent on the screening and treatment of diabetic eye disease in type 2 diabetes patients on insulin has produced health gains valued at $36.00.

The management of type 2 diabetes has evolved significantly over the past few decades, due most recently to an increased understanding of risk factors:

- Advances in self-monitoring blood glucose kits, more accurate hemoglobin Alc tests, and more effective insulin and oral drug therapies have made tight blood glucose control possible.
- Tight control of blood pressure has been identified as an integral part of type 2 diabetes management.
- Statin therapy is routinely used in patients with type 2 diabetes to reduce elevated cholesterol levels.

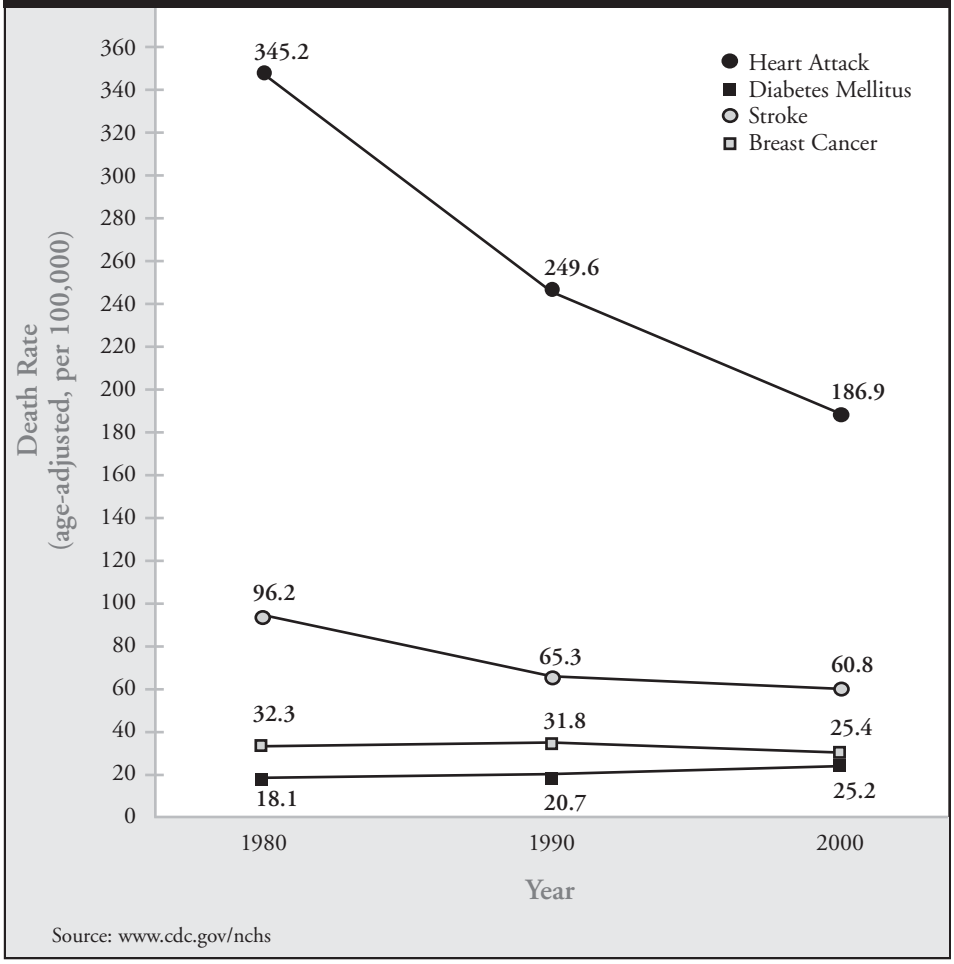
Overall mortality rates for diabetes mellitus have steadily increased over the past 20 years from 18.1 to 25.2 per 100,000 persons, given the increase in the incidence of type 2 diabetes.* However, interventions in type 2 diabetes are expected to improve outcomes by diminishing the risks and occurrence of long-term complications, as shown in several recent studies:

- Stringent control of blood glucose levels leads to reductions in risks for any diabetes-related complication (12%), any diabetes-related death (10%), death due to any reason (6%), and all microvascular complications, including eye, nerve, and kidney disease (25%).
- Tight blood pressure control in type 2 diabetes patients with high blood pressure leads to reductions in all diabetes complications (24%), deaths due to diabetes (32%), strokes (44%), heart failure (56%), and all microvascular complications, including eye, nerve and kidney disease (37%).
- When cholesterol is lowered with statin therapy, the risk of coronary events is reduced by 25% in type 2 diabetes patients.

Stroke

Stroke is the third leading cause of death in the U.S. and the leading cause of adult disability; roughly 1.6% of the U.S. population have suffered a stroke. Two-thirds of stroke survivors suffer from significant long-term physical and emotional disabilities. Given the impact of stroke on victims and their families, progress in prevention, diagnosis, and treatment is critical. To this end, significant advances in diagnosis and therapy have improved patient care and reduced the mortality rate from stroke.

Figure 6 ■ Death Rates for Conditions Studied, 1980-2000



Source: www.cdc.gov/nchs

** Mortality statistics from the CDC do not distinguish between type 1 and type 2 diabetes. However, 90% of all diabetes diagnoses are for type 2 diabetes, suggesting most of the diabetes-related deaths are most likely due to type 2.*

Based on a study of claims data for Medicare patients who suffered from stroke, every additional dollar spent on the overall treatment of stroke has produced health gains valued at $1.55.

Evidence of the value of health gains associated with specific investments in management of stroke suggests that every additional dollar spent on antiplatelet therapy vs. aspirin for the prevention of stroke in high-risk patients has produced health gains valued at $2.00 to $6.00.

Some of the noteworthy progress in the management of stroke includes:

- Advances in surgical techniques (e.g., carotid endarterectomy, early aneurysm surgery, minimally invasive microcoil devices used to treat brain aneurysms) and better drug therapy (e.g., combination therapy with dipyridamole and aspirin, anticoagulants, and antithrombolytics) are expected to reduce the incidence of stroke, both primary stroke in high-risk patients and recurrent stroke in patients previously suffering a stroke.
- "Clot-busting" therapy is routinely used immediately following acute stroke.
- Advances in brain and vascular imaging—such as computed tomography (CT) and magnetic resonance imaging (MRI) scans of the brain and ultrasound images of the vessels—enable more rapid diagnosis and treatment of stroke.
- Glycoprotein inhibitors are often used to reduce the risk of recurrent coronary events (such as stroke) in individuals who have suffered a primary coronary event.
- The increased use of acute and subacute rehabilitation improves and speeds up post-stroke recovery.

This progress has led to improved outcomes for stroke survivors.

- Stroke mortality rates have significantly declined in the past 20 years, falling from 96.2 to 60.8 per 100,000 persons, as shown in Figure 6.
- Due to the reduced mortality rates, the estimated number of non-institutionalized stroke survivors increased by 400,000 (from 2.0 to 2.4 million) between 1980 and 1991.

Breast Cancer

Breast cancer is one of the most commonly diagnosed cancers among women in the U.S., affecting 2.2 million women out of a total of 143.4 million women (1.5% among all women in the U.S.; 0.7% of the entire U.S. population) in 2000. About 40% of these women lived with breast cancer for 10 or more years. In 2001 alone, an estimated 192,000 new cases of invasive breast cancer were diagnosed. While substantial progress has been made in diagnosing and treating breast cancer, researchers continue their efforts to improve the outcomes for women affected by this disease.

Based on a study of claims data for Medicare patients with breast cancer, every additional dollar spent on overall breast cancer treatment has produced health gains valued at $4.80.

Evidence of the value of health gains associated with specific investments in breast cancer management includes:

- Every additional dollar spent on stereotactic core needle biopsy (vs. surgical biopsy) has produced health gains valued at $3.70 to $4.83.
- Every additional dollar spent on newer, less toxic hormonal therapy has produced health gains valued at $27.03 to $36.81.

The period since the 1970s has seen the following noteworthy advances in the diagnosis and treatment of breast cancer:

- The increased emphasis on mammograms at an earlier age allows for earlier diagnosis and initiation of treatment.
- Recent years have seen a shift towards less invasive diagnostic procedures. For example, stereotactic core needle biopsy allows removal of only a microscopic sample.
- Breast-conserving surgery offers a greatly improved cosmetic and psychological outcome over the traditional, more invasive mastectomy.
- New and better-tolerated hormonal treatments (used to block the effects of estrogen on the growth of cancer cells) improve rates of cancer-free survival without major side effects.

As the health interventions for breast cancer have advanced, health outcomes have improved.

- Overall mortality from breast cancer has declined from 32.3 in 1980 to 25.4 deaths in 2000 per 100,000 persons, as shown in Figure 6.
- Five-year survival rates have increased from 76.9% in 1980 to 86.6% in 1995.
- For a 54-year-old woman diagnosed with lymph node-positive breast cancer, the risk of developing metastatic disease has declined from 40% to 15%.

Conclusion

Expressed in dollar terms, the value of improved health in the U.S. population over the past 20 years significantly outweighs the additional health care expenditures during this period. *The Value of Investment in Health Care* adds further significant evidence showing that our increased spending on health care is well worth the cost. This evidence is consistent with economic theory: continued investment in health care reveals society's preference and implicit belief that the expected benefits are worth the costs. Over the past 20 years, patients have benefited from longer, better lives, as well as reduced disability and less hospitalization. The value of these improvements alone, which do not capture all the patient and societal benefits provided through health care, far outweigh increases in health care spending.

This report underscores a critical fact that must be part of every health policy discussion: health benefits have ***clear, quantifiable, economic value***. Such policy discussions should encompass elements of not only costs of health care, but also the added benefits. Policymakers in the U.S. are increasingly interested in whether, and the degree to which, investments in health care are worth the costs. This report provides important new findings that quantify improvements in health resulting from these investments. These improvements and this report represent an essential element of the debate over health care costs, building upon a growing body of evidence that suggest these benefits are, indeed, worth the costs.

Introduction

While investment in health care has increased over the past 30 years, the resulting gains to patients and society through better health have been far greater.

In this study, we present evidence from a variety of sources that shows that the value of the health gains during this time period are ***higher*** than the increased health care expenditures during this time period, indicating that these additional investments in health care add value to the U.S. population.

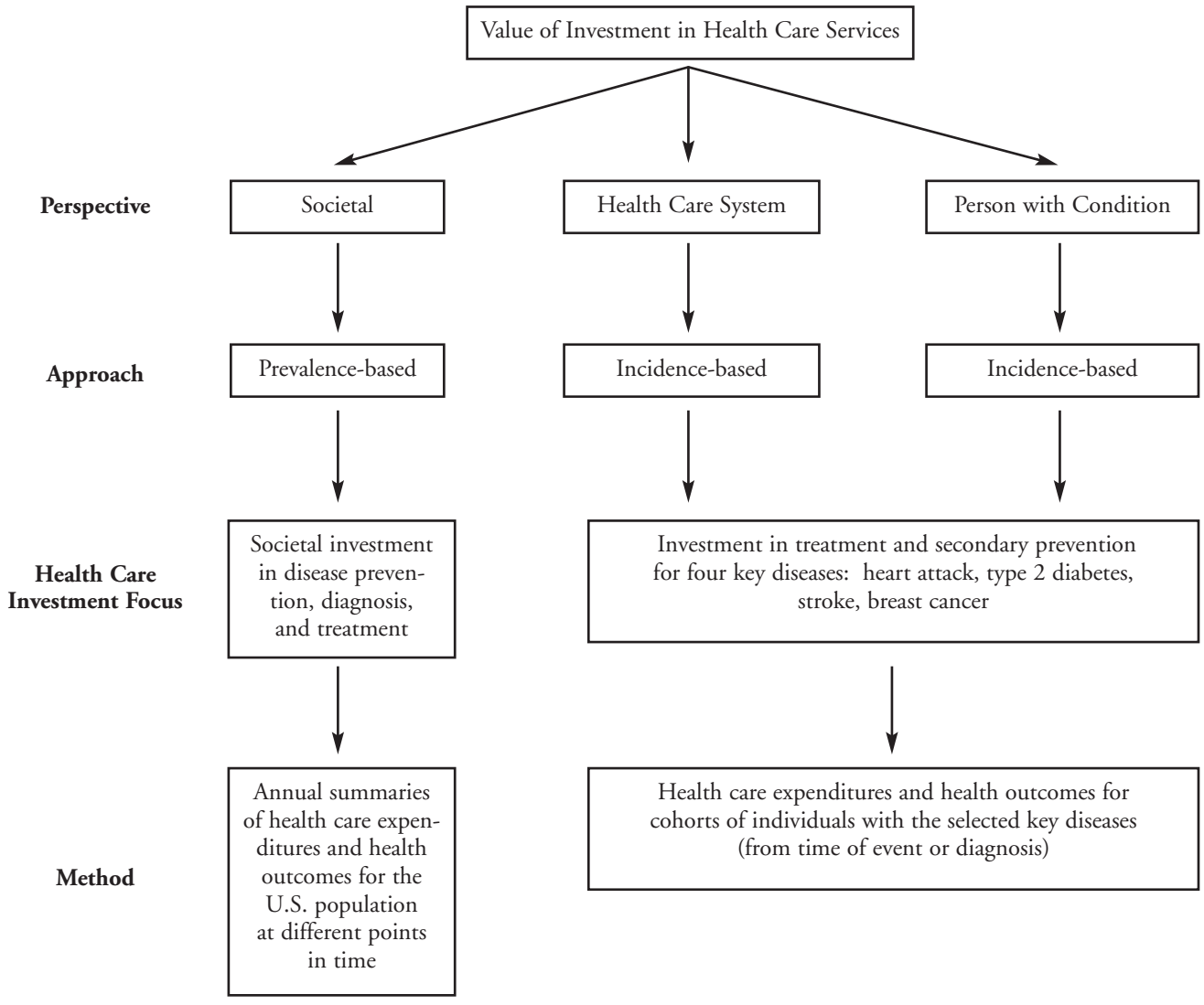
In this study, we define the value of investment (VOI) in health care services as:

The value gained associated with expenditures on health care services for prevention, diagnosis, and treatment of health conditions measured as:

- *Health benefits (e.g., life-years gained and deaths avoided),*
- *Monetized health benefits (by applying a dollar value to a life-year gained or death avoided), and*
- *Indirect benefits (e.g., productivity).*

This study looks at the value of investment in health care for overall health care expenditures as well as for expenditures for the management of four key health conditions —heart attack, type 2 diabetes, stroke, and breast cancer. Perspectives taken in this study include those of society, the health care system, and the person who experiences the health condition. The diagram on the following page illustrates the methods used to estimate the value of investment in health care.

Framework for Assessing Value of Investment in Health Care



Value of Investment in Overall Expenditures on Health Care

To calculate the value of investment (VOI) in total population expenditures on health care, this study compared changes in total annual health care costs with changes in annual population health outcome measures for 1980 and 2000.

Specifically, the VOI was estimated by:

- Computing the dollar value of gains in annual population health outcomes for 2000 compared to 1980;
- Computing the increased annual health care expenditures (including prevention, diagnosis, and treatment) for 2000 compared to 1980;
- Using the health outcomes and expenditure data to compute the value of the population health gains for every additional dollar invested in health care services in 2000 compared to 1980.

