Summary of Research Activities by Disease Categories
Chronic Diseases and Organ Systems

Two-year-old Hannah’s great-grandmother, who was born in 1900, died of tuberculosis in her thirties. Polio crippled her grandfather, and other family members died at young ages of influenza and typhoid fever. Dramatic improvements in public health and medical practice have made it considerably less likely that these and many other infectious diseases will pose the same threat to Hannah that they did to her ancestors. However, she and her family will almost certainly be affected by one or more chronic diseases and conditions—for example, type 2 diabetes, and obesity—whose incidence has risen dramatically in the United States as the burden of infectious disease has diminished. Even more worrisome is that although we think of many chronic diseases as more often affecting adults, such conditions are increasingly appearing in the young. For example, some 16 percent of American children between the ages of six and 19 are overweight—a number unprecedented in history—placing them at greatly increased risk of type 2 diabetes, depression, and, as they grow to adulthood, heart disease and a host of other life-threatening conditions. In fact, former Surgeon General Richard Carmona has said that today’s obese children could be the first generation of Americans with a life expectancy less than that of their parents, to say nothing of the effects of obesity-related conditions on their quality of life. As the burden of chronic disease in children and adults continues to grow in the United States and around the world, biomedical research to understand, predict, prevent, and treat chronic disease is critical.

Introduction

A chronic disease is one that lasts 3 months or longer. In general, chronic diseases cannot currently be prevented by vaccine or cured by medication, nor do they resolve on their own. Not all chronic diseases are fatal, and not all fatal conditions are chronic. Nonetheless, 7 of every 10 Americans who die each year—more than 1.7 million people—succumb to a chronic disease. Health-damaging behaviors, such as tobacco use, lack of physical activity, poor eating habits, and excessive alcohol use contribute to many chronic diseases, whereas others may represent the long-term effect of early exposure to toxins and/or other environmental factors, especially in individuals with a higher genetic risk of disease. A shared aspect of many chronic diseases is chronic pain and other disease-associated disability that interferes with quality of life.

Many of the most burdensome chronic diseases develop over time and become more prevalent with age; less commonly, chronic disease may manifest from birth as a result of one or more faulty genes. Chronic diseases can be common in the U.S. population (e.g., heart disease, the leading cause of death), relatively rare (e.g., cystic fibrosis, which affects approximately 30,000 Americans), or represent a growing medical problem (e.g., type 2 diabetes and obesity).

Most chronic diseases and conditions affect one or more organs. Thus, research to combat chronic illness involves significant trans-NIH collaboration in addition to the mission-specific work of each IC. NIH
supports basic research on both normal and disease states of organ systems to understand the initiation and progression of chronic diseases, as well as translational and clinical research on new biomedical and behavioral strategies to prevent, preempt, diagnose, treat, and cure these diseases. The ultimate goal is to reduce or eliminate morbidity and mortality while improving the quality of life for those living with these often debilitating conditions.

This section focuses primarily on a number of major chronic diseases within NIH’s purview. Additional major chronic diseases are discussed in this chapter in the sections “Cancer” (cancers of all organs and tissues, including blood), “Neuroscience and Disorders of the Nervous System” (e.g., Parkinson’s disease, Alzheimer’s disease), “Autoimmune Diseases” (e.g., lupus, multiple sclerosis), and “Infectious Diseases and Biodefense” (e.g., HIV/AIDS). Because some people with certain chronic diseases require transplantation to replace a diseased organ or tissue, organ transplantation research is highlighted in this section. Research on complementary and alternative medicine (CAM) approaches to combating chronic disease also is discussed. Finally, NIH supports research to reduce the pain associated with long-term diseases and to find innovative and effective forms of palliative care to relieve disease symptoms. Some of these efforts are highlighted in this section; more information on NIH pain research can also be found at the NIH Pain Consortium Web site.

**Burden of Illness and Related Health Statistics**

The prevalence and burden of chronic diseases are substantial. In fact, the burden of chronic diseases is rapidly increasing worldwide. In 2005, chronic diseases contributed approximately 60 percent of the 58 million total reported deaths in the world and almost three-quarters of the burden of disease (measured in disability-adjusted life-years) in those age 30 or older. By 2015, deaths from chronic disease will be the most common cause of death even in the poorest countries. Considering the totality of chronic diseases in the United States, more than 7 percent of adults age 45 to 54 have three or more chronic conditions and 36 percent of adults age 75 and older have three or more chronic conditions. Chronic disease disables or limits activity for almost 12 percent of all adults and more than 34 percent of adults age 65 and older. Moreover, annual mortality from chronic diseases in the United States is more than 1.7 million. For details on the depth and breadth of this burden, see the table of data, presented by disease and condition, at the end of this section.
ABOUT VARIOUS CHRONIC DISEASES AND CONDITIONS

Links to detailed information on many specific chronic health conditions can be found at “http://health.nih.gov.” Following are examples of chronic diseases and conditions addressed by NIH-funded research, with links to major associated research programs and NIH research fact sheets.

**Cardiovascular Diseases:** Heart disease is the leading cause of death in the United States. Coronary heart disease, the most common type of heart disease, occurs when the arteries that supply blood to the heart muscle become hardened and narrow. Coronary heart disease can cause angina (chest pain) or a heart attack and, over time, contribute to serious disability or death. Other chronic, serious cardiovascular conditions include hypertension, heart failure, atrial fibrillation, and peripheral arterial disease. Rare cardiovascular disorders include Marfan syndrome, a connective tissue disorder that affects growth and development, including the heart and blood vessels; long QT syndrome, a disorder of the heart’s electrical activity that may cause a sudden, uncontrollable, and dangerous heart rhythm; and congenital heart defects.

**Lung Diseases:** Chronic obstructive pulmonary disease, the fourth leading cause of death in the United States, causes airflow obstruction in the lungs that makes breathing difficult. Asthma, the most common chronic disease of childhood, is characterized by inflamed or swollen airways. Asthma can be controlled so that individuals have fewer and less frequent symptoms or can be more active. Rare lung diseases include cystic fibrosis, an inherited disease that affects multiple organs, and idiopathic pulmonary fibrosis, in which lung tissue becomes thick and stiff, resulting in loss of function.

**Diabetes Mellitus:** Diabetes is characterized by abnormally high levels of glucose (sugar) in the blood. It can be caused by either autoimmune destruction of cells in the pancreas (type 1) or the inability of tissues such as the muscles and liver to properly use insulin (type 2). Diabetes can result in complications such as heart disease, stroke, hypertension, and nerve damage. It is also the leading cause of kidney failure and nontraumatic lower limb amputation in the United States and of new cases of blindness among working-age Americans.

**Obesity:** Obesity, which has risen to epidemic levels in the United States, is a chronic, relapsing health problem caused by an interaction of genes, environment, and behavior. A common measure of overweight and obesity in adults is body mass index (BMI) a calculation based on height and weight. For most people, BMI correlates with their amount of body fat, and it is used as an indicator of weight-related health risks. An adult with a BMI between 25 and 29.9 is considered overweight, whereas an adult with a BMI of 30 or higher is considered obese. BMI numbers are interpreted differently for children; however, as with adults, rates of overweight and obesity have risen dramatically for children in recent years. Obesity increases the risk of other chronic conditions, including type 2 diabetes, heart disease, certain cancers, osteoarthritis, liver and gallbladder disease, urinary incontinence, sleep apnea, and depression.

**Kidney Diseases:** Chronic kidney disease is the progressive, permanent loss of kidney function that can result from physical injury or from a disease that damages the kidney, such as diabetes,
high blood pressure, or polycystic kidney disease. Patients with advanced chronic kidney disease may progress to irreversible kidney failure and require immediate, life-saving dialysis or a kidney transplant. Chronic kidney disease is a growing problem in the United States; between 1990 and 2000, the number of people with kidney failure requiring dialysis or transplantation doubled.

**Digestive and Urologic Diseases:** Diseases of the digestive system involve many organs (e.g., intestine, stomach, liver, gallbladder, and pancreas) and include disorders such as irritable bowel syndrome, ulcerative colitis, Crohn's disease, celiac disease, peptic ulcer disease, gallstones, gastroesophageal reflux disease, and chronic pancreatitis. Illnesses of the genitourinary tract are similarly diverse and include chronic prostatitis, benign prostatic hyperplasia, interstitial cystitis and painful bladder syndrome, urinary incontinence, and urinary tract infections.

**Liver Diseases:** Chronic forms of liver disease include chronic viral hepatitis (B and C), alcoholic and nonalcoholic fatty liver disease, genetic diseases such as hemochromatosis, and autoimmune diseases such as primary sclerosing cholangitis. Significant liver injury can sometimes result from adverse reactions to medical drugs and other compounds. Although many organ systems may be damaged by chronic alcohol use, alcoholic liver disease is the leading cause of death from excessive and long-term alcohol consumption.

**Blood Diseases:** Chronic anemias result from a deficiency of red blood cells or an abnormality in hemoglobin production, as is the case with sickle cell disease and Cooley's anemia. Patients can experience pain, fatigue, and other, serious health problems. Chronic inherited bleeding disorders such as hemophilia and von Willebrand disease leave patients at risk for uncontrollable bleeding. Conversely, clotting disorders such as deep vein thrombosis can lead to the formation of life-threatening blood clots.

**Musculoskeletal Disease:** Osteoarthritis, the most common form of arthritis, is a degenerative disease caused by the breakdown of cartilage, leading to pain, swelling, and stiffness in joints. Osteoporosis, another musculoskeletal disease that causes significant disability, occurs when bones become thin, weak, and fragile. Other chronic bone diseases include osteogenesis imperfecta, a genetic disease that causes bones to become brittle and break for no known reason, and Paget's disease of bone, in which bones grow larger and weaker than normal.

**Skin Disorders:** Skin, the largest organ of the body, separates the internal organs from the outside environment, protects against bacteria and viruses, regulates body temperature, and provides sensory information about surroundings. The most common type of eczema—inflammation of the skin—is atopic dermatitis, which is characterized by dry, itchy skin. Chronic wounds on the skin or impaired wound healing are common in elderly, bed-ridden, and diabetic populations.

**Eye Diseases** and **Deafness:** Diseases of the eyes and ears can lead to chronic impairment or loss of vision and hearing. Middle ear infections (otitis media) can cause temporary hearing loss in children that can become permanent. Age-related macular degeneration (loss of cells in the retina) or hearing loss can reduce independence and quality of life in the elderly. Uveitis (inflammation of the eye) and glaucoma (damage to the optic nerve) are significant causes of
new blindness in adults.

**Dental and Craniofacial Disorders:** Periodontal disease is a disorder of the gingiva and tissues around the teeth. It varies in severity but can lead to bleeding, pain, infection, tooth mobility, and tooth loss. Periodontal disease can affect other organs and has been linked to cardiovascular disease, diabetes, and pulmonary disease. Temporomandibular joint and muscle disorders, commonly called TMJD, are a group of conditions that cause pain and dysfunction in the jaw joint and the muscles that control jaw movement. The primary symptom of these disorders is pain, which can become permanent and debilitating.

**Mental Illness** and **Addiction:** Mental disorders are the leading cause of disability in the United States and Canada. Mental illness can also coexist with a number of other chronic diseases. For example, unipolar depressive disorder, a major contributor to disability worldwide, can be triggered by chronic diseases such as cancer or stroke in those who are prone to the disorder. Conversely, depression is associated with an increased risk for other diseases, such as coronary heart disease. Mental disorders often co-occur with alcohol dependence and other substance abuse, making treatment of either disorder more difficult. Addictions to alcohol and other drugs of abuse also are chronic diseases that have both physiological and behavioral components.

**NIH Funding for Chronic Diseases and Organ Systems Research**
Currently, NIH does not collect the data necessary to provide an aggregate figure for expenditures on chronic diseases and organ systems research. The table at the end of this chapter provides funding estimates for many of the areas of research associated with chronic diseases and organ systems (see “Estimates of Funding for Various Diseases, Conditions, and Research Areas”). Because of overlap among the areas of research listed in the table, and because research on chronic disease and organ systems may account for only a portion of the funding for a given area, the figures in that table cannot be used to provide an aggregate number.

**Summary of NIH Activities**
To alleviate the public health burden of chronic diseases, NIH supports research on the development and progression, detection and diagnosis, prevention, and treatment and management of these diseases. Because of the impact such diseases have on public health and the national economy, NIH directs significant resources toward the study of common chronic diseases, such as asthma, heart disease, diabetes, and many others. However, NIH also support research on many less common chronic conditions. This research has the potential to improve the health and quality of life of thousands of Americans who suffer with these “rare” diseases but also can yield fundamental information on normal physiology as well as the pathophysiology of other, more common diseases. For example, long QT syndrome, which results from genetic mutations that lead to disruption of the normal electrical rhythms of the heart, affects an estimated 1 in 5,000 individuals and results in 3,000 deaths per year in the United States. However, studies of long QT syndrome also have shed light on the causes and treatments of more common, nongenetic cardiac arrhythmias that contribute to 300,000 sudden deaths each year.

This section highlights some key examples of challenges, progress, and emerging opportunities in NIH-
supported research on chronic diseases and organ systems. Through its multifaceted research efforts, NIH is providing a solid foundation for improved patient health and well-being.

**Understanding Fundamental Mechanisms of Organ Health and Disease**

Basic research supported by NIH provides the foundation for understanding and addressing chronic diseases. Understanding fundamental biological mechanisms at the molecular, cellular, tissue, and organ levels provides the basis for formulating new theories of disease causation, identification of novel treatment targets, and development of innovative strategies for disease prevention, diagnosis, or treatment. For example, NIH has made advances in understanding the mechanisms of chronic periodontitis, a disease that leads to tooth loss and affects 80 percent of the U.S. adult population. NIH-supported scientists have discovered that patients with chronic periodontitis have elevated levels of SHIP, a protein that impairs their ability to mount a robust immune attack on bacteria associated with the disease. In another study, NIH-supported scientists identified two pathways associated with chronic periodontitis in diabetic patients who experience increased incidence and severity of this disease. Although studied in different contexts, each of these advances paves the way for potential new targets for preventing or treating this highly prevalent disease. In another effort to increase understanding of the mechanisms of a chronic disease, NIH has initiated a Specialized Center of Clinical Research focused on understanding the key structural and regulatory processes mediating mucus clearance and their dysfunction in cystic fibrosis and COPD. The concepts emerging from the center are expected to stimulate development of new therapies to enable treatment early in the course of disease.

Some diseases, such as drug and alcohol addiction, affect nearly every organ system. NIH supports research to uncover fundamental mechanisms of alcohol-induced tissue injury that are common to many organs and tissues throughout the body, including the brain and liver. Program initiatives to elucidate the underlying mechanisms of alcohol-induced tissue injury will lead to the identification of biomarkers for early detection of disease and new strategies for treatment. Other diseases, such as osteoporosis, have a more limited but still significant impact on the body by affecting key tissues or organs. Because bone loss occurs without symptoms, people may not know that they have osteoporosis until a sudden strain, bump, or fall causes a disabling fracture. NIH supports a number of research projects aimed at elucidating the underlying mechanisms of osteoporosis and other bone diseases. Still other chronic diseases, such as diabetes, affect multiple organs and body systems but might be effectively treated or even cured by replacing a single type of tissue. For example, death of the insulin-producing beta cells of the pancreas results in type 1 diabetes, whereas type 2 diabetes arises when beta cells are present but not working properly. The NIH-supported Beta Cell Biology Consortium is studying how beta cells are made during development, maintained in sufficient numbers in healthy individuals, and function to release insulin in precise response to the body's needs. This research will provide the foundation for strategies to replace beta cells in patients with type 1 diabetes and to repair defective beta cells in those with type 2 diabetes.

A related line of inquiry is the study of processes that may either contribute to or signify the presence of chronic disease. For example, inflammation is a normal and necessary reaction of the body to infections, chemical irritants, and other harmful substances or injury. However, unresolved or chronic inflammation underlies or contributes to many chronic diseases. Researchers are working to elucidate the role of inflammation in a number of chronic diseases; for example, using a mouse model of glaucoma, researchers have discovered that a key inflammation marker, TNF-a, might be the link between elevated eye pressure and damage to the optic nerve. Another team found that resolvin E1, a form of omega-3 fatty acid, can alter the course of inflammation associated with periodontitis. In addition, researchers
are building on advances in the fundamental biology of inflammation to investigate age-related inflammatory processes in the elderly, such as vascular inflammation and neurotoxicity in the brain and inflammatory responses to sleep loss.

A critical dimension of basic research on chronic diseases and organ systems is the development of innovative technologies, research tools, and materials that are revolutionizing our understanding of the human body and laying the groundwork for cutting-edge therapies. Heart and vascular diseases represent only one example of many chronic diseases that benefit from technology research. Use of new, noninvasive imaging techniques in the Jackson Heart Study, a longitudinal study of heart and cardiovascular disease in African Americans in Mississippi, is expected to provide important new insights into the origins of heart disease in this population. Likewise, advances from disciplines such as materials science, tissue engineering, bioengineering, and computational sciences are providing a foundation for the development of replacements for damaged or diseased small blood vessels, from which thousands of patients with vascular disease could benefit each year.

**Detecting and Diagnosing Chronic Disease**

Early detection and diagnosis of a chronic disease or of damage to an organ allows patients to seek appropriate care and, in some cases, improve their outcomes or prevent progression of the disease. NIH fosters research on disease detection and diagnosis through the identification of biomarkers that predict disease or its progression, as well as the development of technologies or resources to promote early detection. For example, the NIH-supported Drug-Induced Liver Injury Network (DILIN) performs research on liver toxicity caused by prescription drugs or CAM. Among many research projects, DILIN researchers are developing better diagnostic tools and studying the mechanisms of liver injury. Related clinical research on acute liver failure from drug-induced liver injury conducted by the Acute Liver Failure Study Group has identified a potential biomarker for liver injury caused by excessive amounts of the over-the-counter pain reliever acetaminophen, which could be used clinically to aid diagnosis. In another example, the Alcohol Biosensors Program is engineering devices for the continuous measurement of alcohol concentrations that will provide new tools for clinical and basic research on alcohol use disorders.

In addition to advanced technology, the dissemination of knowledge to health care providers is one of the most important tools for disease detection and diagnosis. NIH has updated the booklet *Helping Patients Who Drink Too Much: A Clinician’s Guide* to educate primary care and mental health clinicians on evidence-based methods to screen, diagnose, and manage patients who may have alcohol use disorders. In addition to traditional printed handouts and fact sheets, NIH also offers information for doctors and other health professionals in electronic formats. Two CD-ROMs, Bone Health Information for You and Your Patients and Lupus and Other Related Information for You and Your Patients, provide print-friendly PDF files of health education brochures and professional educational resources, as well as Web links to current clinical trials and other resources from Federal agencies and nonprofit organizations. Additional efforts to convey information about chronic disease detection and diagnosis to the medical community are described in the section “Health Communication and Information Campaigns and Clearinghouses” in Chapter 3.
Identifying Risk and Preventing Chronic Disease

Many chronic diseases have genetic or hereditary components that increase the risk of disease in certain individuals or population groups. Chronic diseases also may have known, modifiable risks factors such as diet, smoking, chronic stress, exposure to environmental toxins, or a variety of other factors. Often, disease results from complex and poorly understood interactions among multiple genetic, environmental, and behavioral risk factors. NIH supports research to identify all types of risk factors for chronic diseases and to develop new strategies to modify risk to prevent disease.

