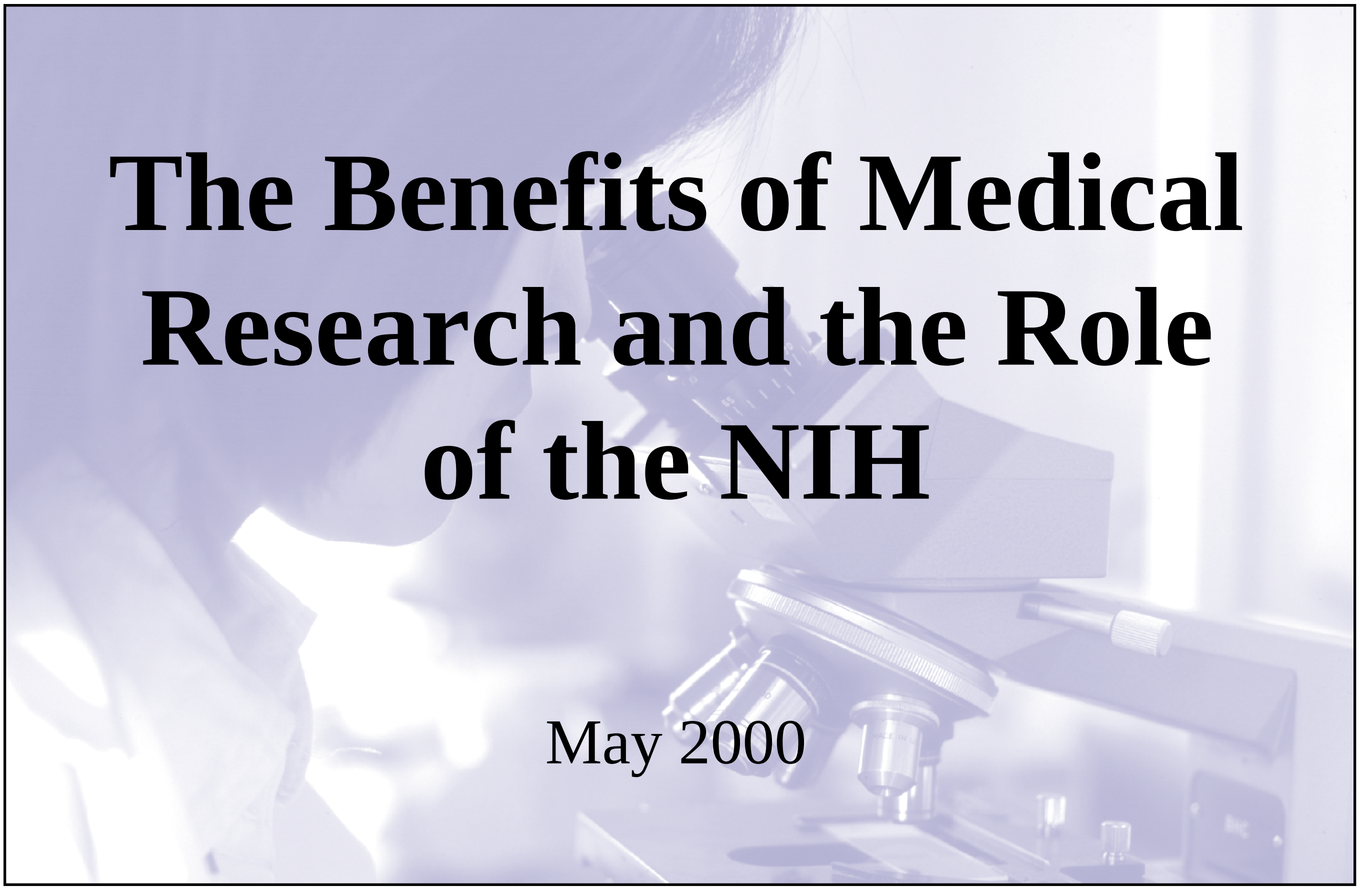

The Benefits of Medical Research and the Role of the NIH

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Office of the Chairman, Connie Mack
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THE BENEFITS OF MEDICAL RESEARCH AND THE ROLE OF THE NIH

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EXECUTIVE SUMMARY

The NIH Leads the Battle Against Disease

- ***Leading the battle against disease***. As the world's leading medical research institution, the NIH funds more than 35,000 research grants each year to scientists across the country making advances against heart disease, cancer, and many other diseases. NIH-funded scientists have won 93 Nobel Prizes over the years, and researchers in the NIH's own labs have won 5 Nobel Prizes.

- ***High returns from federal investments.*** The federal government, mainly through the NIH, funds about 36 percent of all U.S. medical research. Most NIH-funded research focuses on basic science, which creates advances across many disease categories. Publicly funded research in general generates high rates of return to the economy, averaging 25 to 40 percent a year.

- ***Successes against many diseases.*** NIH-funded research has contributed to dramatic decreases in heart disease and stroke mortality rates, increased cancer survival rates, new medications for mental illness, vaccines to protect against infectious diseases, and many other advances in medicine.

- ***NIH behind 7 of 21 top drugs***. Of the 21 most important drugs introduced between 1965 and 1992, 15 were developed using knowledge and techniques from federally funded research. Of these, NIH research led to the development of 7 drugs used to treat patients with cancer, AIDS, hypertension, depression, herpes, and anemia.

Reducing the Economic Costs of Illness

- ***Economic costs of illness.*** The economic costs of illness in the U.S. are approximately $3 trillion annually, representing 31 percent of the nation's GDP. This includes "direct" costs of public and private health care spending of $1.3 trillion, and "indirect" illness costs from reduced ability to work and premature death of $1.7 trillion.

- ***NIH investments are small compared to economic costs of illness***. NIH-funded medical advances are central to lowering the huge economic costs of illness. The NIH is fighting this $3 trillion battle with a budget of just $16 billion, or less than one percent of annual illness costs.

- ***Reducing the <u>direct</u> costs of illness***. Past advances have dramatically reduced health care costs for such illnesses as tuberculosis, polio, peptic ulcers, and schizophrenia. Future advances hold great promise of further reducing costs, such as with drug treatments that decrease hospital stays and invasive surgeries. One study found that, on average, a $1 increase in drug expenditures reduces hospital expenditures by about $3.65.

- ***Reducing the indirect costs of illness***. Medical advances also cut illness costs by reducing lost economic output from disability and premature death. For example, new treatments for AIDS—some developed with funding from the NIH—caused the mortality rate from AIDS to drop over 60 percent in the mid-1990s, thus allowing tens of thousands of Americans to continue contributing to our society and economy.

Illness and the Value of Life

- ***The value of life.*** Most Americans value their life and health very highly. By extending life and improving health, medical research generates great value to us all, in addition to its role in lowering the economic costs of illness.

- ***Longevity is worth trillions of dollars***. U.S. longevity has increased as the overall U.S. death rate has dropped by one-third since 1970. A recent study found that these longevity increases have created net "value of life" gains to Americans of about $2.4 trillion every year. Such estimates place a value on a year of life based on the typical person's "willingness to pay" to avoid various safety risks.

- ***High returns from NIH-funded research***. A portion of the $2.4 trillion in annual longevity gains stem from medical research, and NIH-funded research in particular. If just 10 percent of the value of longevity increases ($240 billion) resulted from NIH-funded research, it indicates a payoff of about 15 times the annual NIH investment of $16 billion.

- ***Cardiovascular disease.*** Advances against the biggest killer of Americans, cardiovascular disease, illustrate the benefits of medical research. The death rate from cardiovascular disease has fallen by more than 50 percent since 1970. About one-third of the decline is the result of advances in medical technology, according to a recent study.

The NIH's Role is More Important Than Ever

- ***Cost of illness threatens to rise.*** The costs of illness may grow higher if we fail to push ahead with further research. Infectious diseases, in particular, are continually creating new health costs. The recent emergence of Lyme disease, *E. coli*, and hantavirus, for example, show how nature continues to evolve new threats to health. In addition, dangerous bacteria are evolving at an alarming rate and grow resistant to every new round of antibiotics.

- ***The NIH agenda.*** NIH-funded research is creating progress in many exciting areas, such as the understanding of Alzheimer's disease and other brain illnesses; better treatment of spinal cord injuries; and greater knowledge of the mechanisms that cause cancer. The human genome project, supported by NIH, holds the prospect of far-reaching advances in gene therapy to treat many illnesses.

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FOREWORD

The United States is the world leader in biomedical research. The benefits derived from our commitment to research have led to life-saving medical breakthroughs and dramatically improved the quality of life for people everywhere. Research has demonstrated that many diseases can be prevented, eliminated, detected or managed more effectively through a vast array of new medical procedures and therapies. But there is much more to learn, and much more we can do to enhance the quality of life for all Americans. We are on the verge of finding cures and new treatments for so many of the diseases that plague our society. Research is the key to unlocking the knowledge we need to find these cures.

The health and well-being of future generations depend on strengthening our dedication to the principle that the federal government, in partnership with the private sector, has a legitimate role in furthering the advancement of science. Investment in basic science helps us compete in the global marketplace in such industries as pharmacology, biotechnology, and medical technologies. I am optimistic that researchers throughout our nation will have the necessary resources to build upon the discoveries of the past, and to continue making new innovations in the future. Turning those discoveries into new methods of treating disease will make every American the beneficiary of these monumental achievements.

That’s what this effort is really about: hope and opportunity. The challenge before us is great, but America has always responded when our people are behind the challenge. America landed a man on the moon. We pioneered computer technology. America won the Cold War. Now it is time to win the war against the diseases that plague our society. We have the knowledge. We have the technology. Most important, we have the support of the American people.

Senator Connie Mack, Chairman
Joint Economic Committee

I. INTRODUCTION

The 20th century witnessed a remarkable string of medical breakthroughs. Federal research funding has provided the foundation for many of them. For more than a century, the lead federal agency responsible for advances in medical research has been the National Institutes of Health (NIH). Efforts by the NIH have had success on many fronts in the battle against disease and in fostering general improvements in health, including the following:

- Reducing the time to discover and develop new cures and treatment options.
- Lowering rates of disease incidence.
- Decreasing mortality rates in people with disease.
- Reducing the economic burden of disease by reducing hospitalization and other costs.
- Decreasing levels of disability.
- Improving quality of life by reducing pain and suffering.
- Sustaining support for university research, education, and tomorrow's leading scientists.

The successes of the NIH have gained it bipartisan support, as Congress and the Administration have increasingly recognized the tremendous potential of federal medical research to improve the lives of Americans. Recognition of the potential of medical research is the basis of a Congressional effort to double the budget of the NIH from a base of $13.6 billion in 1998 to a target of $27.3 billion in 2003. Increasing federal funding for medical research also has wide public support. In a survey, 68 percent of respondents supported doubling spending on government-sponsored medical research.[1]

This report examines how NIH funding for medical research provides economic benefits, reduces suffering from illness, and helps Americans live longer, healthier lives. It supports the case for doubling the budget of the NIH. The NIH at present has a fairly modest budget: its outlays for fiscal year 2000 are expected to be $16 billion. Figure 1 puts that figure in perspective. NIH funding is less than one percent of total federal expenditures, and just 0.5 percent of the total economic cost of illness in the United States. Moreover, the share of national health care spending that goes toward public and non-profit medical research has fallen from 2.2 percent in 1980 to 1.6 percent today.[2] This is a worrisome trend because advances in medical care come from medical research, not from spending more money to apply already known techniques. Shortchanging medical research means shortchanging our own future health and well-being.

As the main federal agency for funding medical research, the NIH is on the front line of the fight against disease. The extensive cross-fertilization between public and private biomedical research has made the United States the world leader in the field. It has produced drugs to combat AIDS, depression, and hypertension, and other advances that have helped millions of Americans live better lives. The NIH has had a crucial role in developing the drugs and medical treatments to combat these diseases and other killers.

Figure 1: NIH Funding in Perspective, 2000
(Ratio of NIH funding to comparison item)

Spending Item	Value	Ratio
NIH budget expenditures	**$16 billion**	**100.0%**
Comparison item:		
Federal R&D expenditures	$83 billion	19.3%
Federal expenditures on health care	$424 billion	3.8%
Total federal expenditures	$1,790 billion	0.9%
Total U.S. health care expenditures	$1,316 billion	1.2%
Economic cost of illness in the U.S.	$3,000 billion	0.5%

Sources: Office of Management and Budget; Health Care Financing Administration; Joint Economic Committee. Figures are estimates based on outlays, except federal R&D, which is budget authority.

Americans today are living longer than ever. A generation ago, in 1970, 9.7 percent of Americans were 65 years old or older. Today, the proportion is 12.4 percent, and a generation hence, in 2030, it is forecast to be 19.8 percent.[3] The aging of America creates new challenges for medicine, because older Americans are disproportionately afflicted with many illnesses. Biomedical research is rising to the challenge. Today, researchers building on decades of NIH-funded work in genetics are beginning to understand the human genetic code. Their work offers the prospect of conquering diseases associated with an aging population, such as Alzheimer's disease, and other persistent unsolved problems, such as cancer and AIDS.

If we are to continue to advance in the fight against illness, it is vital that we increase the NIH’s funding to enable it to handle new challenges and new opportunities for improving the lives of Americans.

II. THE NIH AND FEDERAL FUNDING OF MEDICAL RESEARCH

A. Overview of the NIH

The National Institutes of Health is one of eight health agencies that make up the Public Health Service, which in turn is part of the U.S. Department of Health and Human Services. The NIH was founded in 1887 as the Laboratory of Hygiene, a one-room operation with a budget of $300. Today the NIH comprises 25 institutes and centers, concentrated on a 300-acre campus in Bethesda, Maryland, with estimated budget outlays of $16 billion in fiscal year 2000.

