

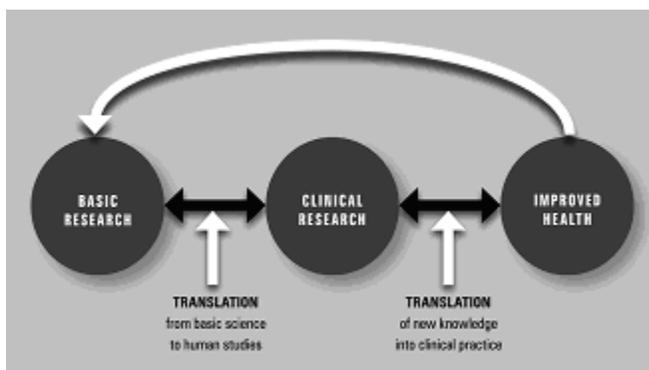
# Summary of Research Activities by Key Approach and Resource

## Clinical and Translational Research

*Decades ago, population studies established that, while most human papillomavirus (HPV) infections clear up on their own, virtually all cases of cervical cancer were caused by HPV infection. National Cancer Institute (NCI) scientists Douglas Lowy, M.D., and John Schiller, Ph.D., saw this discovery as an opportunity to develop a vaccine to prevent cervical cancer. The NCI researchers used genetic engineering technology to isolate a single HPV protein and create virus-like spheres that were able to trigger an antibody response capable of protecting the body from the targeted types of HPV. After subsequent development and clinical trials, the unprecedented result is two FDA-approved vaccines that block infection by the major cervical cancer causing types of HPV. These vaccines have the potential to save thousands of women's lives annually in the United States and several hundred thousand more each year worldwide.*

### Introduction

Delivering new and effective treatments and disease prevention approaches to improve health depends on a research continuum that translates basic biomedical research findings into clinical practice and health care decision-making as rapidly as possible (Figure 1) (see also the section on Molecular Biology and Basic Sciences in Chapter 3). In this report, clinical and translational research are considered together because the two areas overlap, with translational efforts often focusing on overcoming barriers that impede the progress of clinical research.



**Clinical research** encompasses human subjects research (studies that involve direct interaction between investigators and human subjects or use of material of human origin, such as tissues, specimens, and data that retain information that would allow the investigator to readily ascertain the identity of the subject), epidemiologic (see section on Epidemiological and Longitudinal Studies in Chapter 3) and behavioral studies, and outcomes and health services research. Examples of clinical research include studies of mechanisms of human disease, clinical trials, and development of new technologies. Excluded from the umbrella of clinical research, however, are investigations that use anonymous specimens or data from human subjects; such studies would likely fall into the categories of basic or translational research.

**Clinical trials**, a subset of clinical research, often are considered the best method of determining whether interventions are safe and effective in people, including assessing the risks of adverse side effects and other complications. They are designed to answer specific research questions about a biomedical or behavioral

intervention. For example, treatment trials test experimental drugs or devices, new combinations of drugs, or new approaches to surgery or radiation therapy.

Prevention trials seek better ways to prevent a disease or to keep a disease from returning. Screening and diagnostic trials are conducted to find better ways to detect or diagnose diseases or health conditions. Finally, quality-of-life trials (or supportive care trials) explore ways to improve comfort and functioning for individuals with chronic illnesses or approaching the end of life.

Although other entities (e.g., pharmaceutical companies, nonprofit organizations) sponsor a sizeable body of clinical and translational research, the Federal Government plays a critical role in focusing on gaps that otherwise would remain unaddressed. NIH supports clinical and translational investigations unlikely to garner significant investment by other sources because of lack of financial incentives, for example, studies that address rare diseases, involve high costs and high risk, or are based on behavioral changes rather than drugs or devices.

NIH's ICs oversee a broad clinical and translational research portfolio that encompasses intramural and extramural programs. Nearly every NIH component supports clinical and translational research in strategic ways related to its mission. A highlight of the intramural program is the [NIH Clinical Center](#), the Nation's largest hospital devoted entirely to clinical research. The Clinical Center logs more than 7,000 inpatient admissions and 100,000 outpatient visits annually. In order to be seen at the Clinical Center, individuals need to meet the eligibility criteria for a research protocol and agree to participate. The NIH extramural program, in addition to supporting both investigator- and NIH-initiated clinical and translational research, fosters collaborations among institutions, industry (e.g., pharmaceutical companies), and local communities; sets up innovative centers of clinical and translational research; underwrites animal and other preclinical studies; and develops new resources and tools for research. Moreover, the NIH extramural program supports important programs to expand capacity for clinical and translational research. A significant dimension of this capacity building is establishing and enhancing clinical research networks. Other vital aspects of this capacity building are training and career development initiatives to ensure that diverse pools of highly trained clinical and translational scientists are available in adequate numbers and in appropriate research areas to carry out the Nation's biomedical and behavioral research agendas (see the section on Research Training in Chapter 3). To accelerate and strengthen the clinical research process, a set of NIH Roadmap initiatives and follow-on programs are improving the clinical research enterprise. These include infrastructure for clinical research networks, outcome assessment tools, core services and resources, policy enhancement and harmonization, and a program of [Clinical and Translational Science Awards \(CTSAs\)](#). Thanks to such programs, a transformation of the clinical research enterprise is under way to speed new discoveries from bench to bedside to community.