The completion of the Human Genome Project has opened new avenues of research into the genetic causes of chronic diseases. Diseases and conditions for which NIH-supported investigators have recently identified susceptibility genes include:

- Age-related macular degeneration, a common cause of irreversible vision loss (Age-Related Eye Disease Study)
- Inflammatory bowel disease (Inflammatory Bowel Disease Genetics Consortium)
- Alcoholism and related disorders (Collaborative Study on the Genetics of Alcoholism)
- Diabetic Kidney Disease (Genetics of Kidneys in Diabetes Study)

The datasets collected through many NIH-supported genetics studies are available, with appropriate mechanisms in place to safeguard subjects’ privacy, to qualified researchers worldwide.

Ongoing initiatives such as the ENDGAME (Enhancing Development of Genome-Wide Association Methods) consortium are developing new approaches to understanding the role of genetic variation in normal physiology and disease, whereas two major ongoing studies (the Candidate Gene Association Resource and the Framingham SHARE Program) are focusing on the genetics of cardiovascular disease. In addition, a public-private partnership led by NIH—the Genetic Association Information Network (GAIN)—is exploiting the completion of a detailed map of human genetic variation to search for genes involved with specific diseases and to develop tools to understand how environmental factors interact with genetic susceptibilities. (For more on GAIN, see the section “Genomics” in Chapter 3.)

Genetic susceptibility is rarely the only risk factor for developing a chronic disease. NIH also supports research to identify other, nongenetic risk factors that, either alone or in conjunction with genetic factors, influence the development or progression of chronic diseases. Identifying risk factors for a specific disease from the myriad behaviors and environments of individuals requires studying large numbers of people for extended periods of time. Two research studies of osteoporosis and other age-related chronic diseases—the Study of Osteoporotic Fractures and Mr. OS—have uncovered specific risk factors, such as bone mineral density of the hip, that predict the risk of fractures in the elderly. The Osteoarthritis Initiative is tracking 4,800 individuals who are at high risk for knee osteoarthritis to identify biological markers that predict disease progression. NIH-supported researchers also are investigating the complex biological and behavioral factors underlying childhood and maternal obesity and testing behavioral interventions in schools, homes, and the community in an effort to stem the rising obesity epidemic.

Many population groups, whether stratified by race, ethnicity, sex, age, or other characteristics, seem to be particularly vulnerable to specific chronic diseases. NIH research programs that are exploring genetic and nongenetic disease risk factors in specific populations include:

- Cardiovascular disease among African Americans (Jackson Heart Study)
- Heart disease, COPD, kidney disease, and asthma in Latin Americans (Hispanic Community Health Study)
• Obesity and diabetes in the Pima Indians of Arizona (Gila River Indian Community Longitudinal Study)
• Alcohol consumption, drug use, and related disorders in various racial and ethnic groups (National Epidemiologic Survey on Alcohol and Related Conditions)
• Interdisciplinary centers on the influence of sex and gender as it relates to diseases and conditions such as chronic pain, irritable bowel syndrome, and urologic health (Specialized Centers of Research on Sex and Gender Factors Affecting Women's Health)
• Type 1 diabetes in children (The Environmental Determinants of Diabetes in the Young)

Knowing the factors that increase or decrease the risk of disease can help researchers design innovative strategies to prevent disease in susceptible individuals. Interventions are being developed and tested to prevent trauma-related mental health disorders, such as posttraumatic stress disorder, in persons engaged in high-risk occupations such as the military or emergency response. The Diabetes Prevention Program Outcomes Study currently is assessing long-term outcomes in its subjects; the study previously had demonstrated that lifestyle change or treatment with the drug metformin significantly delayed the onset of type 2 diabetes in at-risk individuals. Lifestyle changes (modifications in diet and physical activity) were nearly twice as effective as drug treatment in reducing the risk of developing type 2 diabetes in that study. Furthermore, the physical activity increases in the lifestyle modification group were sustained for 4 years, indicating that modest changes in behavior can be accomplished and maintained for long periods. A related clinical trial, Look AHEAD (Action for Health in Diabetes), is testing whether an intensive lifestyle intervention for weight loss can reduce the incidence of cardiovascular events in 5,100 overweight or obese subjects with type 2 diabetes. Testing strategies for prevention and early treatment of type 1 diabetes is the focus of the TrialNet clinical research network. The network recently began a new clinical study of oral insulin to prevent or delay type 1 diabetes in at-risk individuals.

Prevention of chronic diseases in children is a particularly important focus of NIH research. The onset of a chronic disease in childhood often is associated with serious comorbidities (disorders or diseases in addition to the primary disease); therefore, many of these diseases, if left unchecked, have negative implications for the health of the future adult population. HEALTHY is a multicenter clinical trial testing behavioral interventions aimed at decreasing the risk of obesity and type 2 diabetes in middle school children. Likewise, the goal of the national public education outreach program Ways to Enhance Children's Activity & Nutrition (We Can!) is to reduce childhood obesity by helping children age 8-13 achieve and maintain a healthy weight. Asthma, another serious disease of childhood, is strongly related to environmental exposures such as indoor allergens. Researchers in North Carolina are conducting a dust mite reduction study in the homes of study subjects between ages 5 and 15 to determine whether this strategy can reduce or prevent asthma and other adverse outcomes related to dust mite exposure. The Underage Drinking Research Initiative supports multiple efforts to understand and prevent alcohol use by children and adolescents and its progression to abuse and dependence, and the Rapid Response Program supports the implementation and evaluation of programs to reduce underage alcohol use on college campuses.

NIH also sponsors awareness campaigns and other educational efforts to disseminate the results of its prevention research to the general public (see the section “Health Communications and Information Campaigns and Clearinghouses” in Chapter 3). One such campaign, The Heart Truth, takes a multifaceted approach to educate women on the risk factors for heart disease, the leading cause of death in American women.
Treating Chronic Disease and Comorbidities

Despite the remarkable advances of modern medicine, chronic diseases, by definition, require long-term medical or behavioral intervention or a combination of multiple treatment modalities. For some diseases, no effective therapies or cures are currently available, and the diseases can only be managed to control symptoms. Daily management of chronic diseases to prevent or slow the progression or development of comorbidities often imposes a significant burden on patients and their families. For example, type 1 and type 2 diabetes can be managed by injections of insulin or by taking insulin-sensitizing drugs; however, optimal control of diabetes to reduce the risk of complications also requires careful and continuous monitoring of blood glucose levels, diet, and physical activity throughout the day. A major focus of NIH research is the development and testing of new therapies for chronic disease that will cure disease, ease the process of disease management, treat patients who are not helped by current therapies, or otherwise reduce the burden of chronic illness. (For a general discussion of treatment and other clinical research, see the section “Clinical and Translational Research” in Chapter 3.) To facilitate clinical trials for many diseases, NIH supports multiple networks of investigators at medical centers across the country who can conduct studies more efficiently by working together. In addition, NIH is investing in the development of a Patient-Reported Outcomes Measurement Information System that will devise standardized measurements of symptoms that affect quality of life. Validated measures of patient-reported symptoms such as pain, fatigue, emotional distress, and others will revolutionize clinical research across a spectrum of chronic diseases and conditions.

The NIH clinical research portfolio comprises numerous trials to evaluate the safety and efficacy of therapies for many chronic diseases. The examples described here illustrate the diversity of diseases and potential therapies being studied with NIH support. Information about these and other NIH-supported clinical trials is available at [http://clinicaltrials.gov](http://clinicaltrials.gov).

- **Diabetes:** The long-running Diabetes Control and Complications Trial and its follow up, the [Epidemiology of Diabetes Interventions and Complications](https://www Диабет 1 и 2 типа может быть управляется с помощью инъекций инсулина или инсулиночувствительных препаратов; однако, достижение оптимального контроля диабета для снижения риска осложнений также требует постоянного и тщательного контроля уровней сахара в крови, диеты, и физической активности в течение дня. Основной акцент NIH заключается в развитии и тестировании новых терапий для хронических заболеваний, которые смогут вылечить болезнь, упростить процесс ее управления, лечить пациентов, которые не реагируют на существующие терапии, или в противном случае снизить бремя хронического недуга. (Для общего обсуждения лечения и других клинических исследований, смотрите раздел “Клиническая и трансляционная разработка” в главе 3.) Чтобы упростить клинические исследования для многих заболеваний, NIH поддерживает множество сетей исследователей в медицинских центрах по всей стране, которые могут проводить исследования более эффективно, работая вместе. В дополнение, NIH инвестирует в развитие Пациент-Отчетных Мероприятий Информационной Системы, которая будет разрабатывать стандартизированные измерения симптомов, влияющих на качество жизни. Подтвержденные измерения симптомов, отчитываемых пациентами, таких как боль, усталость, эмоциональное напряжение, и другие, позволят революционизировать клиническое исследование по спектру хронических заболеваний и состояний.

Портфель исследований NIH включает в себя множество испытаний, которые оценивают безопасность и эффективность терапии для многих хронических заболеваний. Приведенные здесь примеры илюстрируют разнообразие заболеваний и потенциальных терапий, которые могут быть изучены с использованием поддержки NIH. Информация о этих и других поддерживаемых NIH клинических испытаниях доступна на [http://clinicaltrials.gov](http://clinicaltrials.gov).

- **Diabetes:** Долговременное исследование Диабета 1 и 2 типа и его продолжение, [Интервенции и осложнения диабета Эпидемиология](https://www.Diabetes Control and Complications Trial), демонстрируют, что интенсивная терапия инсулином, несмотря на отсутствие лекарств для лечения диабета, может значительно сократить риск осложнений глаз, нервов, почек и сердца.

- **Chronic Obstructive Pulmonary Disease (COPD):** Исследование [Долгосрочного лечения гипоксемии](https://www.Long-Term Oxygen Treatment Trial) оценивает роль терапии кислородом в домашних условиях для пациентов с COPD и умеренной гипоксемией (низким уровнем кислорода в крови).

- **Idiopathic Pulmonary Fibrosis:** Клиническая исследовательская сеть была создана для лечения пациентов с новым диагнозом идиопатической псишемической фиброза, используя комбинации препаратов, которые могли бы атаковать процесс фиброза на нескольких уровнях и тем самым стабилизировать или улучшить болезнь.

- **Nonalcoholic Steatohepatitis (NASH):** Исследование [NASH Clinical Research Network](https://www.NASH Clinical Research Network) исследует, является ли витамин E или препарат пиоглитазон эффектным лечением для ненаркотических взрослых с NASH, болезнь печени, связанная с ожирением и диабетом.

- **Hepatitis C:** Исследование [Hepatitis C Антивирусный долгосрочный против цирроза (HALT-C)](https://www.HALT-C) изучает, может ли долговременное антивирусное лечение предотвратить прогрессию болезни печени у пациентов, у которых есть инфекция с гепатитом C и которые не были помогут коротким терапевтическим курсом.

- **Polycystic Kidney Disease (PKD):** Исследование [HALT-PKD] оценивает использование контроля давления крови в комбинации с медикаментами в качестве средства для замедления прогрессии PKD в пациентах с ранней или более продвинутой формой заболевания.

- **Age-Related Macular Degeneration (AMD):** В 2005 году NIH-сponsored исследование показало, что определенные витамины и минералы могут замедлить прогрессию AMD, одного из главных причин слепоты у пожилых; вторая часть [Age-Related Eye Disease Study](https://www.Age-Related Eye Disease Study), продолжает этот результат, используя для тестирования дополнительных препаратов, которые могут замедлить прогрессию AMD.
• **Uveitis**: Localized steroid treatment is being testing in the Multicenter Uveitis Steroid Treatment (MUST) trial as a therapy for this major cause of blindness. If successful, this trial would improve on current treatments for uveitis that expose the entire body to corticosteroids and immune suppression drugs.

• **Ulcerative Colitis**: Many patients with ulcerative colitis do not respond to currently available treatments. A clinical trial is under way to determine whether a drug used to treat type 2 diabetes (rosiglitazone) can also control the symptoms of ulcerative colitis.

• **Drug Abuse and Addiction**: NIDA’s National Drug Abuse Clinical Trials Network is a multisite research project that tests the effectiveness of new and improved behavioral, pharmacological, and integrated treatment interventions in real-life community settings with diverse populations. Children do not always respond to treatments in the same way as adults. For this reason, NIH is committed to conducting clinical intervention trials to identify therapies that are safe and effective for use in children with chronic diseases. For example, the NASH Network (see above) is testing the use of the drug metformin or vitamin E as a treatment for fatty liver disease in children. Type 2 diabetes—a disease that was previously seen primarily in adults—is becoming more prevalent in children, and the safety of long-term use of adult diabetes drugs in children is not known. The Treatment Options for Type 2 Diabetes in Youth (TODAY) study is evaluating three strategies for treating children and adolescents with type 2 diabetes. NIH supports a multipronged approach to developing and testing therapies for asthma. The Inner-City Asthma Consortium (ICAC) evaluates immune-based therapies for asthma in inner-city children, who are disproportionately affected by the disease. At the same time, the Asthma Exacerbations: Biology and Disease Progression program is conducting basic and clinical research to facilitate development of new treatments to control asthma symptoms in children and adults.

In addition to drug development and evaluation, NIH supports research on nonmedicinal interventions for chronic diseases, including behavioral and surgical approaches. For example, researchers have developed two effective behavioral therapies—the Matrix Model and Motivational Incentives for Enhanced Drug Abuse Recovery—that help people overcome methamphetamine addiction. A clinical trial infrastructure also has been set up to facilitate testing of innovative treatments for mental disorders such as schizophrenia, bipolar disorder, and depression that include medical and/or behavioral therapies. The Health Maintenance Consortium is fostering collaboration among independent research projects aimed at promoting behavior change in areas such as diet, exercise, HIV prevention, smoking cessation, and others. Many diverse strategies are being tested for treatment of obesity, including the use of bariatric surgery. The Longitudinal Assessment of Bariatric Surgery (LABS) is evaluating the risks and benefits of bariatric surgery in obese adults, and a related observational study, Teen-LABS, is collecting data on the use of this procedure in obese adolescents.

Organ transplantation is a surgical option for some chronic diseases. Transplantation can alleviate disease, prolong survival, and improve quality of life, but the procedure carries its own risk of complications, including those caused by drugs that prevent organ rejection. Researchers are investigating the use of MRI to noninvasively monitor transplant rejection. If successful, this technology could be used by physicians to modulate drug regimens to precise levels that prevent rejection while allowing the patient’s body to maintain enough immune activity to ward off infections. NIH established the Clinical Trials in Organ Transplantation program to further improve the outcome of organ transplantation. Researchers also are studying transplantation of specific organ tissues to treat disease, such as transplanting the insulin-producing islet cells of the pancreas to treat type 1 diabetes. The international Clinical Islet Transplantation Consortium is developing and conducting clinical studies that could improve this treatment approach for people with type 1 diabetes.
An important aspect of the NIH mission is to communicate the results of its research so that patients and the public can benefit from up-to-date information on treatment options (see the section “Health Communication and Information Campaigns and Clearinghouses” in Chapter 3). Sometimes this goal is accomplished through public awareness campaigns, such as one for COPD called “COPD: Learn More, Breathe Better,” which distributes materials on COPD to patients, persons at risk, health care professionals, and community-level organizations to raise awareness of COPD. COPD is a disease that often goes undiagnosed, and therefore untreated, in an estimated 12 million Americans. For other diseases, translational researchers are exploring the best ways to transfer knowledge from controlled research settings into standard medical practice and the community to achieve maximum benefits for public health. Research is ongoing to find sustainable and cost-effective means to translate the successes of clinical trials for the treatment of diabetes and obesity into the real world. NIH-supported scientists also are identifying ways to promote the use of evidence-based interventions for treatment of mental illnesses.

A 2002 survey conducted by NIH and CDC found that one-third of American adults use some form of complementary and alternative medicine (CAM) to prevent or treat disease, including diverse modalities such as acupuncture, meditation, megavitamin therapy, herbs, special diets, chiropractic care, prayer, and other methods. The goal of NIH research on CAM is to provide an evidence-based assessment of the safety and effectiveness of CAM practices in order to guide and protect patients and consumers who are making treatment choices. NIH has developed a 5-year strategic plan to define priorities for CAM research, much of which pertains to a variety of organ systems and chronic diseases.

NIH-supported studies of popular dietary supplements have reported mixed results. One study showed that high doses of a form of vitamin E did not lower cholesterol in the blood, whereas in another study, glucosamine and chondroitin sulfate supplements did not relieve osteoarthritis pain in the general study population, although patients with moderate-to-severe pain did benefit. In other ongoing research, multidisciplinary teams are uncovering scientific explanations for some of the effects of acupuncture in relieving pain and are evaluating the use of this technique in patients with coronary artery disease, spinal cord injury, post-thoracotomy pain syndrome, and a number of other chronic conditions.

**Addressing Pain and Palliative Care in Chronic Diseases**

Pain and palliation—care to alleviate the symptoms of disease and improve quality of life—are issues associated with many chronic diseases, regardless of the organ system affected. NIH supports research to understand the origins of pain, develop therapies to manage pain effectively, and design palliative therapies to reduce suffering and improve disease outcomes. NIH is pursuing multidisciplinary approaches to the discovery of non-opioid pain medications that can selectively and safely treat chronic pain without creating drug dependence. For example, basic pharmacological research has uncovered previously unknown receptor combinations in the body that represent new targets for pain control. Nonpharmacological strategies for pain management also are being closely studied. For example, researchers have confirmed that acupuncture is an effective add-on to conventional treatment for osteoarthritis, a common cause of pain and reduced quality of life in elderly patients. The Spine Patient Outcomes Research Trial has determined which patients with back pain are most likely to benefit from surgical intervention. The Orofacial Pain: Prospective Evaluation and Risk Assessment study is seeking better ways to manage the chronic pain of temporomandibular muscle and joint disorders.

Because of the broad diversity of chronic diseases associated with pain, NIH established the NIH Pain Consortium to enhance research and promote collaboration among the many ICs that have an interest...
in pain and pain management research. Since its establishment, the consortium has sponsored two symposia featuring new and exciting advances in pain research and pain management. Consortium ICs also have issued an NIH-wide research initiative to encourage pain research and delineate cross-cutting NIH interests in pain.

NIH research addresses the application of palliative care at all stages of a disease process, including at the end of life, and encompasses the needs of patients and their caregivers. Behavioral strategies have been shown to improve patient outcomes for several chronic diseases, including diabetes, irritable bowel syndrome, and asthma. Researchers also have developed a support intervention that significantly improves the quality of life for caregivers of patients with Alzheimer's disease; further research is needed to determine how best to implement this intervention through community health service networks so that more caregivers can benefit. In FY 2006, the proceedings of an NIH-sponsored State-of-the-Science Conference on Improving End-of-Life Care were published as a supplement to the Journal of Palliative Medicine. This special supplement reported on the state of the science in end-of-life care and proposed new research directions to improve care for all patients and their families in the final stages of disease.