We have assumed that all improvements in health outcomes observed in 2000 compared to 1980 are attributable to the increased expenditures on health care services. In particular, we assumed that changes in other factors associated with health outcomes (behavioral, environmental, and socioeconomic) over this time period had mixed effects on health outcomes, some improving them and some worsening them for a zero net effect (Appendix A).[1]

The VOI analysis used data from multiple sources including "Health United States: 2002" and data from the U.S. Census 2000, as well as data from other U.S. National Health surveys and data from published sources. The data sources were identified through Internet searches using Google and through journal searches using PubMed. The results of the VOI analysis are presented in three sections:

- Improvements in health: 1980 to 2000
- Additional investments in health care: 1980 to 2000
- Value of additional investments in health care: 1980 to 2000

Between 1980 and 2000:

- *The annual number of deaths fell by 16%*
- *Life expectancy increased across all age groups by an average of 5%*
- *The number of people over 65 years of age with disabilities fell by 25%*
- *The number of hospital days fell by 56%*

Improvements in Health: 1980 to 2000

During the period 1980 to 2000, there were significant reductions in mortality, disability over age 65 years, and hospital days (used here as a measure of population functional status) in the U.S. population as well as an increase in life expectancy. Table 1 presents these health gains for the U.S. population. The table compares 1980 and 2000 death rates, annual deaths, disability rates for those over 65 years, number of people over 65 with disabilities, life expectancy, and hospital days. The 1980 figures are adjusted to reflect the size and age distribution of the 2000 population.

Annual per person health care costs increased by $2,254 (102%) between 1980 and 2000.

Additional Investments in Health Care: 1980 to 2000

During the period 1980 to 2000, total annual health care expenditures increased in the U.S. by more than $664 billion.

[1] The health of the U.S. population is affected by both the health care system and other factors, such as health care behaviors (e.g., nutrition, exercise), environmental factors (e.g., pollution), and socioeconomic factors (e.g., crime, substance abuse, accidents, the economy). These non-health care factors have both positively and negatively impacted health outcomes over the past few decades. In this report we assume that the net impact on health of these other factors over the past few decades is zero.

Table 1 ■ Health Gains from 1980 to 2000

Annual Health Outcomes	1980 Values*	2000 Values	Difference (%)
Death Rate (per 100,000)	1,039.1	872	-167.1 (-16.1%)
Number of Deaths	2,924,255**	2,453,999	-470,256 (-16.1%)
Disability Rate (>65 years)	26.2***	19.7	-6.5 (-24.8%)
People with Disability	9,290,300**	6,985,455	-2,304,845 (-24.8%)
Life Expectancy (LE) From birth	Incremental (total) 73.7	Incremental (total) 76.9	Difference (%) 3.2 (4.1%)
From 20 years****	55.46 (75.46)	57.8 (77.8)	2.34 (4.2%)
From 40 years****	36.79 (76.79)	38.9 (78.9)	2.11 (5.7%)
From 65 years****	16.51 (81.51)	17.9 (82.9)	1.39 (8.4%)
From 75 years****	10.48 (85.48)	11.3 (86.3)	0.82 (7.8%)
Average change in LE (all ages)			2.18 (5.2%)
Hospital Days	365,004,334	159,312,994	-205,691,340 (-56.4%)

**1980 values were age-adjusted to match the 2000 population*
***1980 rates are multiplied by the number of people in the 2000 U.S. population*
****Disability rates for 1982 instead of 1980*
***** Incremental life expectancy is the additional years of life one is expected to live from a given age (20, 40, 65, or 75 years). Total life expectancy is the total years of life, assuming one lives to the given age.*

Table 2 ■ Increased Health Care Expenditures from 1980 to 2000

	1980 Values*	2000 Values	Difference
Population Size	226,546,000	281,421,906	54,875,906
Per Person Health Care Costs	$2,207	$4,461	$2,254
Total Health Care Costs	$621 billion **	$1,255.4 billion	$634.4 billion

**1980 expenditures inflated to 2000 U.S. dollars using all items from the CPI and per person costs are age-adjusted to match the 2000 population.*
***1980 per person costs are multiplied by the number of people in the 2000 U.S. population.*

Per person annual health care expenditures increased in the U.S. by $2,254. Table 2 compares the 1980 and 2000 total health care costs and per person health care costs for the U.S. population in 2000. The 1980 per person costs are age-adjusted to account for the higher percentage of people over age 65 in the 2000 population compared to the 1980 population. The 1980 costs are also inflated to 2000 U.S. dollars using all items from the consumer price index. The 1980 total costs are computed by applying the adjusted 1980 per person costs to the 2000 U.S. population size.

For every additional $1 spent on health care, the value of the health gains ranged from $2.40 to $3.00.

Value of Investment in Health Care

To compute the value of investment in health care, we converted the mortality or life expectancy gains into dollars. Published estimates of the value of a statistical life (VSL) method of calculating the value of small reductions in mortality risks derived using data on risk-compensating wage differences, consumption activity which affects risk, or hypothetical markets yield values of life that range from $1 million to $9 million (Blomquist 2001). The VOI analysis in this study uses $4 million for VSL, an estimate towards the mid-point of this range. Based on this VSL, a value of $100,000 was used as the net present value of an undiscounted life-year gained and $2,455 as the annual consumption value[2] of an increase of 1 year in life expectancy (Mauskopf et al. 1991, Nordhaus 2002).

Using these standard economic values for avoided deaths or increased life expectancy, the value of investment for every $1 spent on health care ranged between $2.40 and $3.00, depending on the outcome chosen (Table 3).

The value of investment in health care is positive under a wide range of alternative assumptions. As an example, for every additional dollar spent on health care, the value

[2] Annual consumption value is defined as the dollar amount in additional consumption each year for the person's remaining lifetime that gives a net present value equal to the value of one life-year.

Table 3 ■ Value of Investment Calculations: 1980 to 2000

Annual Outcomes	Changes in Outcomes	$ Value of Changes in Outcomes	Value of Investment of $1 in Health Care Services*
Deaths	-470,256	$1,881 billion **	$3.00
Average Life Expectancy	2.18	$1,509 billion ***	$2.40

** Change in outcome valued in dollars/change in annual health care costs between 1980 and 2000 ($661.5 billion)*
***Assuming the value of an avoided death is equal to $4,000,000.*
****Assuming the annual consumption value of an increased year of life expectancy is $2,455 at 0% discount rate—this value is equivalent to a net present value of a life-year of approximately $100,000 at a 0% discount rate.*

Table 4 ■ Productivity Gains associated with Treatment for Type 2 Diabetes

Condition and treatment (source)	Productivity Measures	Financial Measures
Diabetes- Glipazide (Testa 1998)	Number of workdays lost per 500 workdays were less with glipazide (5 days) versus placebo (24 days)	$91 a month reduction in absenteeism costs per worker with diabetes per month

of the investment remains greater than $1 for all scenarios where one life is valued at >$1.4 million and for all scenarios where a life-year is valued at >$40,000. Alternatively, assuming our base case values of $4 million for the value of one life and $100,000 for the value of a life-year, for every additional dollar spent on health care, the value of the investment remains greater than $1 for all scenarios where at least 40% of the life expectancy gains are directly attributable to the additional health care expenditures.

Using a similar methodology, several researchers have computed a value of investment in overall health care expenditures for the U.S. for different time periods:

- Nordhaus (2002) ⧫ between $1.90 and $2.60 for every additional $1 invested between 1980 and 1990
- Murphy and Topel (2003) ⧫ $1.60 for every additional $1 invested since 1970
- Cutler and McClellan (2001) ⧫ $3.71 for every additional $1 invested between 1950 and 1990

These figures are likely to underestimate the value of investment in health since they do not include the value of the morbidity gains from the reduction in disability over age 65 and gains in worker productivity and quality of life attributable to new treatments for specific health conditions. Over the past 20 years, significant gains in productivity and quality of life associated with health care interventions in those under 65 years have been shown for several diseases including influenza, migraine, diabetes, and depression but comprehensive national estimates of changes in U.S. productivity or quality of life attributable to health conditions are not available. An example of productivity gained for diabetes is shown in Table 4.

In this study, we examine both overall health care indices relative to overall health care costs and indicators for four major diseases (heart attack, type 2 diabetes, stroke, and breast cancer). These diseases were chosen based on several factors listed below.

- Each disease is widely prevalent (Table 5), thereby leading to high death and disability rates with costly implications.
- Virtually everyone in the U.S. is at risk for one or more of these diseases. A broad spectrum of demographic groups are affected, across gender, race, and age, to a lesser degree.
- Effective health care management practices, including technological innovations and advances in drug therapy, have been made over the past years for these particular diseases.
- Major financial investments have been made in the chosen diseases over the past few decades, which raises the question of the value to society of those investments.

The subsequent sections of this report include the following components for each of the four diseases (heart attack, type 2 diabetes, stroke, and breast cancer):

- Innovations in the management of each health condition;
- Impact on health outcomes due to innovations; and
- Value of investment for innovations.

Table 5 ■ Prevalence of Conditions Studied in Report

	Heart attack	Type 2 Diabetes	Stroke	Breast Cancer
Prevalence	2.6%	6%	1.6%	0.7%
Number of people affected	7.6 million	17 million	4.7 million	2.2 million

Heart Attack

One of the great achievements in medicine in the past few decades is the dramatic reduction of disease and death due to heart attacks (also known as myocardial infarctions). Each year in the U.S., about 1.5 million people suffer a heart attack, with 2.6% of all people having suffered a heart attack at some point in their lives (American Heart Association 2003).

Cardiovascular disease, of which heart attacks are a serious consequence, continues to be the leading cause of death and disability in the U.S. Improvements in medical technology (e.g., electrocardiograms, diagnostic imaging, stents), increased use of percutaneous coronary interventions (PCI) (e.g., percutaneous transluminal coronary angioplasty [PTCA] with or without stenting), and noteworthy progress in thrombolytic therapy immediately following an acute heart attack have improved survival significantly.[3] Overall, mortality due to heart attacks has been cut by nearly half, with rates falling from 345.2 to 186.9 per 100,000 persons.

Death rates from heart attacks have fallen by nearly half over the past 20 years from 345.2 to 186.9 per 100,000 persons.

Innovations in the Management of Heart Attack

From 1970 to 2000 advances in the treatment of heart attack include thrombolysis (use of drugs that dissolve clots, often called "clot busters," such as urokinase, streptokinase, anisoylated plasminogen streptokinase activator complex, recombinant tissue-type plasminogen activator [rt-PA]), PCI (e.g., primary angioplasty with or without a stent),[4] and the use of pharmaceutical agents to prevent heart attacks (e.g., cholesterol-lowering, blood pressure-lowering drugs). A history of innovations in heart attack treatment is presented below in Table 6.

30-day mortality rates from heart attack have fallen over the past 20 years from 24.3% to 13.0%.

Improvements in Health Outcomes for Heart Attack

Innovations used to manage heart attacks have included improvements in health care technology (e.g., more effective and less invasive surgical procedures) and drug therapy (e.g., thrombolytics, antiplatelets). The impact of these innovations has led to improvements in overall and 30-day mortality rates from heart attacks. Clinical benefits realized from key advances are listed below.

- Overall mortality rates from heart attack have fallen over the past 20 years from 345.2 to 186.9 per 100,000 persons (www.cdc.gov/nchs)(Figure 7).
- 30-day mortality rates in the initial period following a heart attack have declined from 24.3% in 1980 to 13.0% in 1990.
- Using rt-PA (vs. alternative drug therapy) immediately following an acute heart attack leads to a 15% reduction in 30-day mortality rates (GUSTO 1993).

[3] While beyond the scope of this study, it is important to note that significant progress also has been made in the prevention of first heart attacks. Identification of important risk factors (diabetes, obesity, smoking, etc.), new blood tests, increased knowledge of lifestyle's impact on cardiovascular disease, drug therapy with cholesterol—and blood pressure-lowering medications, and, when appropriate, use of elective procedures, have all contributed to an important reduction in first heart attacks.

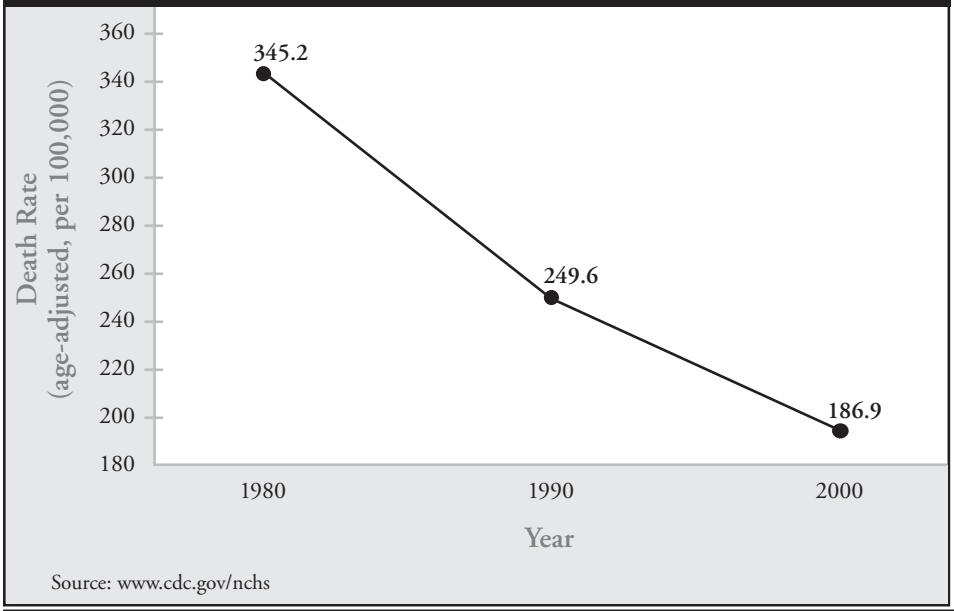
[4] There is an important distinction between angioplasty/PTCA and primary angioplasty/primary PTCA. Primary angioplasty (or primary PTCA) is a treatment for an acute heart attack; it is used in the period immediately following the heart attack. Conventional angioplasty/PTCA is used as treatment for coronary heart disease. When we refer to primary angioplasty/PTCA throughout this report, we are using it as acute treatment of a heart attack.

- Primary angioplasty leads to a reduction in risk for 30-day mortality ranging from 34% (Weaver et al. 1997) to 50% (Grines et al. 1993).
- Combined rates of occurrence for overall mortality and nonfatal recurrent heart attacks have improved for primary angioplasty (7.2%) and thrombolytics (11.9%) (Weaver et al. 1997).
- Compared with angioplasty without a stent,[5] adding a stent after angioplasty leads to reductions in 30-day rates of recurrent heart attacks (0.4% vs. 1.1%) (Grines et al. 1999).
- Early initiation of treatment with statins following an acute heart attack reduces the risk of fatal heart disease or a recurrent heart attack by 24% (Sacks et al. 1996).
- Maintenance therapy with an antihypertensive agent in patients who have suffered a heart attack leads to reductions in one-year mortality rates ranging from 19% for ACE inhibitors (Pfeffer et al. 1992) to 22% for beta-blockers (Phillips et al. 2000).
- The use of glycoprotein inhibitors has been shown to reduce the risk of death, a second heart attack, or revascularization by 48-52% in patients who have suffered a first heart attack (Sabatine & Jang 2000).