Translational research drives progress along the research continuum and encompasses two separate stages. The first translational stage involves applying discoveries generated during research in the laboratory to the development of studies in humans. Such preclinical translational investigations often are carried out using animal models, cultures, samples of human or animal cells, or experimental systems. The second translational stage takes results from studies in humans and applies them to research on enhancing the adoption of best practices in the community.

Although sometimes referred to as bench-to-bedside research, translational research really is a two-way street. Basic research scientists provide clinicians with new tools for use with patients, and clinical researchers make new observations about the nature and progression of disease that often stimulate basic investigations. Research on new outreach approaches and the cost-effectiveness and real-world feasibility of prevention and treatment strategies are important aspects of this endeavor, as they provide the feedback necessary to ensure the practicality of interventions.

A special aspect of the scope of NIH activities in translational research is its collaboration with NIH's sister HHS agencies. Most ICs are engaged in such collaborations, which involve almost every other HHS agency. The collaborations include working groups and committees such as the Biomedical Imaging in Oncology Forum, the Joint Working Group on Telehealth, and the Health Literacy Workgroup; a wide range of translational research

such as projects on vaccine safety, child abuse and neglect, Diabetes Prevention Program Outcome Study, and Native American Research Centers for Health; database development and management such as the Stem Cell Therapeutics Outcomes Database; and health surveys such as the National Health and Nutrition Examination Survey (NHANES).

## Summary of NIH Activities

NIH nurtures strategies for bringing basic research discoveries to human studies, optimizing the conduct of clinical research, facilitating the transfer of new knowledge gained through research into clinical practice, and aligning and reinforcing the entire continuum. The following sections delineate some specific strategies employed by the ICs to drive research along the research continuum and highlight a few examples from NIH's robust portfolio of clinical and translational research.

### Preclinical Research: Translating Basic Science Discoveries to Human Studies

Before investigators can conduct human studies, much preliminary (basic and preclinical research) work must be done, and a supportive infrastructure must be in place. NIH equips preclinical translational scientists with research tools, enhances opportunities for collaborative research, and provides resources for developing and testing new drugs before progressing to human studies.

### Research Tools and Resources

Among the research tools that NIH provides to promote preclinical translational studies are its myriad biosample and data repositories. A central repository allows additional studies on human samples and data collected during clinical studies, enhancing the value of each study and making optimal use of samples and data. It also ensures that samples are stored under uniform conditions and simplifies access to samples by the scientific community. Samples and data are labeled with codes, keeping the study subjects' information confidential. A notable example of such a repository was established through the [Genetics of Kidneys in Diabetes](#) (GoKinD) study. It facilitates investigator-driven research into the genetic basis of diabetic kidney disease by collecting, storing, and distributing genetic samples from patients with type 1 diabetes and diabetic nephropathy and from control type 1 diabetes patients without kidney disease. By gathering information and samples of the kind, quality, and quantity that individual researchers would be unable to collect on their own, GoKinD facilitates research on the genetics of diabetic kidney disease. (See also the section on *Disease Registries, Databases, and Biomedical Information Systems* in Chapter 3).

Animal models are critical components of translational research. They enable discoveries that are directly related to human health and are used in preclinical research to test therapies and vaccines. [Resource Centers](#) funded by NIH provide investigators with the animals, reagents, and information needed to develop animal models to uncover clues about the effects of specific genes on human health and disease and to gain insights into, for example, basic cellular processes. Additionally, NIH is establishing a new informatics resource to help researchers analyze preclinical research results of diverse studies involving animal models to determine whether a given new scientific discovery merits future development as a potential therapeutic approach (see also the section on *Technology Development* in Chapter 3).

Several preclinical cancer researchers are identifying and developing new biomarkers, which are physical, functional, or biochemical indicators of physiologic or disease processes. Some biomarkers play important roles in disease diagnosis, identifying patient populations that could benefit from particular therapies and monitoring treatment effectiveness. Through such programs as the [Early Detection Research Network](#) and the [Strategic Partnering to Evaluate Cancer Signatures](#) initiative, NIH brings together interdisciplinary teams at dozens of institutions to discover, develop, and test biomarkers and provide advanced analysis and tools that can be used to characterize an individual's disease or tumor so that personalized medical strategies can be developed.

Other translational research at NIH capitalizes on the intricate and interconnected pathways that link and enable communication among genes, molecules, and cells. These molecular pathways work together in a feat of biological

teamwork to promote normal development and sustain health. Many NIH-sponsored studies entail research into such pathways to determine how disturbances in them can lead to disease and to develop new therapies targeted at restoring normal function in disease-disrupted pathways. For example, one NIH initiative—[Asthma Exacerbations: Biology and Disease Progression](#)—was designed to improve understanding of what happens in the body at a molecular level to cause asthma flare-ups. The program could help identify and characterize molecular pathways that might provide a rational basis to develop new medications for preventing or treating such episodes.