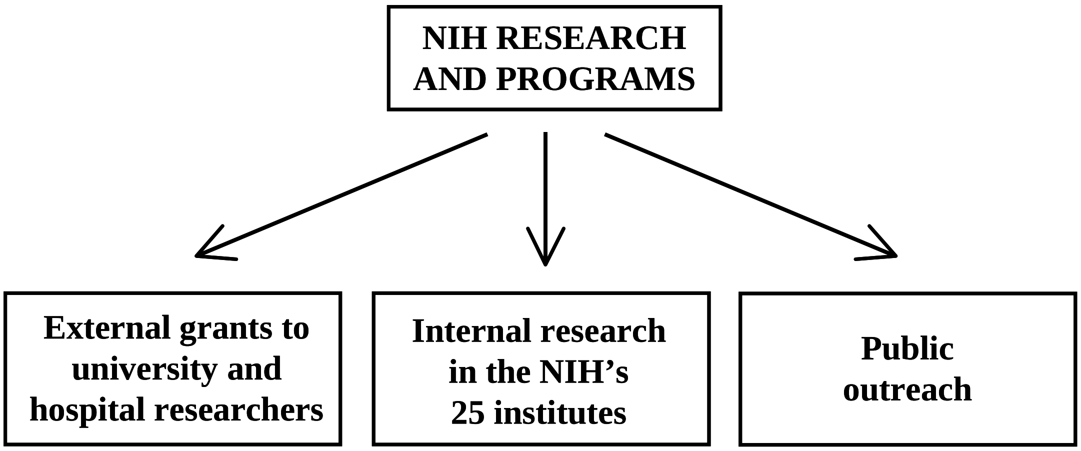
The NIH is the focus for medical research by the federal government. Its mission is to acquire new knowledge to treat illnesses, from the rarest genetic disorder to the common cold. In pursuit of its mission, the NIH performs a wide range of activities, which fall under the broad headings of external (extramural) research, internal (intramural) research, and public outreach. Figure 2 summarizes the NIH's activities.

The NIH spends about 80 percent of its budget on *external (extramural) research* by funding promising medical research at more than 2000 universities, hospitals, and other institutions across the United States. The NIH funds approximately one-third of all research and development conducted in U.S. colleges and universities. The list of medical advancements made by extramural researchers is immense. It includes discoveries of the neurotransmitters in the brain that cause depression, identification of over 20 cancer-related genes, and demonstration that cholesterol levels are linked with the potential for heart attacks. *The NIH has funded no less than 93 Nobel Prize winners through its external research programs.*[4]

The NIH reviews about 50,000 research and training applications a year. A call for grant proposals by the NIH Center for Scientific Review can generate over 10,000 applications. In fiscal year 1999, the NIH spent $11.2 billion to support 38,385 external research grants. For fiscal year 2000, nearly 80 percent of NIH funding will be distributed to external researchers.[5] Most NIH grants are investigator-initiated, single-project grants with one principal researcher. However, the NIH also makes "program project grants," which support multidisciplinary projects conducted by several investigators, and "center grants," which fund multidisciplinary programs of medical research, integrate basic research with applied research, and promote research on clinical applications. Grants include money for equipment needed for research, supplies, costs of using patients in research, and salaries for scientists and technicians. The Appendix contains statistics about NIH grants and recipients.

The NIH Center for Scientific Review and individual NIH institutes and centers apply rigorous standards in evaluating grant applications. Reviewers are experts in the fields under review. The percentage of successful applications for grants is falling. *In 1999 the NIH funded 32 percent of applications, in 2000 it will fund 31 percent, and in 2001 it expects to fund only 26* *percent.*[6] *For lack of funding, the NIH is unable to approve many grants that receive excellent*

Figure 2: The Role of the NIH



External grants to university and hospital researchers

- 80 percent of the NIH's budget funds researchers at over 2,000 institutions across the country.
- More than 35,000 external grants and contracts are awarded each year to university and hospital researchers.
- The NIH funds a third of all R&D in U.S. universities. The NIH has funded 93 Nobel Prize winners.
- Past NIH research has made key advances in treating depression, cancer, and heart disease.

Internal research in the NIH's 25 institutes

- Past research in NIH labs has made key advances in knowledge about cell communication, brain neurotransmitters, and amino acid function.
- Five Nobel Prizes have been awarded to NIH researchers.

Public outreach

- The NIH is the primary disseminator of medical information in the United States.
- The NIH receives over 2 million requests for medical information each year.
- The NIH has pioneered electronic medical databases used by doctors worldwide.
- The NIH has played a key role in creating awareness of the dangers of high blood pressure, cancer, and sudden infant death syndrome.

ratings from review panels. This represents lost opportunities for funding high-quality research that could help improve the health of Americans significantly. Increased funding will allow more high-quality research to be undertaken.

The NIH began as an institution doing *internal (intramural) research.* Today its 2,000 or so internal research programs comprise only about 10 percent of its budget, but they remain central to its scientific efforts. According to the NIH, "First-rate scientists are key to NIH intramural research. They collaborate with one another regardless of institute affiliation or scientific discipline, and have the intellectual freedom to pursue their research leads in NIH's own laboratories. These explorations range from basic biology, to behavioral research, to studies on treatment of major diseases."[7] *Researchers on the staff of the NIH have included winners of five Nobel Prizes in medicine or chemistry.*[8]

Each NIH institute and center has its own research division. Facilities located at the NIH campus in Bethesda, Maryland, include the Warren G. Magnuson Clinical Center; the Mark O. Hatfield Clinical Research Center (opening in 2002); and the National Library of Medicine, the world's largest medical library and producer of MEDLINE and other medical databases used worldwide. NIH facilities located elsewhere include the National Institute of Environmental Health Sciences in Research Triangle Park, North Carolina; the Addiction Research Center of the National Institute on Drug Abuse and the Gerontology Research Center, both in Baltimore; the Rocky Mountain Laboratories of the National Institute of Allergy and Infectious Diseases in Hamilton, Montana; and the NIH Animal Center in Poolesville, Maryland.[9]

The internal research programs of the NIH train a large number of scientists. NIH researchers also participate in ensuring that external research is performed according to high scientific standards, devising research protocols (such as standards for treating patients in clinical trials), and facilitating collaborations between researchers where appropriate.

The NIH also performs substantial *public outreach.* As a government agency, the NIH is ultimately accountable to the public. Medical research is not truly complete until its outcome is public knowledge. That is why the NIH devotes considerable attention to serving as a clearinghouse of medical information and to educating the public.

The NIH devises public education campaigns to help Americans improve their health. For example, the Heart, Lung and Blood Institute created the National High Blood Pressure Program in 1972 to educate the public about hypertension. The National Institute of Child Health and Human Development, working with Gerber (best known as makers of baby food) and children's advocacy groups, devised the "Back to Sleep" campaign to inform the public about sudden infant death syndrome (SIDS). The campaign educated parents and care givers how to prevent SIDS from happening to their infants. From 1992, the year the campaign began, to 1997, SIDS-related deaths fell 43 percent.

The NIH makes vast amounts of medical information available through the Internet, through such services as the Health Information Index, an A-Z subject guide that provides direct links to the specific NIH institutes supporting research related to particular concerns about

Figure 3: Top Ten Diseases and Conditions by Level of NIH Funding, Fiscal Year 2000

Disease or Condition	NIH Funding
Cancer	$3.86 billion
HIV / AIDS	$2.01 billion
Heart research	$1.42 billion
Mental disorders	$853 million
Digestive diseases	$731 million
Drug abuse	$697 million
Diabetes	$525 million
Eye diseases	$485 million
Alzheimer's disease	$466 million
Smoking	$393 million

Source: National Institutes of Health.

health; MEDLINEplus, a service for anyone with a medical question, which provides up-to-date information from the NIH's National Library of Medicine, the world's largest medical library; and ClinicalTrials.gov, a consumer-friendly database with information on federal and private medical studies at thousands of locations nationwide.

The NIH receives more than 2 million inquiries a year from the public and mails out 700,000 requested publications a year. In 1998, the main Web page of the NIH was, along with the Library of Congress, the second most visited Web site of any federal government agency. The NIH responds to more than 1,000 inquiries from the mass media each month.[10]

Figure 3 shows the top ten funded diseases and conditions by NIH funding levels for fiscal year 2000. Appendix Figure A-4 contains more detail about common diseases that afflict Americans.

B. Complementary Roles of NIH and Private Research

The federal government, mainly through the NIH, funds about 36 percent of all biomedical research in the United States. Nonprofit organizations fund about 7 percent, and private industry funds about 57 percent.[11]

Measuring the economy-wide rate of return to publicly funded research involves difficult problems of quantification. However, *direct estimates that have been made in econometric studies place the economy-wide rate of return on publicly funded research on the order of 25 to 40 percent a year*. This finding agrees with estimates of the rate of return of *privately* funded research and development.[12] By way of comparison, the average before-tax profits of nonfinancial corporations in the United States ranged from 8.5 percent to 14.3 percent in the most recent ten years for which data are available (1988 to 1997), and corporations often use an expected rate of return of 15 percent as the minimum for considering investments.

The federal government funds both applied research and basic research, but its role has been especially large in basic research. Basic research generally aims at discovering new scientific principles. Researchers or their backers often cannot receive enforceable property rights, such as patents, that would enable them to recover their investment in the ideas they have discovered. Once knowledge discovered by basic research has been disseminated, anyone can use it without charge. Therefore, investment in basic research can be unprofitable for private industry except insofar as it has well-defined links with applied research.

The results of basic research can sometimes not be patented because, and most countries have found it beneficial that the results of such research be widely disseminated and available at low cost. However, this implies that the economy-wide rate of return on basic research is higher than the private rate of return that industry can capture—a situation that creates a case for government support of basic research, such as medical research.

Applied research generally aims to use already known scientific principles. Worthwhile applications can be patented to give companies enforceable property rights to the fruits of their research—a drug, a piece of medical equipment, or a medical device. This creates strong incentives to further invest in potential breakthroughs. Also, patent royalties can add to returns and help companies generate enough revenue to make applied research profitable. Even here, though, a case may exist for government support if market factors are not fully favorable. For example, some devastating diseases affect only a small number of Americans. Privately funded research may consider the potential market too small to serve. Publicly funded research offers a channel for helping such groups.

Federal research and private research are complementary. Private research in the United States has produced a cornucopia of medicines, medical devices, and techniques. Private research has built on a foundation funded by federal research. Many of the ideas underlying private research and commercialization were developed by federally funded research. Together, federal funding and private funding have produced networks of innovative research that have served the American public well.

III. REDUCING THE HIGH COSTS OF ILLNESS WITH MEDICAL RESEARCH

A. The High Costs of Illness

The costs of illness are enormous from any perspective. Millions of Americans deal with the pain and suffering caused by disease; many die prematurely each year from illnesses; and families deal with the emotional pain created by loved ones with disease. In addition, illness imposes large costs on the economy, which includes the nation's expenditures on health care of $1.3 trillion annually, and about $1.7 trillion a year in lost economic output attributable to incapacitated workers and premature death.

Figure 4 classifies the main costs of illness into ***direct costs***, ***indirect costs***, and ***intangible costs***.[13]

Direct costs are the total costs of the health care system, including diagnosis, surgery, treatment, care, and rehabilitation by doctors, hospitals, nursing homes, and other institutions. In 2000, total U.S. public and private health care expenditures are estimated to amount to $1.3 trillion, or 14 percent of gross domestic product (GDP).[14]

Indirect costs include lost worker output from reduced job performance and missed work due to illness (morbidity), and lost output due to premature death (mortality). Indirect cost estimates may also include other losses to the economy that result from illness. Indirect cost estimates typically use the "human capital" approach to valuation, which accounts for reduced productivity through losses to earnings.

Intangible costs are burdens in addition to the direct and indirect costs of illness. They include the emotional and physical pain and suffering that illness causes to patients and families. The intangible costs of illness are large, but difficult to value monetarily. Individuals place great value on their own lives, and would be willing to pay substantial amounts to avoid illness and premature death.[15]

Direct and *indirect* costs together may be thought of as the *economic costs of illness*. Researchers have produced a variety of estimates for various components of the economic costs of illness.[16] To estimate an overall cost for the United States, we examined figures collected by the NIH that show direct and indirect costs by major illness.[17] These are summarized in Figure 5 below. The estimates are collected from numerous academic studies, each typically focusing on a single illness. Figure 5 reports the ratio of indirect to total economic costs for each illness. The overall weighted average for 25 major illnesses shown is 56 percent.[18] Note that the studies may use different methodologies and are for different years, so this figure should be considered a rough summary statistic for the average magnitude of indirect economic costs for all illnesses.

Figure 4: The Benefits of Medical Research

MEDICAL R&D

MEDICAL ADVANCES

- **Pharmaceutical products**
- **New knowledge of disease and better health care procedures**
- **New machines and equipment for diagnosis and treatment**

Reduction in direct costs of illness

- Medical advances can bring savings in hospital, nursing home, surgery, and other health care expenses.
- Total "direct" costs of illness equal total U.S. health care expenditures of $1.3 trillion annually.

Reduction in indirect costs of illness

- Lowering morbidity (illness) reduces lost economic output by reducing sick days and unemployment, and maximizing worker productivity.
- Lowering mortality (death rates) also reduces lost economic output. Years of productive work may be saved by reducing premature deaths.
- Total "indirect" costs of illness from lost productivity and other factors may total $1.7 trillion.

Reduction in intangible costs of illness

- Medical advances add years to many Americans' lives.
- New pharmaceuticals and other technologies reduce patient pain and suffering.
- Valuations of life based on "willingness to pay" studies indicate benefits from improved health in the trillions of dollars.

A comprehensive 1997 study by the Canadian government investigating the total economic costs of illness in Canada found a similar ratio of direct and indirect costs. Direct costs of disease represented 46 percent of Canada's total costs, while indirect costs represented 54 percent.[19] Like most U.S. studies investigating the economic costs of illness, the Canadian study used the "human capital" approach to measuring indirect costs. Estimates for total economic costs have been completed for the U.S. producing somewhat varying results.[20]

In the United States, total direct costs of illness are represented by the $1.3 trillion Americans will spend this year on health care. Based on the average indirect cost ratio computed in Figure 5, *the total economic costs of illness in the United States are about $3 trillion annually, of which 44 percent ($1.3 trillion) are direct costs and 56 percent ($1.7 trillion) are indirect costs. These costs represent about 31 percent of U.S. gross domestic product.*

B. Direct Cost Savings from Medical Research

Medical research holds great potential to reduce the direct, indirect, and intangible costs of illness alike. Past breakthroughs in research have lowered the direct costs of illness by reducing the incidence of or eradicating diseases, shortening hospital stays, and diminishing the

Figure 5: Economic Costs of Major Illnesses

		billions of dollars			
Illness	**Year**	**Direct costs**	**Indirect costs**	**Total costs**	**Ratio of indirect to total costs**
Injury	1995	89.0	248.0	337.0	74%
Heart diseases	1999	101.8	81.3	183.1	44%
Disability	1986	82.1	87.3	169.4	52%
Mental disorders	1992	66.8	94.0	160.8	58%
Cancer	1994	41.4	68.7	110.1	62%
Alzheimer's disease	1997	15.0	85.0	100.0	85%
Diabetes	1997	44.1	54.1	98.2	55%
Chronic pain conditions	1986	45.0	34.0	79.0	43%
Arthritis	1992	15.2	49.6	64.8	77%
Digestive diseases	1985	41.5	14.7	56.2	26%
Stroke	1998	28.3	15.0	43.3	35%
Kidney and urological diseases	1985	26.2	14.1	40.3	35%
Eye diseases	1991	22.3	16.1	38.4	42%
Pulmonary diseases	1998	21.6	16.2	37.3	43%
HIV / AIDS	1999	13.4	15.5	28.9	54%
Other *(10 further illnesses)*	various	53.4	23.9	77.2	31%
Total - 25 illnesses		**707.1**	**917.5**	**1624.0**	**56%**

Source: Based on National Institutes of Health, *Disease Specific Estimates of Direct and Indirect Costs of Illness*, 2000.