Value of Investment in Heart Attack Management

After an exhaustive literature search for cost-effectiveness studies that evaluated heart attack treatments, we identified eight studies that met all of our inclusion criteria (Appendix D). These studies evaluated therapies included in our timeline of treatment innovations. Based on the published literature, the value of health gains associated with the investment in heart attack treatment ranged from $1.42 to $38.44 for each additional dollar spent (Table 7).[6] The exact figure depends on the patient population and type of treatment included in each study.

Figure 7 ■ Decline in Death Rates due to Heart Attacks, 1980-2000



Source: www.cdc.gov/nchs

For Medicare heart attack patients, the value of health gains associated with overall heart attack treatment is estimated to be $1.10 for every additional dollar spent.

Medicare Expenditures and Outcomes: 1985 to 1999

Estimates of the five-year costs and health benefits for Medicare heart attack patients were generated for three time periods: 1985 to 1989, 1990 to 1994, and 1995 to 1999.

As shown in Table 8, the total five-year costs (Medicare expenses and out-of-pocket expenses paid by Medicare patients) for Medicare patients increased steadily between the 1985 to 1989 period and the 1995 to 1999 period. Specifically, heart attack treatment costs increased by approximately $26,000 per patient between the periods 1985 to 1989 and 1995 to 1999. Concurrently, health gains increased over the time period under study. The net five-year benefits from treatment for heart attack in 1995-1999 were modest compared to those in 1984-1989: an increase of $2,539 per patient.[7] For Medicare heart attack patients, the value of health gains associated with overall heart attack treatment is estimated to be $1.10 for every additional dollar spent.

"Face to Face" Case Study

Cheryl: 1970

Cheryl is a 66-year-old female with hypertension who smokes cigarettes on an ongoing basis. She presents with severe episodes of chest tightness to her primary care physician.

She has been under a lot of stress due to her younger son's divorce, and she is given diazepam for nerves. Two days later, her husband calls an ambulance because she is having a persistent severe episode of chest tightness associated with sweating and shortness of breath.

[5] Although 80% of patients who undergo PCI procedures receive stents, not all patients who suffer a heart attack and undergo primary angioplasty/PTCA require a stent.

[6] Note that both an additional life year gained or additional quality adjusted life year (QALY) gained are valued at $100,000 (if the study did not discount costs and benefits) or $173,000 (if discounting was used) in order to generate these estimates.

[7] These benefits represent estimates based on commonly used values for health gains.

Table 6 ■ History of Innovations (1970 to 2000) in the Treatment of Heart Attack

1970s	■ Cardiac care units are first introduced in the 1970s but will evolve significantly and become widely available 10-20 years later. ■ The use of lidocaine in managing ventricular arrhythmias (irregular heartbeat) leads to improvements in 30-day mortality rates immediately following heart attacks. ■ The use of beta-blocker therapy (a class of drugs used to lower blood pressure) in the first three hours of a heart attack becomes more prevalent and is shown to improve short-term mortality and reduce the incidence of a recurrent heart attack. ■ Streptokinase (SK) demonstrates effectiveness as a thrombolytic and begins to be used widely. ■ In the late 1970s, revascularization (restoration of blood flow to an organ or tissue) through coronary artery bypass surgery (CABG) becomes more prevalent in patients with coronary heart disease. It is used in heart attack patients only after they are completely stable (weeks to months after the initial heart attack), but not as acute treatment in the period immediately following heart attacks.
1980s	■ Blood-thinning agents (e.g., heparin) are used regularly to prevent recurrent heart attacks in the acute period (first 7 days) following a heart attack. ■ Therapy with beta-blockers evolves from short-term therapy immediately following the heart attack to maintenance therapy. Reductions in 2-year mortality rates are observed with this change in treatment patterns. ■ Thrombolytic therapy improves with the introduction of rt-PA in 1987. Improvements in 30-day mortality rates range from 18-50%. ■ Angioplasty is an effective revascularization procedure for heart attack patients after they are completely stable (weeks to months after the initial heart attack). It will eventually become an option as treatment during the acute period following the heart attack.
1990s	■ Ticlopidine and clopidogrel, more effective antiplatelets (a class of drugs used to inhibit clot formation) than aspirin, are introduced in the early 1990s for short-term use (two to three weeks) immediately following a heart attack. ■ Primary angioplasty begins to be used in the mid-1990s for treatment and revascularization in acute heart attacks. In the late 1990s, the use of bare-metal stents (tiny wire mesh devices to keep vessels open) is added to primary angioplasty procedures. At this time, the term "percutaneous coronary intervention" (PCI) begins to be used to refer to interventional procedures, such as angioplasty with or without a stent. ■ Thrombolytic therapy and angioplasty are first-line options for the acute treatment of heart attacks. ■ Cardiac rehabilitation programs are implemented sooner, encouraging patients to walk within the first few days following the heart attack and begin supervised exercise within the first few weeks. ■ Implantable cardiac defibrillators (ICD) (also not used specifically in the treatment of heart attack) are used electively in eligible patients who suffer from irregular heartbeats, which may be due to a prior heart attack. These devices are small enough to be implanted under the skin (vs. open heart surgery) and have been shown to significantly reduce mortality from sudden cardiac death.
2000s	■ Cardiac troponin immunoassay tests provide more specific and sensitive diagnosis of heart attack. ■ Intravenous glycoprotein inhibitors (a class of drugs that inhibit proteins responsible for clot formation originally introduced in the 1990s) are being used more frequently during primary (and conventional) PCI procedures to prevent against thrombosis. ■ Drug-eluting stents (not specifically used in the treatment of heart attack but as part of PCI procedures for other cardiovascular conditions) significantly reduce the rate of re-blockage of clogged arteries, thus reducing the rate of repeat operations to clear arteries. Patient outcomes improve, while the likelihood of additional hospitalization after the procedure declines. ■ FDA approves statins for the reduction of risks of fatal and non-fatal heart attacks and strokes, and decreasing the need for PCIs. ■ Eplerenone is first in a new class of medicines that the FDA approves for improving the survival of congestive heart failure patients following an acute heart attack. ■ The strategy for long-term management of heart attack patients to prevent recurrent heart attacks has evolved as follows: - Patients are continued on maintenance therapy with aspirin. - Anti-hypertensive agents (e.g., ACE inhibitors, beta-blockers) are recommended in patients with high blood pressure who experience a heart attack. - Statin therapy is recommended in heart attack patients with elevated cholesterol levels.

Sources: Published literature and expert opinion.

Table 7 ■ Key Studies used to Calculate Value of Investment in Treatment of Heart Attack

Reference	Comparators	Population	Value of Investment
Cretin (1977)	Mobile coronary care unit vs. usual care	Hypothetical cohort of heart attack patients	For every additional dollar spent, gain of $10
Goldman et al. (1988)	Routine therapy with beta-blockers vs. usual care	Heart attack survivors beginning therapy with beta-blockers	**Low-risk patients:** for every additional dollar spent, gain of $6.49 **Medium-risk patients:** For every additional dollar spent, gain of $23.44 **High-risk patients:** for every additional dollar spent, gain of $35.16
Mark et al. (1995)	tPA vs. alternative drug therapy	Heart attack survivors treated with thrombolytics	For every additional dollar spent, gain of $4
Kuntz et al. (1996)	Coronary angiography and treatment guided by its results vs. initial medical therapy without angiography	Patients with strongly positive exercise tolerance tests or prior heart attack	For every additional dollar spent, gain of $2.62 - $8.19
Phillips et al. (2000)	Routine therapy with beta-blockers vs. usual care	Heart attack survivors beginning therapy with beta-blockers (except those with absolute contraindications)	For every additional dollar spent, gain of $38.44
Cohen et al. (2001)	PTCA + stenting vs. PTCA alone	Patients presenting with a heart attack	For every additional dollar spent, gain of $1.42
Sanders (2001)	ICD vs. amiodarone (preventive use)	Patients with history of heart attack, but no sustained ventricular arrhythmia	Possible gains (up to $2.41) or losses, depending on assumptions
Tsevat et al. (2001)	Statin vs. usual care	Heart attack survivors with average cholesterol levels	For every additional dollar spent, gain of $4.72 - $9.44

She is taken to the emergency department and observed for 12 hours until electrocardiograms (EKG) began to show Q-waves (indicator of heart activity) consistent with an evolving anterior heart attack with 5 millimeters of anterior ST segment elevation.

She is admitted to the coronary care unit and placed on oxygen, continuous EKG monitoring, and complete bed rest. Her vital signs are manually measured every two to four hours, and nurses attend to all personal grooming including feeding. Her heart attack is eventually confirmed by elevated creatinine phosphokinase (CPK; muscle protein) levels. Her chest pain is treated with boluses of intravenous morphine. The use of nitroglycerin and beta-blockers are forbidden in the coronary care unit.

After one day in the hospital, she develops atrial fibrillation (a fast heart rhythm) and congestive heart failure. She is treated with digoxin doses until her heart rhythm slows. She is also given a diuretic to remove fluid. Her blood pressure becomes so low with the diuresis that it has to be stopped. Her course is also complicated by runs of ventricular tachycardia (a type of irregular heartbeat). She is treated with a lidocaine drip and eventually placed on oral quinidine that is continued when she leaves the hospital. She will be scheduled to return 4 months after discharge for direct current cardioversion of her rhythm.

She is transferred to the regular hospital ward 6 days after admission and continued on total bed rest for an additional week. She is discharged from the hospital after a 5-week stay and cautioned against any major physical activity for months. She continues to smoke cigarettes, as no mention is made of the need to stop.

Two months after discharge, she remains severely limited by heart failure symptoms including shortness of breath with any activities, fatigue, and ankle swelling. One morning, she cannot be woken up by her husband and the ambulance crew declares her deceased.

Monique: 2000

Monique is a 66-year-old female with hypertension who smokes cigarettes on an ongoing basis. She presents with severe episodes of chest tightness to her primary care physician.

She has been under a lot of stress due to her younger son's divorce. The physician obtains an EKG which shows non-specific T-wave (indicator of heart activity) abnormalities and schedules her for a stress test later in the week. She is also given a prescription for an anxiety drug, along with instructions detailing how to recognize the warning signs and symptoms of a heart attack and the importance of seeking immediate medical attention.

Two days later, her husband calls an ambulance because she is having a persistent, severe episode of chest tightness associated with sweating and shortness of breath. The EKG administered by the paramedics shows an anterior heart attack with 5 millimeters of anterior ST segment elevation. In consultation with the emergency department physician and excluding any bleeding contraindications, the paramedics begin fibrinolytic therapy[8] (hereinafter referred to as thrombolytics) to open the blocked artery. She is also given an aspirin.

On arrival to the emergency department, her chest pain has resolved and the EKG shows resolution of the anterior ST segment elevation. She is placed on a heparin drip and a beta-blocker and transferred to the coronary care unit. The following morning, an ACE inhibitor and a statin are started. She is allowed to use a bedside commode, and encouraged to increase her activity including walking as tolerated.

During her stay, doctors diagnose her as having atrial fibrillation (a fast, irregular heart rhythm) and moderate congestive heart failure. She is treated with an analgesic and a sedative and undergoes cardioversion with a biphasic depolarization at 50 joules. After returning to a regular rhythm, she remains in heart failure with a low blood pressure. An intra-aortic balloon pump (device used to increase blood flow to coronary arteries) is placed and she is taken to the cardiac catheterization laboratory. She is found to have two blocked coronary arteries including a 95% obstruction of the left anterior descending artery with slow flow beyond (the heart attack related artery) and a 75% obstruction of the right coronary artery. Both blockages are opened with balloon angioplasty and placement of stents. She is treated with a glycoprotein inhibitor during the procedure, and placed on combination antiplatelet therapy (most likely clopidogrel + aspirin) for at least one month following the procedure.

One day after the angioplasty, her heart failure and low blood pressure have improved, and the balloon pump is removed.

Her course is complicated by the development of a large hematoma in her right groin adjacent to the angioplasty catheter access site. Ultrasound reveals a pseudoaneurysm (persistent hole in the artery). This is closed with injection of a drug that induces blood clotting.

Two days after the angioplasty, she begins to have runs of ventricular tachycardia. She is placed on intravenous amiodarone. Repeat catheterization shows both stented areas to be open (and not blocked), and her left ventricular ejection fraction to be 30%. She undergoes an electrophysiology study that demonstrates inducible sustained ventricular tachycardia. An implantable cardioverter defibrillator (ICD)† is placed.

As part of the hospital quality assurance project, she receives pre-printed instructions on discharge that include directions to stop smoking. These instructions also indicate that her treatment should include aspirin, a beta-blocker, an ACE inhibitor, and cholesterol therapy, unless otherwise instructed by her physician. She is discharged 7 days after hospital admission.

She progresses well, and 2 weeks after discharge, begins cardiac rehabilitation, including supervised exercise, and instruction on diet and other risk-factor modification activities.

Table 8 ■ Five-Year Treatment Costs and Health Outcomes for Heart Attack

	Average Life Years	Value of Additional Life-Years* (1)	Average Costs (2)	$ Net Benefits (1-2)
1985 to 1989 (Period 1)	2.52		$45,711	
1990 to 1994 (Period 2)	2.67		$67,252	
1995 to 1999 (Period 3)	2.82		$71,804	
Change between Periods 1 and 2	0.15	$21,961	$21,541	$420
Change between Periods 1 and 3	0.30	$28,632	$26,093	$2,539

Value of $100,000 per life year gained without an activity limitation, $50,000 per life year gained with an activity limitation, and $2,500 decrease per life year for each cognitive question answered incorrectly

[8] Fibrinolytics were classified as thrombolytics in the 1980s and 1990s but are still referred to as thrombolytics in this report.

† Note that an implantable cardioverter defibrillator is also known as an implantable cardiac defibrillator.

A few months after discharge, her ICD fires and wakes her up from sleep. The device is interrogated in the emergency department, and found to have properly discharged for a run of sustained ventricular tachycardia. After her examination is negative for other signs of acute coronary disease, she is discharged home.

Differences between the 1970s and 2000

The most critical changes in the management of heart attack patients involve revascularization therapy and prevention of recurrent heart attacks. It is well-documented that an acute heart attack is due to the obstruction of a coronary artery by plaque rupture and clot. As a result, strategies have been developed to rapidly open the blocked artery and reestablish blood flow to the damaged heart muscle. The relationship between early treatment and improved survival is now recognized (e.g., the sooner the artery is opened, the more likely a patient is to survive with minimal damage to the heart muscle), such that the health system is now focused on early recognition and rapid treatment.