## Collaborative Science

Oftentimes, translational research can be streamlined or conducted more economically when scientists within NIH, private industry, academia, private practices, or other institutions work in partnership to complement each other's strengths and share costly resources or infrastructure. For this reason, NIH launched its [Centers of Research Translation](#) to unite basic and clinical research in a way that translates basic discoveries into diagnostic approaches and treatments through robust collaborative efforts. The first set of centers focuses on lupus, orthopedic trauma care, scleroderma, and a genetic form of rickets. In addition to these centers, various ICs also have entered into numerous public-private partnerships. One such public-private partnership is conducting animal studies to test promising compounds for treating fragile X syndrome (FXS), the most common cause of inherited mental impairment. By combining samples and data to increase their collective statistical power, collaborating scientists can conduct studies of rare diseases, such as FXS, more quickly than would be possible if they were working on their own.

## Resources for Developing and Testing Investigational Drugs

NIH helps bridge the gap between drug discovery and clinical testing of promising new agents. Translating promising compounds into drugs for human use is an exacting task that requires very specific, interrelated activities. NIH provides state-of-the-science preclinical drug development resources. Specifically, NIH helps investigators by screening investigational drugs for possible activity against human disease, manufacturing them on a large scale, and clarifying regulatory issues so that FDA requirements are likely to be satisfied when the new investigational drugs are ready for testing in the clinic. One aspect of the [NCI Experimental Therapeutics Program \(NExT\)](#), for example, safely shortens the timeline for taking anticancer drugs from the laboratory to the clinic by combining NIH's expertise in drug development with that found in excellent research facilities.

Similarly, to move basic research on [Alzheimer's disease into translational research](#) and drug testing in clinical trials, NIH provides drug development and toxicology services to academic and small-business investigators who lack the resources needed to perform the required preclinical studies on promising therapeutic compounds. In addition, an entire menu of preclinical drug development contract resources is available through one of NIH's Roadmap initiatives, the [Rapid Access to Intervention Development \(RAID\)](#) programs. The [Type 1 Diabetes RAID program](#) is designed to facilitate translation to the clinic of novel therapeutic interventions for type 1 diabetes and its complications. Another RAID program is in place for [investigational cancer therapeutics](#).

## Clinical Research: Learning Which Interventions Work

Clinical research helps scientists develop and test interventions and new treatments. There are many types of clinical research. For example, some observational clinical research studies involve following a group of patients with a condition and determining their symptoms and responses to treatment in order to try and refine medical practice. Some studies help researchers and clinicians determine whether dosing schedules, behavioral changes, and other elements of a treatment plan are realistic and appropriate. Clinical research sometimes overlaps with the category of epidemiological studies, which is described earlier in this chapter. These research studies can help researchers develop new interventions that can later be evaluated in clinical trials.

Generally, clinical trials, particularly those evaluating drugs or medical devices, are conducted in phases, each of which helps scientists answer different questions. In Phase I trials, researchers test an experimental drug or treatment in a small group of people (20-80) for the first time to evaluate its safety, determine a safe dosage range, and identify side effects. Phase II trials involve a larger group of people (100-300) to evaluate the safety and

effectiveness of the study drug or treatment. In Phase III trials, the experimental study drug or treatment is given to large groups of people (1,000-3,000) to confirm its effectiveness, monitor side effects, compare it to commonly used treatments, and collect information that will allow it to be used safely. Phase IV, or postmarketing, studies are conducted to gather information associated with long-term use in various populations.

The randomized clinical trial has long been considered the gold standard for evaluating the effectiveness of investigational treatments. “Randomization” means that subjects are assigned by chance to either the investigational intervention or the control group. The control group might include interventions such as usual care; best proven care; if known, or no treatment. The specific clinical trial design, including the types and number of intervention and control groups, is dependent upon the medical questions being posed. In addition to the use of control groups, clinical trials often use “blinded” or “masked” study designs, in which subjects are purposely not told whether they are in the intervention or the control group. If feasible, clinical trials are often “double-blinded” or “double-masked” so that the subjects as well as those conducting the study are unable to distinguish between the intervention and control groups.

Participation in clinical trials gives people an opportunity to contribute to the research effort and potentially gain early access to experimental treatments that might prove effective. For some research subjects, participating in a study can provide them with expert medical care at a leading health care facility. To help people access information about clinical trials for which they may be eligible, a Web site (<http://www.clinicaltrials.gov>) offers general information about clinical trials and provides a searchable database of specific studies around the world<sup>9</sup>. Research risks and potential benefits are carefully balanced and the burdens and benefits of participating are shared equally by appropriately including both sexes, people of all races/ethnicities (see Appendix E), and children. Balanced inclusion in trials allows investigators to know whether an intervention works equally well, or not, in all populations. NIH supports outreach efforts to recruit and retain children, women, minorities, and their subpopulations in clinical studies. In addition, NIH holds training events designed to help the research community better understand and be equipped to implement inclusion policy requirements. In 2006, in collaboration with FDA, NIH developed a Web-based course to create a strong foundation for implementation of the requirements for inclusion of minorities and women. The course addresses the scientific basis of known sex and gender differences and explores the influence of sex and gender differences on health outcomes and illness. Recognizing the importance of developing sound scientific bases for pediatric care while protecting children adequately in research settings, NIH policy requires that children (i.e., individuals younger than age 21) be included in human subjects research conducted or supported by the NIH, unless there are sound scientific and/or ethical reasons for excluding them.