Note: All costs are in selected year unadjusted dollars.

invasiveness of surgery. Medical advances have reduced the indirect costs of illness by extending life spans and enabling people with disease to take more active roles in work and society. Enabling people to live longer, healthier lives has also reduced the intangible costs of illness.

Here are examples of illnesses whose direct costs have been reduced by medical research:

- ***Tuberculosis.*** Before antibiotics were developed, tuberculosis patients often spent years in sanatoriums and had a high chance of death. Today, patients typically recover within a year with antibiotic treatments. As a result, the U.S. health care system saves about $5 billion annually in institutional care costs for the 300,000 or so patients who would have had this disease.[21]

- ***Polio.*** For years, the best the medical profession could offer polio sufferers was management of the disease by the use of expensive iron lungs. With the discovery of the polio vaccine, the disease has been eliminated in the United States: no new cases have been reported since 1991. If a vaccine had not been found, U.S. health care costs would have been about $30 billion a year higher, according to one estimate.[22]

- ***Peptic ulcers.*** Operations for peptic ulcers plunged 80 percent between the late 1970s and late 1980s as new pharmaceuticals were introduced to replace surgery.[23] Further research found that ulcers can be complicated by a bacterium. The bacterium can now be treated with antibiotics. This discovery resulted in cost savings of about $600 million annually.[24]

- ***Clinical depression***. New drugs developed during the past two decades have dramatically cut treatment costs for the approximately 6 million Americans with clinical depression. Anti-depression drugs save the health care system about $6.5 billion annually.[25]

- ***Other mental illnesses.*** Mental hospitals used to hold about 400,000 schizophrenia patients and other mental patients, but new drugs enabled 95 percent of patients to be treated on an outpatient basis by the late 1980s, saving up to $25 billion annually.[26] Lithium treatment for manic depression is saving over $9 billion per year in hospital costs since being introduced about 30 years ago.[27]

- ***Chronic disability.*** Long-term disability rates among the elderly have been falling as new treatments have become available, thus reducing the need for nursing homes. One study found that reduced nursing home usage saved $17 billion from 1980 to 1994.[28]

These are just a few of many medical advances that have reduced the nation's direct health care costs. A 1995 survey listed 63 cases of multi-million and multi-billion dollar savings made possible from medical research and development.[29] A study by the Wisconsin Association for Biomedical Research and Education estimated that the direct cost savings from medical research advances during the past six decades totals more than $100 billion a year.[30]

New drugs in particular have already created large savings and provide great potential for further savings. A 1996 statistical study examined the aggregate impact of new drugs on health care costs in the United States.[31] The study used data on drugs prescribed, hospital admissions, surgical procedures performed, and other variables across all kinds of patients and doctors throughout the country. The study found that from 1980 to 1992, hospital and surgery indicators declined most rapidly for those diagnoses that had the largest increase in drugs prescribed. An increase in prescriptions was found to reduce hospital admissions, number of hospital days, and the number of surgical procedures performed. The study concluded that *on average, a $1 increase in spending on drugs reduced hospital care expenditures by $3.65.*

Despite the great success of medical advances in reducing health care costs for many diseases, there is concern that new medical technologies continue to drive health care spending upward. Certainly, NIH funding has created an increased *supply* of new technologies for diagnosis and treatment. However, the main reason that health care costs have risen quickly is the prevalence of third-party payers in the U.S. health care system. Third-party payment in its current form artificially increases *demand* for health care by reducing incentives to use cost-saving technology.[32]

Many experts believe that future breakthroughs offer even greater potential than we have already experienced for innovations that reduce costs.[33] For example, new drugs may reduce costs of treatment for many illnesses. In addition, biotechnology promises to improve our understanding of the fundamental mechanisms that cause disease. A 1999 paper by five health industry experts was optimistic that "improved understanding of human biology at the molecular level may make invasive surgery, intensive care units, and long-term nursing home care far less necessary."[34] Many costly interventions may eventually be replaced by far less expensive genetically engineered drugs or gene therapy.

Even new technologies that result in higher spending on health care should not automatically be considered problematic, as some commentators are quick to assume. Spending on health care has increased from 8.9 percent of U.S. GDP in 1980 to 14.3 percent in 2000,[35] but so has the share of GDP devoted to other products, such as recreation, whose demand has also risen with rising incomes.

One reason Americans want to spend more on health care is that as life expectancy has increased the value of further medical breakthroughs has also increased.[36] Decades ago, developing a terminal illness at age 30 reduced average life expectancy by roughly 30 years; today it reduces life expectancy by about 50 years. Consequently, it makes sense for the United States to spend greater amounts on medical discovery and health care, because successful treatment adds more years of life than before.

In summary, new revolutions in medicine will provide great opportunities to reduce costs with new pharmaceuticals and other technologies. But even more important than medical research's impact on direct health care costs is its enormous potential to reduce the indirect and intangible costs of illness.

C. Indirect Cost Savings from Medical Research

Rising levels of health and longevity have reduced the indirect costs of illness, including lost economic output from mortality and morbidity. Reduced mortality enables people to work and contribute to society for more years. Reductions in AIDS and other diseases that incapacitate or kill people in their prime earning years can create particularly large gains to the economy. Moreover, if new medicines can shorten spells of hospitalization and incapacity, reduce pain, and increase mobility, workers can be more economically productive.

Many factors have improved the life expectancy and health of Americans over the decades. Much progress stems from advances in medical research, including new drugs, diagnostic equipment, and treatments. Improved sanitation, purer food, greater public knowledge of health issues, and healthy life styles have also helped. Behind it all has been the continuing growth in the U.S. economy. Higher incomes have increased Americans' ability to afford high levels of medical research and top-quality health care.

The impact of medical research on improved health cannot readily be disentangled from other factors that have improved health. However, many specific examples of the role of medical research in fighting particular diseases are dramatic:

- ***Infectious diseases.*** The development of antibiotics and vaccines in the early and mid 1900s has saved millions of lives formerly claimed by killers such as syphilis, diphtheria, whooping cough, measles, and polio. For example, the death rate from influenza and pneumonia has been reduced by 85 percent.[37]

- ***Heart disease and stroke*****.** Since 1970, the death rate from stroke has fallen 60 percent, and the death rate from heart disease has fallen by 48 percent.[38] Cardiovascular drugs such as anti-hypertensives and beta-blockers have played a key role in these death rate declines.[39] One study found that changes in pharmaceutical treatments were responsible for half the reduction in heart attacks in recent years.[40]

- ***AIDS.*** Deaths from AIDS (acquired immunodeficiency syndrome) in the United States have plummeted in recent years as new drug therapies have extended the life span of those with the disease. Drug therapies helped reduce the AIDS death rate by more than 60 percent during the mid-1990s.[41]

- ***Emphysema.*** Anti-inflammatory drugs and other products have reduced emphysema deaths by 57 percent in recent decades.[42]

Of the different types of improvements in health resulting from medical technology, it is least difficult to measure those created by new drugs, because of the well-defined dates of introduction and often dramatic effects that new drugs have. A study of the period 1970 to 1991 found a strong relationship between the introduction of new drugs and reductions in mortality across disease categories. The diseases that had the most rapid introduction of new drugs realized the greatest increase in years of life to patients. Drug innovations increased life expectancy 0.75 to 1.0 percent per year. In economic terms, the study found that spending an additional $15 billion on research and development would save lives whose economic value was conservatively measured at about $27 trillion, thus suggesting a high rate of return.[43]

A study by the Wisconsin Association for Biomedical Research and Education examined the reductions in U.S. mortality and morbidity between 1930 and 1994.[44] From these changes, the study calculated what the gain in economic output has been from improvement over 1930 rates of illness. The estimated gain from medical advances over 64 years was about $5,600 per person in the United States. To arrive at this figure, the authors assumed that 30 percent of the improvements in mortality and morbidity resulted from advances in medical research as opposed to advances from other factors, such as better sanitation or healthier behavior.

D. Intangible Cost Savings from Medical Research

The burden of pain, suffering, and premature death to individuals is much more difficult to value than the direct and indirect economic costs of illness. One way researchers have attempted to place a dollar value on these “intangible” costs is to estimate individuals' "willingness to pay" to avoid illness or death. Such valuations are often used in cost-benefit analyses of public policy issues such as environmental hazards.

A 1999 study by University of Chicago economists Kevin Murphy and Robert Topel estimated the benefits of increases in U.S. life expectancy that have occurred in recent decades.[45] The authors found that *the increases in longevity between 1970 and 1990 created annual net gains worth about $2.4 trillion (in 1992 dollars). Note that if only 10 percent of these increases in value ($240 billion) are the result of NIH-funded medical research, it indicates a payoff of about 15 times the taxpayers’ annual NIH investment of $16 billion*.[46]

An assumption that the NIH is responsible for about 10 percent of the nation's steady improvements in health appears to be reasonable. A number of studies have found that medical advances, in general, are behind about one-third of all health advances. For example, a study discussed below found that about one-third of the decline in deaths from cardiovascular diseases during recent decades stemmed from medical technology advances. Another study found that about one-third of the long-term decline in U.S. disability rates has been from innovation in medical technologies, such as new drugs and surgical techniques. The NIH funds about one-third of the medical research that leads to these advances.[47] One-third of one-third is 11 percent. And, as described later, NIH-funded research helped lead to the development of one-third of the most important drugs introduced in recent decades.

Looking forward, Murphy and Topel believe reductions in prevalence of major diseases would generate monumental gains. For example, *completely curing cancer would be worth roughly $47 trillion, and curing heart disease would be worth roughly $48 trillion.* These figures are present values of all future benefits from longer lives.

Based on these results, the authors conclude that the returns to new medical discoveries are enormous. Reducing deaths from cancer by one percent, for example, would generate gains of about $500 billion. Murphy and Topel remark, "To put this value in perspective, consider a federal commitment of an additional $100 billion for cancer research … Our estimates imply that the program would be worthwhile if it had only a one-in-five chance of producing a 1-percent reduction in cancer mortality."[48] Note that the federal government currently invests just $3.9 billion annually on cancer research. It cannot readily be estimated how much of the nation's reduced mortality in recent decades has stemmed from which factors, but the authors conclude that "even if a small fraction of this improvement is due to medical research, the economic return to that research could be substantial."[49]

Another recent study, by William Nordhaus of Yale University, also attempts to value the reductions in mortality of recent decades.[50] Increasing longevity is akin to rises in average income levels: both have boosted U.S. living standards in recent decades. Like Murphy and Topel, Nordhaus bases his valuations of increased longevity on studies that estimate individuals' willingness to pay to avoid risks. Looking at the period 1975 to 1995, Nordhaus calculates that the value of improvements in life expectancy is about as large as the value of the growth in consumption of all other goods and services.

Another way that Nordhaus considers the benefits of our improved health is as a return on investment in the health care system, which he finds has been very high. For example, health care spending per person in the United States increased $1,200 from 1980 to 1990, but the value of improved longevity for the average American rose $2,300 to $3,100 during that period, so the benefits of greater health care spending were about twice as large as the costs. Adding the value of reduced morbidity to the value of increased longevity, which Nordhaus does not do, would make the return to health care spending even larger.

In a 1999 paper, David Cutler and Srikanth Kadiyala examine the economics of improved cardiovascular health.[51] Deaths from heart disease have fallen about 60 percent in the past three decades. The authors attribute about a third of the decline to medical advances such as better acute management and new drugs such as beta-blockers. They estimate that the average American has gained a value of $85,000 in increased longevity from medical advances in heart disease since 1950, and that this has cost about $35,000 per person in research spending. In other words, the gross investment return was about 240 percent of costs.

E. Implications

The costs associated with illness in the United States, including the direct, indirect, and intangible costs, are enormous. However, they would be much larger without the many advances brought about by medical research. Today, we are on the cusp of making many further great strides against some of the biggest killers. These strides are likely to be made at one of the nation's many universities and medical research centers with research underwritten by the NIH.

Consider treatment of cancer as an example of the potential gains from research. Cancer causes about 540,000 deaths a year in the United States, and its direct and indirect costs are about $110 billion a year. A major cancer research task force in 1998 suggested that if cancer research spending (now just $3.9 billion annually) were increased, and other recommendations of the study were implemented, it would be possible to reduce the incidence of cancer by about 30 percent in 20 years and save 369,000 lives each year by the end of the period.[52] The potential for cost savings from cancer research therefore appear to be very large.

It is also important to keep in mind that, as is the case with many diseases, the costs of cancer are not static. Costs may increase over time unless science makes progress against the disease. The 1998 cancer research task force believed that the costs of cancer may climb to over $200 billion a year within a decade, up from about $110 billion a year today.

Infectious diseases are also constantly pushing U.S. health care costs upwards because harmful organisms are always mutating and evolving. The emergence of Lyme disease, *E. coli*, HIV, and hantavirus (a distant cousin of the deadly ebola virus), are just some of the latest growing threats to health.[53] Tuberculosis, dengue, and malaria have also re-emerged as threats in recent decades. And bacteria continue to evolve rapidly and repeatedly grow resistant to new antibiotics.

We must keep innovating with our medicines so that deadly microbes do not gain the upper hand. Infectious diseases as a group are the third largest killers of Americans, after heart disease and cancer. And 25 percent of all visits to the doctor are related to infectious disease.[54] We cannot expect the current costs of illness to stand still; we must make substantial investments in medical research just to keep pace with the enormous economic and intangible costs of disease.

This section has discussed how medical advances in general have reduced the costs of disease. The next section examines in greater detail medical advances that stemmed directly from research supported by the NIH.