- In the 1970s, patients admitted with an acute heart attack were hospitalized for five to seven days in a critical care unit followed by an additional three to four weeks in an open ward; today's patients face much shorter stays in the hospital.
- Reperfusion through thrombolytic therapy has improved dramatically.
- Primary angioplasty is a common approach to revascularization. Not even available in the 1970s, the procedure is now used routinely for revascularization in acute heart attacks. In addition, conventional angioplasty is used in stable patients as a means of improving long-term survival.
- Bare-metal stents have been added to primary angioplasty procedures to minimize the occurrence of restenosis. More recently, drug-eluting stents (not specifically used in the immediate treatment of heart attack but used for other cardiovascular conditions), are added to reduce rates of artery re-blockage and rehospitalization.
- Antiplatelet therapy for heart attack survivors was limited to aspirin but today includes other antiplatelets whose short-term use improves mortality outcomes compared with aspirin alone.
- During the period following a heart attack, patients in the 1970s were strictly limited in their physical activity including complete bed rest in the initial one to two weeks. Today, cardiac rehabilitation programs are implemented sooner, encouraging patients to walk within the first few days following the heart attack and begin supervised exercise within the first few weeks.
- There is a much greater emphasis today on the prevention of heart attacks, including the identification of important risk factors (diabetes, obesity, smoking, etc.) and the initiation of therapy to minimize these risks. The strategy for long-term management of heart attack patients has evolved as follows:
  - Patients are continued on maintenance therapy with aspirin.
  - Anti-hypertensive agents (e.g., ACE inhibitors, beta-blockers) are recommended in patients with high blood pressure who experience a heart attack.
  - Statin therapy is recommended in heart attack patients with elevated cholesterol levels.
- ICDs are used in eligible patients who suffer from irregular heartbeats, which are often associated with prior heart attacks. These devices, which can be implanted percutaneously (rather than through open heart surgery), have been shown to significantly reduce mortality from sudden cardiac death-the leading cause of death in the U.S.
- Advances in diagnostic imaging technologies, including ultrasound and cardiac catheterization, provide valuable information on heart functioning and performance thereby aiding in treatment planning and improving outcomes.
- These types of advances have led to dramatic reductions in the risk of recurrent heart attacks and similarly dramatic improvements in mortality rates associated with heart attack.

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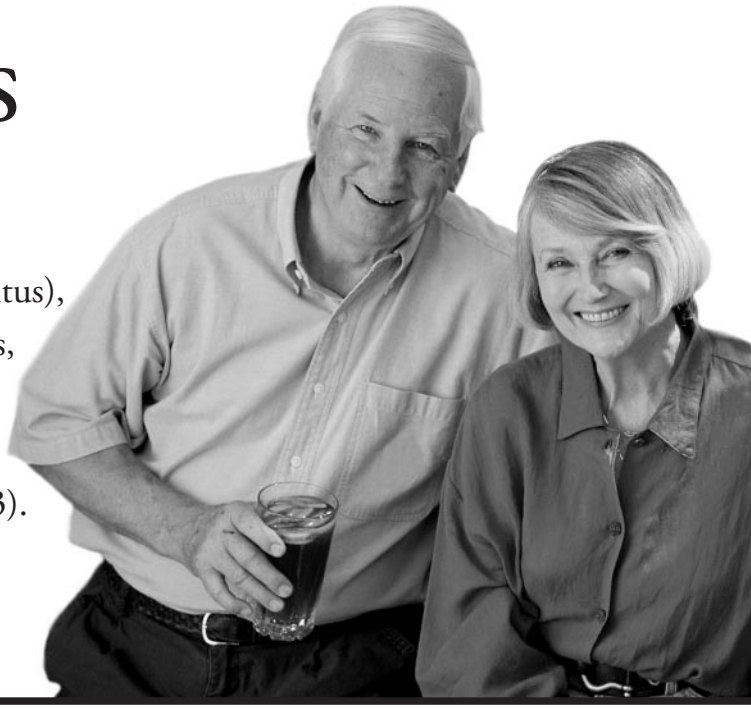
Type 2 Diabetes

Type 2 diabetes (also known as non-insulin-dependent diabetes mellitus), is the most common form of diabetes, affecting approximately 17 million individuals (6%) in the U.S. (American Diabetes Association 2003).



Unfortunately, poorly managed diabetes can result in long-term complications such as diseases of the eye, kidney, and nervous system, as well as cardiovascular disease. Such complications can lead to blindness, nerve damage, kidney failure, heart attack, stroke, and death. According to Caro et al. (2002), type 2 diabetics are expected to accrue $47,240 per patient over a 30-year period for the management of these different complications. Brandle et al. (2003) point out that annual medical costs to treat type 2 diabetes increases dramatically as long-term complications arise. Costs of treating a patient with these complications can be 10% to 90% greater vs. costs of treating a patient with well-controlled diabetes (Brandle et al. 2003).

Innovations in the Management of Type 2 Diabetes

Although type 2 diabetes cannot yet be cured, it can be effectively managed, thereby potentially decreasing both the incidence and costs of long-term complications. From 1970 to 2000, numerous advances have been achieved that are expected to improve the long-term outlook for patients with type 2 diabetes (Table 9). These advances primarily include improved diagnostic and monitoring techniques, such as hemoglobin A1c tests (lab test that measures blood glucose levels) and self-monitoring blood glucose kits, improvements in oral and insulin therapy, and widespread recognition of the relationships between type 2 diabetes, elevated cholesterol levels and high blood pressure and the need to treat these comorbid conditions.

Tight blood glucose and blood pressure control, as well as reductions in elevated cholesterol levels, are all shown to reduce the occurrence of long-term complications associated with type 2 diabetes.

Improvements in Health Outcomes in Type 2 Diabetes

In the 1990s, the incidence of obesity increased, which resulted in an increase in the incidence of type 2 diabetes (Mokdad et al. 2001). Overall mortality rates have steadily increased over the past 20 years from 18.1 to 25.2 per 100,000 persons (www.cdc.gov/nchs)(Figure 8*). However, recent studies suggest that prevention of type 2 diabetes, as well as better management of patients with existing type 2 diabetes, result in better clinical outcomes and lower complication rates.[9] As seen in the U.S. Diabetes Prevention Program, either diet combined with exercise, or therapy with one of the newer oral agents (metformin), dramatically reduces the risk of type 2 diabetes in high-risk individuals by 58% and 31%, respectively. Interventions (e.g., tight blood glucose control, made possible with better self-monitoring of blood glucose levels and hemoglobin A1c tests, and improved management of blood pressure) in treating diabetic patients have significantly changed how type 2 diabetes is managed today. These innovations are expected to boost outcomes by diminishing the risks and occurrence of long-term complications.

Early findings from the United Kingdom Prospective Diabetes Study (UKPDS), the largest and longest study of type 2 diabetic patients, were published in the late 1990s. Between 1977 and 1991, this trial recruited 5,102 patients with newly diagnosed type 2 diabetes in 23 centers within the U.K. Patients were followed for an average of 10 years, with the following results:

- When blood glucose was tightly controlled (hemoglobin A1c levels maintained at 7.0%, which is slightly lower than the

[9] While these clinical trial findings are too recent to be observed in "real-world" settings, they are critical in helping us understand the importance of managing risk factors for type 2 diabetes.

Table 9 ■ History of Innovations (1970-2000) in the Treatment of Type 2 Diabetes

1970s	■ Lifestyle changes, such as diet modification and exercise, are recommended to treat type 2 diabetes. ■ The most commonly used medication options include insulin and sulfonylureas, one of the first classes of oral drugs used to treat type 2 diabetes. ■ In 1978, home blood glucose monitoring (self-monitoring of blood glucose) is introduced. This technique will eventually revolutionize how diabetes is managed. ■ The creation of a lab test called hemoglobin A1c (which tests for an average blood glucose level over 2-3 months) improves a doctor's ability to monitor blood glucose levels.
1980s	■ Self-monitoring of blood glucose takes on a larger role as an innovation that improves patient awareness of their blood glucose levels. While initially used in patients with type 1 diabetes, it will eventually be recommended for use in type 2 diabetics. ■ Two second-generation sulfonylureas (glyburide, glipizide) are approved for use, increasing the available options for oral agents. ■ Combination therapy, usually with insulin and a sulfonylurea becomes a common alternative for individuals not controlled on a single agent. ■ Although first introduced in the 1970s, photocoagulation therapy (laser surgery used to prevent vision loss) and vitrectomy (surgical removal of the gel-like substance in the center of the eye) become widely used as treatments for diabetic retinopathy (eye disease due to diabetes). ■ As hemoglobin A1c tests improve, predicting the development of diabetes-related complications becomes easier.
1990s	■ This decade marks an initial recognition that tight blood glucose control is needed to manage type 2 diabetes effectively. ■ Additional classes of oral agents are approved, including biguanides (decreases glucose release from the liver), thiazolidinediones (increases muscle and fat sensitivity to insulin), and alpha-glucosidase inhibitors (decreases carbohydrate digestion and absorption). Metformin, a biguanide, eventually becomes one of the most widely prescribed oral agents for patients with type 2 diabetes. ■ Throughout the 1990s, innovations in insulin therapy (human vs. recombinant DNA; short-acting vs. long-acting) significantly improve patient management with insulin. ■ The medical community recognizes that controlling blood pressure and cholesterol levels has beneficial effects on diabetes-related complications. ■ Two recently published trials highlight the importance of using medication to reduce high blood pressure and lower cholesterol levels: the UK Prospective Diabetes Study (UKPDS) and Cholesterol And Recurrent Events (CARE) trial.
2000s	■ Combination therapy for oral agents is now offered as one pill (vs. multiple pill combination therapy prescribed in the 1990s). Options include rosiglitazone + metformin and glyburide + metformin. Compliance with oral diabetes therapy is expected to increase with combination therapy. ■ Devices for self-monitoring of blood glucose continue to improve, as glucometers become more convenient and less painful. ■ The first drug in a new class of drugs (D-phenylalanine derivatives) for the treatment of type 2 diabetes is approved. Drugs in this class stimulate rapid, short-acting insulin secretion from the pancreas, effectively lowering overall blood glucose levels by minimizing the increase in these levels that most people with type 2 diabetes experience after meals.

Sources: Published literature and expert opinion.

original recommendation of 7.9% in the 1990s), the overall rate of microvascular complications (diseases of the eye, nerve, and kidney due to diabetes) fell by 25% (UKPDS 1998a).

For Medicare patients with type 2 diabetes, the value of health gains associated with overall type 2 diabetes treatment is estimated to be $1.49 for every additional dollar spent.

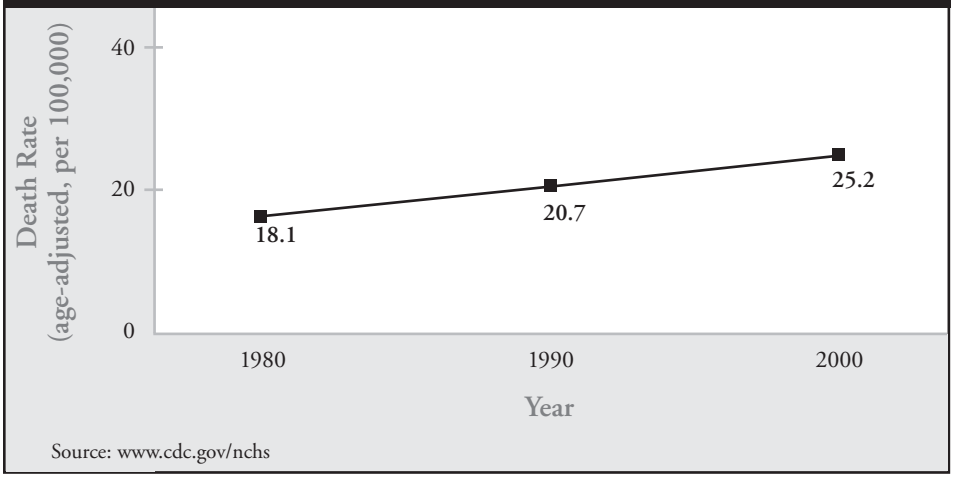
- Reductions of 10% in diabetes-related deaths, 6% in deaths due to any cause, and 18% in the occurrence of fatal and nonfatal heart attacks were observed with tight blood glucose control (UKPDS 1998a).
- Tight blood pressure control (blood pressure maintained below 150/85 mmHg) in type 2 diabetic patients led to reductions in any diabetes complications (24%), deaths due to diabetes (32%), strokes (44%), heart failure (56%), and all microvascular complications (37%) (UKPDS 1998b).

Results from other clinical trials have shown equally promising effects on disease outcomes:

- When cholesterol was lowered by 19% with statin therapy (a class of drugs used to lower cholesterol levels) to an average level of 170 mg/dL, risk reduction of coronary events in patients with type 2 diabetes was 25% (Goldberg et al. 1998).
- Among patients whose diabetic eye disease was detected early and treated, an 84% reduction in progression to severe vision loss was determined (Ferris 1993).

*Mortality statistics from the CDC do not distinguish between type 1 and type 2 diabetes. However 90% of all diabetes diagnoses are for type 2 diabetes, suggesting most of the diabetes-related deaths are most likely due to type 2.

Figure 8 ■ Increase in Death Rates due to Diabetes Mellitus, 1980-2000



Source: www.cdc.gov/nchs

Mortality statistics from the CDC do not distinguish between type 1 and type 2 diabetes. However 90% of all diabetes diagnoses are for type 2 diabetes, suggesting most of the diabetes-related deaths are most likely due to type 2.

- When type 2 diabetes was well-managed with drug therapy (vs. poorly managed with placebo), individuals were more likely to remain employed (97% vs. 85%) and were more productive (99% vs. 87%), with fewer days missed from work (decrease of 0.8% vs. increase of 8.1%) (Testa & Simonson 1998).

Value of Investment in Type 2 Diabetes Management

Our literature review identified several key cost-effectiveness articles regarding the impact of tight glucose control, tight blood pressure control, and the reduction of elevated cholesterol levels in patients with type 2 diabetes (Table 10).

Medicare Expenditures and Outcomes: 1985 to 1999

Estimates of the five-year costs and health benefits for Medicare patients with diabetes were generated for three time periods: 1985 to 1989, 1990 to 1994, and 1995 to 1999.

As shown in Table 11, the total five-year costs (Medicare expenses and out-of-pocket expenses paid by Medicare patients) for Medicare patients with type 2 diabetes increased over time, and health gains were achieved. Specifically, treatment costs for type 2 diabetes increased by approximately $11,300 between the periods 1985 to 1989 and 1995 to 1999. The net five-year benefits from treatment for type 2 diabetes in 1995-1999 were higher compared to those in 1984-1989: an increase of $5,593 per patient.[10] For Medicare type 2 diabetes patients, the value of health gains associated with overall type 2 diabetes treatment is estimated to be $1.49 for every additional dollar spent.

"Face to Face" Case Study

JB: 1970

JB is a 46-year-old African-American woman with a family history of diabetes who has been experiencing unexplained weight loss for two months as well as excessive thirst and urination. She has a family history of diabetes and is a nonsmoker.

Upon examination, it is discovered that JB is obese with a weight of 198 pounds. Her blood pressure is considered normal at (128/70). Her physical examination is unremarkable. A urinalysis shows high levels of sugar but no protein or ketones. Some blood work is drawn off and sent to the lab for studies.

The blood work returns a few days later, showing a high sugar level at 240 mg/dL. Based on the patient's symptoms and elevated blood sugar, she is diagnosed with diabetes. Her initial treatment regimen consists of diet and exercise. To get started, her physician suggests that she start walking short distances, gradually working up to two miles a day. JB is restricted to a 1500-calorie diet composed in part of 55% complex carbohydrates—those that are absorbed more slowly and do not raise blood glucose levels as quickly as the simple variety. All food and drink containing sugar must be eliminated, and carbohydrate intake will be controlled using the special dietary exchange system. JB will also need to measure sugar in her urine four times a day, recording the values in a log book. She will also check her urine every morning for ketones (chemicals the body makes that spill into the urine when there is not enough insulin in the blood). After six weeks she must return to the clinic for a fasting blood glucose test.

When JB returns to the clinic her fasting blood glucose reads 180 mg/dL, and she has gained several pounds. However, fluid intake is decreasing, as is her urinary output. Urine sugars average 1+ to 2+ in the morning and 3+ to 4+ before lunch, dinner and at bedtime, and her blood pressure is now elevated 150/100. JB's physician adds the drug chlorpropamide to better help control her blood glucose and instructs her on how to recognize the symptoms of low blood glucose as well as what she should do if the symptoms arise. The importance of eating meals and eating at the proper time is impressed upon her as is the directive that she should not use salt on foods with an already high salt content. JB is instructed to return in 4 weeks for a fasting blood glucose test and another clinic visit.