### Notable Examples of NIH Activity

**Key for Bulleted Items:**

- E = Supported through Extramural research
- I = Supported through Intramural research
- O = Other (e.g., policy, planning, or communication)
- COE = Supported through a congressionally mandated Center of Excellence program
- GPRA Goal = Concerns progress tracked under the Government Performance and Results Act

#### Understanding Fundamental Mechanisms of Organ Health and Disease

**Innovative Technologies for Engineering Small Blood Vessels:** NIH has initiated a program of basic research studies for the future development of replacements for damaged or diseased small blood vessels. Thousands of patients each year could benefit from small blood vessel substitutes (e.g., to bypass coronary artery or peripheral vascular occlusions or to establish arteriovenous shunts for hemodialysis), but currently available replacement grafts have a high failure rate. Recent advances in materials science, bioengineering, and tissue engineering, as well as the availability of better computational tools, are providing opportunities for the development of replacement blood vessels with properties that closely match those of natural blood vessels.

- This example also appears in Chapter 3: Molecular Biology and Basic Sciences and Chapter 3: Technology Development.
- (E) (NHLBI)

**Interagency Registry for Mechanically Assisted Circulatory Support (INTERMACS):** In a joint effort, NHLBI, the Center for Medicare and Medicaid Services, and FDA created INTERMACS, a national registry for patients who are receiving mechanical circulatory support device therapy to treat advanced heart
failure. Data from INTERMACS are expected to improve patient evaluation and management; aid in the development of safer, more effective devices; and enhance research.

- For more information, see [http://www.uab.edu/ctsresearch/mcsd](http://www.uab.edu/ctsresearch/mcsd)
- This example also appears in Chapter 3: *Disease Registries, Databases, and Biomedical Information Systems*
- (E) (NHLBI)

**Women's Health Initiative:** In January 2007, NIH awarded support for a dozen 2-year research projects to apply genomics, proteomics, and other innovative technologies to improve understanding of several major diseases that commonly affect postmenopausal women. The new endeavor builds on the long-running Women's Health Initiative, which conducted several clinical trials and an observational study to examine strategies for preventing heart disease, breast and colorectal cancers, and osteoporosis in a cohort of more than 160,000 subjects. Investigators will use stored blood, DNA, and other biological samples and associated clinical data to analyze genetic factors and biological markers that may be useful in predicting disease outcomes or the effects of therapeutic and preventive regimens in postmenopausal women.

- This example also appears in Chapter 3: *Epidemiological and Longitudinal Studies* and Chapter 3: *Genomics.*
- (E) (NHLBI)

**Inflammation in the Elderly:** Inflammatory processes, particularly those mediating chronic inflammation, have been implicated as predictors or initiators of or contributors to a number of chronic diseases and conditions of aging. NIH currently supports research to determine relationships of age-related changes in inflammation and inflammatory mediators to physiologic and pathophysiologic aging changes, risks and progression of age-related morbidity and disability, and changes in tissue and organ function. Funded projects include studies of vascular inflammation and neurotoxicity in the aging brain and inflammatory responses to sleep loss.

- For more information, see [http://tinyurl.com/22o9mv](http://tinyurl.com/22o9mv) (Obesity chapter)

**Neurobiology of Appetite Control:** NIH supports research to elucidate the complex biologic pathways that converge in the brain to regulate appetite. Examples include research on how serotonin reduces appetite; the actions of the protein mTOR in sensing nutrients in the body so as to modulate food intake; and a strategy to block ghrelin, a stomach-secreted hormone that signals the brain to increase food intake. This research has implications for new therapies for obesity.

- For more information, see [http://tinyurl.com/22o9mv](http://tinyurl.com/22o9mv) (Obesity chapter)
- This example also appears in Chapter 2: *Neuroscience and Disorders of the Nervous System.*
- (E) (NIDDK)

**Lymphatic System in Health and Disease:** NIH recently announced two funding opportunities for research to increase understanding about the lymphatic system and its function in health and disease.
The lymphatic system plays a critical role in the well-being of many other systems in the body. When it is not working properly, a broad array of diseases and disorders can result, including lymphedema (characterized by accumulation of lymph fluid that often results in swelling of the arms or legs), inflammation and infections, cancer, and metabolic disorders. In July 2007, NIH issued the Program Announcement “Lymphatic Biology in Health and Disease” to encourage research on the biology of the lymphatic system and potential new therapeutic approaches. In addition, in December 2006, NIH re-issued the Program Announcement “Pathogenesis and Treatment of Lymphedema and Lymphatic Diseases” to stimulate research on the lymphatic system and lymphatic dysfunction and related diseases, as well as to develop new diagnostic methods and treatment interventions.

- This example also appears in Chapter 3: Molecular Biology and Basic Sciences.
- (E) (NHLBI, NCCAM, NCI, NIAMS, NIBIB, NICHD, NIDDK, NINR)

**Understanding the Mechanisms of Alcohol-Induced Tissue Injury:** Virtually every organ system of the body is impacted by heavy alcohol use (the most vulnerable being the brain and liver), and the resulting pathological conditions contribute to increased mortality and morbidity among all age and racial/ethnic groups and genders. NIH is especially interested in elucidating mechanisms of injury common to multiple body and organ systems. A number of Program Announcements and RFAs have been issued to support research to increase our understanding of the underlying cellular and molecular mechanisms of tissue injury caused by alcohol consumption, including alcohol's genetic, epigenetic, and metabolic effects. The long-term goals of these initiatives are to identify biomarkers for alcohol exposure and for the early detection of alcohol-induced tissue injury, and to develop new therapeutics that control or modify outcomes of chronic alcohol use.

- This example also appears in Chapter 2: Life Stages, Human Development, and Rehabilitation, Chapter 2: Neuroscience and Disorders of the Nervous System, and Chapter 3: Molecular Biology and Basic Sciences.
- (E/I) (NIAAA)

**Jackson Heart Study Advanced Imaging Component:** The Jackson Heart Study is a longitudinal study of heart disease and cardiovascular disease in about 5,000 African Americans in the Jackson Mississippi area. Data collection for this study began in 2000. New imaging techniques that include dynamic MR imaging of the heart to assess cardiac function and CT imaging to assess visceral abdominal fat and calcification of the aorta and coronary vessels can provide significant additional understanding of heart disease in this minority population. NIH is in the process of adding these valuable components to the study of heart disease. The CT studies began in spring of 2007 and the MR studies are being set up now and will begin in early 2008.

- For more information, see [http://www.nhlbi.nih.gov/about/jackson/index.htm](http://www.nhlbi.nih.gov/about/jackson/index.htm)
- This example also appears in Chapter 2: Minority Health and Health Disparities
- (E) (NIBIB, NCMHD, NHLBI)
**Systems Biology Approach to Salivary Gland Physiology:** Previous research has catalogued the genes and proteins expressed in the salivary glands. This initiative puts those catalogues into context by defining when and where genes and proteins are expressed and how they function as parts of a fully integrated biological system. The initiative combines the power of mathematics, biology, genomics, computer science, and other disciplines to translate this highly detailed information into more precise and practical leads to treat Sjögren’s syndrome, a debilitating autoimmune disorder that affects millions of Americans. The initiative also will help in learning to use saliva as a diagnostic fluid for a variety of conditions, from AIDS to cancer to diabetes.

- For more information, see [http://www.nidcr.nih.gov/GrantsAndFunding/See_Funding_Opportunities_Sorted_By/ConceptClearance/CurrentCC/SysAppySal.htm](http://www.nidcr.nih.gov/GrantsAndFunding/See_Funding_Opportunities_Sorted_By/ConceptClearance/CurrentCC/SysAppySal.htm)
- For more information, see [http://grants2.nih.gov/grants/guide/rfa-files/RFA-DE-08-001.html](http://grants2.nih.gov/grants/guide/rfa-files/RFA-DE-08-001.html)
- This example also appears in Chapter 2: *Autoimmune Diseases* and Chapter 3: *Genomics*.
- (E) (NIDCR)

**Beta Cell Biology Consortium (BCBC):** The BCBC is collaboratively pursuing key challenges relevant to the development of therapies for type 1 and type 2 diabetes, including studying pancreatic development to understand how insulin-producing beta cells are made, exploring the potential of stem cells as a source for making islets, and determining the mechanisms underlying beta cell regeneration. The BCBC has generated key research resources, such as animal models, microarrays, and antibodies, which are available to the scientific community.

- For more information, see [http://www.betacell.org](http://www.betacell.org)
- This example also appears in Chapter 2: *Autoimmune Diseases* and Chapter 3: *Molecular Biology and Basic Sciences*
- (E) (NIDDK)

**Urinary Tract Infections:** NIH supports a Specialized Center of Research on Sex and Gender Factors Affecting Women’s Health. This program advances new understanding of host-pathogen interactions that occur throughout the infectious cycle, including host defense response in the bladder and the virulence mechanisms by which bacterial pathogens subvert the defenses.

- For more information, see [http://clinicaltrials.gov/ct/show/NCT00068120](http://clinicaltrials.gov/ct/show/NCT00068120)
- This example also appears in Chapter 2: *Infectious Diseases and Biodefense*.
- (E) (NIDDK)

**Systems Science and Health:** Solutions to complex problems like chronic disease require approaches that can address a broad range of factors within a single framework—from genetic to environmental, cellular to behavioral, and biological to social. A 2007 Symposium Series on Systems Science and Health focuses on approaches that consider how numerous factors interact nonlinearly over time in multiple feedback loops to influence health. These approaches show promise for unlocking the secrets of complex, multidimensional health problems and for transforming this knowledge into effective interventions that can fundamentally change population health.

- For more information, see [http://obssr.od.nih.gov/Content/Lectures+and+Seminars/Systems_Symposia_Series/SEMINARS.htm](http://obssr.od.nih.gov/Content/Lectures+and+Seminars/Systems_Symposia_Series/SEMINARS.htm)
- (O) (OBSSR, CDC, FIC, NCI, NICHD, NIGMS)
Mechanisms of Action of CAM: Important and potentially promising findings from recently reported research aimed at elucidating the fundamental mechanisms of various CAM interventions include the following:

- Extracts of turmeric (a common component of Ayurvedic traditional Indian medicines and ingredient in Indian cuisine) containing compounds known as curcuminoids prevent experimental rheumatoid arthritis in an animal model.
- Green tea is widely promoted for a variety of health-related benefits. It contains a group of chemicals called catechins, one of which is known as epigallocatechin gallate (EGCG). Investigators recently reported that an EGCG-enriched extract of green tea significantly improves glucose and lipid metabolism in an animal model of obesity/insulin resistance/metabolic syndrome.

- This example also appears in Chapter 3: *Molecular Biology and Basic Sciences*
- (E) (NCCAM)

Inflammatory Factor Mediates Nerve Degeneration in Glaucoma Model: In glaucoma, elevated eye pressure plays a role in damaging fibers in the optic nerve, which relays visual signals to the brain. However, the link between pressure and nerve damage is not well understood. Recent research in mice suggests a critical role for the protein TNF-a in developing glaucoma. A molecular target in the glaucoma disease pathway opens up doors for drug therapy.

- This example also appears in Chapter 2: *Neuroscience and Disorders of the Nervous System.*
- (E) (NEI)

Wound Healing and Skin Biology: Recent advances in wound healing research have brought greater understanding to skin biology, with implications for hair growth and skin diseases, as well as treatment of chronic wounds. When skin is wounded, a protein, S100A7, is released and attaches to and reduces survival of potentially disease-causing bacteria on the skin, preventing the development of wound-related infections.

- (E) (NIAMS)

Leiomyomata Uteri (Uterine Fibroids): Some estimates suggest that uterine fibroids could affect as many as 77 percent of women nationwide and that more than 25 percent have active symptoms. NIH researchers recently found that, unlike normal uterine tissue, abnormal fibroid tissue is not affected by reproductive hormones. This suggests that the conventional hormone therapies used to treat fibroid tumors are unlikely to yield lasting improvements. Based on the findings, NIH researchers are planning studies to test two new drug treatments. One would block collagen from forming to help keep existing fibroids from growing larger; the second would help to break apart collagen fibrils in an attempt to shrink existing tumors.

- (E/I) (NICHD)
Anti-inflammation/Resolution Regulator May Be Involved in a Wide Range of Human Diseases:
Resolvin E1 (RvE1) is a new family of bioactive products of omega-3 fatty acid. Using periodontitis as a model disease, a team of NIH-funded researchers recently reported that RvE1 can dramatically alter the progression of microbe-initiated local inflammatory disease. RvE1 therapy demonstrates greater efficacy without the side effects of chronic antibiotic usage. The results of their study provide new directions for treatment of localized aggressive periodontitis and other inflammation-related bone disorders. In many chronic disorders similar to periodontitis, prolonged and unresolved inflammation contributes to pathogenesis. It is now clear that several endogenous biochemical pathways activated in the host during defense reactions can counter-regulate inflammation. This study provides evidence for the role of resolvin E1 as an endogenous anti-inflammation/resolution regulator that may be involved in the pathogenesis of a wide range of human diseases.

- This example also appears in Chapter 3: *Molecular Biology and Basic Sciences.*
- (E) (NIDCR)

New Molecular Targets to Halt Periodontal Bone Loss: Approximately 80 percent of American adults have some form of periodontal disease. Chronic periodontitis erodes supporting structures of the tooth, leading to tooth loss. The risk of periodontal diseases is higher in smokers and individuals with diabetes; 18 million Americans suffer from diabetes and related complications, including increased incidence and severity of periodontitis. This higher incidence and severity is associated with increased cell death in bone and tissue-forming cells called osteoblasts and fibroblasts. The loss of these cells results in decreased capacity to repair tissue and bone. NIH-supported investigators published two separate papers describing the mechanisms by which the diabetic state enhances cell death. The papers suggest that diabetes-induced cell death and compromised tissue repair are mediated by the TNF-a pro-apoptotic pathway, the major effector being caspase-3. Inhibition of TNF-a or caspase-3 activity rescues cell death and restores repair capacity. Discrimination between harmful microbes and commensal species is a critical property of the mucosal immune system, which is essential for maintaining health. Host immune cells have surface receptors that recognize bacterial species such as those known to be associated with periodontitis. Host immune cells can selectively learn to respond strongly or to tolerate endotoxin produced by recognized bacteria. NIH-supported scientists found that patients with chronic periodontitis overproduce a molecule known as SHIP, which plays an important regulatory role in signaling immune cells to tolerate endotoxin. Data from these studies suggest possible targets for developing new ways to treat or prevent chronic periodontitis.

- This example also appears in Chapter 2: *Autoimmune Diseases* and Chapter 3: *Molecular Biology and Basic Sciences.*
- (E) (NIDCR)

Advances in Treatment Development for Mental Disorders: NIH continues to fund research into the development of new, targeted medications and treatments for mental disorders:

- Drug Development for Cognitive Impairments in Schizophrenia: The Treatment Unit for Research on Neurocognition in Schizophrenia program is a network that is testing the safety and efficacy of new therapeutic compounds for treating the cognitive deficits of schizophrenia.
- (E) (NIMH)
Studies of Fragile X Syndrome: NIH has entered into a public-private partnership to study and test possible medications for treating fragile X syndrome, the most common cause of inherited mental impairment. Fragile X syndrome is caused by a single gene mutation that ultimately results in exaggerated activity of a brain protein called mGluR5. Researchers will study, in animals, the safety of chemical compounds known to block this mGluR5 activity. If this phase goes well, researchers will move forward with clinical studies.

- (E) (NIMH, NINDS, NICHD)

Faster-Acting Depression Treatments: A recent NIH-funded study found that people with treatment-resistant depression experienced relief in as little as 2 hours after a single intravenous dose of ketamine, a medication usually used in higher doses as an anesthetic. Used in very low doses, ketamine is important for depression research but at higher doses could have side effects that may limit its clinical use. Nevertheless, this research could inform the development of faster- and longer-acting medications for treating depression.

- For more information, see [http://www.nimh.nih.gov/press/ketamine.cfm](http://www.nimh.nih.gov/press/ketamine.cfm)
- This example also appears in Chapter 2: Neuroscience and Disorders of the Nervous System and Chapter 3: Clinical and Translational Research.
- (NIMH)

Detecting and Diagnosing Chronic Disease

Helping Patients Who Drink Too Much: A Clinician's Guide: In January 2007, NIH issued an update to its 2005 edition of this clinician's guide. Targeted to primary care and mental health clinicians, the guide presents a user-friendly, research-based approach to screening, diagnosing, and managing patients with heavy drinking and alcohol use disorders. The updated guide offers the following new resources: CME/CE credits for physicians and nurses available through Medscape; support for medication-based therapy in non-specialty settings; a new handout with strategies to help patients reduce or quit drinking; a new dedicated Web page devoted to the guide and supporting resources for clinicians and patients; and an updated PowerPoint presentation for educators and instructors. NIH has worked closely with several organizations to disseminate the guide to their memberships.

- For more information, see [http://www.niaaa.nih.gov/Publications/EducationTrainingMaterials/guide.htm](http://www.niaaa.nih.gov/Publications/EducationTrainingMaterials/guide.htm)
- This example also appears in Chapter 3: Health Communication and Information Campaigns and Clearinghouses
- (E) (NIAAA)

Alcohol Biosensors Program: This Advanced Research Program, modeled on DoD's DARPA (Defense Advanced Research Projects Agency) program, was developed by NIH to generate a technical solution to address the need for continuous measurement of alcohol concentrations over time in clinical and basic research on alcohol use disorders. NIH awarded five research and development contracts for alcohol biosensor development. Each research group employed a different technological approach for alcohol measurement, and all have made substantial progress in engineering commercially viable alcohol biosensors, some of which are likely to make their way to market in the next few years.

- This example also appears in Chapter 3: Technology Development.
- (E) (NIAAA)
Drug-Induced Liver Injury Network (DILIN): DILIN is addressing the problem of drug-induced liver toxicity, which is increasing in the United States and has serious consequences for individuals and society. This Network enables research on liver toxicity due to prescription drugs or complementary and alternative medicines. Current studies are developing better tools for diagnosing, and ultimately preventing, drug-induced liver injury, as well as enhancing knowledge of disease processes. The Network has evolved into a resource on drug-induced liver toxicity for the national clinical community and the public.

- For more information, see http://dilin.dcri.duke.edu
- (E) (NIAAA)

Identifying Risk and Preventing Chronic Disease

Genome-Wide Association (GWA) Studies and Database of Genotype and Phenotype (dbGaP): In December 2006, NIH released the initial dbGaP dataset, using GWA data from the Age-Related Eye Diseases Study (AREDS), a landmark study of the clinical course of age-related macular degeneration (AMD) and cataracts. AREDS documents, protocols, and aggregated data are made available with no restrictions. To protect patient confidentiality, de-identified, individual-level patient characteristics and family data are accessible only by authorized investigators. Correlating phenotype and genotype data provides information about the genetic and environmental interactions involved in a disease process or condition, which is critical for better understanding complex diseases and developing new diagnostic methods and treatments. Using these data, recent studies have linked two genes with progression to advanced AMD. After other factors were controlled for, certain forms of the genes increased the risk of AMD progression by 2.6- to 4.1-fold; smoking and body weight further increased risk with these gene variants.