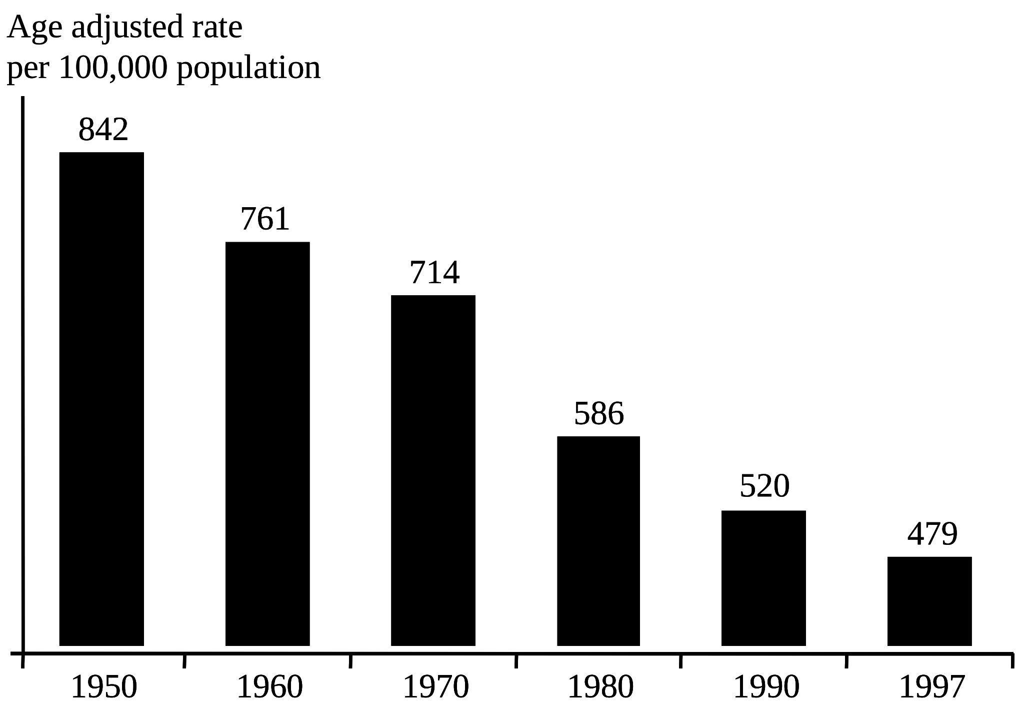
IV. SUCCESS OF THE NIH IN REDUCING DISEASE

A. The Role of the NIH in Improving American Health

During the 20th century, average life expectancy in the United States rose from 47 years to more than 76 years. Much of this increase, particularly in recent decades, is the result of medical advances stemming from research. Many of these advances have been connected to the programs and research funding of the NIH.

Longevity has increased as medicine has had great success in lowering death rates from some of the biggest killers. Figure 6 shows that the overall U.S. death rate from all causes has fallen one-third since 1970. (The numbers are adjusted for changes in the age composition of the population.) Although new threats to health such as AIDS have arisen, we have made great progress against the three biggest killers of Americans: heart disease, cancer, and stroke.

Figure 6: U.S. Death Rate from All Causes



Source: Centers for Disease Control.
Note: Age adjusted rate based on 1940 standard.

Perhaps the biggest success of medical research has come from the huge decline in the death rate from heart disease, which still results in over one-quarter of all U.S. deaths. Figure 7 shows the age-adjusted death rate from heart disease fell 48 percent since 1970, and 57 percent since 1950. This reduction can be attributed to numerous advances stemming from medical research, including new drug treatments such as beta-blockers and calcium channel blockers.[55]

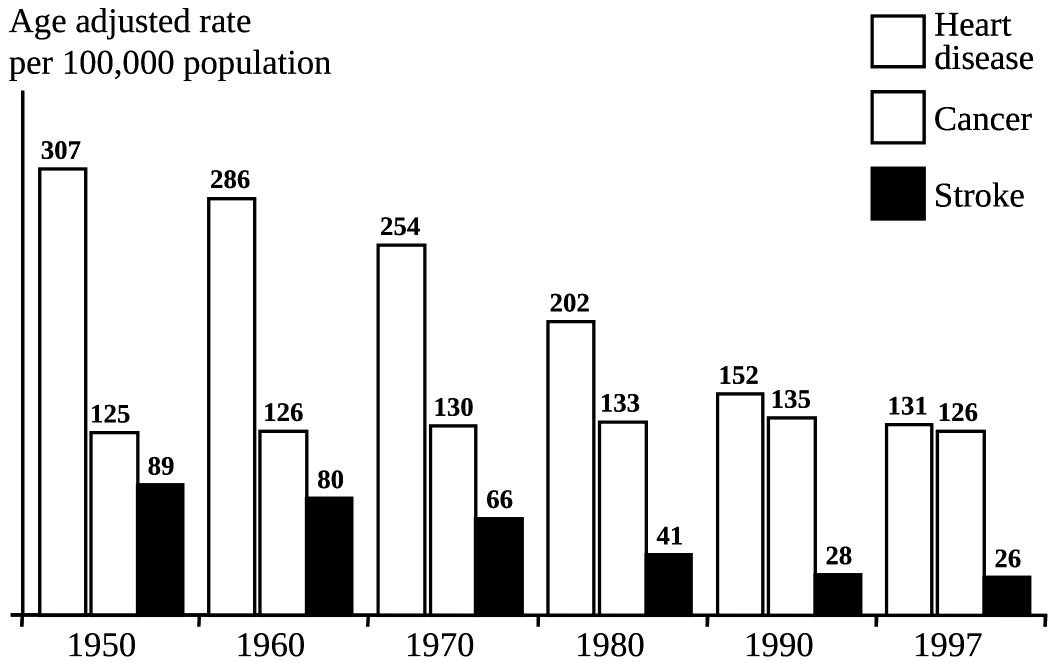
Medical research has also generated new information on how changes in lifestyle can substantially affect heart disease risks. Information as simple as detecting high blood pressure, often a precursor to heart disease, and medicating when necessary, has been effective in helping to reduce heart disease death rates. Medical research has shown that a person's age, family history, cholesterol level, and tobacco intake, among other factors, can detect who is at risk for heart disease. The NIH has played a central role in making the research possible and spreading knowledge of it.

A parallel success story has been the huge drop in death rates from America's third largest killer, stroke. Figure 7 shows that the stroke death rate has plummeted 61 percent since 1970, and 71 percent since 1950. Again, medical research has played an instrumental role. Research has shown, for example, that rapid treatment can greatly reduce the effects of stroke on victims. If individuals receive new blood clot-dissolving drugs within hours of a stroke, their chance of fully recovering in three months is at least 30 percent higher. Medical research has also documented the link between hypertension and stroke. Proper treatment for hypertension and awareness of the signs of stroke, which include numbness of limbs and blurred vision, have helped reduce the death rate from stroke. The NIH played a major role in developing anti-clotting medicines, which have cut by 80 percent the risk of stroke from a common heart condition known as arterial fibrillation.

Cancer is the second leading cause of death in the United States today; it causes more than half a million deaths each year. After decades of steady increases in cancer death rates, the 1990s have finally seen the beginning a downward trend (see Figure 7). But death rates only tell part of the story, since many factors may have caused cancer incidence to rise, even as we are having more success treating it. In fact, our success fighting cancer with new drugs and technologies is illustrated by the substantially higher survivor rates of individuals with cancer diagnoses. Figure 8 shows that five-year cancer survival rates have been rising steadily, from about 35 percent in the 1950s to more than 60 percent today.

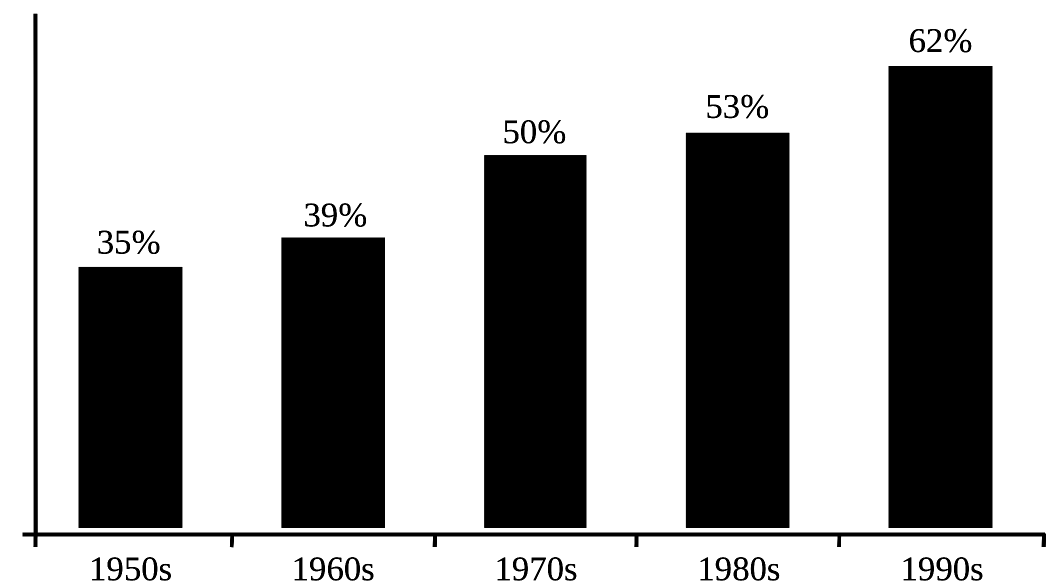
Cancer survival rates have increased because of earlier detection from cancer screenings; improvements in chemotherapy; and drug treatments such as cisplatin, tamoxifen, and taxol. While we have not yet won the battle against the many types of cancer, medical research into drugs such as tamoxifen, which can actually *prevent* breast cancer, indicates that we are gaining the knowledge to win the fight against cancer.

Figure 7: Death Rate from Leading Illnesses



Source: Centers for Disease Control.
Note: Age adjusted rate based on 1940 standard.

Figure 8: Five-Year Cancer Survival Rate



Source: Based on data from National Cancer Institute.
Note: Survival rates are based on the following years and groups: 1950s—1950-54, whites only; 1960s—1960-63, whites only; 1970s—1974-76, all races; 1980s—1985, all races; 1990s—1992, all races.

In addition to these successes against the three largest killers, the NIH has played a major role in the successes against many other diseases, including:[56]

- New medications for schizophrenia have reduced dangerous symptoms such as delusions and hallucinations in 80 percent of patients.

- Development of many vaccines to protect against infectious diseases that once killed and disabled millions.

- Better treatments for spinal cord injury with the development of new steroids, which have significantly reduced paralysis.

- Research that provided the basis for new classes of anti-depression drugs, allowing millions of Americans to have fuller and more productive lives.

NIH-funded research continues across many disease categories and scientific disciplines. In the past year alone, NIH-funded research has contributed to the following successes:

- Completed the first sequence of human chromosome 22, the chromosome that is linked to the functioning of the immune system, congenital heart disease, schizophrenia, mental retardation, birth defects, and several cancers. This is the longest continuous chain of DNA yet deciphered.

- Lowered the transmission rate of the HIV virus from mother to infant. Clinical trials done with scientists from Uganda have found that when given to the HIV-infected mother during labor and to the infant within three days of birth, the drug nevirapine reduced HIV transmission rates to newborns while also being less expensive. The treatment could prevent 300,000 to 400,000 HIV infections in newborns each year.

- Discovered chemical imbalances in pregnant women with preeclampsia, a condition causing high blood pressure and severe headaches. The discovery of these chemical imbalances (of prostacyclin and thromboxane) that control blood pressure may help prevent preeclampsia from evolving to the more severe condition, eclampsia, which causes convulsions and birth complications.

- Discovered the gene that makes salmonella bacteria. The discovery will aid in developing antibiotics and vaccines that will be effective not only against salmonella, but also many other types of bacteria containing the discovered gene.[57]

B. Cost Savings from NIH Research

Not only are NIH scientists in the forefront of new research and treatments; they are also devising treatments that reduce medical costs. The following examples show some of the cost savings that have resulted from applied and clinical research supported by institutes and centers of the NIH. Dollar amounts are in 1992 dollars, and the dates of each research effort are in parentheses.[58]

- A $50,000 research effort by the Warren G. Magnuson Clinical Center proved that it is unnecessary to screen donated blood for HIV-antigen if it has already tested negative for HIV-antibody. Potential savings are $37 million to $49.4 million a year (1988).

- The National Cancer Institute developed combination chemotherapy with cisplatin for treating advanced testicular cancer. A clinical trial showed that patient response rate to the therapy was 77 percent and the cure rate was 60 to 65 percent. The study cost $71.6 million; estimated savings from improved survival rates were $134 million to $178.7 million a year (1970-87).

- The National Eye Institute evaluated laser treatment for blindness caused by diabetes. The research effort cost $180.6 million; reduced risk and costs of vision loss were estimated at $1.1 billion to $1.6 billion a year (1971-92).

- The National Heart, Lung, and Blood Institute compared medical versus surgical treatment for people whose coronary artery bypass surgery could be deferred. The research effort cost $36.5 million; estimated savings are $402 million to $804 million a year in lower treatment costs (1973-84).

- The National Institute for Allergy and Infectious Diseases formulated the hepatitis B vaccine. The research effort cost $31.8 million; estimated savings are $73.7 million to $147.6 million a year (1964-81).

- The National Institute for Allergy and Infectious Diseases formulated intervention for two-month-old infants of haemophilus influenzae type b, the leading cause of bacterial meningitis in the United States. The research effort cost $20.1 million; reduced medical costs and indirect costs of sickness and death are $346.6 million to $462.1 million a year (1972-89).

- The National Institute for Child Health and Human Development used mass screening for identifying hypothyroidism in infants and helping prevent mental retardation. The research effort cost $1.6 million; potential savings are $193 million to $436.2 million a year (1979-86).

- The National Institute for Diabetes and Digestive and Kidney Diseases discovered preventive measures for the recurrence of kidney stones. The research effort cost $920,000; potential savings from reduced treatment costs were $436.2 million to $872.4 million a year (1980-84).

- The National Institute of Dental and Craniofacial Research has done research leading to adoption of preventive oral hygiene measures including the use of fluoride, dental sealants, appropriate diet and oral hygiene practices, and pharmacologic agents. The research effort cost $3.1 billion; savings in reduced treatment costs are $2.9 billion to $3.8 billion a year (1950-90).

- Research by the National Institute for Diabetes and Digestive and Kidney Diseases has improved the efficacy and safety of kidney transplants for patients with kidney failure. The research effort cost $571.9 million; savings from lower treatment costs and recovery of lost earnings are potentially $359.3 million to $479.1 million a year (1970-89).