Four weeks later her fasting blood glucose has dropped to 120 mg/dL and her excessive thirst and urination has dissipated, but she has gained several more pounds and now weighs 193. Her blood pressure is 160/90 so a blood pressure lowering medication is added to her treatment. JB's urine sugar readings have dropped to 0 to 1+ before breakfast and 1+ to 2+ before lunch and dinner. Pre-bedtime values are 1+.

[10] These benefits represent estimates based on commonly used values for health gains.

Table 10 ■ Key Studies Used to Calculate Value of Investment in Treatment of Type 2 Diabetes

Reference	Comparators	Population	Value of Investment
Eastman et al. (1997)	Goal of blood glucose control to achieve normal glucose levels vs. no specific goal	Patients newly diagnosed with type 2 diabetes (ages 19-75)	For every additional dollar spent on controlling glucose levels, gain of $8.65
CDC (2002)	Goals of intensive blood glucose control, intensified blood pressure control, reduction in cholesterol level vs. standard of care for each of these parameters	Patients newly diagnosed with type 2 diabetes (ages 25 or older)	For every additional dollar spent on intensive blood glucose control, gain of $3.77 Intense blood pressure control actually leads to savings in overall treatment costs as well as health gains For every additional dollar spent on lowering cholesterol levels, gain of $3.00
Elliott et al. (2000)	Goal of intense vs. less stringent blood pressure control	Patients with type 2 diabetes (ages 60 or older) who also suffer from high blood pressure	Intense blood pressure control actually leads to savings in overall treatment costs as well as health gains
Golan et al. (1999)	Treatment with ACE inhibitors vs. treatment with ACE inhibitors based on screening	Newly diagnosed type 2 diabetes patients (ages 50 or older)	For every additional dollar spent on treatment with ACE inhibitors (vs. screening first for appropriateness), gain of $21.36
Grover et al. (2001)	Treatment with statin vs. no treatment	Diabetics without cardiovascular disease (CVD)	For every additional dollar spent on statin therapy in diabetic patients without CVD, gain of $7.00 to $31.00
Javitt and Aiello (1996)	Screening and treatment of diabetic retinopathy vs. no screening	All type 2 diabetics who use insulin for control	For every additional dollar spent on screening and subsequent treatment (vs. no screening), gain of $36.00

For the next 18 months, JB maintains fasting blood glucose between 120 and 150 mg/dL. Urine sugars are mostly 1+ to 2+ with a rare 0. Occasionally, JB has an episode of low blood glucose which is treated successfully with 4 ounces of orange juice. Her blood pressure is 150/90 but her weight varies and is typically between 200 and 210 pounds. She is also showing traces of protein in her urine.

Three years later, in 1977, JB weighs 205 pounds and her blood pressure is higher at 160/100. Her urine sugars are consistently high at 3+ to 4+, and her fasting blood glucose is 190 mg/dL. A urinalysis shows protein in the urine. Overall, JB feels weak and tired and is again growing thirstier. Upon further examination, her ophthalmologic examination now shows hard areas of her eye that are oozing and flame-shaped hemorrhages. Her physician concludes that she is failing to respond to chlorpropamide so it is discontinued and she is started on two injections of porcine insulin a day. Without a quick way to check her blood sugars, JB must be very careful to eat at regular intervals to avoid low blood sugar episodes. JB is also started on additional blood pressure medication.

JB's new insulin regimen is helpful and keeps her symptom-free over the next several years. However, her fasting blood glucose and random blood glucose levels range from 150 to 300 mg/dL and she still shows high amounts of protein in her urine. In addition, she is beginning to show signs of problems with her eyes and low blood glucose episodes continue to occur at infrequent intervals. Over the course of the next few decades, JB is at high risk to develop many of the complications of diabetes including renal disease, nerve disease, blindness, amputation, heart attacks, and strokes.

Alicia: 2000

Alicia is a 46-year-old African-American woman with a family history of diabetes who has been experiencing unexplained weight loss for two months as well as excessive thirst and urination. She has a family history of diabetes and is a nonsmoker.

Table 11 ■ Five-Year Treatment Costs and Health Outcomes for Type 2 Diabetes

	Average Life Years	Value of Additional Life-Years* (1)	Average Costs (2)	$ Net Benefits (1-2)
1985 to 1989 (Period 1)	3.48		$83,467	
1990 to 1994 (Period 2)	3.64		$88,477	
1995 to 1999 (Period 3)	3.73		$94,804	
Change between Periods 1 and 2	0.16	$11,565	$5,010	$6,555
Change between Periods 1 and 3	0.25	$16,930	$11,337	$5,593

**Value of $100,000 per life year gained without an activity limitation, $50,000 per life year gained with an activity limitation, and $2,500 decrease per life year for each cognitive question answered incorrectly.*

Upon examination, it is discovered that Alicia is obese; her weight is 198 pounds and her height is 5'6". This translates to a Body Mass Index (BMI) of 44.5. Her blood pressure is considered normal (128/70). Her physical examination is unremarkable. Alicia's physician conducts a random blood glucose test in the office in just a few seconds with a glucometer, and this shows her random blood glucose level is 240mg/dL. A urine dip reveals a blood glucose reading of 2+, but no protein and no ketones. These findings, combined with her risk factors, raise the possibility of type 2 diabetes.

Alicia returns the next morning for a fasting blood glucose test which is 150mg/dL, well above the suggested range. Thus, she is diagnosed with type 2 diabetes. At this point, her physician refers her to a certified diabetes educator and nutritionist, starts her on a combination of diet and exercise, and refers Alicia to an ophthalmologist for a baseline retinal exam. In addition, he checks her A1C levels, baseline chemistry, and urine for microalbumin; starts the patient on aspirin therapy to decrease the risk of cardiovascular complications; and gives Alicia the pneumovax immunization to prevent pneumococcal disease (a disease caused by common bacteria called the pneumococcus, which can invade the brain, for example, and cause meningitis).

Results from the lab show that the patient's A1C, representing a 3 month average of her blood sugar, is slightly above goal, but ideally this will be managed with diet and exercise. Her cholesterol and blood pressure are within target (cholesterol LDL <100mg/DL and BP <130/80mmHg). Her urine microalbumin is high, which may be an indicator of early kidney disease. She is started on an ACE inhibitor to delay progression of such disease.

Alicia does well with a regimen of diet and exercise for the next year. She monitors her glucose levels regularly with a glucometer at home, and every 3-4 months she visits her physician for follow up. However, during her third year post-diagnosis, her stress level is high and she has difficulty maintaining her diet and exercise habits. This results in a slightly elevated blood pressure and additional weight gain. Her physician repeats her A1C test and the results indicate the number is well above goal. A repeat fasting lipid profile also reveals an elevated LDL cholesterol. Alicia is encouraged to continue following her diet and exercise plan and is referred for more diabetes education.

In addition, she is started on oral diabetes medication to lower her fasting blood glucose level. She is able to tolerate this medication well without problems of low blood sugars. Since her blood pressure is also above goal, her physician increases the dosage on her ACE inhibitor until her blood pressure falls below the goal of 130/80. Finally, she is also started on statin therapy to treat her high cholesterol, with a goal to lower her LDL cholesterol or "bad cholesterol" to within a desired range.

More than likely, in a few years, a second oral agent for glucose control will be added. If this combination therapy is not effective in maintaining the proper blood glucose levels, Alicia may also need insulin injections. Newer genetically engineered insulins will help to better control JB's blood sugar with less risk of abnormal lows or highs. Eventually there is a chance that the patient will develop long-term complications of diabetes, such as kidney, nerve or eye disease, or cardiovascular disease—but her more aggressive management is likely to help to prevent these complications.

Differences between the 1970s and 2000

In addition to advances in oral drugs and insulin therapy, perhaps the most noteworthy event has been the recognition of the interrelationships between type 2 diabetes, elevated cholesterol levels, and uncontrolled blood pressure and glucose levels. Recent years have highlighted the need to treat these comorbid conditions together to successfully minimize long-term complications associated with type 2 diabetes. Specific progress made since the 1970s is outlined below.

- Diabetes was initially classified as juvenile and adult-onset, with the role of insulin resistance (insulin-dependent, non-insulin dependent) recognized only in the late

1970s. The distinction between type 1 and type 2 diabetes was made much more recently, with a recognition today that many obese adolescents can develop type 2 diabetes (originally known as adult-onset).

- Obesity and lack of exercise as contributing factors for adult-onset diabetes were touched upon in patient management, but their roles were not emphasized nearly as strongly as they are today.
- Development and widespread availability of the hemoglobin Alc test, the primary lab test for diabetes, allows physicians to better manage their diabetic patients, improving the patients ability to live with diabetes.
- Oral pharmacologic treatment consisted almost exclusively of sulfonylureas, with many centers refusing sulfonylureas because of a fear of negative side effects on the heart. Today, safer sulfonylureas are available, along with several other classes of oral agents (biguanides, thiazolidinediones, alpha-glucosidase inhibitors).
- Although available since before the 1970s, insulin therapy was limited to short-acting agents with inconvenient dosing schedules (usually had to be taken before every meal and every night before bedtime). Today's options include long-acting insulin that offer better dosing schedules and possibly better patient compliance with therapy.
- Recombinant DNA is also used today to make insulin, which was not available in the 1970s.
- Self-monitoring and physician monitoring of glucose levels are far more accurate today than it was in the 1970s, thanks to advances in home glucose monitoring kits and hemoglobin A1c tests. New non-invasive tests that can check blood glucose levels without puncturing the skin also make management of diabetes easier.
- In the 1970s, little was known about the importance of controlling factors other than blood glucose. Since then, extensive research has been conducted that highlights the importance of controlling blood pressure and cholesterol levels, in addition to blood glucose.

- Recognition of these inter-relationships is expected to lead to declines in the incidence of long-term, diabetes-related complications (diabetic diseases of the eye, nerves, or kidneys; cardiovascular illness related to diabetes).
- Patients who develop these long-term complications have more alternatives for treatment. For example, advances in photocoagulation and vitrectomy procedures have shown promise for patients suffering from diabetic eye disease. Progress in dialysis and kidney transplants has occurred, offering patients with diabetic nephropathy better quality of life.

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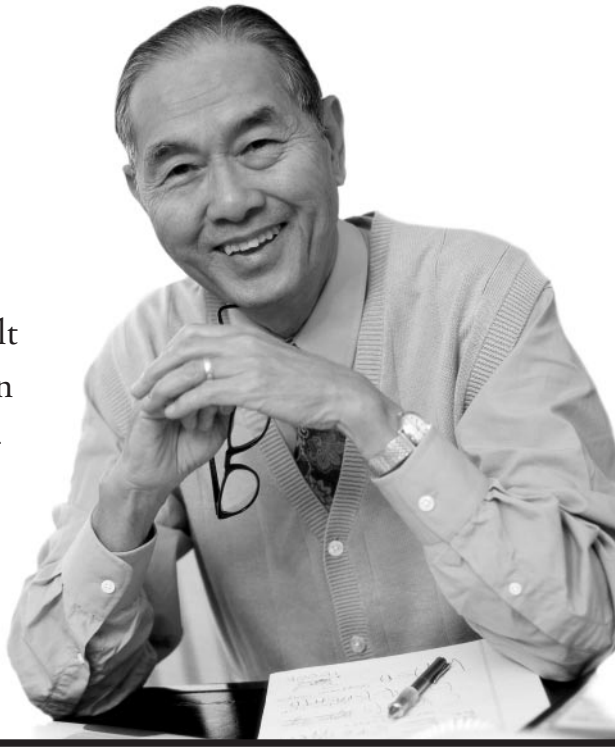
Stroke

Stroke is the third leading cause of death in the United States and the leading cause of adult disability; roughly 1.6% of the U.S. population has suffered a stroke. Consequently, the condition and disabilities associated with it cost the U.S. $30-40 billion a year.



Two-thirds of stroke survivors suffer from significant long-term physical and emotional disabilities. Given the impact of stroke on victims and their families, progress in prevention, diagnosis, and treatment is critical.

Innovations in the Management of Stroke

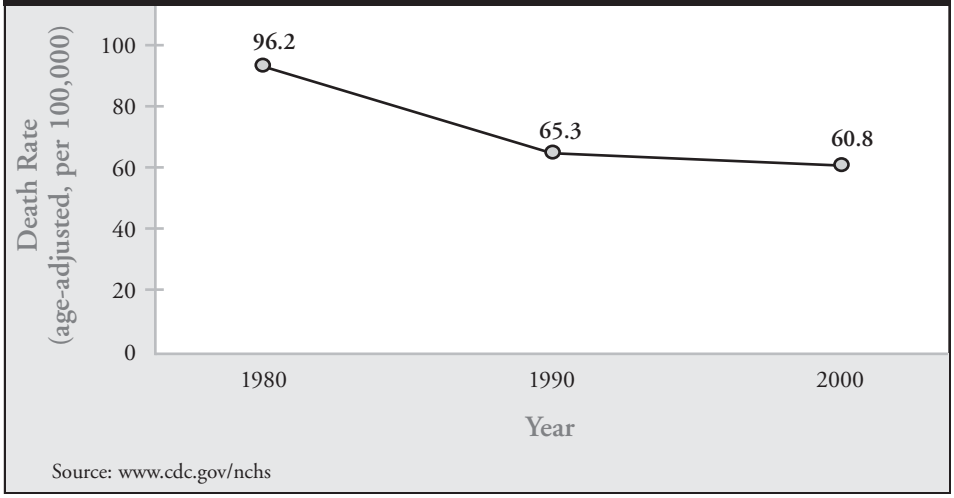
Key advances in the prevention and treatment of stroke between 1970 and 2000 are shown in Table 12. These advances include the development of safer, more effective drugs that prevent and reduce blood clotting, better tolerated and more effective drugs for controlling high blood pressure and cholesterol, and the advent of carotid endarterectomy (surgical procedure to remove plaque build-up in carotid arteries). The 2003 American Stroke Association practice guidelines recommend immediate intravenous administration of recombinant tissue-type plasminogen activator (rt-PA; part of a class of drugs known as thrombolytics or "clot-busting" drugs because of their ability to dissolve blood clots) in patients who are suffering an acute ischemic stroke. To date, rt-PA is the only therapy established as safe and effective and approved by the FDA for the immediate treatment of stroke.

Improvements in both brain imaging (e.g., CT and MRI scans of the brain, diffusion-weighted imaging, perfusion-weighted imaging, PET scans) and vascular imaging (e.g., ultrasounds of vessels, MRA, SPECT, and transthoracic and transesophageal echocardiography) enable a much faster diagnosis of stroke and its possible cause, thereby allowing treatment to begin more quickly.

Improvements in Health Outcomes for Stroke

Mortality has steadily fallen from 96.2 deaths per 100,000 individuals in 1980 to 60.8 deaths per 100,000 persons in 2000 (www.cdc.gov/nchs)(Figure 9). Other outcome improvements are noted below.