In keeping with ethical mandates, NIH clinical research encompasses the principles of respect for persons, beneficence, and justice. Various NIH initiatives and programs seek to harmonize regulatory aspects governing the conduct of clinical research to ensure that studies are conducted with scientific rigor, with minimal burdens on research subjects and investigators, and with utmost consideration for the safety of subjects. In addition, NIH seeks to bolster participation in clinical trials by providing [clinical trial educational materials](#), such as those targeted to cancer patients, health care professionals, and the general public to increase awareness of cancer clinical trials.

## Fostering Collaborative NIH Clinical Research

NIH's efforts to bolster activities along the research continuum are enriching the pipeline of biomedical discoveries. To test investigational therapeutic and preventive strategies in the most expeditious way and hasten their entry into the clinic, NIH is supporting a wide variety of collaborations, research centers, and networks to conduct efficient clinical trials.

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<sup>9</sup> As required by the NIH Reform Act of 2006, NIH provides an annual report to the U.S. Food and Drug Administration identifying all trials registered in [www.clinicaltrials.gov](http://www.clinicaltrials.gov).

Collaborations can consist of scientists at several institutions working together, or they may be intradepartmental or interagency government projects. As an example of such collaboration, NIH and the Centers for Medicare & Medicaid Services, which has an interest in developing an evidence base for Medicare coverage decisions,

<sup>9</sup>As required by the NIH Reform Act of 2006, NIH provides an annual report to the U.S. Food and Drug Administration identifying all trials registered in [www.clinicaltrials.gov](http://www.clinicaltrials.gov).

launched the largest ever randomized clinical trial of the effectiveness and safety of [long-term home oxygen therapy](#) for patients with chronic obstructive pulmonary disease.

NIH funnels the majority of its clinical trials funding to its extramural partners, which operate at the regional, State, and local levels. Many studies are conducted not just at one institution, but at many. Such multisite clinical trials help investigators quickly recruit enough subjects for studies; give the public the widest possible access to clinical studies; and address the special health concerns of high-risk populations, hard-to-reach communities, and individuals with rare or understudied conditions. This approach was used in several practical clinical trials, the primary and secondary phases of which were recently completed. These studies examined treatment effectiveness for such mental disorders as [schizophrenia](#), [bipolar disorder](#), and [depression](#), involving more than 10,000 subjects at more than 200 sites. The infrastructure developed for each of these trials forged collaborative relationships among scientists and clinicians around the country. The platform developed for the trials 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 future studies.

Large studies conducted at multiple sites often are best conducted through networks of investigators who are equipped with tools to facilitate collaboration and information sharing. NIH supports many clinical research networks by funding ongoing infrastructure that provides means of standardizing data reporting to enable seamless data- and sample-sharing across studies. Through NIH-funded informatics and other technologies, researchers are better able to broaden the scope of their research and avoid duplicating research efforts, thereby freeing time and funds to address additional research questions. Among the numerous networks established by NIH that have generated significant findings are the [Maternal and Fetal Medicine Units Network](#), [Neonatal Research Network](#), [Obstetric Pharmacology Research Network](#), [Collaborative Pediatric Critical Care Research Network](#), Pelvic Floor Disorders Network, Traumatic Brain Injury Clinical Trials Network, and Global Network for Women's and Children's Health Research. Additionally, the Community Cancer Centers Program, a 3-year pilot program to improve delivery of cancer care, builds upon the exemplary and long-lived Community Clinical Oncology Program, a network established in 1983 for conducting cancer prevention and treatment clinical trials. It has enrolled more than 200,000 people in treatment and prevention trials.

The [Diabetic Retinopathy Clinical Research Network](#) is a collaborative, nationwide public-private network of eye doctors and investigators at 165 clinical sites conducting clinical research on diabetes-induced retinal disorders with the aim of evaluating promising new therapies. This model network provides the infrastructure to facilitate clinical trials of innovative therapies, rapidly develop and initiate new protocols, and interact with industry partners while ensuring scientific rigor and high ethical standards.

## Addressing Gaps in Research

In terms of clinical evaluation of drugs, there is no clear line where NIH work stops and the pharmaceutical industry picks up. Every drug candidate presents its own profile of financial risk and benefit and potential for gains in public health. NIH's aim is to be sure that all important leads are followed until they are mature enough to attract private-sector interest or until they reach a dead end. About half of the chemotherapeutic drugs currently used by oncologists for cancer treatment were discovered and/or developed by NIH. Cisplatin for treating testicular, ovarian, and lung cancer, and paclitaxel (Taxol) and fludarabine phosphate for treating several cancers and lymphoma, respectively, are examples where NIH involvement in early-stage drug development resulted in products that eventually were licensed to commercial organizations and reached the market. Recently, large-scale clinical trials of compounds that may prevent substance-abuse relapse demonstrated that the compounds were effective according to scientifically valid criteria accepted by FDA. If their efficacy is confirmed in NIH-sponsored

trials, these drugs will be the first generation of medications for treating stimulant dependence. In addition, NIH involvement has been central in developing effective interventions for diagnosis, management, or monitoring of HIV/AIDS, tuberculosis, arthritis, malaria, and many other conditions.