In response to the Government Performance and Results Act of 1993,[59] the NIH has developed an independent assessment process for evaluating the outcomes of NIH-supported research. The assessment gauges the NIH's stewardship of medical research.[60] The fiscal year 1999 version of the assessment document exceeds 500 pages. It describes how NIH-supported research has added to the knowledge about biological functions and behavior; developed new or improved instruments and technologies for research and medicine; developed new or improved approaches to disease and disability; developed new or improved methods for diagnosing disease and disability; and developed new or improved approaches for treating disease and disability. Each section of the assessment is divided into three parts: Science Advances, describing a specific scientific discovery published within the last year and supported by NIH funding; Science Capsules, providing a snapshot of the breadth and scope of the results of NIH research programs; and Stories of Discovery, each discussing a single finding and how it fits into the overall development of treatments that improve health and the quality of life.

C. Case Studies of the NIH's Role in Pharmaceutical Development

Research done by the NIH has resulted in thousands of important medical discoveries and advancements, many arising from basic medical research. As Dr. Arthur Kornberg, a Nobel Prize-winning scientist, has observed,

"Investigations that seemed totally irrelevant to any practical objective have yielded most of the major discoveries of medicine. X-rays were discovered by a physicist observing charges in vacuum tubes; penicillin came from enzyme studies of bacterial lysis and the polio vaccine from learning how to grow cells in culture. Cisplatin, a widely used drug in cancer chemotherapy, was a fortuitous discovery of how electric fields affect the growth of bacteria. All these discoveries have come from the pursuit of curiosity about questions in physics, chemistry and biology, apparently unrelated at the outset to a specific medical or practical problem."[61]

Figure 9: Benefits of Drugs with NIH Research Involvement

Generic name *(trade name)*	Illness	NIH role	Nonmonetary benefits	Dollar savings
Acyclovir ***(Zovirax)***	Herpes simplex virus (HSV)	NIH-funded researchers discovered how HSV enters nerves cells and purified HSV enzymes	Prevents neonatal herpes	Reduces treatment in pregnant women with HSV from $1.3 mn. per neonatal infection prevented to $493,000
AZT ***(Retrovir)***	HIV	National Cancer Institute helped screen AZT, the first anti-HIV therapy	Reduces transmission of HIV from mother to child in 66% of potential cases	HIV transmission rate from mother to child was 15-30% before 1994; now it is 5-10%
Captopril ***(Capoten)***	Hypertension, diabetes-induced kidney failure	NIH funded research to find the drug that would inhibit the enzyme causing hypertension	Reduces risk of kidney failure, dialysis, transplantation, and death in 50% of patients with insulin-dependent diabetes mellitus	Use in patients with insulin-dependent diabetes mellitus saves $32,550 per patient in direct costs and $45,730 in indirect costs over a lifetime
Cisplatin ***(Platinol)***	Testicular, ovarian, and cervical cancer	National Cancer Institute developed cisplatin combination chemotherapy for testicular cancer	77% patient response rate for testicular cancer; 60-65% cure rate	Cost savings from testicular cancer treatment average over $156 million a year
Erythropoietin ***(Epogen)***	Anemia	National Institute of Diabetes and Digestive and Kidney Diseases funded research identifying the cells that produce the erythropoietin hormone	Reduces need for blood transfusions in anemic patients and allows them to be more vigorous; also reduces mortality	Reduces hospital days for anemic patients from 19.3 days a year to 11.6 days; saves thousands of units of blood transfusions
Fluoxetine ***(Prozac)***	Depression	National Heart, Lung, and Blood Institute and National Institute of Mental Health researchers discovered serotonin	Avoids side effects prevalent in earlier antidepressants	Lower total costs of health care compared to earlier antidepressants
Tamoxifen ***(Nolvadex)***	Breast cancer	National Cancer Institute performed laboratory and live subject testing of the effects of tamoxifen	Five years of tamoxifen treatment reduces breast cancer mortality 26% and reoccurrence 47%; tamoxifen prevents breast cancer in 50% of high-risk patients	Successful tamoxifen therapy saves “end-stage” treatment costs of $22,142 per patient; direct cost savings from tamoxifen use are $41,372 per year of life gained for women 35-49

A study of the 21 drugs introduced between 1965 and 1992 that were considered by experts to have had the highest therapeutic impact on society found that public funding of research was instrumental in the development of 15 of the 21 drugs (71 percent). Three—captopril (Capoten), fluoxetine (Prozac), and acyclovir (Zovirax)—had more than $1 billion in sales in 1994 and 1995. In addition to these drugs, other members of the group of 21 drugs, including AZT, acyclovir, fluconazole (Diflucan), foscarnet (Foscavir), and ketoconazole (Nizoral), had NIH funding and research to help in clinical trials.[62] Seven of the 21 drugs have specific ties to the NIH; Figure 9 summarizes their stories, which follow. They illustrate the importance of the NIH's role in improving the health of Americans.

Acyclovir (Zovirax)

Approximately 45 million Americans have herpes simplex virus. Each year, Americans make nearly 500,000 clinical visits and file more than 2 million pharmacy claims related to genital herpes. Acyclovir, a drug used to treat herpes simplex virus infection, was the first drug that inhibited the replication of the virus without harming the patient's replication of cells.

In the 1960s, researchers in NIH-supported laboratories found that the herpes simplex virus enters nerve cells through their endings in the skin. Using knowledge generated from NIH-funded research into genetics, particularly DNA (deoxyriboneucleic acid), NIH-funded researchers detected and purified enzymes made by the herpes simplex virus. These and related discoveries led scientists at Burroughs Wellcome (now Glaxo Wellcome) to develop acyclovir to inhibit those enzymes and halt the spread of the virus.

The direct medical costs of treating herpes simplex virus were estimated at $166 million annually for 1992-94, or $207 million in 1999 dollars. Of these costs, medical care accounted for 36 percent and drug treatment for 64 percent.[63] In pregnant women with genital herpes, use of acyclovir reduces the costs[64] of treatment from $1.3 million per neonatal infection prevented to $493,000 per infection prevented.

AZT (Retrovir)

In the United States, 650,000 to 900,000 people have human immunodeficiency virus (HIV), which causes AIDS.[65] Some 40,000 new HIV cases are reported each year, and there have been 410,800 AIDS-related deaths through 1998.[66]

In the early 1980s, scientists at Burroughs Wellcome (now Glaxo Wellcome) discovered that AZT (zidovudine) may be a promising treatment against HIV and AIDS.[67] Collaboration between Burroughs Wellcome and the NIH's National Cancer Institute led to the screening of AZT as a therapy for AIDS. Use of AZT alone has now been eclipsed by combination drug "cocktails" for treating many occurrences of HIV and AIDS. (The NIH has done research that has been used in developing the cocktails.) However, use of AZT alone remains important for treating HIV-infected mothers at risk of passing the virus to their babies. Before 1994, the transmission rate was 15 to 30 percent, meaning that 1,000-2,000 babies were born with HIV each year. A 1994 study by the NIH in 1994 showed that treating pregnant HIV-positive women with AZT could reduce the transmission of the virus to babies in about two-thirds of cases.[68]

The age-adjusted death rate from AIDS in the United States fell 47 percent from 1996 to 1997 because of anti-HIV drugs. Therapies using drug cocktails cost $10,000 to $15,000 a year per patient, but reduce other, more expensive costs of treatment. Hospital treatment alone for advanced AIDS costs about $100,000 a year. According to a Los Angeles medical practice treating AIDS patients, each dollar spent on drug therapy saved two dollars in overall treatment costs. A study on AIDS treatment costs at St. Vincent's Hospital in New York City found that new drug treatments caused the monthly average number of patients of hospitalized patients to decrease by 45 percent between February 1995 and September 1996. Moreover, according to a study by the Department of Veteran Affairs, giving patients full access to new AIDS drugs helped save $18 million in treatment costs in 1997.

Captopril (Capoten)

Approximately 14 million Americans have diabetes. Of those, more than 5 million are likely to develop diabetic nephropathy, a condition that ultimately leads to kidney failure, also called end stage renal disease.[69] In 1990, the most recent year for which data were available, 45,000 new cases of kidney failure were diagnosed in the United States; diabetes accounted for about 15,000 of those cases. Of patients with diabetes and kidney failure, 25 percent will eventually need dialysis or a kidney transplant to survive; the costs of such procedures exceed $7 billion a year.[70] Even then, only 20 percent can expect to live as long as five years. In 1990 alone, 200,000 people in the United States experienced kidney failure, resulting in direct and related expenditures of $7.3 billion.[71]

Captopril, a drug originally developed to treat hypertension, was found to be effective at treating kidney failure caused by diabetes. The development of captopril used research results from work funded by the NIH extending back to the mid 1950s. The drug company Squibb (now Bristol-Myers Squibb) worked with Dr. John H. Laragh and an NIH-funded academic laboratory to discover a drug to inhibit an enzyme that creates hypertension; from this research Squibb scientists were able to synthesize captopril.

Trials have shown that, compared to controlling blood pressure alone, using captopril cut in half the risk of progressive kidney failure and the related risk of dialysis, transplantation, and death in patients with an illness called insulin dependent diabetes mellitus. Studies show that the savings for these patients are $32,550 per person in direct costs and $84,390 in indirect costs over the course of a lifetime, compared to no treatment. For patients with non-insulin dependent diabetes mellitus, the savings are $9,900 per patient in direct costs and $45,730 indirect costs. If captopril therapy had been initiated in 1995 for patients with either kind of diabetes mellitus and kidney failure, the total direct savings would have been $189 million a year for 1999 and $473 million a year in 2004.[72]

Cisplatin (Platinol)

Cisplatin is an anti-cancer drug discovered at Michigan State University by biophysicist Barnett Rosenberg, who found that electric currents prevented bacteria from dividing. Rosenberg brought his initial discovery to the National Cancer Institute, whose scientists completed the pharmacology, toxicology, formulation, production, and clinical trials. Michigan State University licensed its patent for cisplatin to Bristol Myers (now Bristol-Myers Squibb).[73]

Cisplatin is now used to treat several types of cancer, including testicular cancer, ovarian cancer, and cervical cancer. The NIH's National Cancer Institute developed combination chemotherapy with cisplatin for the treatment of advanced stage testicular cancer. Clinical trials performed in 1977 demonstrated that treatment with cisplatin, vinblastine, and bleomycin resulted in a 77 percent response rate when used to treat testicular cancer and a 60 to 65 percent cure rate for the disease. The total costs of developing the treatment over the period 1970 to 1987 were $71.6 million, but the potential savings from use in treatment are $134 million to $178.7 million a year.[74]

In 1996, studies done by the United States Gynecologic Oncology Group found that the combination of cisplatin and paclitaxel (Taxol) may increase long-term survival rates for patients suffering from ovarian cancer. Every year, more than 27,000 new cases of ovarian cancer are diagnosed and almost 15,000 women die from the disease. The combination therapy extended the median survival of patients to 38 months, 14 months longer than standard treatment. Almost 19 percent of women are still alive after eight years, versus 8 to 9 percent of women receiving the older treatment.[75]

Cervical cancer is diagnosed in 14,000 women in the United States a year; almost one-half of the cases are already in the advanced stage. Reports from the *New England Journal of Medicine* indicate that a combination therapy of cisplatin and radiation reduced the relative risk of death by 50 to 72 percent for these women.[76]

The National Cancer Institute continues to study cisplatin and its potential for treating other types of cancer. Studies underway show that cisplatin chemotherapy and radiation increases overall survival rates for patients with head and neck cancer, while studies conducted during the past decade have shown that cisplatin therapy in conjunction with other therapies can modestly improve the condition of lung cancer patients.

Erythropoietin (Epogen)

More than 230,000 Americans are being treated for kidney failure. One of the common symptoms of the disease is anemia, a condition that makes it difficult for patients to work, do household tasks, or simple activities of daily living. Approximately 25 percent of patients undergoing kidney dialysis require intermittent or regular transfusions of red blood cells to treat symptoms associated with anemia.

External researchers funded by NIH's National Institute of Diabetes and Digestive and Kidney Diseases identified the cells that are responsible for producing erythropoietin, the hormone made by the kidneys that regulates production of red blood cells. The biotechnology company Amgen was able to identify the erythropoietin gene and create a recombinant form of erythropoietin. Erythropoietin therapy reduces the need for blood transfusions, improves cardiac output and cognitive functioning, increases exercise capability, decreases risk of hospitalization, and decreases mortality in patients with anemia caused by kidney failure. For example, a study of 333 patients receiving shots of erythropoietin found that within two months of therapy the need for transfusions was eliminated in all patients.[77] A 1995 study found that time spent in the hospital by patients treated with erythropoietin fell from 19.3 days a year to 11.6 days.[78]

Fluoxetine (Prozac)

Depression affects 18 million Americans, and by 2020 it is projected to become the second most disabling disorder in the country.[79] In 1954, an external researcher funded by the NIH's National Institute of Mental Health found that the chemical reserpine could produce depression in humans. Work through the 1960s by internal researchers at the NIH's National Heart, Lung, and Blood Institute and the National Institute of Mental Health, as well as external researchers funded by NIH, led to a series of discoveries indicating that depression was caused by lack of certain chemicals in the brain, notably serotonin. In 1970 Dr. Julius Axelrod of the National Institute of Mental Health received a Nobel Prize for his research on the subject. Also during the 1960s, Eli Lilly & Co. began searching for a drug to target serotonin. Lilly developed fluoxetine, which eliminates the side effects caused by earlier antidepressants.

In 1990, the last year for which data are available, the estimated costs of depressive illness in the United States were $43.7 billion: $12.4 billion in direct costs and $31.3 billion in indirect costs. Using fluoxetine instead of certain rival antidepressants decreases annual healthcare charges by $16.48 per patient for each percentage point increase in the number of patients remaining on initial therapy for six months.[80] The costs of treating patients who did not follow instructions and overdosed on fluoxetine were $1,269, compared to $5,764 for those who overdosed on certain rival antidepressents.[81]

Tamoxifen (Nolvadex)

About 180,000 women in the United States are diagnosed with breast cancer each year; 44,000 died from it in 1998. Tamoxifen, produced by the drug company AstraZeneca (formerly Imperial Chemical Industries, or ICI), slows or stops the growth of cancer cells. It is used in patients with advanced breast cancer and in treating early stage breast cancer after mastectomy.