- Seddon JM, et al. JAMA 2007;297:1793-800, PMID: 17456821
- This example also appears in Chapter 3: Disease Registries, Databases, and Biomedical Information Systems and Chapter 3: Genomics.
- (E) (NEI, NIA, NLM)

Diabetes Prevention Program Outcomes Study (DPPOS): The landmark NIH Diabetes Prevention Program (DPP) clinical trial showed that lifestyle change or treatment with the drug metformin significantly delayed the development of type 2 diabetes in people at high risk. The DPPOS is a long-term follow-up study of DPP subjects that is determining the durability of the interventions in preventing disease. DPP researchers recently confirmed that a variant in a gene predisposes people to type 2 diabetes. DPP subjects at highest genetic risk benefited from healthy lifestyle changes as much or more than those who did not inherit the variant. Participants over 60 years of age responded especially well to the lifestyle intervention, showing a 71 percent risk reduction in the incidence of diabetes, compared to groups treated with metformin or standard medical advice. The lifestyle intervention had greater impact with increasing age (from age 25 to over 60); the metformin treatment had progressively less impact with increasing age.

- For more information, see http://tinyurl.com/24okog
- For more information, see http://tinyurl.com/295h4l
- This example also appears in Chapter 3: Clinical and Translational Research and Chapter 3: Epidemiological and Longitudinal Studies.
The Heart Truth: The Heart Truth, NIH's national awareness campaign for women about heart disease, continues to extend the reach of campaign messages and promotion of the Red Dress as the national symbol for women and heart disease. Hundreds of locally sponsored Heart Truth events have taken place, and more than a billion media impressions have been achieved. The Heart Truth Road Show helps subjects learn about heart disease risk factors, provides free health screenings, and disseminates educational materials. In April 2006, the campaign launched the Heart Truth Champions program to recruit health advocates and educators in local communities to increase awareness about women and heart disease. National Wear Red Day—the first Friday in February—has become an annual event when Americans wear red clothing and accessories in recognition of the importance of heart disease in women.

- For more information, see http://www.nhlbi.nih.gov/health/hearttruth
- This example also appears in Chapter 3: Health Communication and Information Campaigns and Clearinghouses.
- (E) (NHLBI)

Ways to Enhance Children's Activity & Nutrition (We Can!): This national public education outreach program, focusing on parents and families in home and community settings, is designed to help children 8-13 years old achieve and maintain a healthy weight. We Can! program materials offer tips and activities to encourage healthy eating, increase physical activity, and reduce sedentary or computer and television screen time. Many national partners and supporting organizations are promoting the We Can! messages and materials, and the program is being implemented in a variety of settings. In 2007, NIH began the We Can! city program to assist towns and cities in mobilizing their communities to prevent childhood obesity. The first three cities that will participate in the new effort have pledged to offer We Can! evidence-based obesity prevention programs to parents and youth in collaboration with community-based partners. In addition, each city will distribute We Can! tips and information to city employees.

- For more information, see http://www.nhlbi.nih.gov/health/public/heart/obesity/wecan/
- For more information, see http://public.nhlbi.nih.gov/newsroom/home/GetPressRelease.aspx?id=268
- This example also appears in Chapter 3: Health Communication and Information Campaigns and Clearinghouses
- (E) (NHLBI, NCI, NICHD, NIDDK)

National Epidemiologic Survey on Alcohol and Related Conditions (NESARC): This nationally representative survey collected comprehensive, detailed data from approximately 40,000 individuals on alcohol consumption, use of 10 categories of drugs, and symptoms of alcohol and specific drug use disorders, as well as mood, anxiety, and personality disorders. In addition to diagnostic criteria, NESARC assessed indicators of impairment and distress due to each disorder, as well as disorder-specific treatment and help seeking. Analysis of these data is ongoing and continues to provide valuable information such as prevalence and comorbidity of mental health and substance use disorders. In addition, because NESARC data include a representative sample of ethnic and racial minority populations in the United States, a better assessment of the needs of specific populations can be made. One recent study using these data examined differences in the use of alcohol treatment services across the three largest ethnic groups in America. It showed that Hispanics and African Americans with higher
levels of problem severity were less likely to have used treatment services than were Whites with 
problems of comparable severity, providing useful information about disparities in treatment utilization.

- This example also appears in Chapter 2: *Life Stages, Human Development, and Rehabilitation*, Chapter 3: *Epidemiological and Longitudinal Studies*, and Chapter 2: *Minority Health and Health Disparities*.
- (E/I) (NIAAA)

**Osteoporosis**: NIH supports several longstanding prospective cohort studies, including the Study of Osteoporotic Fractures (SOF) in women and Mr. OS, a study of osteoporosis and other age-related diseases in men. Major contributions from the SOF, which began in 1986, include findings that bone mineral density of the hip is one of the best predictors of fracture for women. Recently, Mr. OS researchers identified specific lifestyle, medical, and demographic characteristics associated with low bone mass and fracture risk in older men.

- For more information, see [http://www.niams.nih.gov/News_and_Events/Advisory_Council_Minutes/2006/sum01_06.asp](http://www.niams.nih.gov/News_and_Events/Advisory_Council_Minutes/2006/sum01_06.asp)
- This example also appears in Chapter 3: *Epidemiological and Longitudinal Studies*.
- (E) (NIAMS, NIA)

**Childhood and Maternal Obesity**: As the maternal and childhood obesity epidemic grows, researchers are trying to understand the interaction among the many complex biological and behavioral factors that contribute to this rise, identify the long-term impact on mother and child, and develop effective interventions to reverse these trends. NIH obesity research, which includes a range of racial and ethnic groups, is examining topics such as:

- Basic research on the physiology, psychology, and genetics of obesity in children
- Developing working definitions of the metabolic syndrome in children and adolescents
- Linking maternal obesity, reproductive health, and pregnancy to adverse health outcomes
- Behavioral intervention trials in schools, the home, and the community

- This example also appears in Chapter 2: *Life Stages, Human Development, and Rehabilitation*.
- (E/I) (NICHD, NCCAM, NCI, NCMHD, NHLBI, NIDCR, NIDDK, NINR, OBSSR, ODP/ORD)

**Trial to Reduce the Incidence of Type 1 Diabetes for those Genetically at Risk (TRIGR)**: Researchers are conducting a study to determine whether the onset of type 1 diabetes can be delayed or prevented by weaning genetically susceptible infants to Nutramigen®, a hydrolysate of cow milk protein, instead of to a standard cow milk-based infant formula. Earlier studies in animal models have shown that hydrolyzed protein diets prevented the onset of type 1 diabetes. TRIGR is the first large effort designed to ascertain whether a simple nutritional intervention during infancy can delay or prevent the onset of type 1 diabetes in children who are at high genetic risk for the disease. Enrollment for the study was recently completed, totaling more than 2,000 children from 15 countries.

- For more information, see [http://www.nichd.nih.gov/research/supported/TRIGR.cfm](http://www.nichd.nih.gov/research/supported/TRIGR.cfm)
- This example also appears in Chapter 2: *Life Stages, Human Development, and Rehabilitation*. 
HEALTHY: The HEALTHY multicenter clinical trial aims to prevent risk factors for type 2 diabetes in middle-school children. A pilot study for HEALTHY found that an alarmingly high 15 percent of students in middle schools enrolling mainly minority youth had three major risk factors for diabetes; about half of the children were overweight. These data suggest that middle schools are appropriate targets for efforts to decrease the risks for obesity and diabetes. In the full-scale HEALTHY trial, 42 enrolled middle schools receive the intervention, which includes changes to school food service and physical education classes, behavior change, and communications campaigns. Over 80 percent of the enrolled students are from minority populations.

- This example also appears in Chapter 2: Life Stages, Human Development, and Rehabilitation and Chapter 2: Minority Health and Health Disparities.
- (E) (NIDDK)

Inflammatory Bowel Disease Genetics Consortium: This consortium of researchers in the United States and Canada applies knowledge from the Human Genome Project to the identification of genetic factors influencing the development of inflammatory bowel diseases. A genome-wide screen of samples collected recently identified three new inflammatory bowel disease susceptibility genes. The identification of such genetic factors can provide key insights into disease development and targets for designing more effective therapies for inflammatory bowel disease.

- This example also appears in Chapter 3: Genomics.
- (E) (NIDDK)

Irritable Bowel Syndrome: Center for Neurovisceral Sciences and Women's Health: Irritable bowel syndrome is a common disorder that occurs much more frequently in females than in males. The Women's Health and Functional Visceral Disorders Center at the University of California—Los Angeles studies the role of sex-related factors in the development of irritable bowel syndrome and its response to treatment. Basic and clinical research involving patients, animal models, and functional brain imaging techniques are exploring sex differences in stress responses within the central nervous system, colon, and hormonal and immune systems. Researchers hope to identify factors that can form the basis of more effective treatment options for irritable bowel syndrome.

- For more information, see [http://www.cns.med.ucla.edu](http://www.cns.med.ucla.edu)
- (E) (NIDDK, ORWH)

Environmental Intervention in the Prevention of Asthma: Asthma is strongly related to environmental exposures. Exposure to indoor cat, dog, house dust mite, cockroach, and mold allergens is of particular concern because about 75-80 percent of children with asthma have significant allergies, which can trigger asthma, and thus these allergens have considerable medical and economic impact. Recent data have documented the ubiquity and specific levels of critical indoor allergens. In addition, a number of studies have shown that sensitization to indoor allergens (including those that derive from house dust mites, cats, dogs, rodents, cockroaches, and fungi) is a risk factor for the subsequent development of asthma. These studies include case-control studies, prospective studies, and allergen avoidance trials. Because house dust mites have been shown to be one of the strongest risk factors for persistence of asthma, an environmental intervention dust mite reduction study is under way in North Carolina.
Volunteers between the ages of 5 and 15 years who are allergic or sensitive to dust mites are being recruited for the study. A study team will visit the homes of subjects four times over a 12-month period to measure indoor dust mite levels and collect information about the home. The results of the study will provide information that will help reduce or prevent adverse health outcomes from exposure to house dust mites and other allergens.

- For more information, see [http://www.niehs.nih.gov/health/topics/conditions/asthma](http://www.niehs.nih.gov/health/topics/conditions/asthma)
- (NIEHS)

**Head Off Environmental Asthma in Louisiana:** Nearly 20 million people, 6.5 million of them children, suffer from asthma in the United States, and minorities are disproportionately represented. NIEHS, with the National Center on Minority Health and Health Disparities (NCMHD) and others, co-funds the Head Off Environmental Asthma in Louisiana (HEAL) project to assess the impact on asthma of environmental health conditions that were caused and exacerbated by Hurricane Katrina in New Orleans children, as well as implement an intervention program to address these problems. The Project's three main goals are (1) to conduct an extensive epidemiology study to assess the nature of the environmental and psychological impacts on children in New Orleans of Hurricane Katrina and subsequent flooding; (2) to examine the genetic and environmental risk factors for asthma, including genetic susceptibility to mold toxins, and gene interactions; and (3) to design, implement, and evaluate a case management program to meet the health care needs of children with asthma in a disrupted and highly challenging environment. The project has a clear plan for informing the community of the goals, implementation, and outcomes, as well as for receiving input from the community.

- For more information, see [http://heal.niehs.nih.gov](http://heal.niehs.nih.gov)
- This example also appears in Chapter 2: *Minority Health and Health Disparities* and Chapter 3: *Clinical and Translational Research.*
- (NIEHS, NCMHD)

**The Collaborative Study on the Genetics of Alcoholism (COGA):** In its 18th year, COGA is a multisite, multidisciplinary family study with the overall goal of identifying and characterizing genes that contribute to the risk for alcohol dependence and related phenotypes. COGA investigators have collected data from more than 300 extended families (consisting of more than 3,000 individuals) who are densely affected by alcoholism. Several genes have been identified, including *GABRA2, ADH4, ADH5,* and *CHRM2,* that influence the risk for alcoholism and related behaviors, such as anxiety, depression, and other drug dependence. In addition to genetic data, extensive clinical neuropsychological, electrophysiological, and biochemical data have been collected, and a repository of immortalized cell lines from these individuals has been established to serve as a permanent source of DNA for genetic studies. These data and biomaterials are distributed to qualified investigators in the greater scientific community to accelerate the identification of genes that influence vulnerability to alcoholism. COGA will continue to identify genes and variations within the genes that are associated with an increased risk for alcohol dependence and will perform functional studies of the identified genes to examine the mechanisms by which the identified genetic variations influence risk.

- For more information, see [http://zork.wustl.edu/niaaa](http://zork.wustl.edu/niaaa)
- This example also appears in Chapter 2: *Neuroscience and Disorders of the Nervous System,* Chapter 3: *Genomics,* and Chapter 3: *Molecular Biology and Basic Sciences*
- (E) (NIAAA) (GPRA Goal)

**Look AHEAD (Action for Health in Diabetes):** This multicenter NIH-led clinical trial is examining the health effects of an intensive lifestyle intervention designed to achieve and maintain weight loss over
the long term through decreased caloric intake and increased physical activity. The impact of the intervention on the incidence of major cardiovascular events will be evaluated in 5,100 overweight or obese subjects with type 2 diabetes. Look AHEAD is one of four trials that collectively address GPRA Goal SRO-6.2.

- For more information, see [http://tinyurl.com/2xaypk](http://tinyurl.com/2xaypk)
- This example also appears in Chapter 3: Clinical and Translational Research and Chapter 2: Minority Health and Health Disparities
- (E/I) (NIDDK, CDC, NCMHD, NHLBI, NINR, ORWH)(GPRA Goal)

**International Tobacco and Health Research and Capacity Building Program:** Without a significant shift in worldwide smoking patterns, tobacco is projected to cause approximately 10 million deaths each year by 2025; 70 percent of this increase will occur in developing countries. To address this rising epidemic, NIH reissued the International Tobacco and Health Research and Capacity Building Program for funding in 2007. Grantees are generating a solid evidence base that can inform effective tobacco control strategies and policies. The program focuses on five critical areas: (1) epidemiology and surveillance, (2) susceptibility and risk for smoking uptake, (3) behavioral and social sciences, (4) effective interventions, and (5) policy-related research. The program also emphasizes research on determinants of youth smoking in diverse cultural and economic settings. A central goal of this program is to strengthen capacity in tobacco research in low- and middle-income nations, which advances the science and permits greater international collaboration.

- For more information, see [http://www.fic.nih.gov/programs/research_grants/tobacco/index.htm](http://www.fic.nih.gov/programs/research_grants/tobacco/index.htm)
- (E) (FIC, NCI, NIDA, NIDCR, ORWH)

**Jackson Heart Study:** The Jackson Heart Study, a large epidemiological study of cardiovascular disease among more than 5,300 African American residents of Mississippi, has been renewed through FY 2013. The project is exploring genetic, biological, and environmental factors that influence the development and course of cardiovascular disease in African Americans. It is also seeking to expand minority participation in public health and epidemiological research by providing classes and hands-on training to interested undergraduate students. Moreover, a community health education component is using data derived from the study cohort to develop and disseminate up-to-date information on reduction of risk factors, practice of healthy lifestyles, and adherence to proven risk-reducing therapies.

- For more information, see [http://jhs.jsums.edu/jhsinfo](http://jhs.jsums.edu/jhsinfo)
- This example also appears in Chapter 2: Minority Health and Health Disparities and Chapter 3: Epidemiological and Longitudinal Studies.
- (E) (NHLBI, NCMHD)

**Osteoarthritis Initiative (OAI):** The OAI is a long-term effort, developed with support from private sector sponsors and with the participation of the Food and Drug Administration, to create a resource to identify and evaluate biomarkers of osteoarthritis to be used in clinical research. The OAI, which began in FY 2002, has recruited 4,800 subjects who are at high risk for knee osteoarthritis.

- For more information, see [http://www.niams.nih.gov/Funding/Funded_Research/Osteoarthritis_Initiative/default.asp](http://www.niams.nih.gov/Funding/Funded_Research/Osteoarthritis_Initiative/default.asp)
- (E) (NIAMS, NCCAM, NCMHD, NIA, NIBIB, NIDCR, ORWH)
Genetics of Kidneys in Diabetes (GoKinD): This program facilitates investigator-driven research into the genetic basis of diabetic kidney disease through a biospecimen repository. Individuals with type 1 diabetes were screened to identify two subsets, one with clear-cut kidney disease and another with normal kidney function despite long-term diabetes. Nearly 10,000 DNA, serum, plasma, and urine samples—plus genetic and clinical data—from more than 1,700 adults with diabetes have been collected. The entire GoKinD collection is being genotyped for whole-genome association studies as part of the previously described Genetic Association Information Network (GAIN).

- For more information, see http://www.jdrf.org/index.cfm?fuseaction=home.viewPage&page_id=B9C33021-1321-C834-0382E079E7865807
- This example also appears in Chapter 3: Clinical and Translational Research and Chapter 3: Genomics.
- (E) (NIDDK)

The Environmental Determinants of Diabetes in the Young: Pinpointing the environmental factors, such as infectious agents or diet, that can trigger type 1 diabetes in genetically susceptible individuals is crucial to developing prevention strategies. To address this knowledge gap, NIH established The Environmental Determinants of Diabetes in the Young (TEDDY) consortium. This international consortium is enrolling newborns at high genetic risk and following them until age 15 to identify environmental triggers for type 1 diabetes. The study is amassing the largest set of data and samples in the world for newborns at risk for type 1 diabetes.

- For more information, see http://teddy.epi.usf.edu
- This example also appears in Chapter 2: Life Stages, Human Development, and Rehabilitation and Chapter 3: Epidemiological and Longitudinal Studies.
- (E) (NIDDK, CDC, NIAID, NIEHS)

The Gila River Indian Community Longitudinal Study: NIH’s Phoenix Epidemiology and Clinical Research Branch studies type 2 diabetes as it occurs among Pima Indians of Arizona, who have the highest prevalence of diabetes in the world. Working closely with Pima volunteers, the Branch has made substantial progress in identifying genetic, physiologic, and behavioral factors that lead to obesity and diabetes. The Branch also has facilitated improved treatment and prevention services in this community, leading to improved blood glucose control and blood pressure in Pima with diabetes. One important result is that the rate of kidney failure due to diabetes in Pima age 45 and older has declined since 1990.

- For more information, see http://intramural.niddk.nih.gov/research/labbranch.asp?Org_ID=503
- This example also appears in Chapter 2: Minority Health and Health Disparities and Chapter 3: Epidemiological and Longitudinal Studies.
- (NIDDK)

Type 1 Diabetes TrialNet: NIH is supporting this international network of investigators, clinical centers, and core support facilities that conducts research to advance knowledge about type 1 diabetes and tests strategies for its prevention and early treatment. TrialNet recently launched a clinical trial to test whether oral insulin could prevent or delay type 1 diabetes in people with a certain disease marker. The network also completed enrollment of two trials to determine whether medicines to slow the immune response could prevent further insulin-producing beta cell destruction in people newly diagnosed with type 1 diabetes. The TrialNet infrastructure is critically important for testing emerging therapies for prevention and early treatment.
Prevention of Trauma-Related Mental Disorders in High-Risk Occupations: NIH is supporting a research initiative to develop and test preemptive interventions to prevent trauma-related disorders, such as posttraumatic stress disorder, among occupational groups at high risk for trauma exposure, such as the military, fire fighters, police, and rescue workers.

- This example also appears in Chapter 2: Neuroscience ad Disorders of the Nervous System and Chapter 3: Clinical and Translational Research.
- (E) (NIMH)

The U.S. Surgeon General's Family History Initiative: Many people see most diseases as the result of interactions of multiple genes and environmental factors. Health care professionals have known for a long time that common diseases, such as heart disease, cancer, and diabetes, and rare diseases, such as hemophilia, cystic fibrosis, and sickle cell anemia, can run in families. The U.S Surgeon General's Family History tool was created in a collaborative effort among the Office of the Surgeon General, NIH, CDC, AHRQ, and the Health Resources and Services Administration (HRSA). The U.S. Surgeon General's Family History tool (available in both English and Spanish) is free and has proven to be an effective personalized tool for individualizing preventive care and disease prevention—in other words, maintaining good health. Recently updated, this tool allows an individual to record health conditions that have affected his or her relatives. It utilizes a three-generation pedigree to gather information on health conditions in one's family to help doctors take action to keep individuals and families healthy.