Because behavioral interventions generally do not involve marketable products or services, NIH has a special role to play in research on how changes in behavior can improve health. For example, the objective of [Look AHEAD](#) (Action for Health in Diabetes) is to examine cardiovascular outcomes in people with type 2 diabetes using the effects of a lifestyle intervention designed to achieve and maintain weight loss over the long term through decreased caloric intake and exercise. This multicenter, randomized clinical trial involves several ICs as well as the Centers for Disease Control and Prevention. A second example is the landmark NIH Diabetes Prevention Program clinical trial, which showed that lifestyle change or treatment with the drug metformin significantly delayed development of type 2 diabetes in people at high risk for the disease. Researchers in a follow-on study found that study subjects benefited from healthy lifestyle changes regardless of their genetic disposition for developing the disease.

As noted earlier, government-funded research is particularly vital for the study of rare diseases. Not only do affected individuals benefit from new treatments that industry does not have the incentive to bring to market, but insights gained from such research often provide knowledge relevant to understanding more common diseases. For these reasons, NIH-funded investigators are studying an inherited retinal degenerative disease called Leber's congenital amaurosis (LCA), which causes severe vision loss in infancy or early childhood. Translational studies showed that vision could be restored in dogs with LCA using gene therapy to replace defective copies of the retinal gene RPE65. Phase I clinical trials of this type of gene therapy are now under way to determine whether this approach can help people with the condition.

## Putting Clinical Research Results into Practice

Throughout this report are descriptions of important studies that are changing the way health care is practiced in this country, improving public health and enhancing well-being. To fully realize the potential of new interventions, research results must be disseminated and put into widespread use. NIH investigates strategies for adoption of new evidence at the community level, trains health care providers in best practices, carries out effectiveness research (head-to-head trials of known interventions), disseminates information to providers and the public based on the latest research findings, and sponsors research to learn about the most effective ways to disseminate such findings.

## Changing Clinical Practice

It is not enough merely to have the infrastructure needed to address the ambitious goal of implementing science-based interventions and practices into community settings. In partnership with the Substance Abuse and Mental Health Services Administration and with researchers, clinicians, practitioners, and State alcohol and drug abuse directors, NIH is sharing strategies for incorporating research-based treatment findings into community settings. To accelerate the translation of research into practice in the case of addiction research, NIH embarked on the landmark Blending Initiative. This initiative takes what we know from science, identifies needed products, and disseminates them to providers of drug abuse and addiction treatment programs. The [Blending Initiative](#) also includes training components for addiction treatment practitioners.

The largest dataset ever assembled containing information about people with bipolar disorder has produced results with important implications for the way the condition is treated. NIH has taken important steps to ensure that findings from the [Systematic Treatment Enhancement Program for Bipolar Disorder](#) (STEP-BD) are translated into clinical practice. For the study, 4,360 individuals with bipolar disorder received best-practice treatments and were monitored throughout their participation in the study. As a critical translational step, participating doctors received expert training and became STEP-BD-certified in the best treatments for bipolar disorder. Among the consequential outcomes of the research was the finding that patients taking medications to treat bipolar disorder are more likely to get well faster and stay well if they also receive intensive psychotherapy.

NIH studies have transformed the management of antiretroviral therapy (ART) by directly comparing therapy regimens and determining which best extends survival of adults and children with HIV/AIDS. Results from the [SMART study](#), one of the largest HIV/AIDS treatment trials ever conducted, showed that continuous ART is better than periodic therapy for treatment-experienced patients. Deliberately interrupting ART more than doubles the risk of developing AIDS or dying from any cause. The results of these studies stimulated immediate and significant changes in HIV treatment

## Disseminating Research Findings

NIH is taking the lead in identifying the best ways to inform the public and health care practitioners about research results with the potential to improve the Nation's health (see the section on Health Communications in Chapter 3). For example, several large studies of type 1 and 2 diabetes established the importance of patients carefully maintaining blood-sugar control as a way to dramatically reduce the devastating complications of diabetes. Unfortunately, the therapies proven to delay or prevent complications in these studies are not widely incorporated into health care practice. Therefore, NIH is supporting projects exploring ways to disseminate knowledge from successful clinical research into medical practice and community settings. Many of these studies focus on minority populations disproportionately burdened by [type 2 diabetes and obesity](#).

NIH continues to support research designed to strengthen the dissemination and implementation of evidence-based medicine. One example of many such initiatives is improving mental health practices by encouraging transdisciplinary teams to identify and overcome barriers to the adoption of evidence-based interventions. For example, a [recent study](#) reported that providing a minimal level of enhanced care for employees' depression would result in significant savings to employers.

NIH also promotes the fruits of its research by cataloging and disseminating data. For example, NIH leads the [National Toxicology Program](#), an interagency initiative that produces the biennial *Report on Carcinogens*. Under this program, NIH staff members organize and publish data gleaned from numerous sources on some of the more than 80,000 chemicals registered for use in the United States. The 11th edition of the report identifies and discusses agents, mixtures, or exposure circumstances that could pose a health hazard because of carcinogenicity. It includes data on the carcinogenicity, genotoxicity, and biologic mechanisms of the listed substances in humans and/or animals; the potential for human exposure to these substances; and Federal regulations to limit exposures.