The National Cancer Institute, part of the NIH, has sponsored 140 clinical trials of tamoxifen. It also participated in pre-clinical trials, consisting of both in vitro (laboratory) and in vivo (live subject) tests. Five years of treatment with tamoxifen have shown an annual reduction in mortality of 26 percent. Tamoxifen prevents breast cancer from reoccurring in 47 percent of patients. Recent studies have shown that taking tamoxifen can also prevent breast cancer in women who are at high risk of developing the disease. Tamoxifen therapy caused a 49 percent decrease in the relative risk of developing invasive breast cancer for women of all age groups and a 50 percent reduction in the number of noninvasive breast cancers.

The average base cost of invasive breast cancer is $14,100 per patient, while the average annual cost of tamoxifen therapy is $1,050. Tamoxifen therapy saves "end-stage" treatment costs averaging $22,142 for each patient in whom it prevents breast cancer from reoccurring. The saving in direct costs from tamoxifen was $41,372 per life year gained for women 35 to 49 years old, $68,349 for women 50 to 59, and $74,981 for women 60 to 69 years.[82]

D. Federal Research Spurring Private Sector Medical Advances

Federal research and private research in medicine are complementary. As medical knowledge grows, federal research and private research are becoming more intertwined, building the networks of knowledge that are important for generating new discoveries and applications.

Federal research has been essential for discovering knowledge that has later been used to develop important drugs. A study of 32 innovative drugs introduced before 1990 found that without the contributions of government laboratories and other noncommercial institutions, approximately 60 percent of the drugs would not have been discovered or would have had their discoveries markedly delayed.[83] As has been mentioned, a later study by other researchers of 21 drugs, partly overlapping and partly updating the earlier study, found that an even higher proportion—71 percent (15 drugs)—were developed with input from the public sector. This suggests that public sector research is becoming more important over time.[84]

A striking feature of the publicly funded research on which the drugs relied is how old much of it was. Drugs not marketed until the 1990s relied on research conducted as far back as the 1940s. Nor was the research on which they relied limited to basic science; most of the drugs in the 21-drug study also relied heavily on publicly funded research for clinical (applied) knowledge. For example, thanks to NIH studies we know that reducing even moderately elevated blood pressure can improve health. Fifty years ago this connection was not evident to medical researchers. Drug companies have developed medications to reduce blood pressure based on the NIH studies. For AZT, used in the treatment of AIDS, public- and private-sector research were so intertwined that the attribution of the discovery of the drug was controversial.

Publicly funded research has also discovered new uses for existing drugs, such as the potential of aspirin for preventing heart attacks. Where drugs are still covered by patent protection, publicly funded research can be especially important, because drug companies are forbidden to promote uses of their product not approved by the Food and Drug Administration. This restriction, which includes funding research, was developed to protect consumers. Publicly funded research can fill the gap. Therefore, as the authors of the 21-drug study summarized, "the private sector draws from the public [sector] throughout the life of a drug: as a source of fundamental knowledge that might lay the groundwork for new drugs, as a source of clinical knowledge for the design of drugs once they have been discovered and as a source of clinical knowledge about additional indications for drugs once they have been approved."[85]

Federal research has been important in developing the current generation of genetically engineered drugs just as it was with previous generations of drugs that relied on older technologies. A case in point is Genentech, one of the first biotechnology companies. In the early 1970s the biochemist Dr. Herbert Boyer, of the University of San Francisco, began doing research with the geneticist Dr. Stanley Cohen of Stanford University. Dr. Cohen joined Stanford after receiving training at NIH, and NIH has funded research by Cohen and Boyer. In 1975 Boyer met Robert Swanson, an employee of a venture capital firm, and in 1976 they founded Genentech. The new company's first big project was to use bacteria to make human insulin, a goal it achieved in 1978. (Previously, insulin had been made from the pancreases of pigs and sheep. Human insulin avoided some problems that arose in treating diabetics with non-human insulin.) Genetech licensed production of human insulin to Eli Lilly and Co. In 1985 Genentech became the first biotechnology company to launch its own biopharmaceutical product: human growth hormone, a drug that enables children who otherwise would have stunted growth to develop into adults of normal size. Genentech has since gone on to produce interferon alpha-2a to treat leukemia, t-PA to treat blood clots in heart-attack victims, a vaccine for hepatitis B, an antibody that helps treat certain kinds of breast cancer, and other products. In 1999 Genentech had revenues exceeding $1.4 billion and employed 3,883 people.

The presence of NIH in Bethesda, Maryland has spurred development of a number of biotechnology companies nearby to take advantage of the talent pool of NIH-trained scientists. In a sampling of 55 founders of biotechnology companies in Maryland from 1973 to 1998, 16 came from the NIH, six from the Walter Reed Army Institute of Research and other federal government research institutions, and six more from institutions that receive substantial federal funding, such as Johns Hopkins University.[86] One of these companies is MedImmune, founded by alumni of the Walter Reed Institute. Its flagship product is palivizumab (Synagis), a treatment for a respiratory virus that hospitalizes 90,000 infants and kills 4,500 infants annually. In 1999 MedImmune had revenues of $383 million and employed 528 people.

The cases of Genentech and MedImmune illustrate the economic benefits arising from the combined network of federal and private research. Like many other modern industries, biotechnology has the potential to be located almost anywhere. It does not have to be situated near the sources of raw materials, since shipping costs are not an important factor in its profitability. Researchers for biotech firms are mobile nationally and even internationally. However—and this is the key point—researchers tend to cluster near existing centers of research. For example, Genentech started in the San Francisco area because of the proximity of Drs. Boyer and Cohen. The biotechnology industry is concentrated in the United States rather than Germany, India, or elsewhere because research and business conditions created a "first-mover" advantage. Like many other areas of science, biotechnology involves extensive knowledge best gained from apprenticeship to leading researchers; reading publications reporting their research is not sufficient. Federal research contributes to the U.S. lead in the science and commercial applications of biotechnology.[87]

V. FUNDING THE COMING REVOLUTIONS IN MEDICINE

For the 2000 fiscal year, the NIH has identified four broad “research themes”: exploitation of genomic discoveries; interdisciplinary research with other scientific disciplines; reinvigoration of clinical research; and elimination of health disparities. In addition to these themes, which cover all NIH institutes and centers, the NIH has identified seven “areas of research emphasis” that appear to be ripe with scientific opportunity: the biology of brain disorders, including neurodegenerative disorders; new approaches to pathogenesis (disease origins and development); new preventive strategies against disease; new avenues for development of therapeutics; genetic medicine; bioengineering, computers, and advanced instrumentation; and health disparities.[88]

Here are examples of how the NIH will address some of these research themes and areas of research emphasis, and indications of the potential benefits of the research.

A. Brain Disorders

Brain disorders. The NIH’s National Institute of Neurological Disorders and Stroke conducts and supports research on the brain and nervous system, while the National Institute on Aging has primary responsibility to understand, diagnose, prevent, treat, and cure Alzheimer's disease.

Brain disorders affect people of every age, not just the elderly. Research on brain disorders by the National Institute of Neurological Disorders and Stroke and the National Institute on Aging has changed long-held notions, provided improved knowledge and treatments, and charted the course for future discoveries and breakthroughs. For example, it was long thought that adult human brains did not add new nerve cells. Recently, however, scientists have learned that throughout life new nerve cells are added in one part of the brain, the hippocampus, an area that plays a vital role in learning and memory. This process occurs at a slower pace in adults than in the young. However, research has found that reducing levels of the hormone corticosteroid in older rats returns the rate of nerve cell growth in the hippocampus almost to the same level found in young rats. This discovery provides new insights into memory loss associated with aging and into the role of stress in that process. It may also lead to therapies to prevent age-related memory loss in humans.

Stroke. A severe reduction in the blood supply to the brain, a condition known as ischemia, causes many strokes. Ischemia creates damaging conditions that can kill brain cells and produce severe disability. For some time, scientists have known that mild ischemic events increase the ability of brain cells to tolerate later more severe disruptions of blood flow, but they did not understand why. Recently, researchers have discovered a chemical signal, known as ceramide, that is part of the sequence by which brain cells develop tolerance after moderate ischemia. The detection of the chemical ceramide has offered a new treatment to decrease the injuries caused by stroke. This discovery may lead to a greater understanding of stroke and help bring about future treatments for the condition.

Alzheimer's disease. Scientists estimate that as many as four million Americans presently suffer from Alzheimer's disease. Roughly 360,000 new cases will arise each year, and this figure will increase as the general population ages.

The National Institute on Aging has the primary responsibility at the NIH for Alzheimer's research. Reflecting the complex nature of the disease, the National Institute on Aging collaborates with the National Institute of Neurological Disorders and Stroke, the National Institute of Mental Health, the National Institute of Nursing Research, private firms, volunteer groups, and nonprofit agencies. For example, researchers supported by the National Institute of Neurological Disorders and Stroke and the National Institute on Aging have tested the relationship between the severity of dementia and the loss of brain volume. Scientists supported by the National Institute of Neurological Disorders and Stroke are conducting research on potential new treatments of the disease. The National Institute of Mental Health supports studies on the causes of Alzheimer's disease, the role of depression in Alzheimer's patients, and the significance of the chronic inflammatory state that seems to exist in the brain of Alzheimer's patients.

Alzheimer’s disease causes many nerve cells to cease functioning, lose connections with other nerve cells, and die. Both genetic and nongenetic factors are at work in causing the disease. New theories suggest that among the nongenetic factors may be that oxidation and free radicals damage nerve cells. Another possibility is that inflammation in the brain may play an important role in the onset of Alzheimer's disease. New research has also demonstrated a possible connection between stroke and Alzheimer's disease. Within the last few years scientists have also uncovered important similarities between Alzheimer's disease and other neurological diseases, such as Parkinson's disease, that involve involving deposits of abnormal proteins in the brain.

While presently there is no cure for Alzheimer's disease, recent research has developed improved treatments, including drugs to control symptoms. These drugs do not stop or reverse the progression of the disease, and they seem to help only some patients for a limited time. However, researchers are studying the possible benefits of a variety of new treatments, including estrogen replacement therapy and the regular use of anti-inflammatory or anti-oxidant drugs to combat the disease. Eventually, scientists hope to develop medications that attack the fundamental Alzheimer's processes, preventing them from taking effect.

B. Injury, Pain, and Depression

Spinal cord injury. Roughly 250,000 Americans currently suffer from traumatic spinal cord injury. Until recently, little treatment has been available for them. However, new discoveries increasing the knowledge of how the spinal cord develops and what stops the growth of nerve cells in adults are charting a course toward repairing injured spinal cords. Because many injuries leave much of the spinal cord unbroken, it may be possible to restore some functions by reactivating "spinal pattern generators." The National Institute of Neurological Disorders and Stroke is advancing new projects to build upon recent discoveries about the nerve cell circuits of the spinal cord and the cellular mechanisms that promote regeneration of the spinal cord.

Pain. One of the great mysteries of medicine is understanding and treating pain. Severe and chronic pain has often been misunderstood and therefore largely untreatable. Despite recent progress in understanding the mechanisms of pain, millions of Americans still continue to suffer from pain in various forms. Pain still poses one of the most difficult challenges of medicine, because scientists know relatively little about how the brain processes the subjective experience of pain. Until recently, doctors could only rely upon what patients communicated to measure the degree of pain and to understand how the brain treats pain signals. Today, researchers are using techniques such as magnetic resonance imaging (MRI) and positron emission tomography (PET) to map what happens to specific regions of the brain when people feel pain. Their research is only the first step towards a full understanding of how to treat pain, but it has already helped to disprove some old ideas regarding pain and may spur new ideas for treatment and prevention.

Depression. Depression afflicts more than one in fifteen Americans. Prior to the 1950s, there were no real medical treatments for this debilitating illness. It was only then that the discovery of psychotropic drugs made it possible for many patients to live outside mental hospitals, forever changing the treatment of mental illness. In 1954, NIH-funded work made the initial discovery of the impact of the chemical reserpine on depression. This and later discoveries about the roles of dopamine, norepinephrine, serotonin, and other chemicals that exist in the brain eventually helped prompt the discovery of the drug fluoxetine (Prozac) to treat depression. Fluoxetine is widely prescribed, because it is effective and produces fewer side effects than traditional antidepressant drugs. Research continues, though, in the hopes of finding even better medications to treat and possibly prevent depression.

C. Cancer

Remarkable progress was made in the 20th century in our knowledge of cancer biology. We are now beginning to understand what turns a normal cell into a cancerous cell. Recently developed molecular-based technologies are providing even greater insights into the steps involved in the transformation of cells allowing for early detection and diagnosis of cancer. Advances in technology, including imaging techniques, new drugs and treatments, therapeutic interventions, and insights and discoveries into the fundamental nature and causes of cancer, have led to cures and to improved quality of life for people diagnosed with cancer.

Cancer surveillance—identifying and tracking trends in cancer cases, and monitoring the factors that influence them—is crucial to the effort to prevent and control cancer. America’s investment in cancer research is paying off: between 1990 and 1996, the incidence of cancer and death rates from cancer dropped for all cancers combined and for most of the top 10 cancer sites in the United States, reversing a decades-long trend.

The National Cancer Institute's surveillance efforts are being expanded to cover groups not fully represented in cancer registry programs, including American Indians, Alaskan natives, rural dwellers, and Hispanics of Caribbean origin. New investments in surveillance research on groups such as these will make it possible to connect information on prevention, risk factors, screening, treatments, and patterns of care with incidence, quality of life, and survival.

The research investment of the past decade has brought about a dramatic increase in the number of new therapeutic and preventive agents showing enough promise to warrant testing in clinical trials. However, our present clinical trials system is not keeping pace. Fewer than three percent of patients with cancer participate in the clinical trials that define effective new prevention and treatment approaches. The number and complexity of cancer trials needed to determine the therapeutic roles of the new generation of agents continues to grow. Many more patient-volunteers are needed to help establish the benefits of new agents and new combination treatments, and a sufficient infrastructure to support these studies is needed. A bill that would help achieve this is the Medicare Cancer Trials Coverage Act (H.R. 1388 and S. 784), introduced by Representatives Nancy Johnson (R-Connecticut) and Ben Cardin (D-Maryland) and Senators Connie Mack (R-Florida) and Jay Rockefeller (D-West Virginia).

Because advances in basic research, prevention, and treatment are incremental, it often takes years to see the cumulative effects of our efforts on populations at risk, patient survival, and improved quality of life. Moving from an insight to a tested, successful intervention in people takes time, and there will always be a lag between our investment in developing a solid knowledge base and the payoff for a person with cancer or one at risk for the disease. Yet every day, thanks to the dedicated efforts of cancer researchers and clinicians, we are growing closer to our goal of overcoming cancer. For example, if breast cancer is detected at an early stage, the survival rate is 94 percent; another example is that 80 percent of all children diagnosed with some forms of leukemia are alive and free of the disease five years after the initial diagnosis.