- For more information, see [http://www.hhs.gov/familyhistory](http://www.hhs.gov/familyhistory)
- For more information, see [https://familyhistory.hhs.gov](https://familyhistory.hhs.gov)
- This example also appears in Chapter 3: Genomics.
- (O) (OD, NHGRI)

Transdisciplinary Tobacco Use Research Centers: Multiple Institutes at NIH are co-funding seven collaborative, transdisciplinary centers to identify familial, early childhood, and lifetime psychosocial pathways related to smoking initiation, use, cessation, and patterns of dependence. Research on genetics of addiction, physiological biomarkers, and the use of advanced imaging techniques can lead to individualized and community approaches for tobacco prevention and treatment. This model demonstrates the feasibility and benefits of scientific collaboration across disciplines and public-private partnerships.

- For more information, see [http://dccps.nci.nih.gov/tcrb/tturc](http://dccps.nci.nih.gov/tcrb/tturc)
- This example also appears in Chapter 2: Cancer and Chapter 2: Life Stages, Human Development, and Rehabilitation.
- (E) (NCI, NIAAA, NIDA)

Retinopathy Occurs in Middle-aged Adults Even Without Diabetes: Signs of retinopathy are common in the eyes of the elderly, particularly in those with diabetes. In the Atherosclerosis Risk in Communities (ARIC) study, African American subjects were significantly more likely to have signs of retinopathy (13 percent) compared with White subjects (5.5 percent). Among people with diabetes, 27 percent had
signs of retinopathy. Unexpectedly, retinopathy signs were also observed in 4.3 percent of people who did not have frank diabetes but tended to have elevated blood pressure. Future studies will examine whether these signs of retinopathy result from high blood pressure and whether they indicate an increased risk of systemic cardiovascular disease or predict a subsequent diagnosis of diabetes.

- For more information, see [http://www.cscc.unc.edu/aric](http://www.cscc.unc.edu/aric)
- This example also appears in Chapter 2: *Minority Health and Health Disparities* and Chapter 3: *Epidemiological and Longitudinal Studies.*
- (E/I) (NHLBI, NEI)

**Environmental Triggers and Skin Diseases:** CDC has excluded patients with eczema (also known as atopic dermatitis) from smallpox vaccination programs (in response to bioterrorism threats). There is concern of the risk of spreading vaccinia virus from the vaccine to the skin, which can cause eczema vaccinatum, an overwhelming and potentially lethal systemic infection. Researchers have learned that vaccinia virus grows much more in atopic dermatitis skin samples than in normal skin. Also, atopic dermatitis skin samples have lower levels of naturally occurring antimicrobial peptides, which could contribute to atopic dermatitis patients' susceptibility to eczema vaccinatum.

- Howell MD et al. *Immunity* 2006;24:341-8, PMID: 16546102
- (E) (NIAMS, NIAID)

**Osteoarthritis:** African Americans have a higher risk of bilateral radiographic (x ray-defined) osteoarthritis of the knee and hip than Whites. Two NIH-funded studies have revealed that mechanical stress can increase the production and release of osteoarthritis-related biomarkers. The research highlights the importance, when analyzing biomarkers, of considering the type and degree of physical activity in which patients with osteoarthritis participate.

- O'Kane JW et al. *Osteoarthritis Cartilage* 2006;14:71-6, PMID: 16188465
- This example also appears in Chapter 2: *Minority Health and Health Disparities.*
- (E) (COE) (NIAMS, NIA)

**Bone Health:** NIH researchers have established reference curves for bone mineral content and density in children. The early findings are now available according to age, sex, and race and can be used to help identify children with bone deficits and to monitor changes in bone in response to chronic diseases or therapies. Early study findings showed that bone minerals continue to accrue beyond the teenage years, so the study will continue as the adolescent subjects approach young adulthood. In another study, NIH scientists discovered two genes for osteogenesis imperfecta, or brittle bone disease. The genes affect how collagen, an important building block for bone, is formed. Although there is no treatment for the disorder, the findings allow researchers to test families who have lost a child to osteogenesis imperfecta for the presence of the defective genes.

- This example also appears in Chapter 2: *Life Stages, Human Development, and Rehabilitation.*
The Rapid Response Program: In April 2002, the Task Force on College Drinking released its seminal report A Call to Action: Changing the Culture of Drinking at U.S. Colleges. As part of its college focus, NIH initiated support of collaborations between university personnel who have responsibility for alcohol programs on various campuses and established researchers in college drinking to implement and evaluate programs to reduce underage alcohol use and its consequences. These programs include:

- RFA AA-03-008: “Research Partnership Awards for Rapid Response to College Drinking Problems.” Five U01 (cooperative agreement) 5-year grants were awarded in December 2002.
- PAR-03-133: “Rapid Response to College Drinking Problems.” Fifteen 3-year grants were awarded in June 2003.

This rapid funding mechanism (U18, cooperative agreement) supports timely research on interventions to prevent or reduce alcohol-related problems among college students. It was intended to support studies of services or interventions that could capitalize on “natural experiments” (e.g., unanticipated adverse events, policy changes, new media campaigns, campus-community coalitions, etc.). Each U18 grantee was required to partner with a U01 grantee. Together, these pairs, working with NIH Scientific Staff Collaborators, jointly design, develop, implement, and evaluate college drinking projects on their campuses.

- This example also appears in Chapter 2: Life Stages, Human Development, and Rehabilitation, Chapter 3: Epidemiological and Longitudinal Studies, and Chapter 3: Health Communication and Information Campaigns and Clearinghouses.
- (E) (NIAAA)

Underage Drinking Research Initiative: In 2004, NIH launched this ongoing initiative with the goal of obtaining a more complete and integrated scientific understanding of the environmental, biobehavioral, and genetic factors that promote initiation, maintenance, and acceleration of alcohol use among youth, as well as factors that influence the progression to harmful use, abuse, and dependence, all framed within the context of overall development. Activities and accomplishments in 2007 include:

- Provided the scientific foundation for The Surgeon General’s Call to Action to Prevent and Reduce Underage Drinking (released March 6, 2007) and for the ongoing work of the Interagency Coordinating Committee on Preventing Underage Drinking
- Convened scientific meetings of experts, including the Underage Steering Committee, which met four times over a 2-year period; a Meeting on Diagnosis of Alcohol Use Disorders among Youth (April 2006); and a Meeting on Screening for Child and Adolescent Drinking and Alcohol Use Disorders Among Youth (June 2007)
- Issued three RFAs, including “Underage Drinking: Building Health Care System Responses” (four projects awarded in FY 2006), “Impact of Adolescent Drinking on the Developing Brain” (five projects awarded in FY 2007), and “Alcohol, Puberty and Adolescent Brain Development” (three projects awarded in FY 2007)
- Published Alcohol Research & Health Volume 28, Number 3, “Alcohol and Development in Youth: A Multidisciplinary Overview”
- Published a supplement of seven developmentally focused papers covering a broad range of underage drinking topics (accepted for the journal Pediatrics).

For more information, see http://www.niaaa.nih.gov/AboutNIAAA/NIAAASponsoredPrograms/underage.htm
• This example also appears in Chapter 2: *Life Stages, Human Development, and Rehabilitation*, Chapter 2: *Neuroscience and Disorders of the Nervous System*, and Chapter 3: *Health Communication and Information Campaigns and Clearinghouses*.

• (E) (NIAAA)

**Specialized Centers of Research on Sex and Gender Factors Affecting Women's Health (SCORs):** ORWH led the development and implementation of a second round of SCORs with co-funding from five NIH institutes and FDA. The interdisciplinary nature of these research centers provides innovative approaches to advancing research on the influence of sex and gender as it relates to health and disease. Primary research areas funded include chronic pain, pregnancy, substance abuse, irritable bowel syndrome and interstitial cystitis, mental health, polycystic ovarian syndrome, and urologic health.

• For more information, see [http://orwh.od.nih.gov/interdisciplinary/SCORs.html](http://orwh.od.nih.gov/interdisciplinary/SCORs.html)

• (E) (ORWH, NICHD, NIDA, NIDDK, NIMH, and NIAMS)

**Gene Influences Antidepressant Response:** Whether depressed patients will respond to an antidepressant depends in part on which version of a gene they inherit. Having two copies of one version of a gene that codes for a component of the brain's mood-regulating system increased the odds of a favorable response to an antidepressant by up to 18 percent, compared to having two copies of the other, more common version.


• This example also appears in Chapter 2: *Neuroscience and Disorders of the Nervous System* and Chapter 3: *Genomics*

• (E) (NIMH)

**Genetic Resources/Tools**

**Medical Sequencing:** The completion of the human genome sequence, as well as genomic sequences of numerous other organisms, has already made a substantial impact on both biological and medical research. Public access to the raw data produced from these large-scale sequencing efforts has empowered many additional studies about the genomic contributions to disease. To expedite the transition from research data to medical practice, NIH supports initiatives that both drive technology that will make whole-genome sequencing affordable and produce data useful to biomedical research. Making affordable the sequencing of any individual's complete genome will allow personalized estimates of future disease risk and improve prevention, diagnosis, and treatment of disease. NIH's medical sequencing program is utilizing DNA sequencing to identify the genes responsible for rare, single-gene diseases; sequence all of the genes on the X chromosome to identify the genes involved in sex-linked diseases; and survey the range of variants in genes known to contribute to common diseases.

• For more information, see [http://www.genome.gov/15014882](http://www.genome.gov/15014882)

• This example also appears in Chapter 3: *Genomics*

• (E/I) (NHGRI)

**Population Genomics, GAIN, and GEI:** In February 2006, HHS announced the creation of two related groundbreaking initiatives in which NIH is playing a leading role. The Genetic Association Information Network (GAIN) and the Genes, Environment, and Health Initiative (GEI) will accelerate research on the causes of common diseases. GAIN is a public-private partnership among NIH, the Foundation for NIH, Pfizer, Affymetrix, Perlegen, the Broad Institute, and Abbott. GEI is a trans-NIH effort combining comprehensive genetic analysis and environmental technology development to understand the causes
of common diseases. Both GAIN and GEI are powered by completion of the “HapMap,” a detailed map of the 0.1 percent variation in the spelling of our DNA that is responsible for individual predispositions for health and disease. Data from GAIN will help to narrow the hunt for genes involved in six common diseases. In June 2007, the first GAIN dataset, on attention deficit hyperactivity disorder, was released. GEI will provide data for approximately another 15 disorders and will develop enhanced technologies and tools to measure environmental toxins, dietary intake, and physical activity, as well as an individual's biological response to those influences.

- For more information, see [http://www.genome.gov/19518664](http://www.genome.gov/19518664)
- For more information, see [http://www.genome.gov/19518663](http://www.genome.gov/19518663)
- For more information, see [http://genesandenvironment.nih.gov](http://genesandenvironment.nih.gov)
- For more information, see [http://www.genome.gov/11511175](http://www.genome.gov/11511175)
- This example also appears in Chapter 3: Genomics and Chapter 3: Technology Development.
- (E/I) (NHGRI)

**Multiplex Initiative:** With the completion of the sequence of the human genome, genetic susceptibility tests that give personalized information about risk for a variety of common health conditions are now being developed and marketed. This genetic information ultimately will improve primary care by enabling more personalized treatment decisions for common diseases like diabetes and heart disease. This information also might motivate patients to change unhealthy behaviors. NIH investigators have teamed with the Group Health Cooperative in Seattle and the Henry Ford Health System in Detroit to launch a study to investigate the interest level of healthy young adults in receiving genetic testing for eight common conditions. Called the Multiplex Initiative, the study will also look at how people who decide to have the tests interpret and use the results in making health care decisions. One thousand subjects who meet the study's eligibility requirements will be offered free multiplex genetic testing. The testing is designed to yield information about 15 different genes that play roles in common diseases such as type 2 diabetes and coronary heart disease. Trained research educators will make follow-up telephone calls to help subjects interpret and understand test results, and subjects will receive newsletters to update them on new developments about the tested genes. This research should provide insights into how best to utilize the powerful tools of genomic medicine to improve health.

- For more information, see [http://www.genome.gov/25521052](http://www.genome.gov/25521052)
- This example also appears in Chapter 3: Clinical and Translational Research and Chapter 3: Genomics.
- (E/I) (NHGRI)

**Candidate Gene Association Resource:** Over the years, NHLBI has supported a number of major population studies that have collected extensive data on cardiovascular disease and its risk factors and manifestations. To increase the utility of the data for conducting genetic association studies, NIH initiated the Candidate Gene Association Resource program in FY 2006. This new resource will have the capacity to perform high-throughput genotyping for up to 50,000 subjects in cohort studies that have stored samples and data available on a wide array of characteristics (phenotypes) associated with heart, lung, blood, and sleep disorders. The linked genotype-phenotype data will form an invaluable resource for investigators seeking to identify genetic variants related to those disorders.

- This example also appears in Chapter 3: Disease Registries, Databases, and Biomedical Information Systems and Chapter 3: Genomics.
- (E) (NHLBI)
Enhancing Development of Genome-wide Association Methods (ENDGAME): The ENDGAME consortium, which comprises 11 interactive teams of investigators, has been initiated to explore new approaches for designing and conducting genome-wide association studies (GWAS) of complex diseases. ENDGAME investigators are developing and testing innovative, informative, and cost-effective study designs as well as analytical strategies and tools for performing the studies. All strategies and tools developed will be made available to the scientific community. Results from ENDGAME are expected to greatly enhance the utility of GWAS for increasing understanding about genetic variations and their role in health and disease.

- This example also appears in Chapter 3: Genomics
- (E) (NHLBI, NCI, NHGRI, NIEHS, NIGMS)

Framingham SNP-Health Association Resource (SHARE): The Framingham SHARE is a comprehensive new effort by NIH and the Boston University School of Medicine to pinpoint genes underlying cardiovascular and other chronic diseases. The program builds on the Framingham Heart Study, which was begun in 1948 to identify factors that contribute to cardiovascular disease, and on other NIH-funded research demonstrating that common but minute variations in human DNA, called single nucleotide polymorphisms (SNPs), can be used to identify genetic contributors to common diseases. The initiative will examine more than 500,000 genetic variants in 9,000 study subjects across three generations. NIH will develop a database to make the data available to researchers around the world. The database will help researchers integrate the wealth of information collected over the years in the Framingham study with the new genetic data, resulting in an increased understanding of genetic influences on disease risk, manifestation, and progression. Because of its uniqueness in including three generations of subjects with comparable data obtained from each generation at the same age, the Framingham Heart Study is the first study to be included in the SHARE initiative. NIH is currently considering expansion of SHARE to include other large longitudinal studies, such as the Jackson Heart Study and the new Hispanic Community Health Study.

- For more information, see http://public.nhlbi.nih.gov/newsroom/home/GetPressRelease.aspx?id=2460
- This example also appears in Chapter 3: Epidemiological and Longitudinal Studies and Chapter 3: Genomics.
- (E) (NHLBI, NLM)

Hispanic Community Health Study: In October 2006, NIH began the largest long-term epidemiological study of health and disease ever conducted in people of Latin American heritage living in the United States. The project, which will include about 16,000 subjects, is designed to identify factors that predispose individuals to develop heart disease, stroke, asthma, COPD, sleep disorders, dental disease, hearing loss, diabetes, kidney disease, liver disease, cognitive impairment, and other chronic conditions. Characteristics such as diet, physical activity, obesity, smoking, blood pressure, blood lipids, acculturation, socioeconomic status, psychosocial factors, occupation, health care access, environment, and use of medications and dietary supplements will be assessed.

- For more information, see http://www.nhlbi.nih.gov/new/press/06-10-12.htm
- This example also appears in Chapter 2: Minority Health and Health Disparities and Chapter 3: Epidemiological and Longitudinal Studies.
- (E) (NHLBI, NCMHD, NIDCD, NIDCR, NIDDK, NINDS, ODS)
Treating Chronic Disease and Comorbidities

HBO “Addiction” Documentary: NIH collaborated with Home Box Office (HBO) to create a 90-minute documentary, “Addiction,” which aired on March 15, 2007. An NIH expert in the treatment of alcoholism was one of several principal spokespersons for the documentary and was featured in a supplementary broadcast on treatment advances. Several NIH grantees appeared in the documentary. A general-audience HBO book was produced to accompany the film.

- For more information, see http://www.hbo.com/addiction
- This example also appears in Chapter 3: Health Communication and Information Campaigns and Clearinghouses.
- (E) (NIAAA, NIDA)

Success in Treating Drug Addiction Internationally: International efforts to disseminate effective drug abuse treatments have seen success in countries with epidemic opiate addiction and/or HIV problems. Because of NIH research demonstrating that addiction is a chronic, relapsing disease that can be effectively treated, a culture change is starting to occur in these countries. For example, despite experiencing severe drug problems, Malaysia lagged behind in the treatment of drug addiction and related disorders, even as it coped with having the second-highest HIV prevalence rate among adult populations and the highest proportion of HIV cases from injection drug use. Historically, drug abusers were “rehabilitated” involuntarily in correctional facilities, and although 60 percent of prisoners had drug-related offenses, no or minimal treatment was available in prison and no medications were permitted. This primarily criminal treatment approach had limited effectiveness, which led to widespread public dissatisfaction and the recent introduction of medications for addiction. These include naltrexone (1999), buprenorphine (2001), and methadone (2003). These drug treatment programs, which were rapidly embraced by the country's medical community, have resulted in tens of thousands of opiate-dependent patients receiving medical treatment. Now the Ministry of Health, rather than the Ministry of Security, has authority for providing medical treatment for heroin addiction. This shift signals a remarkable change in Malaysian policies and approaches to addiction and an important opportunity to develop, implement, and disseminate effective treatments. A similar success story is starting to unfold in China as well.

- This example also appears in Chapter 2: Infectious Diseases and Biodefense and Chapter 3: Clinical and Translational Research
- (E) (NIDA, NIAID)

Diabetes Control and Complications Trial (DCCT)/Epidemiology of Diabetes Interventions and Complications (EDIC): The DCCT demonstrated that intensive control of blood glucose levels reduced complications of the eyes, nerves, and kidneys in patients with type 1 diabetes. Long-term findings from the follow-on EDIC study show that intensive control lowers risk of heart disease. This research revolutionized disease management, leading to the recommendation that patients should begin intensive therapy as early as possible. EDIC recently found that recurrent hypoglycemia associated with intensive control does not affect patients' long-term cognitive function. After more than 20 years of studying this patient cohort, crucial insights continue to emerge.