In its quest to help clinicians and patients make appropriate decisions about health care, NIH periodically convenes expert panels that review the cumulative research and publish clinical practice guidelines that describe a range of generally accepted approaches for the diagnosis, management, or prevention of specific diseases or conditions. The guidelines, which address such topics as asthma, cholesterol management, overweight and obesity, and HIV management, provide recommendations that patients and their doctors can use to develop individual treatment plans tailored to the specific needs and circumstances of the patient.

Located in the NIH Office of the Director, the [Office of Medical Applications of Research](#) (OMAR) works closely with ICs to assess, translate, and disseminate the results of biomedical research that can be used in the delivery of health services. OMAR coordinates periodic consensus conferences with the goal of reviewing areas of NIH-supported research where there may be a gap between research accomplishments and clinical care. The consensus statements that result from these conferences are shared widely with health care providers, policymakers, patients, and the media. Recent statements have addressed such topics as tobacco use, management of chronic insomnia, and multivitamin/mineral supplements.

## Bolstering the Research Continuum

NIH is committed to reengineering the clinical research enterprise, a key objective of the NIH [Roadmap for Medical Research](#). Three critical components of the Roadmap are capacity building, developing a multidisciplinary scientific

workforce dedicated to a new discipline of clinical and translational research to implement the Nation's research agenda, and harmonizing, streamlining, and optimizing policies and requirements concerning the conduct and oversight of clinical research.

## Building Capacity for Clinical and Translational Research

NIH supports capacity building for clinical and translational research. Drawing on the momentum of the NIH Roadmap and extensive community input, the [Clinical and Translational Science Award](#) program is creating academic homes for the discipline of clinical and translational science at institutions across the country. Beginning with 12 academic health centers located throughout the Nation, the [consortium](#) will eventually link about 60 institutions. The program encourages the development of novel methods and approaches to clinical and translational research, enhances informatics and technology resources, and improves training and mentoring to ensure that new investigators can navigate the increasingly complex research system. The consortium of research institutions is radically changing how clinical and translational research is conducted and ultimately will enable researchers to provide new treatments more quickly to patients.

Researchers are increasingly conducting studies in community clinics, doctors' offices, and other health care facilities as innovative means of building capacity across the Nation and ensuring that diverse populations are involved in research. For example, NIH fosters scientifically rigorous research in oral health care in [three networks](#) of private dental practices to address the longstanding lack of high-quality research data to guide treatment decisions in the dentist's office. Each network is a grassroots effort, involving 100 or more community dentists and hygienists undertaking short-term clinical studies to compare the benefits of different dental procedures, dental materials, and prevention strategies.

Also, NIH is committed to expanding research capacity in the area of complementary and alternative medicine (CAM). By establishing various [Centers of Research](#), both in the United States and abroad, based on collaborations between established biomedical research scientists and experts in CAM or traditional medicine, NIH has made significant advances in our understanding of the scientific basis for the effects of several CAM treatment approaches.

## Developing the Research Teams of the Future

NIH is anticipating and preparing to meet the need for a multidisciplinary, well-trained cadre of researchers at every point in the research continuum through its career development initiatives (see section on Research Training in Chapter 3). For example, a key component of the CTSA program is the creation of one or more graduate degree-granting and postgraduate programs in clinical and translational science, which will provide an enriched environment for educating and retaining the next generation of clinical and translational researchers.

A Research Centers in **Minority Institutions Translational Research Network** (RCMI<sub>net</sub>) will be a cooperative research network that will facilitate clinical research in health disparity areas. This Network will consist of a consortium of clinical investigators from the RCMI, RCMI Clinical Research Infrastructure Initiative (RCRII), and [Clinical Research Education and Career Development \(CRECD\)](#) programs; other NIH-supported Clinical Research Centers; relevant organizations, including community health centers, with an interest in health disparity areas; and a Data and Technology Coordinating Center (DTCC).

To respond to the identified need for more veterinarians in the field of biomedical research, NIH funds [career development programs for veterinarians](#) and veterinary studies, which are an important link between the use of animal models and their application to problems involving human health and disease.

## Optimizing Policy

The NIH [Clinical Research Policy Analysis and Coordination \(CRpac\)](#) program serves as a focal point for the ongoing harmonization, streamlining, and optimization of policies and requirements concerning the conduct and oversight of clinical research. It is widely recognized that the efficiency and effectiveness of the clinical research enterprise is

hampered by variability in regulations and policies that pertain to the conduct and oversight of clinical research. The CRpac program reflects NIH's sense of responsibility, as the lead Federal agency supporting clinical research, to promote the efficiency and effectiveness of the clinical research enterprise by facilitating compliance and oversight. Its objective is to develop and implement coordinated policies and practices reflective of the needs and points of view of NIH's varied stakeholders. The CRpac program works on an array of issues and activities usually in close collaboration with other Federal agencies and offices that have responsibilities concerning the oversight of clinical research. CRpac's current focus includes issues related to Federal adverse event reporting requirements; clinical research review and oversight mechanisms; clinical trial monitoring; Federal regulations and policies governing research with human specimens and data; informed consent; and clinical trial design.