Figure 9 ■ Decline in Death Rates due to Stroke, 1980-2000



Source: www.cdc.gov/nchs

Table 12 ■ History of Innovations (1970-2000) in the Treatment of Stroke

1970s	■ Aspirin is shown to be effective in treating patients suffering from stroke. ■ The development of Computed Tomography (CT) and Positron Emission Tomography (PET) scanning allows clinicians to distinguish ischemic (clotting) from hemorrhagic (bleeding) stroke (and the diagnosis of other conditions), leading to more effective and targeted treatments.
1980s	■ Early surgery for an aneurysm (widening of a vessel that results in a "bulge" and weakens the vessel wall, possibly causing a rupture) is shown to be effective in improving mortality rates after a patient suffers from a hemorrhagic stroke. ■ Development of magnetic resonance imaging (MRI) further improves evaluation of persons with cerebrovascular disease, including stroke. ■ Emphasis on identifying and modifying risk factors for stroke is increased. This includes, but is not limited to, smoking and high blood pressure. ■ In the mid to late 1980s, a new thrombolytic (class of "clot-busting" drugs) called tissue-type plasminogen activator (tPA) shows promise in treating blood clots that travel to the brain. ■ Acute rehabilitation (greater than three hours of therapy) is routinely used to improve the functional recovery of stroke patients.
1990s	■ Carotid endarterectomy is proven effective in preventing stroke among eligible patients with severe narrowing of these neck arteries. ■ Anticoagulants (blood thinners) are shown to be effective in lowering the risk of stroke in people with atrial fibrillation. ■ A combination platelet product (aspirin + dipyridamole) is approved to reduce the risk of recurrent stroke in patients suffering a mini-stroke (transient ischemic attack) or a full-blown ischemic stroke. ■ The roles of blood pressure control and reduced cholesterol levels become even more recognized and important in the prevention of recurrent stroke in patients who have suffered a stroke or other coronary illness. ■ Glycoprotein inhibitors (a class of drugs that inhibit proteins responsible for clot formation) are approved for use to reduce the risk of coronary events in patients suffering a stroke or other coronary event. ■ The use of recombinant tPA (rt-PA) is approved to treat ischemic stroke in the first three hours following the onset of symptoms. ■ Microcoils (surgical device used to treat aneurysms) are introduced as effective, minimally invasive treatment for brain aneurysms, which helps in the prevention of stroke and leads to minimal patient discomfort. ■ Brain imaging improves significantly and includes options such as CT scan of the brain, diffusion-weighted imaging, perfusion-weighted imaging, and PET scans. Imaging helps determine if carotid endarterectomy is an appropriate option, as narrowing of carotid arteries may not have caused initial stroke. ■ Subacute rehabilitation (therapy less than three hours a day) becomes an option to improve the functional recovery of stroke patients while reducing costs. ■ Integrated stroke intervention teams, stroke units, rehabilitation facilities, and stroke care maps are actively used as a way to improve the outcomes of stroke patients.
2000s	■ Although introduced in the 1990s, use of vascular (vessel) imaging increases and today includes ultrasonography, magnetic resonance angiography (MRA), single-photon emission computed tomography (SPECT), and transesophageal and transthoracic echocardiography (tests enabling clinicians to view the heart and its major vessels either by inserting a probe down the patient's throat or placing a probe on the patient's chest). ■ Fiber optic endoscopy to evaluate swallowing and laryngeal function is a new technology that allows physicians to insert a fiber optic scope and determine if swallowing is obstructed in stroke patients, which could then lead to aspiration, a common cause of stroke-related pneumonia. This procedure is now an integral component of modern stroke care maps (organized systems for patient management). ■ Losartan, an angiotensin II receptor antagonist originally approved for the treatment of high blood pressure, is additionally approved to reduce the risk of stroke in patients with high blood pressure and left ventricular hypertrophy.

Source: adapted from http://www.americanstroke.org and published literature

- Patients treated with rt-PA are at least 30% more likely to have minimal or no disability at three months compared with patients who are not treated with anything in the period immediately following a stroke (NINDS 1995).
- Ticlopidine has been found to reduce the risk of stroke by 21% (vs. aspirin) in high-risk patients suffering a prior transient ischemic attack or minor stroke (Hass et al. 1989).
- Short-term therapy with clopidogrel is also more effective than aspirin in reducing the combined risk of ischemic stroke, heart attack, and vascular death. In high-risk patients, a risk reduction of 8.7% across all three events in the first few years following an atherosclerotic vascular event can be realized with the administration of clopidogrel vs. aspirin (CAPRIE 1996).
- In the prevention of stroke in eligible patients, carotid endarterectomy has been shown to extend the average quality-adjusted life expectancy by 13.8 months vs. no therapy and by 11.2 months vs. aspirin (Nussbaum et al. 1996).

Value of Investment in Stroke Management

Because the emphasis in recent years has been on the prevention of both primary and recurrent stroke, data regarding the cost-effectiveness of the treatment of stroke is limited (compared with the literature published on the cost-effectiveness of preventing stroke). Key studies looking at the cost-effectiveness associated with either the prevention or the treatment of stroke are summarized in Table 13. Conducted in the U.S., these studies are representative of treatments presented in the treatment innovation timeline.

For Medicare stroke patients, the value of health gains associated with overall stroke treatment is estimated to be $1.55 for every additional dollar spent.

[11] These benefits represent estimates based on commonly used values for health gains.

Medicare Expenditures and Outcomes: 1985 to 1999

Estimates of the five-year costs and health benefits for Medicare stroke patients were generated for three time periods: 1985 to 1989, 1990 to 1994, and 1995 to 1999.

Table 14 shows that the total five-year costs (Medicare expenses and out-of-pocket expenses paid by Medicare patients) for Medicare stroke patients increased over time, and health gains were achieved. Specifically, treatment costs for stroke increased by roughly $16,000 between the periods 1985 to 1989 and 1995 to 1999. The net five-year benefits from treatment for stroke in 1995-1999 were substantial compared to those in 1984-1989: an increase of $8,900 per patient.[11] For Medicare stroke patients, the value of health gains associated with overall stroke treatment is estimated to be $1.55 for every additional dollar spent.

"Face to Face" Case Study

Robert: 1970

Robert is a 68-year-old man with a history of high blood pressure and diabetes. He suddenly has difficulty talking and is unable to move his right arm. In addition, his right leg becomes weak and cannot support his weight.

His wife notices the problem immediately and calls their doctor who tells them to go to the emergency room at the local hospital. Once there, Robert waits several hours before being seen by a physician. His general examination was normal aside from a blood pressure reading of 180/95 mmHg. His neurological examination reveals a speech deficit (expressive aphasia), an inability to move his right arm and weakness in his right leg. The patient is admitted to the hospital for routine lab tests, which include blood work, urinalysis, chest X-ray and electrocardiogram. Several days later, he aspirates his food, which leads to pneumonia, requiring antibiotic treatment and

Table 13 ■ Key Studies used to Calculate Value of Investment in Treatment of Stroke

Reference	Comparators	Population	Value of Investment
Oster et al. (1994)	Ticlopidine vs. aspirin for the prevention of stroke	Patients who suffered a transient ischemic attack, reversible ischemic neurological deficit, ischemic amaurosis fugax, or minor stroke	For every additional dollar spent on ticlopidine (vs. aspirin), gain of $2 to $4
Nussbaum et al. (1996)	Carotid endarterectomy (CEA) vs. aspirin	Patients who suffered a transient ischemic attack	Use of carotid endarterectomy (vs. aspirin) actually leads to savings in overall treatment costs as well as health gains
Sarasin et al. (2000)	Clopidogrel vs. aspirin for the prevention of a recurrent stroke	Patients who suffered a first stroke	For every additional dollar spent on clopidogrel (vs. aspirin), gain of $6
Fagan et al. (1998)	rt-PA vs. no therapy in the first three hours following stroke for treatment of stroke	Patients who suffered a stroke	Use of rt-PA actually leads to savings in overall treatment costs as well as health gains

prolonged hospitalization by one week. Neurologically he still cannot communicate or use his right arm or right leg. He is discharged to a nursing home.

Thomas: 2000

Thomas is a 68-year-old man with a history of high blood pressure and diabetes. He suddenly has difficulty talking, is unable to move his right arm and experiences weakness in his right leg, which can no longer support his weight.

His wife notices the problem immediately and calls '911.' Emergency medical services arrive in 20 minutes and after a brief assessment determine the patient has symptoms consistent with stroke. He is brought to the Emergency Department at a local hospital where the staff is alerted to a possible stroke code while the ambulance is in-route. Thomas arrives at the hospital just one hour after the onset of his symptoms. At that time the emergency physician performs a brief assessment and activates a stroke code. A neurologist assesses the patient and finds a normal general examination aside from a blood pressure of 180/95 mmHg. His neurological examination does reveal a speech problem, an inability to move his right arm and weakness of the right leg. Blood count and coagulation (clotting) studies are performed and analyzed immediately. Blood glucose is 145mg/dL. The emergency department pharmacist is alerted that the patient might be a candidate for rt-PA. Thomas is sent for an emergency CT scan of the brain that does not show any abnormalities. On returning to the Emergency Department, intravenous rt-PA is administered. Following the hospital's stroke care map, Thomas is admitted to a unit with nurses who are trained in stroke care. Evaluation by a speech pathologist finds that the patient is at risk for aspiration. Therefore, specific dietary recommendations are made. Thomas is also evaluated by a physical therapist and begins a rehabilitative program.

However, by 48 hours Thomas is able to use his arm, walk and effectively communicate. Two days later, he is reassessed with a fiber optic swallowing evaluation. Results indicate that he is able to swallow safely. At the same time, he has several additional studies performed to identify the cause of his stroke. An intracranial/extracranial MRA (procedure that injects a dye into the arteries to detect blockages) does not show any narrowing of the major arteries supplying the brain. A brain MRI shows a small area of injury due to a blockage in the left frontal lobe. A transthoracic echocardiogram is normal, but because of suspicion of an embolic cause, he has a transesophageal echocardiogram that detects a clot in the left atrium of the heart. The patient is started on a blood thinner and has additional assessments for lipid abnormalities and blood homocysteine (protein that stimulates plaque build-up but can also promote blood clotting) levels. He is discharged and will receive outpatient physical therapy. Within three months of having his stroke Thomas returns to all of his previous activities.

Differences between the 1970s and 2000

The differences in stroke-related care between 1970 and 2000 are remarkable. Significant advances have been made because of interventions aimed at improving diagnosis, reducing stroke-associated neurological deficits (such as loss of speech or movement), avoiding complications, and providing effective secondary prevention.

- In the 1970s, patients were less likely to recognize the symptoms of stroke and probably would not arrive at the hospital so soon after the onset of symptoms as they do today.
- Once reaching the hospital, patients typically waited several hours before being seen. Additionally, no specific interventions (besides general care) were undertaken.
- It was also typical for patients to be discharged to nursing homes following strokes, vs. the acute and subacute rehabilitation facilities that are available today.

Table 14 ■ Five-Year Treatment Costs and Health Outcomes for Stroke

	Average Life Years	Value of Additional Life-Years* (1)	Average Costs (2)	$ Net Benefits (1-2)
1985 to 1989 (Period 1)	2.19		$74,346	
1990 to 1994 (Period 2)	2.30		$85,168	
1995 to 1999 (Period 3)	2.40		$90,381	
Change between Periods 1 and 2	0.11	$10,315	$10,822	-$507
Change between Periods 1 and 3	0.21	$24,903	$16,035	$8,868

** Value of $100,000 per life year gained without an activity limitation, $50,000 per life year gained with an activity limitation, and $2,500 decrease per life year for each cognitive question answered incorrectly*

- Speech and physical therapy interventions were delayed until discharge to a suitable care facility, unlike today, where these interventions begin much earlier.
- Rudimentry echocardiography was available in 1970, but was not in widespread use, and the images were not high quality. Today, the use of vascular (vessel) imaging has increased and includes ultrasonography, MRA, SPECT, and transesophageal and transthoracic echocardiography. These imaging technologies dramatically improve the ability to diagnose and treat stroke patients.
- Brain imaging has improved significantly and includes options such as CT scan of the brain, diffusion-weighted imaging, perfusion-weighted imaging, and PET scans. Such technologies are used to determine whether carotid endarterectomy is an appropriate option.
- Carotid endarterectomy can potentially be used to prevent stroke among eligible patients with severe narrowing of these neck arteries.
- Rehabilitation facilities for stroke patients were available; however, stroke patients were not discharged to these facilities until much later than they are today.
- Aspirin was one of the few drugs available to prevent stroke; today, clopidogrel (in combination with aspirin) is routinely used in the short-term to prevent stroke (and other coronary events, including heart attack and vascular death), showing better effectiveness than aspirin alone.
- Microcoil devices provide effective, minimally invasive teratment for brain aneurysms and help in the prevention of stroke.
- The use of rt-PA immediately following stroke was not an option in the 1970s. Today, its frequent use has been shown to improve short-term survival and disability associated with stroke. Patients are less likely to have minimal or even no disability following a stroke.
- Glycoprotein inhibitors are routinely used to reduce the risk of coronary events in patients suffering a stroke or other coronary event, having shown significant improvements in outcomes for stroke patients. Like rt-PA, this drug was not available in the 1970s and was approved for stroke patients in the U.S. only in the 1990s.

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Breast Cancer

Breast cancer is one of the most commonly diagnosed cancers among women in the U.S., affecting 2.2 million women out of a total of 143.4 million women (1.5% among all women in the U.S.; 0.7% of the entire U.S. population) in 2000 (SEER 2002).

About 40% of these women lived with breast cancer for 10 or more years. In 2001 alone, an estimated 192,000 new cases of invasive breast cancer were diagnosed. While substantial progress has been made in diagnosing and treating breast cancer, researchers continue their efforts to improve the outcomes for women affected by this disease.

Innovations in the Management of Breast Cancer

From 1970 to 2000 the main changes in breast cancer treatment have been in the use of less invasive surgical and diagnostic techniques and in the addition of long-term hormone therapy to prevent or delay cancer from spreading (metastatic cancer). A history of innovations is presented in Table 15.

Mortality rates from breast cancer have fallen over the past 20 years from 32.3 to 25.4 per 100,000 persons.

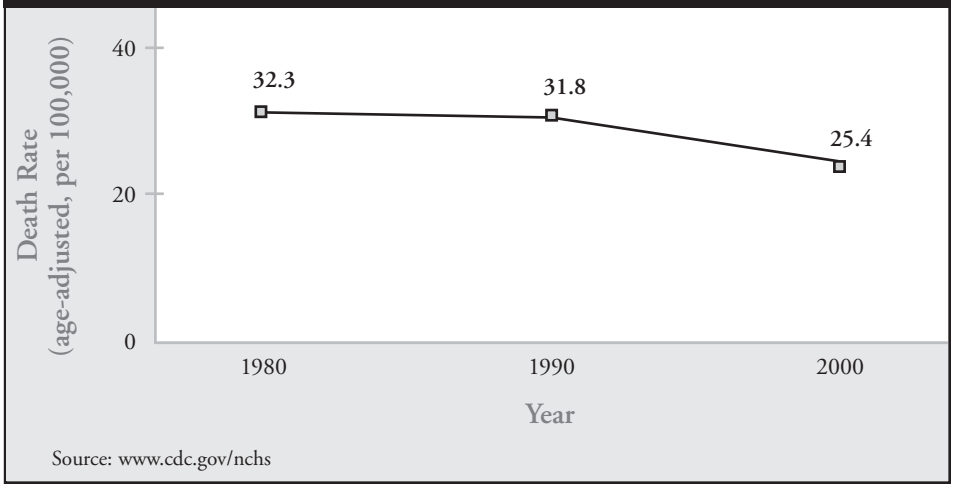
Improvements in Health Outcomes for Breast Cancer

Overall mortality rates for breast cancer held steady in the 1980s, with rates beginning to decline in the early 1990s. Rates fell from 32.3 in 1980 to 25.4 in 2000 per 100,000 persons (www.cdc.gov/nchs)(Figure 10).