- For more information, see http://www.bsc.gwu.edu/bsc/studies/edic.html
- This example also appears in Chapter 2: Autoimmune Diseases and Chapter 3: Epidemiological and Longitudinal Studies.
- (E) (NIDDK)
Practical Clinical Trials: NIH has completed primary and secondary phases of several practical clinical trials that have examined treatment effectiveness for mental disorders such as schizophrenia, bipolar disorder, and depression. The infrastructure developed for each of these large multisite trials—involving more than 10,000 subjects at more than 200 sites—has forged efficient, effective, and collaborative relationships between scientists and clinicians throughout the country. To capitalize on the national networks established for the trials, NIH will fund infrastructure-only support for the platform of clinical sites and an administrative core. It is anticipated that the platform will serve as a critical foundation for supporting subject enrollment, facilitating communication among trial sites, maintaining up-to-date training in diagnosis and treatment, and providing needed administrative organization.

- For more information, see [http://www.nimh.nih.gov/healthinformation/catie.cfm](http://www.nimh.nih.gov/healthinformation/catie.cfm)
- For more information, see [http://www.nimh.nih.gov/healthinformation/stard.cfm](http://www.nimh.nih.gov/healthinformation/stard.cfm)
- For more information, see [http://www.nimh.nih.gov/healthinformation/stepbd.cfm](http://www.nimh.nih.gov/healthinformation/stepbd.cfm)
- This example also appears in Chapter 2: Neuroscience and Disorders of the Nervous System and Chapter 3: Clinical and Translational Research.
- (E) (NIMH)

Scientific Basis of the Placebo Effect: The placebo effect can be defined as the measurable, observable, or felt changes that occur during, but are not directly attributable to, a specific health intervention. It is a ubiquitous and frequently powerful phenomenon that operates in all forms of medicine, so good clinical research is designed to account for its effects as well as those of the intervention under study. Because of the power of the placebo effect, it is equally important to understand the mechanisms by which it operates and to explore how its benefits might be maximized to enhance the quality and effectiveness of all forms of health care. An ongoing NIH initiative is examining multiple aspects of the placebo effect through interdisciplin ary investigations employing molecular, physiological, biochemical, immunological, genetic, behavioral, and social science approaches. This work is beginning to shed light on many facets of the placebo effect. For example, one recently published study showed that placebo-associated pain relief was correlated with activation of areas of the brain that are associated with pain relief that occurs through both innate mechanisms and with use of opioid narcotics. Other ongoing studies are examining the role and importance of the placebo effect in the relationship between patient and health care provider.

- This example also appears in Chapter 2: Neuroscience and Disorders of the Nervous System and Chapter 3: Clinical and Translational Research.
- (E) (NCCAM)

The Scientific Basis of Acupuncture: Ongoing research on acupuncture includes a substantial portfolio of basic and translational studies employing state-of-the-art neuroimaging technology. This work is beginning to provide powerful scientific insight into the potential neurobiological mechanisms of action by which acupuncture might work. Clinical trials of acupuncture for a number of medical conditions are also under way, including studies examining (1) the potential role of traditional acupuncture as an additive/alternative treatment for the prevention of acute cardiac events in patients with coronary artery disease, (2) whether manual or electro-acupuncture contributes to neurological recovery after spinal cord injury, and 3) the efficacy of acupuncture in relieving post-thoracotomy pain syndrome (severe and persistent aching or burning pain along surgical scars in the chest).

- This example also appears in Chapter 2: Neuroscience and Disorders of the Nervous System and Chapter 3: Clinical and Translational Research.
Gene Therapy for Leber's Congenital Amaurosis (LCA): LCA is a rare, inherited retinal degenerative disease that causes severe vision loss in infancy. Although the disease is currently untreatable, NIH-funded investigators have restored vision in dogs with LCA by using gene therapy to replace defective copies of the retinal gene RPE65. Furthermore, new evidence suggests retinal activity also restores function to the brain's visual center. Investigators have recently begun to translate this promising therapy to patients with LCA.

- This example also appears in Chapter 3: Clinical and Translational Research.
- (E) (NEI)

Multicenter Uveitis Steroid Treatment (MUST) Trial: Uveitis, a disease that causes inflammation in middle layers of the eye, is a major cause of blindness in the United States and often requires systemic, long-term treatment with oral corticosteroids and immunosuppressants. Ideally, a local therapy impacting only the eye is preferable to systemic therapy. This comparative effectiveness trial tests a new intraocular implant therapy in patients with severe uveitis.

- For more information, see http://www.musttrial.org
- This example also appears in Chapter 3: Clinical and Translational Research.
- (E) (NEI)

COPD: Learn More, Breathe Better: Through its new education campaign, “COPD: Learn More, Breathe Better,” NIH is raising public and professional awareness about chronic obstructive pulmonary disease (COPD). Launched in January 2007, the campaign is a cooperative effort, engaging the public, health care providers, health insurers, and researchers in improving COPD diagnosis and treatment. The campaign relies on print and radio public service announcements and printed informational materials intended for distribution to patients with COPD, persons at risk for the disease, health care professionals, and community organizations. Joining NIH in implementing this new campaign by promoting it among their constituencies are more than 20 partners, including the American Academy of Family Physicians, the American Lung Association, the American Thoracic Society, the American College of Chest Physicians, and the U.S. COPD Coalition.

- For more information, see http://www.nhlbi.nih.gov/health/public/lung/copd
- This example also appears in Chapter 3: Health Communication and Information Campaigns and Clearinghouses.
- (E) (NHLBI)

Pediatric Circulatory Support: Options for the circulatory support of pediatric patients younger than age 5 are currently limited to short-term extracorporeal devices, the use of which is often complicated by infection, bleeding, and blood clots. Recognizing the need for additional options, NIH established a program to facilitate the development of new circulatory support systems for infants and children with congenital or acquired cardiovascular diseases. The program supports five research groups developing a variety of devices for different pediatric applications. The common objective for the devices is to provide reliable circulatory support for infants and children while minimizing adverse effects.

- For more information, see http://grants.nih.gov/grants/guide/notice-files/NOT-HL-03-004.html
- This example also appears in Chapter 3: Technology Development.
- (E) (NHLBI)
**Sildenafil for Pulmonary Hypertension in Adult Patients with Sickle Cell Disease:** In 2006, NIH began a new study to evaluate a course of treatment with sildenafil in patients with sickle cell disease who have pulmonary hypertension. A randomized, double-blind, placebo-controlled, Phase II clinical trial is testing the drug's safety and efficacy in improving exercise capacity, symptoms, and measures of circulatory function. The trial involves approximately 180 patients at extramural sites and at the NIH Clinical Center. Because pulmonary hypertension occurs frequently in persons with sickle cell disease and confers a high risk of death, a positive outcome of this trial would represent an important step toward improved patient care.

- For more information, see [http://www.clinicaltrials.gov/ct2/show/NCT00492531?term=sildenafil&rank=7](http://www.clinicaltrials.gov/ct2/show/NCT00492531?term=sildenafil&rank=7)
- This example also appears in Chapter 2: *Minority Health and Health Disparities* and Chapter 3: *Clinical and Translational Research*.
- (E/I) (NHLBI)

**Monitoring Organ Rejection Using MRI:** Organ transplants give patients a new lease on life. However, preventing their immune systems from rejecting the transplanted organ sometimes presents a challenge. Physicians must strike a balance between suppressing the immune system so that it does not reject the organ and maintaining enough immune activity to ward off infections. Tracking how the body accepts the new organ is critical to this process. The current “gold standard” for monitoring organ rejection is tissue biopsy, an invasive procedure in which a physician removes a small sample of the transplanted organ for testing. Biopsy has two drawbacks: patient discomfort (the physician must perform the procedure multiple times) and poor selectivity (biopsy removes tissue from only a limited number of sites and can miss rejection starting elsewhere in the organ). To overcome these limitations, NIH-supported researchers are developing a new method to monitor organ rejection with MRI. They label macrophages (immune cells) with polymer-coated, micron-sized iron oxide particles. These magnetic particles allow the migration of the macrophages to rejection sites in the transplanted organ to be clearly tracked by MRI. At present, this work is being performed on rats, but the investigators are extending it to large animals and humans. If successful, the approach could be used to optimize the administration of immunosuppressant drugs in clinical situations.

- For more information, see [http://www.nibib.nih.gov/HealthEdu/eAdvances/25Sep06](http://www.nibib.nih.gov/HealthEdu/eAdvances/25Sep06)
- This example also appears in Chapter 2: *Autoimmune Diseases* and Chapter 3: *Clinical and Translational Research*.
- (E) (NIBIB)

**Asthma Exacerbations—Biology and Disease Progression:** In FY 2005, NIH began a basic and clinical research initiative to improve understanding of the causes of asthma exacerbations and to facilitate the development of more effective treatments to control symptoms. Twelve projects have been funded under this initiative. As part of NIH GPRA reporting activity, NIH is assessing the progress of the initiative through an ongoing GPRA goal, “to identify and characterize two molecular pathways of potential clinical significance that may serve as the basis for discovering new medications for preventing and treating exacerbations, by 2014.”

- This example also appears in Chapter 3: *Clinical and Translational Research* and Chapter 3: *Molecular Biology and Basic Sciences*.
- (E) (NHLBI, NIAID) (GPRA Goal)
Long-Term Oxygen Treatment Trial (LOTT): Although oxygen therapy is known to benefit patients with COPD who experience severe hypoxemia (low blood oxygen level) when resting, the value of this treatment in patients with less serious disease is not known. In November 2006, NIH and the Centers for Medicare and Medicaid Services launched the LOTT, the largest-ever randomized clinical trial of the effectiveness and safety of long-term, home oxygen therapy for patients with COPD and moderately severe hypoxemia. Results are expected to shed light on the role of oxygen therapy in the management of these patients and to provide a basis for Medicare coverage decisions. The LOTT trial is the focus of a new NIH GPRA goal to be included in GPRA reporting in 2007: “by 2012, assess the efficacy of long-term oxygen treatment in patients with COPD and moderate hypoxemia.”

- For more information, see http://www.jhuacct.com/lott/
- For more information, see http://www.nhlbi.nih.gov/new/press/06-11-20.htm
- This example also appears in Chapter 3: Clinical and Translational Research.
- (E) (NHLBI) (GPRA Goal)

Programs to Accelerate Medication Development for Alcoholism Treatment: Alcoholism is a complex heterogeneous disease caused by the interaction between multiple genetic and environmental factors that differ from one drinker to another. Therefore, a diverse repertoire of medications is needed to provide effective therapy to a broad spectrum of alcohol-dependent individuals. Although promising compounds have been identified, developing medications is a long and costly process with a low probability of success for any single agent. NIH has initiated collaborations with the pharmaceutical industry to ensure their interest in taking promising compounds through the final phase of clinical trials and subsequent FDA consideration. As part of this approach, two new programs have been initiated:

- Laboratories have been established to screen promising compounds with animal models, enabling faster determination of those that merit advancement to large, multisite studies. Animal studies have already produced several targets for human studies that are now under way, such as rimonabant, a cannabinoid CB1 receptor blocker, and antalarmin, a corticotropin-releasing factor receptor blocker.
- A network of sites is being developed to conduct early Phase II proof-of-concept human trials. NIH will encourage the pharmaceutical industry to screen proprietary compounds in the preclinical models and, when results are positive, test them in the early human trials network.

- This example also appears in Chapter 2: Neuroscience and Disorders of the Nervous System and Chapter 3: Clinical and Translational Research.
- (E/I) (NIAAA) (GPRA Goal)

Improving Transplantation Outcomes: Organ transplantation prolongs survival and improves quality of life for children and adults with a wide range of diseases. Yet despite advances in organ transplantation, organ recipients rarely achieve normal life expectancy and health-related quality of life. To improve the outcome of organ transplantation, NIH supports the Clinical Trials in Organ Transplantation (CTOT) initiative, a cooperative, multisite consortium that conducts interventional and observational clinical studies, as well as studies of the mechanisms of graft rejection. The consortium includes 34 clinical sites and 30 immunology laboratories at 13 universities. Five clinical trials are currently enrolling individuals undergoing kidney, heart, liver, or lung transplantation.

- This example also appears in Chapter 3: Clinical and Translational Research.
- (E) (NIAID, NHLBI, NIDDK) (GPRA Goal)

Blending Initiative: Bench to Bedside to Community: Efforts to systematically move science-based interventions and practices into community settings are exemplified in the testing of drug abuse
treatment approaches directly in the community settings where they will be used by drug treatment professionals who are trained to implement them. This work is occurring through the National Drug Abuse Treatment Clinical Trials Network at NIH, which involves practitioners from community treatment programs not only in formulating research protocols, but also in providing real-world feedback on their success and feasibility. The adoption of the addiction medication buprenorphine by a growing number of community treatment programs treating patients with opioid addiction is an example of real culture change issuing from NIH clinical research. A similar approach is under way to enhance treatment for drug-addicted individuals involved with the criminal justice system through research supported under the Criminal Justice-Drug Abuse Treatment Studies (CJ-DATS) initiative. It seeks to achieve better integration of drug abuse treatment for criminal offenders with other public health and public safety forums and is a collaborative effort by NIH and multiple Federal agencies and health and social service professionals. These initiatives are helping to change the culture of how drug abuse treatment is delivered in this country.

- For more information, see [http://www.drugabuse.gov/CTN](http://www.drugabuse.gov/CTN)
- For more information, see [http://www.cjdats.org](http://www.cjdats.org)
- For more information, see [http://www.drugabuse.gov/Blending](http://www.drugabuse.gov/Blending)
- This example also appears in Chapter 2: *Neuroscience and Disorders of the Nervous System*, Chapter 3: *Clinical and Translational Research*, and Chapter 3: *Health Communication and Information Campaigns and Clearinghouses*.
- (E) (NIDA) (GPRA Goal)

**Treatments to Fight Methamphetamine Addiction:** The abuse of methamphetamine—a potent and highly addictive psychostimulant—is a serious problem in the United States. Methamphetamine abuse can have devastating medical, psychological, and social consequences. Adverse health effects include memory loss, aggression, psychotic behavior, heart damage, and abnormal brain function. Methamphetamine abuse also contributes to increased transmission of hepatitis and HIV/AIDS and can spawn increased crime, unemployment, and other social ills. The good news is that methamphetamine abuse and addiction are treatable, and people do recover. As methamphetamine abuse has increased, so has NIH's support of research to combat it, including research on genetics, brain development, and translation of findings. This research has led to the development of two effective behavioral therapies for methamphetamine addiction: (1) the Matrix Model, consisting of a 16-week program that includes group and individual therapy and addresses relapse prevention, behavioral changes, establishment of new drug-free environments, and other issues; and (2) Motivational Incentives for Enhanced Drug Abuse Recovery, a cost-effective incentive method for cocaine and methamphetamine addiction that has been shown to sustain abstinence in twice the number of subjects engaged in treatment as usual. Increasingly, community treatment providers nationwide are implementing motivational incentives as part of drug addiction treatment.

- For more information, see [http://www.drugabuse.gov/ResearchReports/Methamph/Methamph.html](http://www.drugabuse.gov/ResearchReports/Methamph/Methamph.html)
- For more information, see [http://www.drugabuse.gov/Testimony/6-28-06Testimony.html](http://www.drugabuse.gov/Testimony/6-28-06Testimony.html)
- This example also appears in Chapter 2: *Neuroscience and Disorders of the Nervous System* and Chapter 3: *Clinical and Translational Research*.
- (E) (NIDA)

**Nonalcoholic Steatohepatitis (NASH) Clinical Research Network:** NASH is strongly associated with obesity and type 2 diabetes, conditions that have increased dramatically in recent decades. Network research addresses GPRA Goal SRO-4.3. The Network is conducting a randomized clinical trial to
evaluate the safety and efficacy of the insulin-sensitizing drug pioglitazone or vitamin E compared to placebo for the treatment of non-diabetic adults with NASH. Also, in a separate trial in children, the Network is comparing the insulin-sensitizing drug metformin, vitamin E, and placebo in treating nonalcoholic fatty liver disease.

- For more information, see [http://www.jhuucc.com/nash](http://www.jhuucc.com/nash)
- This example also appears in Chapter 2: Life Stages, Human Development, and Rehabilitation
- (E) (NIDDK, NCI, NICHD) (GPRA Goal)

Age-Related Eye Disease Study, Part 2 (AREDS2): Age-related macular degeneration (AMD) is the leading cause of blindness in the elderly in the United States and will be an increasing burden in future years, based on demographics. The original AREDS study, completed in 2005, demonstrated that antioxidant vitamin and mineral supplements reduced the progression to advanced AMD by 25 percent. Building on these landmark findings, AREDS2 is assessing additional supplements (lutein, zeaxanthin, and long-chain omega-3 fatty acids) as a treatment for AMD and cataracts. AREDS2 is also evaluating the effects of eliminating beta-carotene and/or reducing zinc in the original AREDS formulation on AMD progression. AREDS2 investigators will also explore gene-environment interactions in the development of these conditions, cognitive function, and cardiovascular health.

- For more information, see [http://public.drcr.net](http://public.drcr.net)
- This example also appears in Chapter 3: Clinical and Translational Research.
- (E) (NEI)

Diabetic Retinopathy Clinical Research Network (DRCR.net): Diabetes, a leading cause of blindness in working-age adults, causes blood vessels in the retina to leak and can lead to retinal detachment. Laser treatment is effective but is not optimal. DRCR.net is a collaborative, nationwide, public-private network of eye doctors and investigators in 165 clinical sites conducting clinical research of diabetes-induced retinal disorders (diabetic retinopathy and diabetic macular edema) with the aim of evaluating promising new therapies. DRCR.net serves as a model network to provide the infrastructure to facilitate multiple concurrent and consecutive clinical trials of innovative therapies, to rapidly develop and initiate new protocols, and to interact with industry partners while ensuring scientific rigor and high ethical standards.

- For more information, see [http://public.drcr.net](http://public.drcr.net)
- This example also appears in Chapter 3: Clinical and Translational Research.
- (E) (NEI)

Comprehensive Sickle Cell Centers (CSCCs): The CSCCs were established in 1972 in response to a Presidential initiative and a Congressional mandate to support multidisciplinary research to expedite the development and application of new knowledge for improved diagnosis and treatment of sickle cell disease. In addition to basic research, training, and patient services activities, the CSCCs currently support multicenter Phase II trials, neurocognitive and neuroimaging studies, development of a collaborative database, and a study on the epidemiology of priapism (painful, prolonged erection) among patients with sickle cell disease. Ten centers are funded through FY 2007, and the program will be renewed in FY 2008.

- For more information, see [http://www.sicklecell-info.org](http://www.sicklecell-info.org)
- This example also appears in Chapter 2: Minority Health and Health Disparities and Chapter 3: Clinical and Translational Research.
Improving the Lives of Asthmatic Children in the Inner City: The NIH Inner-City Asthma Consortium (ICAC) evaluates the safety and efficacy of promising immune-based therapies to reduce asthma severity and prevent disease onset in inner-city children, who are disproportionately affected by asthma. An ICAC longitudinal birth cohort study involving 500 inner-city children is investigating the immunologic causes of the development of recurrent wheezing, a surrogate marker for asthma in children younger than age 3. The ICAC is also conducting a multicenter trial to evaluate the safety and efficacy of Xolair (omalizumab) in children with moderate to severe allergic asthma whose symptoms are inadequately controlled with inhaled steroids. Finally, researchers are conducting a clinical trial to determine the safety and dosing levels of a potential new allergy immunotherapy for cockroach allergen, which previous ICAC findings showed are a major determinant of asthma severity among inner-city children.

- This example also appears in Chapter 3: Clinical and Translational Research and Chapter 3: Epidemiological and Longitudinal Studies.