## Conclusions

NIH's expanded commitment to optimizing the continuum spanning basic, translational, and clinical research by applying a new multidisciplinary approach to clinical and translational science marks a real turning point. Scientists will have more freedom to engage in productive collaborations with experts in different fields and follow creative approaches that will better serve human health as new treatments and prevention strategies are developed, tested, and brought more rapidly into practice. The results of NIH's commitment to clinical and translational science are apparent in the following section, which highlights a few of the myriad accomplishments and ongoing initiatives in this rapidly developing area of research.

## 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, and communication)

COE = Supported through a congressionally mandated Center of Excellence program

GPRA Goal = Concerns progress tracked under the Government Performance and Results Act

## Preclinical Research: Translating Basic Science Discoveries to Human Studies

**Rodent Model Resources for Translational Research:** Mouse and rat models are the primary testbed for preclinical research and have played a vital role in most medical advances in the last century. Rodent models comprise about 90 percent of all animal studies enabling a wide range of genetic and physiological research on human disease. NIH plays a major role in supporting the availability of normal and mutant mice and rats for translational research. Recent accomplishments include:

- Knockout Mouse Project (KOMP): A trans-NIH initiative to individually inactivate each protein-coding mouse gene to better understand the genetic functions of the estimated 22,000 mouse genes, which are, in many cases, very similar to human genes.
- KOMP Repository: Established in FY 2007 to acquire and distribute the mouse models produced by the KOMP.
- Mutant Mouse Regional Resource Centers: Distribution of genetically engineered mice increased by 50 percent in FY 2006 because of increased demand.
- Rat Resource and Research Center: Acquisition and distribution of rat models increased by 50 percent in FY 2006 because of increased demand.

- For more information, see [http://www.ncrr.nih.gov/comparative%5Fmedicine/resource\\_directory/rodents.asp](http://www.ncrr.nih.gov/comparative%5Fmedicine/resource_directory/rodents.asp)
- For more information, see <http://www.genome.gov/17515708>

- For more information, see <http://www.genome.gov/25521840>
- For more information, see <http://www.mmrc.org/>
- For more information, see <http://www.nrrrc.missouri.edu/>
- This example also appears in Chapter 3: *Genomics*.
- (E) (NCRR)

**Advances in Treatment Development:** 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 (FXS):** NIH has entered into a public-private partnership to study and test possible medications for treating FXS, the most common cause of inherited mental impairment. FXS is caused by a single gene mutation, ultimately resulting in exaggerated activity of a brain protein called mGluR5. Researchers will study, in animals, the safety of chemical compounds known to block 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 persons with treatment-resistant depression experienced relief in as little as 2 hours following 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 development of faster and longer acting medications for treating depression.
  - For more information, see <http://www.nimh.nih.gov/press/ketamine.cfm>
  - This example also appears in Chapter 2: *Neuroscience and Disorders of the Nervous System*.
  - (I) (NIMH)

**Engineering Stem Cells to Repair or Replace Damaged Tissues:** Guiding a person's own stem cells to repair or replace damaged tissues with healthy tissue is the goal of multiple NIH-supported tissue engineering projects. For example, one team previously reported success creating three-dimensional mandibular (jaw) joints using rodent tissue; their continuing work on the project addresses pragmatic questions that must be answered in order to create functional human joints. Other teams are working on regeneration of the temporomandibular disk, which acts as a "cushion" between the bony components of the jaw joint and on the tissue engineering of skeletal muscle. Tissue engineering holds great promise for regeneration or replacement of dental, oral, and craniofacial structures lost as a result of trauma, disease, or congenital anomalies. The progress seen in this area will also inform tissue engineering solutions for degeneration in other articular surfaces such as knee, hip, and shoulder joints.

- [Mao JJ, et al. \*J Dent Res\* 2006; 85:966-79, PMID: 17062735](#)
- This example also appears in Chapter 2: *Life Stages, Human Development, and Rehabilitation* and Chapter 3: *Molecular Biology and Basic Sciences*.
- (E) (NIDCR)

**Molecular Profiling of Cancer:** The underlying cause of each patient's disease is typically unique to the individual. Because each tumor has its own biological properties, molecular profiling provides advanced analysis and tools to characterize each individual's disease or tumor so that tailored medical strategies can be applied. Several notable examples include:

- *The Early Detection Research Network (EDRN)* brings together dozens of institutions to help detect cancer in its earliest stages. EDRN was formed to bring a collaborative approach to the discovery, development, and validation of early detection markers by accelerating the translation of biomarker information into clinical

applications.

- *The Strategic Partnering to Evaluate Cancer Signatures (SPECS) Program* establishes strategic partnerships to bring together interdisciplinary teams to evaluate the clinical utility of molecular signatures. SPECS focuses on confirming, evaluating, and refining signatures/profiles derived from molecular analysis of tumors (i.e., biomarkers detection) to improve patient management and outcomes.
  - For more information, see <http://cancerdiagnosis.nci.nih.gov/specs/>
  - For more information, see <http://edrn.nci.nih.gov/>
  - This example also appears in Chapter 2: *Cancer*.
  - (E/I) (NCI)

**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 only from 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 using magnetic resonance imaging (MRI). They label macrophages (immune cells) with polymer-coated micron-size 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 the present time 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.