Since that time, mortality rates have steadily decreased across the board for all stages of the cancer (Table 16). Additional outcomes are listed below:

- Five-year survival rates have increased from 76.9% in 1980 to 86.6% in 1995 (SEER 2003).
- Adjuvant chemotherapy (chemotherapy received in addition to the primary course of treatment) alone has increased relative five-year survival rates by 33% (Abraham & Zujewski 2001).
- The risk for a 54-year-old woman diagnosed with lymph node-positive breast cancer of developing metastatic disease has declined from 40% to 15% (Abraham & Zujewski 2001).

Figure 10 ■ Decline in Death Rates due to Breast Cancer, 1980-2000



Source: www.cdc.gov/nchs

Table 15 ■ History of Innovations (1970-2000) in the Treatment of Breast Cancer

1970s	■ Tamoxifen, a nonsteroidal anti-estrogen drug, becomes a standard treatment, demonstrating less toxicity than other drugs with its anti-cancer properties. ■ Systematic mammography screening results in early diagnosis, which contributes significantly to a decline in mortality from breast cancer. ■ Combination chemotherapy after surgery shows an improvement in disease-free survival. ■ Platinum-based chemotherapy is introduced, leading to improvements in disease-free survival rates. ■ Modified radical mastectomy (surgery that removes the breast, most or all of the lymph nodes under the arm, and the lining over the chest muscles) replaces radical mastectomy (surgery to remove the breast, chest muscles, and all of the lymph nodes under the arm) as standard surgery for breast cancer, offering the equal chance of a cure in a majority of women with the benefit of decreased cosmetic deformity.
1980s	■ The National Institutes of Health (NIH) issues a consensus statement recommending breast conserving surgery (lumpectomy plus radiation therapy) as the treatment of choice for most women with early stage breast cancer—it offers a greatly improved cosmetic and psychological outcome over modified radical mastectomy. ■ Breast reconstruction with the free TRAM flap is introduced which is advantageous over prior reconstruction surgery as it preserves the function of the abdominal musculature.
1990s	■ Better tolerated hormonal treatments—such as newer nonsteroidal anti-estrogens, nonsteroidal aromatase inhibitors, gonadotropin-releasing-hormone analogues, and progestins—are introduced. ■ Stereotactic core needle biopsy (use of a needle to remove tissue sample) is developed. This provides advantages including minimal invasiveness; speed; elimination of scarring, stitches, anesthesia and hospitalization; and improved accuracy in targeting specific areas. ■ Digital spot view mammography is developed to allow faster and more accurate stereotactic core needle biopsy. ■ Sentinel lymph node biopsy (removal and examination of the first lymph node to which cancer is likely to spread from the primary tumor) is developed. This provides a minimally invasive alternative to axillary lymph node dissection (ALND), which removes lymph nodes in the armpit region, and may help avoid the complications of ALND, including pain, infection, limited shoulder motion, and numbness and swelling of lymph nodes. ■ Trastuzumab is shown to be effective at stopping or slowing the growth of breast cancer for women with metastatic tumors that make too many HER2 receptors (human epidermal growth factor receptors that lead to the malignant transformation of cells when they are over-expressed). ■ Taxanes (drugs that inhibit cell growth by stopping cell division) are added to standard chemotherapy based on landmark CALGB study, which showed improvements in disease-free survival rates. Improved rates were also seen in patients with breast cancer resistant to anthracycline (type of chemotherapy).
2000s	■ Advances in brachytherapy (type of radiation therapy where source of radiation is placed close to body surface or within body cavity) reduce 1) use of multiple needles inserted into breast, and 2) risk of infection. ■ Computer-aided detection (CAD) systems in mammography substantially improve the detection of early stage malignancies. ■ Intensity-modulated radiation therapy (IMRT) delivers the highest possible radiation dose to tumors while sparing surrounding healthy tissues, thus reducing the likelihood of long-term toxicity. ■ Tests for alteration of the HER-2/neu gene (e.g., using fluorescence in situ hybridization) use tissue-based detection techniques and offer improved accuracy in identifying high-risk breast cancers. ■ Recent research discovers that letrozole reduces the recurrence of breast cancer by 43% in older women initially treated with tamoxifen.

Sources: Published literature and expert opinion.

Value of Investment in Breast Cancer Management

An exhaustive literature search for cost-effectiveness studies that evaluated innovative breast cancer treatments yielded eight studies that met all of our inclusion criteria (Appendix D). These studies represented therapies included in our timeline of treatment innovations. Based on the published literature, the value of health gains associated with the investment in breast cancer treatment ranged from $1.12 to $36.81 for each additional dollar spent (Table 17).[12] The exact figure depends on the patient population and type of treatment included in each study.

We also identified a cost-of-illness study that provides a good value comparison of breast conserving surgery (BCS) versus modified radical mastectomy (MRM). Palit et al. (2000) note that the two surgical options are equivalent in terms of long-term survival but that BCS offers much better cosmetic and psychological outcomes. The study estimated that total costs for BCS—

The value of health gains associated with the use of BCS vs. MRM is estimated to be $6.90 for every additional dollar spent.

[12] Note that both an additional life year gained or additional quality adjusted life year (QALY) gained are valued at $100,000 (if the study did not discount costs and benefits) or $173,000 (if discounting was used) in order to generate these VOI estimates.

Table 16 ■ Trends in Breast Cancer Mortality Rates and 5-Year Survival

	1980	1990	2000
5-YEAR SURVIVAL** Local Disease	89.6%	96.5%	(1995) 97.0%
Regional Disease	70.0%	75.7%	78.2%
Metastatic Disease	18.7%	24.4%	22.2%

Source: www.cdc.gov/nchs
***** National Cancer Institute (NCI)***

including general surgeon and plastic surgeons' fees, hospital inpatient services, and radiotherapy services—were $26,330 compared to $22,720 for MRM. If one assumes a conservative incremental advantage of 0.25 quality-adjusted life-years (QALY)[13] per person receiving BCS vs. MRM, then the incremental cost-effectiveness of BCS would be approximately $14,500 per QALY. The value of health gains associated with the use of BCS vs. MRM is estimated to be $6.90 for every additional dollar spent.

For Medicare breast cancer patients, the value of health gains associated with overall breast cancer treatment is estimated to be $4.80 for every additional dollar spent.

Medicare Expenditures and Outcomes: 1985 to 1999

Estimates of the five-year costs and health benefits for Medicare breast cancer patients were generated for three time periods: 1985 to 1989, 1990 to 1994, and 1995 to 1999.

As shown in Table 18, the total five-year costs (Medicare expenses and out-of-pocket expenses paid by Medicare patients) for Medicare patients decreased between the periods 1985 to 1989 and 1990 to 1994 but increased for the period 1995 to 1999. Specifically, breast cancer treatment costs increased by approximately $4,700 between the periods 1985 to 1989 and 1995 to 1999. Health gains increased over the time period under study. The net five-year benefits from treatment for breast cancer in 1995-1999 were substantial compared to those in 1984–1989: an increase of $17,665 per patient.[14] For Medicare breast cancer patients, the value of health gains associated with overall breast cancer treatment is estimated to be $4.80 for every additional dollar spent.

"Face to Face" Case Study

Maria: 1970

Maria is a 54-year-old female whose primary care physician has detected a lump in her armpit area. A mammogram detects a 5 cm breast mass, which is both firm and immobile.

Maria is referred by her physician to a general surgeon who performs an excisional biopsy two weeks after first seeing Maria. Maria's pathology report reveals infiltrating ductal carcinoma—the most common type of invasive breast cancer. During her follow-up surgical consultation Maria is informed that she has breast cancer and that she should undergo a mastectomy. Just one week later she returns to the hospital where a mastectomy and complete axillary node dissection are performed (i.e., her breast is removed along with the lymph nodes in the armpit area where the 5 cm mass was found). Reconstructive surgery is not offered. Maria is in the hospital for five days, and her final pathology report reveals breast cancer that has infiltrated three lymph nodes.

Maria's risk of the disease spreading in the five years following her diagnosis is approximately 40%. During this time she develops lymphedema (a swelling of the arm) that diminishes her quality of life.

If Maria is part of the 40% in whom the cancer spreads, the following is the most likely scenario:

Two years later Maria begins to complain of bone pain. Upon further testing it is discovered that the breast cancer has spread to her bones. She is now among the 40% whose cancer returns and spreads to other areas of the body. Maria's treatment includes receiving what is termed "palliative chemotherapy"—treatment designed to reduce the symptoms of a disease rather than cure it. Such therapy requires a 48-hour hospital stay every three weeks—and the side effects of the chemotherapy are extremely tough—physically and emotionally grueling. Side effects include, but are not limited to, excessive nausea, vomiting and hair loss. Drops in Maria's blood counts result in subsequent admissions for neutropenic fever and transfusions. Maria dies within six months of the disease spreading to her bones.

Susan: 2000

Susan is a 54- year-old female whose annual mammogram shows a shadowy mass approximately 5 cm in size with irregular borders. A same day ultrasound reveals it to be hypoechoic whereby the echoes are weaker or fewer than normal, indicating a problem.

After discussing the results with her primary care physician, Susan undergoes a stereotactic core biopsy of the lesion, which is performed on an outpatient basis. Her pathology report reveals the most common type of invasive breast cancer—infiltrating ductal carcinoma.

After meeting with a surgeon, Susan carefully plans her operation, choosing to have breast conserving surgery (lumpectomy), which will produce excellent cosmetic results, followed by radiation therapy.

[13] QALYs gained because of a health intervention are defined as the expected number of additional years of life adjusted for the quality of those years.

[14] These benefits represent estimates based on commonly used values for health gains.

Table 17 ■ Key Studies Used to Calculate Value of Investment in Treatment of Breast Cancer

Reference	Comparators	Population	Value of Investment
Desch et al. (1993)	Adjuvant chemotherapy vs. no chemotherapy, following primary surgery	Estrogen-receptor negative, elderly (ages 60-80) women with stage 1 breast cancer	For every additional dollar spent, gain of $2.44
Hayman et al. (1998)	Routine radiation therapy following conservative surgery vs. surgery alone	Women with early-stage breast cancer	For every additional dollar spent, gain of $5.24
Hillner and Smith (1992)	Tamoxifen plus adjuvant chemotherapy vs. tamoxifen alone	Post-menopausal node-positive women	For every additional dollar spent, gain of $1.86
Hillner et al. (1992)	Autologous bone marrow transplant following induction chemotherapy vs. standard chemotherapy	Women with metastatic disease	For every additional dollar spent, gain of $1.12
Karnon and Jones (2003)	Letrozole vs. current standard of care	Post-menopausal women with advanced breast cancer	For every additional dollar spent, gain of $27.03 to $36.81
Lindfors and Rosenquist (1994)	Mammography with stereotactic core needle biopsy vs. observation only and surgical biopsy	Women in two hypothetical cohorts: annual screening vs. no screening	For every additional dollar spent, gain of $3.70 to $4.83
Lindfors and Rosenquist (1995)	Various mammographic screening strategies vs. limited screening	Women in various age groups	For every additional dollar spent, gain of $5.30 (biennial mammography for ages 50-59) For every additional dollar spent, gain of $4.20 (biennial mammography for ages 50-59 + annual mammography for ages 40-49)
Smith and Hillner (1993)	Adjuvant chemotherapy vs. no chemotherapy, following primary surgery	Pre-menopausal women treated after primary surgery	For every additional dollar spent, gain of $3.27 to $7.31

This is done on an outpatient basis. As part of the surgical procedure, a sentinel lymph node biopsy is performed whereby the first lymph node where cancer cells are likely to spread from the primary tumor, is removed. A frozen section shows cancer in the lymph nodes of the armpit, which leads to their removal. That same evening Susan returns home.

After surgery Susan meets with a medical and radiation oncologist. Faced with cancer that has invaded three lymph nodes, she and her medical oncologist agree on an aggressive approach to optimize her chance of a cure: six cycles of adjuvant chemotherapy, given as an add-on to her radiation treatment, along with anti-nausea medicine and growth factor support. Susan's radiation therapy lasts six weeks. Following radiation she begins taking an anti-estrogen drug (tamoxifen)—one pill a day for five years.

As a result of her combination drug and chemotherapy treatments the risk of her cancer spreading to other areas of her body in the five years following her diagnosis is approximately 15%. Fortunately, her cancer does not spread, and she is cured. Additionally, the breast sparing surgery has produced excellent cosmetic results.

Differences between the 1970s and 2000

The most critical advances in the treatment of breast cancer includes better diagnostic techniques and imaging, wider cosmetic appeal of today's surgical procedures, and less toxic but more effective chemotherapy and hormonal regimens. Breast cancer patients today are likely to live longer with better psychological outcomes compared with patients living with breast cancer in the 1970s.

- Patients were hospitalized when they underwent chemotherapy, whereas today more than 90% of chemotherapy is given on an outpatient basis.
- Chemotherapy was poorly tolerated until more effective medicines for nausea, vomiting, and preservation of red and white cells were introduced.
- Virtually all surgeons performed mastectomies; breast conserving surgery was not routinely offered.

- For those women who had mastectomies, the option of reconstructive surgery was infrequent; now it is frequently performed during the same operation.
- There often was very little preoperative counseling; women would go to surgery for a biopsy and wake up with a mastectomy. Today, options are discussed prior to any surgery with informed consent.
- Sentinel lymph node biopsy is widely practiced; this reduces the need for a more extensive lymph node dissection and reduces the chance of lymphedema (swelling of the arm).
- For women electing lumpectomy with postoperative radiation, more sophisticated methods are available for radiation therapy which reduce toxicity to normal tissues.
- During the past three decades mammography has become much more prevalent and has improved dramatically. Digital mammography produces higher resolution and trained mammographers now often read the films. Thus, breast cancers are being detected earlier and while still small, which has contributed significantly to a mortality decline.
- Tamoxifen, a hormonal therapy which can improve five-year disease-free survival by 33% to 50% in women with estrogen-positive breast cancer, was not widely available in the 1970s.
- Nonsteroidal aromatase inhibitors, a new class of hormonal therapy, have become available. In the adjuvant setting, these have been shown to increase disease-free survival compared with nonsteroidal anti-estrogens; in the metastatic setting these have dramatically increased the number of hormonal therapy options for some women, corresponding to less toxicity and improved quality of life.

Table 18 ■ Five-Year Treatment Costs and Health Outcomes for Breast Cancer

	Average Life Years	Value of Additional Life-Years* (1)	Average Costs (2)	$ Net Benefits (1-2)
1985 to 1989 (Period 1)	3.96		$59,638	
1990 to 1994 (Period 2)	4.18		$52,640	
1995 to 1999 (Period 3)	4.28		$64,314	
Change between Periods 1 and 2	0.22	$28,453	-$6998	$35,451
Change between Periods 1 and 3	0.32	$22,341	$4,676	$17,665

** Value of $100,000 per life year gained without an activity limitation, $50,000 per life year gained with an activity limitation, and $2,500 decrease per life year for each cognitive question answered incorrectly*

- Newer agents for breast cancer have become available. Taxanes have led to an increase in cure rate in patients initially presenting. Targeted therapies like trastuzumab have had a dramatic impact on patients with metastatic disease.
- Breast cancer has lost a great deal of its psychological stigma. Cancer advocacy groups, particularly for breast cancer, have been instrumental in increasing the level of funding for research and in raising awareness of breast cancer, encouraging early detection, and providing social support networks for women.