Dialysis Access Consortium: Arteriovenous fistulas and grafts are the two most common methods of gaining repeated access to the circulation of patients on hemodialysis. The Dialysis Access Consortium (DAC) is conducting two trials to assess the impact of anticoagulation reagents in preventing early failure in arteriovenous fistulas and grafts. The Arteriovenous Fistula Trial is evaluating the ability of clopidogrel to maintain access patency, while the Arteriovenous Graft Trial is evaluating the ability of aspirin combined with extended-release dipyridamole to maintain access patency.

- For more information, see http://www.niddk.nih.gov/patient/dac/DAC.htm
- This example also appears in Chapter 3: Clinical and Translational Research.

Inflammatory Bowel Disease: Randomized Trial of Rosiglitazone for Ulcerative Colitis: Current treatments for ulcerative colitis, a form of inflammatory bowel disease, are not effective for all patients. NIH-supported scientists demonstrated that rosiglitazone, a medication used to treat type 2 diabetes, reduced inflammation in an animal model of ulcerative colitis. Subsequently, a small clinical study showed that rosiglitazone was effective in controlling ulcerative colitis symptoms. NIH is now supporting a full-scale clinical trial of this potential new therapy for ulcerative colitis.

- For more information, see http://clinicaltrials.gov/show/NCT00065065
- (E) (NIDDK)

Longitudinal Assessment of Bariatric Surgery (LABS): The multicenter, NIH-funded LABS consortium is analyzing the risks and benefits of bariatric surgery as a treatment for extreme obesity in adults. Because bariatric surgery is also sometimes used in clinical practice as a treatment for severely obese adolescents, NIH is also supporting an observational study of teens already scheduled for surgery, Teen-LABS, to collect data to help determine whether it is an appropriate treatment option for extremely obese adolescents.

- For more information, see http://tinyurl.com/399zmt
- For more information, see http://tinyurl.com/yoer3l
- This example also appears in Chapter 2: Life Stages, Human Development, and Rehabilitation and Chapter 3: Clinical and Translational Research.
Polycystic Kidney Disease (PKD): The Consortium for Radiologic Imaging Studies of PKD (CRISP) showed that MRI could accurately track structural changes in the kidneys of people with the more common form of PKD. An extension, CRISP II, will continue to monitor these patients to determine whether these changes in kidney volume predict changes in kidney function. NIH is also conducting two clinical trials of people with the most common form of PKD; one is in patients with early kidney disease and another is in patients with more advanced disease. These two trials are the largest multicenter studies of PKD conducted to date and are collectively termed HALT-PKD. They are testing whether optimum blood pressure management, in combination with medication, will slow the progression of PKD.

- For more information, see [http://tinyurl.com/2qu94j](http://tinyurl.com/2qu94j)
- For more information, see [http://www.pkd.wustl.edu/pkd-tn/](http://www.pkd.wustl.edu/pkd-tn/)
- This example also appears in Chapter 3: Clinical and Translational Research and Chapter 3: Epidemiological and Longitudinal Studies.
- **(E) (NIDDK)**

Stress Incontinence Surgical Treatment Efficacy (SISTER) Trial: The first of several studies to be conducted by the NIDDK-funded Urinary Incontinence Treatment Network, the SISTER trial recently showed that the sling surgical procedure helps more women achieve dryness than the Burch surgical technique. Two years after surgery, 66 percent of women who had the sling procedure and 49 percent who had the Burch were continent.

- This example also appears in Chapter 3: Clinical and Translational Research.
- **(E) (NIDDK)**

Studies of Diabetes in Youth: Previously known as a disease of adults, type 2 diabetes is increasingly being observed in youth. The Treatment Options for Type 2 Diabetes in Youth study is comparing three different treatment strategies for children with the disease. The SEARCH for Diabetes in Youth Study is providing key data on childhood diabetes incidence and prevalence. SEARCH estimated that 1 of every 523 youths had physician-diagnosed diabetes in 2001. While type 2 diabetes is increasing in children over age 10, particularly minorities, type 1 diabetes accounts for most new cases, with an estimated 15,000 youths diagnosed annually.

- For more information, see [http://www.todaystudy.org/index.cgi](http://www.todaystudy.org/index.cgi)
- For more information, see [http://www.searchfordiabetes.org](http://www.searchfordiabetes.org)
- This example also appears in Chapter 3: Clinical and Translational Research, Chapter 3: Epidemiological and Longitudinal Studies, and Chapter 2: Life Stages, Human Development, and Rehabilitation
- **(E) (NIDDK, CDC)**

The Clinical Islet Transplantation Consortium: The purpose of this international consortium is to develop and implement a program of single- and/or multicenter clinical studies, accompanied by mechanistic studies, in islet transplantation with or without accompanying kidney transplantation, for the treatment of type 1 diabetes. Research pursued through this consortium aims to make improvements in the field of islet transplantation and to share the data and results with the broad scientific community.
Translational Research for the Prevention and Control of Diabetes and Obesity: NIH is supporting research projects to explore ways to bring knowledge from successful clinical research into medical practice and community settings. Studies are seeking to develop effective, sustainable, and cost-effective methods to prevent and treat type 1 and type 2 diabetes and obesity in clinical health care practice and other real-world settings. Many of these studies focus on minority populations disproportionately burdened by type 2 diabetes and obesity.

- For more information, see [www.isletstudy.org](http://www.isletstudy.org)
- (E) (NIDDK, NIAID)

Maintenance of Long-Term Behavioral Change: Behavioral factors contribute to the development and outcomes of many chronic diseases. Successful prevention of and treatment for chronic diseases depend, in part, upon the sustained maintenance of behavior change over time. This initiative supports research projects that examine biopsychosocial processes and test interventions designed to achieve long-term health behavior change. Funded projects focus on diet, physical activity, HIV prevention, smoking cessation, drug abstinence, suicide prevention and mammography screening. In addition, a Health Maintenance Consortium (HMC) comprising NIH program staff, research investigators at the individual sites, and representatives from cosponsoring private foundations has been established to explore the opportunities for further collaboration across the studies.

- This example also appears in Chapter 2: Minority Health and Health Disparities and Chapter 3: Clinical and Translational Research.
- (E) (NIDDK)

Patient-Reported Outcomes Measurement Information System (PROMIS): This NIH Roadmap initiative is developing ways to measure symptoms—such as pain, fatigue, physical functioning, social-role participation, and emotional distress—that influence quality of life across numerous chronic diseases.

- For more information, see [http://www.nihpromis.org/default.aspx](http://www.nihpromis.org/default.aspx)
- For more information, see [http://obssr.od.nih.gov/Content/Research/Request_for_Applications_%28RFAs%29/Behavioral+Change+RFA+Outcome.htm](http://obssr.od.nih.gov/Content/Research/Request_for_Applications_%28RFAs%29/Behavioral+Change+RFA+Outcome.htm)
- This example also appears in Chapter 3: Disease Registries, Databases, and Biomedical Information Systems.
- (E) (Roadmap—all ICs participate) (GPRA Goal)

Comprehensive Review of Meditation Research: A recent comprehensive literature review on meditation research included more than 800 studies of a variety of forms of meditation for a number of chronic conditions, including hypertension, coronary artery disease, and substance abuse. The review concludes that there are promising indications that meditation may have beneficial effects on a variety of outcomes, including blood pressure, perceived stress, anxiety, and behavioral modification, but additional and higher-quality research is needed.

- For more information, see [http://www.ahrq.gov/clinic/tp/medittp.htm](http://www.ahrq.gov/clinic/tp/medittp.htm)
Mind-Body Medicine: NIH supports a substantial portfolio of multidisciplinary clinical, translational, and basic research on mind-body interventions, such as meditation and Tai Chi Chuan. This effort is based on (1) promising findings from preliminary controlled clinical investigations and (2) laboratory evidence suggesting that these interventions often involve or invoke well-known biological mechanisms that are known to play key roles in the cause of and recovery from illness and in the preservation of health and wellness. For example:

- Investigators recently demonstrated that patients who practiced Tai Chi Chuan, a form of moving meditation based on traditional Chinese medicine, experienced significant augmentation in levels of immunity to the virus that causes shingles after vaccination against the virus.
- Other investigators have demonstrated that patients with chronic heart failure show improvements in quality of life, exercise ability, and biomarkers of cardiac health when Tai Chi Chuan is added to conventional medical care.

Research on Popular Dietary Supplements: A significant body of research on CAM practices focuses on documenting the safety and efficacy of various widely used dietary supplements. Important recently reported findings include the following:

- The combination of glucosamine plus chondroitin sulfate did not provide significant relief of pain from osteoarthritis of the knee in the overall study population, although a subset of the study subjects with moderate-to-severe pain showed significant relief with the combined supplements.
- The dietary supplement alpha-tocopherol (a form of vitamin E), administered at a high dosage of 1,200 IU/day for 2 years, had no effect on serum concentrations of total, low-density lipoprotein, or high-density lipoprotein cholesterol.

Losartan Offers Promise for the Treatment of Marfan Syndrome: New research offers hope that losartan, a drug commonly prescribed to treat hypertension, might also be used to treat Marfan syndrome, a genetic disorder that often causes life-threatening aortic aneurysms. After discovering that Marfan syndrome is associated with a mutation in the gene encoding fibrillin-1, researchers tried for many years, without success, to develop treatment strategies that involved repair or replacement of fibrillin-1. A major breakthrough occurred when NIH-funded researchers discovered that one of the functions of fibrillin-1 is to bind to another protein, TGF-beta, and regulate its effects. After careful analyses revealed aberrant TGF-beta activity in patients with Marfan syndrome, researchers began to concentrate on treating the disease by normalizing the activity of TGF-beta. Losartan, which is known to affect TGF-beta activity, was tested in a mouse model of Marfan syndrome. The results showed that the
The drug blocked the development of aortic aneurysms as well as lung defects associated with the disease. Based on the promising results, the NHLBI Pediatric Heart Network, in partnership with the National Marfan Foundation, began a clinical trial in 2007 to assess losartan therapy in patients with Marfan syndrome.

- For more information, see [http://clinicaltrials.gov/show/NCT00429364](http://clinicaltrials.gov/show/NCT00429364)
- For more information, see [http://www.pediatricheartnetwork.org](http://www.pediatricheartnetwork.org)
- This example also appears in Chapter 3: *Clinical and Translational Research* and Chapter 3: *Molecular Biology and Basic Sciences.*
- (E) (NHLBI)

**Acute Liver Failure Study Groups:** The adult and pediatric Acute Liver Failure Study Groups address the problem of acute liver failure due to drugs or other factors. The groups' research has provided knowledge and tools for managing the clinical and public health burden of acute liver failure. In 2002, the adult Study Group highlighted a dramatic increase in liver injury due to the over-the-counter pain reliever acetaminophen. The groups then developed a serum-based assay to detect acetaminophen-induced acute liver failure in adults and children. Current studies are testing potential therapies to improve survival in patients with acute liver failure.

- For more information, see [http://tinyurl.com/2qu94j](http://tinyurl.com/2qu94j)
- This example also appears in Chapter 2: *Life Stages, Human Development, and Rehabilitation.*
- (E) (NIDDK, FDA)

**Hepatitis C Antiviral Long-Term Treatment Against Cirrhosis (HALT-C) Trial:** The HALT-C trial studies whether long-term antiviral therapy can prevent the progression of liver disease in people with hepatitis C who do not respond to standard, short-term therapy. The trial has advanced understanding of the impact of disease severity and antiviral drug dose on response to long-term therapy and yielded a new tool to monitor treatment response. These advances can help health care providers to determine which patients are unlikely to respond to long-term antiviral therapy, so that those patients can be spared from ineffective treatment and its side effects.

- Morishima C et al. *Hepatology* 2006;44:360-7, PMID: 17241864
- For more information, see [http://www.haltctrrial.org](http://www.haltctrrial.org)
- This example also appears in Chapter 3: *Clinical and Translational Research.*
- (E) (NIDDK, NCI, NIAID)

**Multidisciplinary CAM Research:** Investigators are utilizing increasingly sophisticated, multidisciplinary, bedside-to-bench and bench-to-bedside approaches to elucidate the efficacy, safety, and mechanisms of action of a wide variety of CAM practices. Ongoing research encompasses virtually all organ systems and medical and scientific disciplines, as well as numerous CAM modalities and practices spanning the four major CAM domains (biologically based practices, manipulative and body-based practices, energy medicine, and mind-body medicine), as well as the alternative whole medical systems of which they are a part. Guided by its 5-Year Strategic Plan, recommendations of the National Advisory Council for Complementary and Alternative Medicine, the plans of other ICs, and input from expert panels and various stakeholders, NCCAM establishes priorities to fill gaps in the CAM research portfolio, capitalize on emerging opportunities, and leverage resources.

- For more information, see [http://nccam.nih.gov/about/plans/2005/strategicplan.pdf](http://nccam.nih.gov/about/plans/2005/strategicplan.pdf)
- For more information, see [http://nccam.nih.gov/research/priorities/index.htm#5](http://nccam.nih.gov/research/priorities/index.htm#5)
Advancing Novel Science in Women's Health Research (ANSWHR): In FY 2007, NIH published two Program Announcements for a new grants program called Advancing Novel Science in Women's Health Research (ANSWHR). Both announcements are intended to promote innovative, interdisciplinary research that will advance new concepts in women's health research and the study of sex and gender differences.

- (E) (ORWH, NCI, NEI, NHLBI, NHGRI, NIA, NIAAA, NIAID, NIBIB, NICHD, NIDCD, NIDCR, NIDA, NIEHS, NIGMS, NIMH, NINDS, NINR, NLM, FIC, NCCAM, OBSSR, and ODS)

Research Enhancement Awards Program (REAP): NIH successfully implemented a trans-NIH Research Enhancement Awards Program (REAP) in both FY 2006 and FY 2007 by awarding a total of more than $6.8 million dollars. Sixteen grants were awarded in each fiscal year. This program is directed at meritorious grants that have just missed the IC pay line that will advance research on women's health and/or the study of sex and gender factors. Scientific areas covered by these grants include diabetes, fibromyalgia, genetic studies of ovarian failure, health disparities, heart failure evaluation in postmenopausal women, HIV/AIDS, interstitial cystitis, lupus, neuroendocrine development, pain control, rheumatoid arthritis, smoking in pregnancy, substance abuse, and breast cancer and CAM.

- (E) (ORWH)

Trans-NIH Chronic Fatigue Syndrome Research: NIH coordinates chronic fatigue syndrome research through the trans-NIH Working Group on Research on Chronic Fatigue. This working group developed an action plan to enhance the status of chronic fatigue syndrome research at NIH and among the external and intramural scientific communities. The working group held a workshop on grantsmanship in FY 2007 to provide researchers with an overview of funding opportunities, an understanding of the NIH funding process, and an opportunity to meet with program officials. In addition, the Office of Research on Women's Health and a subset of the working group ICs issued an RFA in FY 2006 to explicate how the brain, as the mediator of the various body systems involved, fits into the schema for understanding chronic fatigue syndrome. This RFA solicited proposals from multidisciplinary teams of scientists to develop an interdisciplinary approach to the study of chronic fatigue syndrome in men and women across the lifespan and resulted in seven new research projects on chronic fatigue syndrome.

- For more information, see [http://orwh.od.nih.gov/cfs.html](http://orwh.od.nih.gov/cfs.html)
- For more information, see [http://orwh.od.nih.gov/cfs/2006NIfundedCFSstudies.html](http://orwh.od.nih.gov/cfs/2006NIfundedCFSstudies.html)
- For more information, see [http://orwh.od.nih.gov/cfs/cfsFundingGMWs.html](http://orwh.od.nih.gov/cfs/cfsFundingGMWs.html)
- This example also appears in Chapter 2: Neuroscience and Disorders of the Nervous System.
- (E) (ORWH, NIAID, NIAMS, NIAAA, NIA, NICHD, NIDA, NIDDK, NINDS, NCRR, CSR, NIEHS, NIDCR, NINR, NHLBI, NIMH, NCCAM, FIC, ODS, OBSSR)

Research to Strengthen the Dissemination and Implementation of Evidence-Based Mental Health Interventions: NIH continues to support research designed to strengthen the dissemination and implementation of evidence-based mental health practices. NIH released a Program Announcement to encourage transdisciplinary teams of scientists and practice stakeholders to work together to develop innovative approaches for identifying and overcoming barriers to the adoption of evidence-based
interventions. This Program Announcement also serves as the basis for a GPRA Goal. NIH also supports research designed to enhance implementation by providing evidence of intervention benefits not just to the individual, but to a broader system as well. For example, a recent study reported that providing a minimal level of enhanced care for employees' depression would result in significant savings to employers.

- Wang PS et al, Arch Gen Psychiatry 2006;63:1345-53, PMID: 17146009
- For more information, see http://grants.nih.gov/grants/guide/pa-files/PAR-07-086.html
- For more information, see http://www.nimh.nih.gov/press/cost-benefitsimulation.cfm
- This example also appears in Chapter 3: Clinical and Translational Research.
- (I/E) (NIH, NCI, NIDA, NIDCD, NINR, NIAAA, NIDCR, NIDDK, NICHD) (GPRA)

**Addressing Pain and Palliative Care in Chronic Diseases**

**Improving End-of-Life Care: Special Supplement to the Journal of Palliative Medicine:** In FY 2005, NIH sponsored the State-of-the-Science Conference on Improving End-of-Life Care. This conference addressed the current state of end-of-life care and proposed important new directions for end-of-life research. Key conclusions to emerge from the conference included: the rapid increase in older adults facing the need for end-of-life care requires the development of research infrastructure to better examine end-of-life issues; enhanced communication between patients, families, and providers is crucial to end-of-life care; and improved outcome measures are needed to better conduct end-of-life research. In FY 2006, a special issue of the Journal of Palliative Medicine presented a series of papers developed from this workshop on a wide variety of topics. The supplement includes articles on measuring end-of-life care outcomes; analyzing racial, cultural, and ethnic factors that influence end-of-life care; improving care for dying children and their families; and examining factors in the health care system that influence end-of-life care.