D. The Human Genome Project

The Human Genome Project is an international effort to map human DNA, our genetic blueprint; develop technologies for analyzing genes; examine the ethical, legal, and social implications of human genetic research; and train scientists to use the resources developed through the project to pursue studies that will improve human health.[89]

The Human Genome Project is approximately two-thirds completed. Scientists now know the exact location of 2 billion of the 3 billion chemical letters that make up human DNA. Scientists have identified more than 8,000 human genes, including those linked to breast cancer, colon cancer and Alzheimer's disease. Figuring out how the genes work promises to lead to prevention and treatments. Once the genome has been sequenced, scientists can compare genetic patterns in different people to determine where there are genetic variations that could cause diseases. NIH’s National Human Genome Research Institute believes that screening tests will eventually enable anyone to gauge his or her particular inherited health risks.

Early detection of diseases is just the beginning. Genes help determine not only whether we get sick, but also how we respond to various treatments. The hope among researchers is that drugs can be assigned to attack any mutations and possibly cure the diseases they cause and that genetic science will be used to fix health problems, not just predict them. Only a few gene-based therapies have entered clinical practice so far.[90] Even so, genetic science now informs every branch of medicine, from cancer research to infectious disease, and it is creating countless possibilities for fighting illness.

VI. CONCLUSION

Currently the federal government spends only one percent of its budget on NIH research funding (see Figure 1 above). The share of national health care spending that goes toward public and non-profit medical research has fallen over the last 20 years from 2.2 percent in 1980 to 1.6 percent today. If we expect medical and biomedical advances to continue, funding for such research must outpace inflation. Pressing health problems such as heart disease, Alzheimer's disease, and AIDS cannot be conquered without continued research.

Advances in medicine not only benefit people with illnesses; they benefit their families and coworkers. Reducing or curing illnesses enables families and other caregivers to devote their time to more pleasant activity. It saves coworkers from the losses of productivity that result from being deprived of the energy and talents of their peers.

The research done by scientists with federal funding has made, and will continue to make, important additions to our knowledge about how the human body performs and how to prevent and treat the afflictions that affect it. Federal funding develops new medical knowledge and helps see that it is applied to treat and prevent disease. Funding of medical research develops the human capital—the skilled minds and hands—that will help our economy grow in the future. Finally, the scientific research done with federal dollars helps create a society where all Americans can contribute to the full extent of their abilities.

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APPENDIX: THE NIH IN THE FEDERAL BUDGET

The medical research community has urged Congress to double the NIH's budget over the five fiscal years from 1999 to 2003. Bipartisan support exists in Congress for this goal. In 1999 the NIH's budget authority was $15.6 billion, an increase of 14.4 percent over the previous year. For 2000, the NIH's budget authority is $17.8 billion. For 2001, supporters of the NIH are requesting a 15 percent increase, which would bring the NIH's budget authority to $20.5 billion.

In contrast to the Congressional proposal for doubling the NIH's budget, the Clinton Administration proposes an increase of only 48 percent from 1999 to 2003. The Administration requested $14.7 billion for the NIH in 1999 (an increase of 2.1 percent over the previous year), $15.9 billion in 2000 (an increase of 8.2 percent over the previous year), and $18.8 billion in 2001 (an increase of 5.6 percent).[91]

The NIH budget accounts for 42 percent of the non-defense federal research and development in 2000, making the NIH the federal government's largest civilian research agency.[92] The federal government funds about 57 percent of the research and development performed by colleges and universities, about 51 percent of R&D performed by other nonprofit institutions, and about 11 percent of research and development performed by industry. Many of these federal research dollars come from the money allotted to the NIH.

Dr. Ruth Kirschstein, acting director of the NIH, addressed the concerns about increases in the NIH's budget in testimony to a subcommittee of the House Appropriations Committee on February 15, 2000. Dr. Kirschstein emphasized six priorities that the NIH follows to ensure that its budget is spent wisely. First, the NIH realizes that it has an obligation to respond to public health needs as judged by the incidence, severity, and costs of specific disorders. Second, it recognizes that opportunities exist to capitalize on previous discoveries. These opportunities must be taken advantage of so that even difficult problems will eventually be solved. Third, the NIH maintains a diverse portfolio of research projects, an approach that is necessary to take advantage of scientific opportunity as it presents itself. Fourth, the NIH has an obligation to obtain the services of first-rate scientific employees and research facilities. Fifth, the NIH seeks advice on research from many sources, including the public. Finally, the NIH makes the overall commitment to support scientific research of the highest caliber.[93]

In recent years, Congress has eliminated the practice of earmarking NIH funds (requiring specific amounts of funding to be allocated to specific kinds of research). Earmarking has been criticized because it limits opportunities for allocating resources to the most promising kinds of research. Today, rather than earmarking, lawmakers give advice to the NIH on what areas they would prefer to see researched. The NIH takes Congressional advice seriously and tries to fund research in the advised areas whenever possible.

The Federation of American Societies for Experimental Biology believes that the NIH, in consultation with Congress and the public should set biomedical research priorities.[94] What the Federation means is that instead of specifically earmarking funds, the NIH in consultation with community scientists and with the agreement of Congress should identify areas in which basic research would be beneficial. NIH has followed that approach by introducing four broad research themes and the seven areas of research emphasis for 2000.

Figure A-1: NIH Research Grants, FY 1990-1999

Fiscal year	Total grants		New and competing grants		Non-competing grants	
	Number	Amount	Number	Amount	Number	Amount
1990	27,767	$5.8 billion	5,620	$0.8 billion	16,907	$3.5 billion
1991	29,222	$6.4 billion	6,462	$0.9 billion	16,890	$3.6 billion
1992	29,268	$6.9 billion	6,768	$1.0 billion	17,265	$3.9 billion
1993	28,744	$7.1 billion	6,149	$0.8 billion	17,803	$4.3 billion
1994	29,450	$7.5 billion	6,474	$1.0 billion	17,576	$4.3 billion
1995	29,172	$7.7 billion	6,759	$1.0 billion	17,069	$4.4 billion
1996	29,953	$8.2 billion	6,653	$1.1 billion	17,854	$4.7 billion
1997	31,506	$8.8 billion	7,390	$1.2 billion	18,248	$5.0 billion
1998	33,127	$9.6 billion	7,578	$1.4 billion	19,495	$5.5 billion
1999	35,312	$11.0 billion	8,566	$2.1 billion	20,149	$5.8 billion

Source: National Institutes of Health, *http://www.nih.gov*.

Note: An accepted grant will receive funding for 12 months. It will then be reviewed to consider continued funding. Thus the need for distinguishing between new, competing, and non-competing grants.

Figure A-2: NIH Research Grants by Performing Institution, FY 1999

Institution	Number of institutions	*Research grants* Number	Total funds	Share of total grants
Nonprofit	**918**	**28,958**	**$8.5 billion**	**98.9%**
Higher education	457	23,838	$6.8 billion	78.7%
Medical schools	123	15,943	$4.7 billion	54.8%
Government	40	202	$61.0 million	0.7%
Federal	12	12	$1.9 million	< 0.1%
State and local	28	190	$59.2 million	0.7%
Other non-profit	421	4,918	$1.7 billion	19.4%
Research institutes	170	2,357	$868.4 million	10.1%
Hospitals	105	2,207	$700.1 million	8.1%
Other	146	354	$108.5 million	1.3%
For-profit	**1,068**	**97**	**$59.3 million**	**0.7%**
Research institutes	31	28	$11.0 million	0.1%
Other	1037	69	$48.3 million	0.6%
Other institutions	**103**	**195**	**$35.3 million**	**0.4%**
Total	**2,089**	**29,250**	**$8.6 billion**	**100.0%**

Source: National Institutes of Health, *http://www.nih.gov*.

Figure A-3: Top Institutions Receiving NIH Funding

Institution	*1999 NIH funding* Total funds *(in millions)*	Research grants	Training grants	Fellow-ships	R&D contracts	*Institutional rankings* 1980	1990	1999
Johns Hopkins Univ. *— Baltimore, MD*	$350.9	827	66	86	27	1st	1st	1st
Univ. of Pennsylvania *— Philadelphia, PA*	$290.3	792	67	75	11	4th	8th	2nd
Univ. of Washington *— Seattle, WA*	$278.7	651	69	54	19	11th	3rd	3rd
Univ. of California *— San Francisco, CA*	$255.8	658	3	58	9	3rd	2nd	4th
Washington Univ. *— St. Louis, MO*	$238.9	596	39	39	6	12th	7th	5th
Univ. of Michigan *— Ann Arbor, MI*	$231.0	640	58	39	13	14th	9th	6th
Yale University *— New Haven, CT*	$229.0	621	47	57	3	5th	5th	7th
Harvard Univ. *— Cambridge, MA*	$216.5	447	55	118	0	2nd	10th	8th
Univ. of Pittsburgh *— Pittsburgh, PA*	$201.4	558	22	23	13	n.a.	28th	9th
Univ. of California *— Los Angeles, CA*	$200.5	564	51	24	9	8th	6th	10th
Columbia Univ. *— New York, NY*	$200.0	506	38	35	6	7th	11th	11th
Stanford Univ. *— Stanford, CA*	$190.5	463	38	70	4	6th	4th	12th
Duke Univ. *— Durham, NC*	$172.9	461	28	41	10	15th	13th	13th
Univ. of North Carolina *— Chapel Hill, NC*	$171.3	449	45	37	9	23rd	16th	14th
Univ. of California *— San Diego, CA*	$169.6	423	40	59	5	16th	12th	15th
Massachusetts Gen. Hospital *— Boston, MA*	$158.1	469	16	32	4	32nd	18th	16th
Science Appl. Int'l. Corp. *— San Diego, CA*	$158.1	0	0	0	2	**	**	17th
Case Western Reserve Univ. *— Cleveland, OH*	$156.9	450	30	24	9	n.a.	32nd	18th
Univ. of Minnesota *— Minneapolis, MN*	$152.2	444	33	40	11	9th	15th	19th
Univ. of Alabama *— Birmingham, AL*	$151.0	399	25	8	25	22nd	23rd	20th
Baylor Coll. of Medicine *— Houston, TX*	$149.4	385	24	28	9	n.a.	n.a.	21st
Univ. of Wisconsin *— Madison, WI*	$148.3	457	30	53	6	13th	14th	22nd
Brigham & Women's Hospital *— Boston, MA*	$146.5	391	16	35	5	59th	21st	23rd
Fred Hutchinson Cancer Research Center *— Seattle, WA*	$134.7	187	2	15	6	n.a.	n.a.	24th
Univ. of Chicago *— Chicago, IL*	$125.9	292	28	26	2	n.a.	n.a.	25th

Source: National Institutes of Health, *http://silk.nih.gov/public/cbz2zoz.@www.all.inst.fy99.dsncc*
Note: ** = Research and development contract. n.a. = not available.

Figure A-4: Disease Characteristics in Order of Prevalence

Condition	U.S. prevalence	Notes
Cardiovascular disease[1]	• Affects 58 million in some form • 960,000 annual deaths	• 450,000 Americans aged over 65 require home or hospice care due to cardio-vascular disease • Congestive heart failure is largest cause of hospitalization for aging Americans
Hypertension[2]	• Affects 50 million with high blood pressure • High blood pressure is a factor in 700,000 annual deaths	• Can lead to stroke and cardiovascular problems
Cancer • **Prostate cancer**[3] • **Breast cancer** • **Lung cancer**[4]	• Prostate cancer affects 2.8 million • Breast cancer affects 175,000 • Over 550,000 people die annually due to cancer • Over 43,000 women die from breast cancer each year • More than 175,000 cancer deaths related to tobacco use annually	• About 8 million Americans alive today have a history of cancer • Over 1 million new cases of cancer will be diagnosed each year • Cancer is the second leading cause of death in the United States • The five year survival rate for cancer is over 60% • Treatments for breast, lung, and prostate cancer account for over one-half of direct medical costs
Stroke[5]	• Affects 700,000 Americans each year • 160,000 annual deaths	
Depression[6] **and brain disorders**[7]	• Depression affects 35-40 million sometime during their lifetime • Mental illness affects 5 million per year • More than 120,000 deaths annually	• 80-90% of people with serious brain disorders are unemployed • 160,000 people with severe mental illnesses are in jails and prisons • 150,000 people with severe mental illness are homeless or living in public shelters

Figure A-4: Disease Characteristics in Order of Prevalence *(cont.)*

Condition	U.S. Prevalence	Notes
Alcoholism and alcohol abuse	• Affects 15 million • 100,000 annual deaths	
Diabetes[8]	• Affects about 15 million • More than 60,000 die from diabetes every year	• Physician visits for diabetes patients topped 30 million in 1997 • Diabetes-related hospitalizations totaled almost 14 million days in 1997 • African Americans are 1.7 times more likely to have diabetes than non-Hispanic whites; 25% of all African Americans age 65-74 have diabetes
Kidney disease[9]	• Affects 20 million • 50,000 annual deaths	• About 30 million physician visits yearly are related to kidney and urologic diseases • 6 million hospitalizations yearly are the result of kidney and urologic diseases • 2.5 million surgical procedures are the result of kidney and urologic diseases
HIV/AIDS[10]	• HIV affects 650,000-900,000; 200,000 of these cases are unaware of infection • AIDS affects more than 700,000 • More than 20,000 die from AIDS annually	
Arthritis[11]	• Affects more than 40 million	• Causes nearly 40 million physicians visits and over 500,000 hospitalizations annually • Over one-half of arthritis sufferers are under age 65
Osteoporosis	• Affects more than 23 million women and 5 million men[12]	• 300,000 hip fractures occur each year due to osteoporosis; 50,000 of these individuals will die as a result
Asthma[13]	• Affects nearly 15 million (1995)	• Results in 1.5 million emergency room visits, 500,000 hospitalizations, and 5,500 deaths yearly (1995)

Figure A-4: Disease Characteristics in Order of Prevalence *(cont.)*

Condition	U.S. Prevalence	Notes
Alzheimer's disease[14]	• Affects 4 million • By the year 2050, an additional 10 million will have the disease	
Parkinson's disease [15]	• Affects 1.5 million	
Sickle cell disease[16]	• Affects 70,000	• Each year more than 6,500 sickle cell patients have episodes that require hospitalization • Potential cost savings if patients have access to the drug Droxia is $13.5 million
Spinal cord injury[17]	• Affects 10,000 each year	

Note: It is important to note that "even if consistent and comprehensive estimates of the relative burdens of specific diseases were available, decisions regarding policy and budget would have to include other factors such as the importance of scientific advances and opportunities." (NIH "Disease-Specific Estimates of Direct and Indirect Costs of Illness and NIH Support", 1997 Update.