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Discussion

Although the cost of medical care has been a national preoccupation and concern for years now, the gains in health have not been neglected by the popular media, nor have the impressive array of health care innovations. We are all aware that improved health has value to American society as does access to the latest medical and health care advances.

But quantifying the value of health care gain has received much less attention… in fact, relatively little has been written and disseminated to the general public about the value of investment in health care in the U.S. That is the task we undertook in this study.

To fully appreciate our findings, it is important for the reader to understand several issues and caveats.

First, we attempted to take a broad, representative approach to valuing health care in the U.S. This is important because of the complexity of the question we faced and the imperfect nature of the available evidence. We accomplished this by focusing our research efforts across several dimensions. For instance, we chose to examine both overall health care indices relative to overall health care costs; as well as to examine in more depth four individual yet major diseases (heart attack, type 2 diabetes, stroke, and breast cancer). The diseases were chosen based on several factors, including: a) their high prevalence, high cost and high morbidity and mortality; b) the fact that virtually everyone in the U.S. is at risk for one or more of these diseases and that most major demographic groups were covered, particularly gender and race, to a lesser degree age; c) the belief that effective health care management practices as well as technological innovations have been made over the past years for these particular diseases; and finally, d) the recognition that major financial investments have been made in the chosen diseases over the past few decades which raises the question of the return to society of those investments.

Second, our effort to develop the evidence presented in this study was broad-based in that we researched the existing clinical, economic, technology assessment and outcomes literature, consulted with clinical specialists in each of the four chosen conditions and examined in detail the Medicare claims data base and long-term care survey data. Within the constraints of our study, we did our best to leave no stone unturned.

Third, although our primary task was to estimate the value of investment in health *care*, we fully recognize that many non-health care factors affect the population's health both positively and negatively. It was virtually impossible to neutralize these effects in all cases. For instance, although many non-health care factors have led to positive gains in health (e.g., lower smoking rates), many others (e.g., increased obesity) have led to negative outcomes. Other factors such as rates of exercise and environmental conditions have both positive and negative impacts on overall health indices. Thus, to some unknown degree, these factors cancel one another out. Further, since we were unable to adequately quantify improvements in quality of life, which doubtlessly exist, our findings may even be quite conservative.

The confounding problem noted above is much less of a concern for our disease-specific findings since, for each disease, we generally begin our analysis with a population already afflicted with the disease, then we calculate the gain in health over time relative to the health care cost invested. Thus, for each disease, the reader can more comfortably assume that the estimated benefits are more likely due to the investment in health care.

Fourth, we attempted to evaluate the value of investment in health care as opposed to restricting our efforts to high-technology. For instance, we note the significant advances of more efficient hospital use (lower lengths of stay), better public health-focused surveillance techniques, and better practices in glucose control as well as many innovative pharmaceuticals, medical devices and diagnostic technologies.

Finally, we specifically examined whether the incremental investment in health care has yielded a positive return. We did not address whether society could achieve these same health benefits at a lower cost or whether the health care system is operating efficiently as a whole. This study should, however, provide additional perspective as the nation debates health care cost containment strategies, helping to refocus attention on increasing value rather than cost reduction as the primary objective.

Glossary of Terms

A

ACE Inhibitor (ACEI) – Class of drugs used to lower blood pressure by inhibiting angiotensin-converting enzymes (ACEs), which help the conversion of angiotensin to angiotensin II.

Adjuvant chemotherapy – Chemotherapy received in addition to the primary course of treatment.

Alpha-glucosidase inhibitors – Class of oral drugs used to treat diabetes by decreasing gastrointestinal carbohydrate absorption (delay absorption of carbohydrates from food and their digestion).

Amaurosis fugax – A short-lived episode of blindness in one eye.

Aneurysm – Localized widening/ballooning-out of a vessel, resulting in a "bulge" that can weaken the vessel's wall and cause a rupture; may occur in the brain, increasing blood pressure and resulting in a stroke.

Angiography – X-ray procedure that takes pictures ("angiograms") of blood vessels. It is usually done by inserting a catheter into an artery or vein in the groin.

Angioplasty – Procedure that re-opens blocked/narrowed arteries to the heart by using a catheter to insert a balloon in the blocked/narrowed portion of the artery; the balloon is then inflated to widen the artery. Also known as "percutaneous transluminal coronary angioplasty."

Angiotensin II Receptor Blocker (ARB) – Class of drugs used to lower blood pressure by blocking angiotensin (eventually converted to angiotensin II), which causes blood vessels to constrict, raising heart rate and blood pressure.

Anterior ST segment – Indicator of heart activity seen on an electrocardiogram.

Anticoagulant – Class of drugs that inhibit blood clot formation; also known as "clot-busting" drugs.

Antiplatelet – Class of drugs that inhibit blood clot formation by keeping platelets (the body's natural blood-clotters) from binding together; also known as "clot-busting" drugs.

Atherosclerotic vascular event – Any type of cardiovascular event that is due to the progressive narrowing and hardening of the arteries over time because of fatty build-up, which results in blocked arteries and blood clot formation. These events eventually lead to the atherosclerotic vascular event.

B

Beta-blocker – Class of drugs used to lower blood pressure by blocking beta receptors on the surface of heart cells.

Biguanide – Class of oral drugs used to treat diabetes by decreasing hepatic glucose release.

C

Cardiac catheterization – Process to examine the heart by inserting a thin tube/hollow needle (catheter) into a vein or artery and passing it into the heart, often to open blockages.

Carotid artery – Two large arteries in the front of the neck that provide blood to the brain. A stroke most often occurs when the carotid arteries become blocked and the brain does not get enough oxygen.

Carotid endarterectomy – Surgery to remove plaque build up in the carotid arteries.

Carotid stenosis – Narrowing of the carotid artery.

Clopidogrel – Type of antiplatelet drug approved for use in the 1990s that minimizes risk of recurrent stroke.

Coagulation – Formation of clots.

Computed Tomography (CT) – Method of examining body organs by scanning them with X-rays and then using a computer to construct an image based on the X-rays.

Coronary Artery Bypass Graft (CABG) – Procedure used to re-route blood supply around a blocked section of a coronary artery by removing healthy blood vessels from another part of the body (e.g., leg or chest wall) and surgically attaching these vessels to the diseased artery in such a way that blood flows around the blocked section.

Creatinine Phosphokinase (CPK) – An important enzyme found predominantly in the heart, brain, and skeletal muscle. CPK is released into the bloodstream in increased quantities if muscle is injured.

D

Diabetic nephropathy – Kidney disease due to diabetes.

Diabetic neuropathy – Nerve disorders or damage due to diabetes.

Diabetic retinopathy – Disease of the retina that potentially causes blindness and is due to diabetes.

Duplex ultrasound – Imaging that examines the blood flow in the major arteries and veins in the arms and legs with the use of ultrasound (high-frequency sound waves). The test combines Doppler ultrasonography, which uses audio measurements to "hear" and measure the blood flow and duplex ultrasonography, which provides a visual image.

E

Electrocardiogram – Record of the electrical activity of the heart, using high-frequency sound waves. With each beat, an electrical impulse (or "wave") travels through the heart. This wave causes the muscle to squeeze and pump blood from the heart. This test allows clinicians to diagnose abnormal heart conditions.

Electrophysiology – A division of cardiology that specializes in the electrical system of the heart and in diagnosing and treating heart rhythm disorders.

F

Fiber optic endoscopy – Procedure that allows a physician to insert a scope that enables examination of a patient's anatomy or physiology, such as the swallowing mechanism.

Fibrinolytic – Another term for thrombolytic (class of drugs that dissolve blood clots).

Fibrinolysis – Another term for thrombolysis (dissolving of blood clot).

G

Glucose – Sugar.

Glycoprotein inhibitor – Class of drugs that inhibit proteins that cause clot formation; often used in the management of cardiovascular patients.

H

Hematoma – Collection of blood under the skin; bruise.

Hemoglobin A1c – Measure of blood glucose levels captured in a lab evaluation that provides an average of blood glucose levels over 2-3 months.

Hemorrhagic stroke – Accounting for 20-30% of all strokes, this occurs as a result of bleeding inside the brain, has a much higher death rate than ischemic strokes and is classified as subarachnoid hemorrhagic stroke (blood vessel on the brain's surface ruptures and bleeds into the space between the brain and the skull, but not into the brain itself) or cerebral hemorrhagic stroke (defective artery in the brain bursts, flooding the surrounding tissue with blood).

HER2 receptors – Human epidermal growth factor receptors. An overexpression (large increase) of these receptors on the cell's surface is a key factor in malignant transformation and is predictive of a poor prognosis in breast cancer.

Homocysteine – Byproduct of protein metabolism found in blood that stimulates plaque build-up but can also promote blood clotting.

Hypotension – Low blood pressure.

I

Implantable cardiac defibrillator – Device that delivers pacing or electric countershock to the heart when an abnormal rhythm is detected.

Intra-aortic balloon pumps – Devices designed to reduce the workload of the heart and increase blood flow to the coronary arteries.

Ischemic stroke – Accounting for 70-80% of all strokes, this occurs when a blood clot forms and blocks blood flow in an artery bringing blood to part of the brain.

L

Lumpectomy – Type of breast conserving surgery used with breast cancer in which only the affected "lump" is removed (vs. the entire breast).

Lymphedema – Swelling of the arm.

M

Magnetic Resonance Imaging (MRI) – Method of gathering images of body organs by using nuclear magnetic resonance of protons to produce proton density images.

Mastectomy – Complete removal of the breast.

Microalbuminuria – Elevated levels of urinary albumin (protein manufactured by the liver that assists in keeping liquid in the blood stream instead of leaking into the tissue). Also refers to a test used to diagnose a kidney disorder and conducted after a diagnosis of diabetes or hypertension.

Microcoil surgery – Minimally invasive surgical procedure used to treat aneurysms, which can often lead to stroke if not treated.

Microvascular complications – Collective term that refers to diabetic retinopathy, neuropathy, and nephropathy.

P

Percutaneous Coronary Intervention (PCI) – Collective term used to describe minimally invasive cardiovascular procedures, such as angioplasty and stenting.

Percutaneous Transluminal Coronary Angioplasty (PTCA) – See angioplasty.

Photocoagulation therapy – Laser surgery used to seal leaks in retinal blood vessels, preventing further vision loss.

Positron Emission Tomography (PET) – Scan that uses a small dosage of a chemical called radionuclide combined with a sugar. A PET scanner detects the positron emissions given off by the radionuclide. The imaging technique is used for diagnosis of a variety of conditions including breast cancer and stroke.

Proteinuria – Elevated levels of protein in the urine, which may be a sign of kidney damage.

Q

Quality-Adjusted Life-Year (QALY) – Expected number of additional years of life with improvements in the quality of life because of a health intervention.

Q-wave – Indicator of heart activity as seen on an electrocardiogram.

R

Recombinant DNA (rDNA) – Taking DNA from one organism and introducing it into the DNA of bacteria where it then reproduces, making copies.

Recombinant Tissue-type Plasminogen Activator (rt-PA) – Type of thrombolytic drug used to dissolve clots but with a mode of action different from antiplatelets and streptokinase.

Relook catheterization – Repeat catheterization (where catheters are placed into the heart to evaluate the anatomy and function of the heart and surrounding blood vessels).

Reperfusion – Restoration of blood flow to an organ or tissue.

Restenosis – Re-narrowing of a blood vessel or heart valve that had been previously opened with angioplasty.

Rethrombosis – Recurrent blood clotting within the open cavity of the blood vessels or heart.

Revascularization – Process to restore blood flow to a body part through procedure-based interventions (angioplasy, stents, coronary artery bypass graft), or by dissolving blood clots with drug therapy.

S

SEER – Surveillance, Epidemiology and End Results program that is used to track cancer prevalence and incidence in the U.S.

Statin – Class of drugs that lower cholesterol levels by blocking enzymes essential to cholesterol production.

Stenosis – Abnormal narrowing or constriction of a blood vessel or valve in the heart (often due to an obstruction).

Stent – Tiny wire mesh device used to keep blood vessels open; classified as either bare-metal or drug-eluting.

Stereotactic core needle biopsy – Procedure to obtain tissue sample by taking two separate X-rays of the breast to locate the lump, and then, with only local anesthetic, using a needle to obtain a tissue sample.

Streptokinase – Type of thrombolytic drug used to dissolve clots but with a mode of action different from antiplatelets and recombinant tissue-type plasminogen activator.

Stress nuclear perfusion test – Test involving an injection of a small amount of radioactive material that circulates in the bloodstream and shows if your heart muscle is receiving adequate blood supply under stress and/or rest conditions.

Subarachnoid hemorrhage – Bleeding into the brain.

Sulfonylurea – One of the earliest classes of oral drug therapies used to treat diabetes.

T

Thiazolidinedione – Class of oral drugs used to treat diabetes by increasing muscle and fat insulin sensitivity.

Thrombolysis – Process of dissolving blood clots through drug therapy.

Thrombolytic – Drug used to dissolve or break up clots that block blood flow; also known as "clot-busting" drug.

Thrombosis – Formation of blood clots that block blood flow in coronary arteries and often cause heart attacks when left untreated.

Ticlopidine – Type of antiplatelet drug approved for use in the 1980s that minimizes risk of recurrent stroke.

Transverse Rectus Abdominis Myocutaneous (TRAM) flap – Most frequently used autologous tissue used for breast reconstruction.

Transesophageal echocardiography – Test that enables a clinician to view the internal structures of the heart and the heart's major vessels by inserting a probe down the patient's throat.

Transthoracic echocardiography – Also known as an ECHO, this test enables a clinician to check for problems in and around a patient's heart using a probe on the surface of the chest.

Transient ischemic attack – Also known as a "mini-stroke," this occurs when brain cells temporarily stop working because of insufficient oxygen, causing stroke-like symptoms that resolve completely within 24 hours of onset.

T-wave – Indicator of heart activity as seen on an electrocardiogram.

U

Ultrasound – High-frequency sound vibration that can be translated into an image and is often used to make medical diagnoses.

V

Value of a Statistical Life (VSL) – Convenient way to summarize the value of small reductions in mortality risks (i.e., tradeoffs between money and fatality risks).

Ventricular arrhythmias – Irregular heartbeat (classified as ventricular fibrillation or tachycardia).

Ventricular Fibrillation (VF) – Occurs when the bottom chambers of the heart (the ventricles) "quiver" or "twitch," preventing the heart from pumping blood to the body.

Ventricular Tachycardia (VT) – Potentially lethal disruption of normal heartbeat that may cause the heart to become unable to pump adequate blood through the body. The heart rate may be 160 to 240 (normal is 60 to 100 beats per minute). In VT, the bottom parts of the heart (the ventricles) are beating very fast. If not treated, VT may go into what is known as ventricular fibrillation.

Vitrectomy – Surgical removal of the vitreous (normally clear, gel-like substance that fills the center of the eye, making up approximately 2/3 of the eye's volume, giving it form and shape before birth).

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