- Grady PA, J Palliat Med 2005;8:S1-3, PMID: 16499457
- For more information, see http://www.liebertonline.com/toc/jpm/8/supplement+1
- This example also appears in Chapter 2: Life Stages, Human Development, and Rehabilitation.
- (E) (NINR)

**Promising Approaches to Treating Chronic Pain:** Opioid analgesics are the most powerful pain medications currently available; unfortunately, they can produce drug dependence. Thus, an area of enormous need is the development of potent non-opioid analgesics, for which NIH has implemented an aggressive and multidisciplinary research program. Many of these initiatives are yielding tangible results that stand to revolutionize the field of pain management. At the molecular level, cannabinoid research has shown that it is possible to selectively activate the cannabinoid system to provide analgesia with minimal or no psychotropic side effects or abuse liability. New findings in basic pharmacology reveal previously unrecognized complexity emerging from the natural mixing of different receptors, the targeting of which could provide a vastly expanded range of pharmacotherapeutic effects. This approach has already ushered in the development of promising designer molecules that can block pain more selectively and safely. At the cellular level, active research on a non-neuronal brain cell type, glia, has led to the realization that glia activation can amplify pain. This discovery suggests that targeting glia and their pro-inflammatory products may provide a novel and effective therapy for controlling clinical pain syndromes and increasing the utility of analgesic drugs. At the brain circuit level, a new approach has been developed to harness the brain's intrinsic capacity to train itself through a strategy in which subjects “learn” how to regulate pain by viewing and then controlling images of their own brains in real time.
- For more information, see [http://www.nida.nih.gov/whatsnew/meetings/painopioides](http://www.nida.nih.gov/whatsnew/meetings/painopioides)
- This example also appears in Chapter 2: Neuroscience and Disorders of the Nervous System and Chapter 3: Molecular Biology and Basic Sciences.
- (E) [NIDA, NINDS]

**Resources for Enhancing Alzheimer's Caregiver Health II (REACH II):** Family members and friends who care for people with dementia face a variety of challenges that can seriously compromise their own well-being. Investigators have found that a personalized intervention consisting of home visits, structured telephone support sessions, and telephone “check-ins” can significantly improve the quality of life for caregivers of Alzheimer's disease patients. The study is the first randomized, controlled trial to look at the effectiveness of an Alzheimer’s disease caregiver support intervention for ethnically diverse populations. Follow-up studies are needed to examine how this intervention might be used through existing community health service networks.
- For more information, see [http://www.nia.nih.gov/NewsAndEvents/PressReleases/PR20061120caregiverQOL.htm](http://www.nia.nih.gov/NewsAndEvents/PressReleases/PR20061120caregiverQOL.htm)
- (E) [NIA, NINR]

**NIH Pain Consortium:** The aims of the NIH Pain Consortium are to enhance pain research and promote collaboration among researchers across the many NIH Institutes and Centers that have programs and activities addressing pain. The consortium held its second annual symposium, Advances in Pain Research, on May 1, 2007, to feature new and exciting advances in pain research and pain management. Topics included neuropathic pain, visceral pain, inflammatory pain, and treatment-induced pain. Topics included NIH and extramural scientific communities, health care providers, and the public. Consortium ICs also issued an NIH-wide Funding Opportunity Announcement, “Mechanisms, Models, Measurement, and Management in Pain Research,” to encourage pain research and delineate cross-cutting NIH interests in pain.
- For more information, see [http://videocast.nih.gov/PastEvents.asp](http://videocast.nih.gov/PastEvents.asp)
- For more information, see [http://painconsortium.nih.gov/index.html](http://painconsortium.nih.gov/index.html)
- This example also appears in Chapter 2: Neuroscience and Disorders of the Nervous System
- (E/I) [NIDCR, CC, FIC, NCCAM, NCI, NCRR, NIA, NIAAA, NIAMS, NIBIB, NICHD, NIDA, NIDCD, NIGMS, NIMH, NINDS, NINR, OBSSR, OD, ODP/ORD, ORWH, OTT]

**Behavioral Strategies to Improve Quality of Life and Chronic Disease Outcomes:** As health care advances continue to transform previously acute conditions into chronic conditions and individual life expectancy is increasing, issues of quality of life have become ever more important. Studies focusing on the management of disease- and treatment-related symptoms have demonstrated the capacity for behavioral strategies to mitigate the effects of symptoms and contribute to improving short- and long-term patient outcomes. For example, behavioral strategies have been shown to improve patient outcomes across various diseases, including diabetes, irritable bowel syndrome, and asthma. In recognition of the need for new behavioral strategies to manage chronic illness, NIH has established a goal to develop and test, by 2012, at least two behavioral strategies for the management of symptoms to reduce the effects of disease, disability, or psychological distress on quality of life and outcomes. Beginning in FY 2008, progress toward achieving this goal will be updated annually in the NIH section of the President's budget submission in a report on NIH GPRA responsibilities.
- For more information, see [http://officeofbudget.od.nih.gov/ui/HomePage.htm](http://officeofbudget.od.nih.gov/ui/HomePage.htm)
- (E) [NINR, NCI] (GPRA Goal)
Acupuncture for Osteoarthritis of the Knee: Clinical trials supported by NIH and others suggest that acupuncture may have a useful role in treating a variety of chronic painful conditions, hypertension, and obesity. For example, in 2006 NIH-funded investigators reported findings from the longest, largest, randomized, controlled clinical trial of acupuncture ever conducted. The results demonstrated that acupuncture is an effective adjunct to conventional treatment for osteoarthritis, the most common form of arthritis and a major cause of pain, limitation of activity, and health care utilization among the elderly. Study subjects receiving acupuncture had significantly reduced disability and improved quality of life. The innovative trial design resulted from an interdisciplinary collaboration of rheumatologists, licensed acupuncturists, and biostatisticians, ensuring that the research methodology was scientifically sound and accurately reflected acupuncture as traditionally practiced.

- This example also appears in Chapter 2: *Neuroscience and Disorders of the Nervous System* and Chapter 3: *Clinical and Translational Research*.

Orofacial Pain: Prospective Evaluation and Risk Assessment (OPPERA): This 5-year clinical study’s longitudinal design will greatly accelerate the identification of better treatments to control the pain of temporomandibular muscle and joint disorders. The OPPERA study marks one of the first prospective clinical studies of a chronic pain disorder. A prospective study is the “gold standard” of medical research: it looks forward in time, monitoring the health of those in the study over several years to track the onset or progression of a disease. With the study’s 5-year vantage point, investigators will begin identifying individual genetic, physiologic, and psychological factors that cause or contribute to temporomandibular muscle and joint disorders and advance virtually all aspects of understanding and caring for these disorders.

- For more information, see [see](http://www.nidcr.nih.gov/Research/ResearchResults/InterviewsOHR/TIS012006.htm)
- This example also appears in Chapter 3: *Clinical and Translational Research* and Chapter 3: *Epidemiological and Longitudinal Studies*
- (E) (NIDCR)

Spine Patient Outcomes Research Trial (SPORT): Before SPORT, many patients with back pain were conflicted about whether to undergo surgery. Now, people who have back pain due to a herniated disc can be assured that a surgical procedure called lumbar diskectomy is generally effective in relieving pain from herniated discs, but, if their pain is tolerable, their symptoms will probably subside, even without surgery, over time. On the other hand, if a patient has spondylolisthesis with stenosis, they are likely to benefit more from decompression and fusion surgery than from nonoperative treatments.

- This example also appears in Chapter 3: *Clinical and Translational Research*. 
NIH Strategic Plans Pertaining to Chronic Diseases and Organ Systems

National Heart Lung and Blood Institute (NHLBI)
- NHLBI Strategic Plan: Shaping the Future of Research

National Cancer Institute (NCI)
- NCI Strategic Plan for Leading the Nation

National Institute of Dental and Craniofacial Research (NIDCR)
- NIDCR Strategic Plan

National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK)

Strategic Plans:
- National Diabetes Education Program (NDEP) Strategic Plan
- Overcoming Bladder Disease—a Strategic Plan for Research
- Renal Disease Research Plan
- Strategic Plan for Polycystic Kidney Disease
- Strategic Plan of the National Kidney Disease Education Program (NKDEP)
- Strategic Plan for Pediatric Urology: The Strategic Plan for Pediatric Urology, NIDDK—Research Progress Report

Reports from Planning Activities:
- Clinical Research on Kidney Disease
- NIDDK Annual Compendium of Recent Advances and Emerging Opportunities
- Progress Report on NIDDK Efforts to Promote Translational Research
- Research Needs in Pediatric Kidney Disease—2000 and Beyond
- Strategic Planning for Polycystic Kidney Disease
- Urolithiasis Research Symposium
- Long-Range Research Plan for Digestive Diseases (expected to be completed in 2008)

National Institute of Allergy and Infectious Diseases (NIAID)
- Vaccine Research Center Strategic Plan: Research Toward Development of an Effective AIDS Vaccine (2001)

National Eye Institute (NEI)
• "Progress in Eye and Vision Research 1999-2006"
• "Ocular Epidemiology Strategic Planning Panel Report—Epidemiological Research: From Populations Through Interventions to Translation (2007)"
• "Age-Related Macular Degeneration Phenotype Consensus Meeting Report"
• "Pathophysiology of Ganglion Cell Death and Optic Nerve Degeneration Workshop Report"

National Institute on Aging (NIA)
• "Living Long and Well in the 21st Century: Strategic Directions for Research on Aging"

National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS)
• "NIAMS Long-Range Plan: Fiscal Years 2006-2009"

National Institute of Mental Health (NIMH)
• "NIMH Strategic Plans and Priorities"
• "Breaking Ground, Breaking Through: The Strategic Plan for Mood Disorders Research"
• "Pathways to Health: Charting the Science of Brain, Mind, and Behavior"

National Institute on Drug Abuse (NIDA)
• "NIDA Draft Strategic Plan"

National Institute on Alcohol Abuse and Alcoholism (NIAAA)
• "National Institute on Alcohol Abuse and Alcoholism Five Year Strategic PlanFY08-13"

Recommendations of the NIAAA Extramural Advisory Board (EAB):
• "Developing an NIAAA Plan for HIV-Related Biomedical Research"
• "Fetal Alcohol Spectrum Disorders Research"
• "Mechanisms of Alcohol Addiction"
• "Mechanisms of Behavioral Change"

National Institute of Nursing Research (NINR)
• "NINR Strategic Plan: Changing Practice, Changing Lives"

National Center for Complementary and Alternative Medicine (NCCAM)
• "Expanding Horizons of Health Care: Strategic Plan 2005-2009"

John E. Fogarty International Center (FIC)
• "Pathways to Global Health Research (Draft)"

Office of AIDS Research (OAR)
• "FY 2008 Trans-NIH Plan for HIV-Related Research"

Office of Dietary Supplements (ODS)

Trans-NIH Strategic Plans
## Detailed Burden of Illness and Related Health Statistics

The following summary illustrates the depth and breadth of chronic disease burden (all statistics refer to the U.S. population unless otherwise specified):

<table>
<thead>
<tr>
<th>Cardiovascular Diseases</th>
<th><strong>Coronary heart disease</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mortality: 452,000 (2004)</td>
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<tr>
<td></td>
<td>Prevalence: 15.8 million (2004)</td>
</tr>
<tr>
<td><strong>Heart failure</strong></td>
<td>Mortality: 58,000 (2004)</td>
</tr>
<tr>
<td></td>
<td>Prevalence: 5.2 million (2004)</td>
</tr>
<tr>
<td><strong>Arrhythmias</strong></td>
<td>Prevalence: &gt; 2 million with atrial fibrillation</td>
</tr>
<tr>
<td></td>
<td><strong>Congenital heart defects</strong></td>
</tr>
<tr>
<td></td>
<td>Incidence: 8 of every 1,000 newborns (35,000 per year)</td>
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<tr>
<td></td>
<td>Prevalence: 1 million adults</td>
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<tr>
<td></td>
<td><strong>Peripheral arterial disease</strong></td>
</tr>
<tr>
<td></td>
<td>Prevalence: 8-12 million</td>
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<table>
<thead>
<tr>
<th>Lung Diseases</th>
<th><strong>Chronic obstructive pulmonary disease</strong></th>
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</thead>
<tbody>
<tr>
<td></td>
<td>Mortality: 120,000 (2004)</td>
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<tr>
<td></td>
<td>Prevalence: 12 million people diagnosed; additional 12 million undiagnosed (2004)</td>
</tr>
<tr>
<td><strong>Asthma</strong></td>
<td>Mortality: 4,000 (2004)</td>
</tr>
<tr>
<td></td>
<td>Total costs (direct and indirect): $12.7 billion (1998)</td>
</tr>
<tr>
<td><strong>Cystic Fibrosis</strong></td>
<td>Prevalence: 30,000</td>
</tr>
<tr>
<td></td>
<td>Incidence: 1 in every 3,000 newborns</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Diabetes Mellitus</th>
<th>Mortality: 224,092 (2002); 6th leading cause of death</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Prevalence: 20.8 million (diagnosed and undiagnosed); type 1 diabetes accounts for 5-10% of diagnosed cases (2005)</td>
</tr>
<tr>
<td></td>
<td>Total costs (direct and indirect): $132 billion (2002)</td>
</tr>
<tr>
<td>Condition</td>
<td>Prevalence/Prevalence Details</td>
</tr>
<tr>
<td>-------------------------</td>
<td>-----------------------------------------------------------------------------------------------</td>
</tr>
<tr>
<td><strong>Obesity</strong></td>
<td>Prevalence: 34.1 percent of adults are overweight; 32.2% adults are obese; 18.8% children (aged 6-11) and 17.4% adolescents (aged 12-19) are overweight (2004)</td>
</tr>
<tr>
<td></td>
<td>Cost (direct): $1.1 billion (2000)</td>
</tr>
<tr>
<td></td>
<td><em>Painful bladder syndrome/interstitial cystitis</em> Prevalence: 0.8% of women (1.2 million) and 0.1% of men (0.08 million) (1988-1994)</td>
</tr>
<tr>
<td></td>
<td>Cost (direct): $65.9 million (2000)</td>
</tr>
<tr>
<td></td>
<td><em>Kidney stones</em> Prevalence: 5% of adults (1988-1994)</td>
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<td></td>
<td>Cost: $2.07 billion (2000)</td>
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<td></td>
<td><em>Urinary incontinence</em> Prevalence: 38% of women and 17% of men, aged 60 and older (1999-2000)</td>
</tr>
<tr>
<td></td>
<td>Cost (direct): $463.1 million</td>
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<td></td>
<td><em>Urinary tract infection</em> Prevalence: 34% of adults (62.7 million) self-reported at least one occurrence (1988-1994)</td>
</tr>
<tr>
<td></td>
<td>Cost (direct): $3.5 billion (2000)</td>
</tr>
<tr>
<td><strong>Digestive Diseases</strong></td>
<td>Mortality: 234,000 (2002)</td>
</tr>
<tr>
<td></td>
<td>Disability: 1.9 million people unable to perform daily activities (1990-1992)</td>
</tr>
<tr>
<td></td>
<td>Costs: $85.5 billion (direct); $20 billion (indirect) (1998)</td>
</tr>
<tr>
<td><strong>Chronic Liver Disease</strong></td>
<td>Chronic liver disease or cirrhosis Mortality: 27,013; 12th leading cause of death (2004)</td>
</tr>
<tr>
<td></td>
<td>Prevalence: 5.5 million people (2-3% of adults) (1998)</td>
</tr>
<tr>
<td></td>
<td>Cost (direct and indirect): $1.6 billion (1998)</td>
</tr>
<tr>
<td></td>
<td>Prevalence: 12% of adults (20 million) (1998)</td>
</tr>
<tr>
<td></td>
<td>Cost: $6 billion (1998)</td>
</tr>
<tr>
<td></td>
<td>Viral hepatitis Mortality: 5,000 (Hepatitis B); 8,000-10,000 (Hepatitis C)</td>
</tr>
<tr>
<td></td>
<td>Prevalence: 1.25 million (Hepatitis B); 3.2 million (Hepatitis C) with chronic infection (1999-2002)</td>
</tr>
</tbody>
</table>
| **Blood Diseases** | **Sickle cell disease**  
Prevalence: 70,000; 1 in 500 African American births; 1 in 1,000-1,400 Hispanic-American births  
*Thalassemia* (includes Cooley's anemia)  
Prevalence: 1,000  
*Hemophilia*  
Prevalence: 18,000  
Incidence: 400 newborns each year |
| **Musculoskeletal Diseases** | **Osteoarthritis**  
Prevalence: 12.1% of adults (21 million)  
*Osteoporosis*  
Prevalence: 10 million adults, 80% of whom are women; 34 million have low bone mass  
Disability: >1.5 million fractures  
Costs (direct): $14 billion  
*Osteogenesis Imperfecta*  
Prevalence: 20,000-50,000  
*Paget's disease of bone*  
Prevalence: 1 million |
| **Skin Diseases and Conditions** | Prevalence: At any given time, 1 in 3 people has a skin disease.  
Total health care costs: >$34.3 billion (2003)  
*Atopic dermatitis*  
Prevalence: >15 million  
Costs (to health insurance companies): >$1 billion |
| **Eye Diseases** | **Age-related macular degeneration**  
Prevalence: 1.75 million; leading cause of vision loss in persons age 65 or older (2004)  
*Uveitis*  
Prevalence: 115.3 cases per 100,000 persons (2004)  
Disability: 30,000 new cases of blindness (1990)  
*Diabetic retinopathy*  
Prevalence: 4.1 million adults aged 40 or older (2004)  
*Glaucoma*  
Prevalence: 2.2 million |
| **Deafness** | **Hearing loss**  
Prevalence: 2-3 of 1,000 newborns; 15% (32.5 million) adults; 10% (22 million) adults aged 20-69 suffer hearing damage due to noise exposure |
<table>
<thead>
<tr>
<th>Category</th>
<th>Condition</th>
<th>Prevalence/Description</th>
<th>Cost</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Otitis media</td>
<td>(middle ear infection)</td>
<td></td>
<td>$5 billion</td>
<td></td>
</tr>
<tr>
<td>Balance and dizziness</td>
<td></td>
<td>Prevalence (balance): 4% (8 million)</td>
<td></td>
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<tr>
<td></td>
<td>Prevalence (dizziness): 1.1% (2.4 million)</td>
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<tr>
<td></td>
<td>Cost: $8 billion for falls by older adults</td>
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<tr>
<td>Dental and Craniofacial Disorders</td>
<td><strong>TMJ disorder</strong></td>
<td>Prevalence: 5-12% of the population; twice as prevalent in women as men</td>
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<td></td>
</tr>
<tr>
<td></td>
<td><strong>Chronic periodontitis</strong></td>
<td>Prevalence: 80% of adults with 1 in 5 having severe periodontitis</td>
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<td></td>
<td><strong>Mental disorders</strong></td>
<td>Prevalence: 6% of adults (approximately 12.5 million) have a serious</td>
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<tr>
<td>Mental Illness</td>
<td><strong>Mental disorder</strong></td>
<td>Disability: No. 1 leading cause; accounts for 29.6% of all disability adjusted life years (DALYs) (U.S. and Canada)</td>
<td>$63 billion lost to decreased productivity</td>
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<td></td>
<td><strong>Depression</strong></td>
<td>Prevalence: 2% of adults (approximately 4.4 million) have a serious depressive disorder</td>
<td>Disability: leading cause among mental health disorders; accounts for 11.2% of all DALYs (U.S. and Canada)</td>
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<td></td>
<td>Cost: $36.2 billion due to lost work; $51.5 billion including lost productivity while at work</td>
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<tr>
<td>Alcohol Use Disorders</td>
<td><strong>Alcohol use disorders</strong></td>
<td>Prevalence: 18 million (8.5% of the population aged 18 or older)</td>
<td>$122 billion (est.)</td>
<td>Alcohol use is the 7th leading cause of DALYs</td>
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<td></td>
<td><strong>Alcohol-attributable chronic disease</strong></td>
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<tr>
<td>Alcohol Use Disorders</td>
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<tr>
<td>Addiction</td>
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<td></td>
<td>&gt;$500 billion (est.; includes health- and crime-related costs as well as losses in productivity)-approximately $181 billion for illicit drugs, $168 billion for tobacco, and $185 billion for alcohol.</td>
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<tr>
<td></td>
<td><strong>Abuse or dependence on alcohol and illicit drugs</strong></td>
<td>Prevalence: 22.2 million people or 9.1% of the population aged 12 or older (est.) (2005)</td>
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<td><strong>Cigarette smoking</strong></td>
<td>Mortality: 440,000 (2002)</td>
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</tr>
</tbody>
</table>

56 A composite.