[1] Centers for Disease Control and Prevention, *http://www.cdc.gov/nccdphp/cardiov.htm* and 1999 Task Force for Aging Research Funding, *www.agingresearch.org.*

[2] The Health Authority, *http://www.healthauthority.com* ; National Stroke Association, *www.stroke.org.*

[3] Centers for Disease Control and Prevention, *http://www.cdc.gov/nchs/fastats/prostate.htm.*

[4] American Cancer Society, *http://www.cancer.org.*

[5] The Health Authority *http://www.healthauthority.com* ; National Stroke Association *www.stroke.org,* and 1999 Task Force for Aging Research Funding, *www.agingresearch.org*.

[6] National Foundation for Depressive Illness, Inc., *http://depression.org/biochem.html.*

[7] National Alliance for the Mentally Ill, *http://www.nami.org*.

[8] American Diabetes Association, *www.diabetes.org* and the 1999 Task Force for Aging Research Funding, *www.agingresearch.org.*

[9] National Kidney Foundation, *http://www.kidney.org.*

[10] National Institute of Allergy and Infectious Diseases, *http://www.niaid.nih.gov*.

[11] 1999 Task Force for Aging Research Funding, *www.agingresearch.org.*

[12] National Institute on Aging, *http://www.nih.gov/nia/* and 1999 Task Force for Aging Research Funding, *www.agingresearch.org.*

[13] National Heart, Lung, and Blood Institute, National Institutes of Health. *http://www.nhlbi.nih.gov.*

[14] Alzheimer's Association , *http://www.alz.org/facts/rtstats.htm.*

[15] 1999 Task Force for Aging Research Funding, *www.agingresearch.org.*

[16] National Heart, Lung, and Blood Institute, *http://www.nhlbi.nih.gov* and The Sickle Cell Disease Association of America, Inc., *http://SickleCellDisease.org.*

[17] Centers for Disease Control and Prevention, National Center for Injury Prevention and Control, *http://www.cdc.gov/ncipc/dacrrdp/ dacrrdp.htm*.

GLOSSARY

Antiretroviral—A substance that stops or suppresses the activity of a retrovirus such as HIV. (A retrovirus is made up of RNA instead of DNA.)

Applied research—Work in an applied science, such as physics.

Biomedical research—Inquiry into biological, medical or physical science.

Behavioral research—Science that deals with human action and seeks to generalize about human behavior in society.

Beta-blocker—A class of drugs used to treat high blood pressure and heart disorders by reducing the strength and rate at which the heart pumps.

Biotechnology—Applied biological science.

Chromosome—A structure in the nucleus of a cell that is the bearer of genes. Normally, humans have 46 chromosomes.

Clinical research—Research involving direct observation of the patient, diagnosable by or based on clinical observation.

DNA (deoxyribonucleic acid)—Any of various acids in the nucleus of a cell. In nearly all organisms, DNA is responsible for passing genetic information.

Econometrics—The statistical and mathematical analysis of economic relationships. Used by governments to set economic policy, and by business to make decisions on prices, inventory, and production.

Enzyme—A chemical, originating in a cell, that regulates reactions in the body.

Gene— The basic unit of DNA, which is responsible for passing genetic information; each gene contains the instructions for the production of a certain protein.

Gene therapy—The insertion of genes into cells, usually to replace defective genes.

Genome—The genetic material of an organism.

Hydrolyze—To decompose a chemical compound by reaction with water.

Hypertension—Abnormally high blood pressure, especially in the arteries.

Incidence—The number of new cases of an illness in a population over a period.

Magnetic resonance imaging (MRI)—A technique that uses magnetic fields and radio waves to create cross-sectional images of the body without using radiation.

Morbidity—Being ill or having a disease.

Mortality—The death rate, measured as the number of deaths within a certain group.

Neurodegenerative—Relating to degeneration of nervous tissue.

Neurotransmitter—A chemical that transfer messages from one nerve cell to another or from a nerve cell to a muscle cell.

Patent—A writing securing to an inventor for a term of years the exclusive right to make, use, or sell an invention.

Prevalence—The percentage of a population affected with a particular disease at a given time.

Protease enzyme—Any of numerous enzymes that decompose proteins by reaction with water.

Recombinant DNA—DNA resulting from inserting into a chain a sequence of DNA not originally present in that chain.

Sudden infant death syndrome (SIDS)—Death of an apparently healthy infant of unknown cause; it occurs especially during sleep and so is also called crib death.

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Amgen, Inc. [1999c.] Provided information on Erythropoietin.

Amgen, Inc. [1999d.] "Quality of Life Benefits of Target HB/Hct." Informational material supplied to customers.

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NOTES

[1] Surveys by Research!America, a nonprofit research tracking organization, 1998, 1999.
[2] U.S. Department of Health and Human Services, Health Care Financing Administration (2000).
[3] Social Security Administration (1999).
[4] Institute of Medicine (1998), p. 23.
[5] Funding varies by the type and form of grant. For example, grants dealing with the human genome or AIDS tend to be more expensive than those dealing with nursing. See <http://silk.nih.gov/public/cbz2zoz.@www.trends99.type9099.dsncc>.
[6] Information supplied by Susan Quantius, Associate Director for Budget at the NIH. The proportion of applications for grants that the NIH funds has fallen, but the average size of grants has increased.
[7] See the National Institutes of Health Web site, <www.nih.gov>.
[8] In 1968, Dr. Marshall W. Nirenberg of the National Heart, Lung, and Blood Institute shared the Nobel Prize in Physiology or Medicine for discovering the key to deciphering the genetic code. In 1970, Dr. Julius Axelrod of the NIH shared the Nobel Prize in Physiology or Medicine for finding noradrenaline, an enzyme that terminates the action of the nerve transmitter. He also demonstrated that some antidepressant drugs act by preventing the re-uptake of noradrenaline and thus prolong its action in the brain. In 1972, Dr. Christian B. Anfinsen of the National Institute of Arthritis, Metabolism, and Digestive Diseases shared the Nobel Prize in Chemistry for his work demonstrating that the information required to fold the polypeptide chain of ribonuclease into the specific three-dimensional form of the active enzyme resides in the sequence of amino acids. In 1976, Dr. D. Carleton Gajdusek of the National Institute of Neurological Diseases and Stroke shared the Nobel Prize in Physiology or Medicine for discoveries of new mechanisms for the origin and dissemination of infectious diseases. And in 1994, Dr. Martin Rodbell of the National Institute of Environmental Sciences shared the Nobel Prize in Physiology or Medicine for discovering in that signal transmission between cells requires a cellular molecule called GTP, "G proteins." See <http://www.nih.gov/about/almanac/lectures/nobel-winners.html>.
[9] Information on these facilities can be found at the National Institutes of Health Web site, <www.nih.gov/icd>.
[10] Remarks by Anne Thomas, Associate Director for Communications of the NIH, September 23, 1998.
[11] JEC estimates based on data from Research!America, Pharmaceutical Research and Manufacturers of America, and American Association for the Advancement of Science.
[12] For summaries of the research on returns to publicly and privately funded research, see President's Council of Economic Advisors (1995) and Science Policy Research Unit (1996). A recent paper on the return to private research and development is Jones and Williams (1998).
[13] For a discussion of these three illness cost categories, see Peebles and others (1997).
[14] U.S. Department of Health and Human Services, Health Care Financing Administration (2000).
[15] Note that indirect costs may overlap with measurements of the intangible costs of illness to the extent that indirect costs capture some of people's valuations of their health.
[16] Regarding the indirect costs of illness, one study found, for example, that unpaid health care provided by families to loved ones with illnesses cost the United States about $196 billion a year in lost worker productivity (Arno and others 1999). Other estimates have looked at the economic costs created by premature deaths. The Bureau of the Census publishes figures that apply an economic value to all U.S. deaths each year, based on discounted lost earnings. According to these figures, deaths in 1997 had an economic cost of $330 billion, based on comparisons of age of death to age-specific life expectancies. (These figures are calculated for the Bureau of the Census by Dorothy Rice and Wendy Max, Institute for Health and Aging, University of California at San Francisco).
[17] National Institutes of Health (2000b). We substituted a 1994 estimate of the direct cost of cancer from the National Cancer Institute's web site for the 1990 figure in the NIH report.
[18] The NIH study contains direct and indirect cost data for 30 illnesses. However, we have excluded alcohol abuse, smoking, drug abuse, obesity, and homicide from our calculated average because the cost information may substantially overlap with other illness categories included. Note, however, that the overall average would change very little if these additional illnesses had been included.
[19] Moore and others (1997). The study found that the total direct and indirect costs of illness were $157 billion which represented 22 percent of Canadian gross domestic product.

[20] Rice and others (1988) found that the total economic costs of illness in the United States in 1980 were $455 billion, of which 46 percent were direct costs and 54 percent were indirect costs. A table presented in a February 2000 report by the National Heart, Lung, and Blood Institute, in contrast, shows that direct costs are 67 percent and indirect costs are 33 percent of U.S. economic costs of illness in 2000. Peeples and others (1997) found that indirect costs represented 52 percent of total costs.
[21] Wisconsin Association for Biomedical Research and Education (1995).
[22] Kirschner and others (1994).
[23] Lichtenberg (1996).
[24] Kirschner and others (1994).
[25] Wisconsin Association for Biomedical Research and Education (1995).
[26] Lichtenberg (1996). See also Silverstein and others (1995).
[27] Kirschner and others (1994). See also Funding First (2000).
[28] Cited in Federation of American Societies for Experimental Biology (1999)
[29] Silverstein and others (1995). See also Kirchner and others (1994).
[30] Wisconsin Association for Biomedical Research and Education (1995).
[31] Lichtenberg (1996).
[32] See for example, Murphy and Topel (1999).
[33] See for example, Cutler (1995).
[34] Pardes and others (1999).
[35] U.S. Department of Health and Human Services, Health Care Financing Administration (2000b).
[36] This idea is discussed in Murphy and Topel (1999).
[37] Lichtenberg (1996).
[38] Decline in age-adjusted death rates between 1970 and 1997, based on data from the Centers for Disease Control.
[39] Federation of American Society for Experimental Biology (1999).
[40] As referenced in Lichtenberg (1996).
[41] Decline in age-adjusted death rate between 1995 and 1998, based on data from the Centers for Disease Control. See also Pharmaceutical Research and Manufacturers of America (1998).
[42] Pharmaceutical Research and Manufacturers of America (1998).
[43] Lichtenberg (1998).
[44] Wisconsin Association for Biomedical Research and Education (1995).
[45] Murphy and Topel (1999).
[46] See also Funding First (2000).
[47] Costa (2000) looked at the dramatic declines in disability in older men from the early 20th century to the early 1990s, and found that 24 to 41 percent of the decline was due to medical innovations.
[48] Murphy and Topel (1999), p. 3.
[49] Murphy and Topel (1999), p. 25.
[50] Nordhaus (1999).
[51] Cutler and Kadiyala (1999).
[52] March Research Task Force (1998).
[53] American Society for Microbiology (1997).
[54] American Society for Microbiology (1997).
[55] Cutler and Kadiyala (1999).
[56] This information is from the NIH fact sheet “What Impact has the NIH Had on the Health of the Nation,” which describes areas where it has “played a major role” in successes against disease.
[57] Kirchstein (2000).
[58] U.S. Department of Health and Human Services (1993).
[59] This act, commonly called the Results Act, requires Federal managers to plan and measure performance in new ways. See <http://www.opm.gov/gpra>.
[60] U.S. Department of Health and Human Services (2000).
[61] Kornberg (1997).
[62] Information on the ties of various drugs to the NIH was supplied by the NIH itself.

[63] Tao and others (2000).
[64] Based on hospital costs and the cost of care for babies infected; see Randolph and others (1999).
[65] HIV is characterized by a gradual deterioration of immune function. HIV causes AIDS by directly killing CD4+T cells or interfering with their normal function and weakening the immune system. HIV is a retrovirus, having genes composed of ribonucleic acid (RNA) molecules. Once inside the cell, HIV uses an enzyme called reverse transcriptase to convert RNA to DNA and incorporate into the host's genes, causing AIDS.
[66] National Institute of Allergy and Infectious Diseases Web site < http://www.niaid.nih.gov>.
[67] AZT was discovered in 1964 and originally intended as a drug to be used in the treatment of cancer.
[68] National Institute of Allergy and Infectious Diseases Web site, < http://www.niaid.nih.gov>.
[69] In the United States, 30 to 40 percent of patients with insulin dependent diabetes mellitus and 10 to 40 percent of patients with non-insulin dependent diabetes mellitus will develop nephropathy and eventually require dialysis or transplant.
[70] The figure of $7 billion a year is the total cost for treating all patients with kidney failure, not just those with diabetes and kidney failure.
[71] Rodby and others (1996).
[72] Rodby and others (1996).
[73] Information provided by the NIH.
[74] U.S. Department of Health and Human Services (1993).
[75] Information provided by Bristol-Myers Squibb.
[76] Information provided by Bristol-Myers Squibb.
[77] Eschbach and others (1989).
[78] Amgen, Inc. (1999a).
[79] Information provided by the NIH.
[80] Wilde and Benfield (1998).
[81] 1993 cost figures.
[82] Noe and others (1999).
[83] Maxwell and Eckhardt (1990).
[84] Cockburn and Henderson (1997), pp. 5-6.
[85] Cockburn and Henderson (1997), pp. 10-11.
[86] MdBIO (1998), p. 32.
[87] See Zucker and Darby (1997), pp. 62-3.
[88] Davey (2000).
[89] National Human Genome Research Institute Web site, <http://www.nhgri.nih.gov>.
[90] A recent success is reported in Kolata (2000).
[91] Testimony of acting NIH director Dr. Ruth Kirschstein to the House of Representatives Committee on Appropriations, Subcommittee on Labor, Health and Human Services, February 15, 2000.
[92] Percentage calculated from *Budget of the United States Government, Fiscal Year 2001*.
[93] Testimony of acting NIH director Dr. Ruth Kirschstein to the House of Representatives Committee on Appropriations, Subcommittee on Labor, Health and Human Services, February 15, 2000.
[94] Testimony of John Suttie, former president of the Federation of American Societies for Experimental Biology, to the Senate Committee on Health, Education, Labor, and Pensions, Subcommittee on Public Health, May 1, 1997.