- [Wu YL, et al. \*Proc Natl Acad Sci U S A\* 2006;103:1852-7](#), PMID: 16443687
- For more information, see <http://www.nibib.nih.gov/HealthEdu/eAdvances/25Sep06>
- This example also appears in Chapter 2: *Autoimmune Diseases* and Chapter 2: *Chronic Diseases and Organ Systems*.
- (E) (NIBIB)

**Basic Research on CAM:** In addition to its focus on clinical investigation of complementary and alternative medicine interventions, NIH places a high priority on basic research aimed at filling important gaps in our knowledge about the mechanisms by which they may exert their effects. Recently released initiatives target this area of research. Examples include the following:

- “Omics and Variable Responses to CAM” utilizes genomic, proteomic, and metabolomic technologies to examine potential causes for variation in individual responses to CAM interventions (PAR-07-377).
- “Mechanistic Research on CAM Modalities Purported to Enhance Immune Function” examines the scientific basis for a common but generally unsubstantiated claim made on behalf of a number of CAM modalities (RFA-AT-06-004, RFA-AT-06-005).
- “Research on the Biomechanical, Immunological, Endocrinological, and/or Neurophysiological Mechanisms and Consequences of Manual Therapies” applies state-of-the-art science to investigate the biological basis for CAM interventions, such as spinal manipulation and massage. (PAR-06-312)
  - This example also appears in Chapter 3: *Molecular Biology and Basic Sciences*
  - (E) (NCCAM)

**NCI Experimental Therapeutics Program (NExT):** The NExT program safely shortens the timeline for taking anticancer drugs from the laboratory to the clinic by combining NIH's expertise in drug development with state-of-the-art research facilities. The program also utilizes new FDA guidelines that allow early Phase I clinical trials to

proceed before certain time-consuming and expensive drug development steps occur. The first such study passed the initial stage of clinical examination, demonstrating that this new type of trial can reduce the number of patients required for an early clinical study, and the time necessary to gather critical drug development information.

- For more information, see <http://dctd.cancer.gov/MajorInitiatives/02NExT.htm>
- This example also appears in Chapter 2: *Cancer*.
- (E/I) (NCI)

**The NCI Alliance for Nanotechnology in Cancer:** This is a comprehensive, systematized initiative encompassing the public and private sectors, designed to accelerate the application of the best capabilities of nanotechnology to cancer. The program supports research on novel nanodevices that may detect and pinpoint the location of cancer at its earliest stages, deliver anticancer drugs specifically to malignant cells, and determine in real time if these drugs are effective in killing malignant cells. Nanotechnology will likely change the very foundations of cancer diagnosis, treatment, and prevention.

- For more information, visit <http://nano.cancer.gov/>
- This example also appears in Chapter 2: *Cancer* and Chapter 3: *Technology Development*.
- (E/I) (NCI)

**Biomedical Technology Research Resources (BTRRs):** The BTRRs develop versatile new technologies and methods that help researchers who are studying virtually every human disease, each creating innovative technologies in one of five broad areas: informatics and computation, optics and spectroscopy, imaging, structural biology, and systems biology. This is accomplished through a synergistic interaction of technical and biomedical expertise, both within the Resources and through intensive collaborations with other leading laboratories. The BTRRs are used annually by nearly 5,000 scientists from across the United States and beyond, representing over \$700 million of NIH funding for 22 institutes and centers. As an example, optical technologies enable researchers to:

- Harness the power of light to “see” biological objects, from single molecules to cells and tissues, which are otherwise invisible. New technologies using fluorescence and infrared spectroscopies revealed exquisite details of how proteins fold and interact.
  - Detect and assess malignancy in a rapid, noninvasive manner. Optical technologies have been used successfully to measure responses of breast tumors to chemotherapy and define the margins of tumors so that surgeons can more precisely remove cancerous tissue during surgery.
- For more information, see [www.ncrr.nih.gov/biomedical\\_technology](http://www.ncrr.nih.gov/biomedical_technology)
  - This example also appears in Chapter 3: *Molecular Biology and Basic Sciences* and Chapter 3: *Technology Development*
  - (E) (NCRR)

**Glycomics Technology Development, Basic Research, and Translation into the Clinic:** Complex carbohydrates are ubiquitous, found on the surfaces of cells and secreted proteins. Glycan binding proteins mediate cell signaling, recognition, adherence, and motility and play a role in inflammation, arteriosclerosis, immune defects, neural development, and cancer metastasis. Detection and analysis of carbohydrate molecules are thus critical for basic and clinical research across the spectrum of health and disease but are widely regarded as among the most difficult challenges in biochemistry. Four NIH programs are striving to make this easier by working together across the domains of technology development and basic and translational research.

- Biomedical Technology Research Resources are developing and sharing cutting-edge technologies for analysis of carbohydrates in complex biological systems.
- Consortium for Functional Glycomics creates and provides access to technological infrastructure for carbohydrate biology and analysis in support of basic research.

- Alliance of Glycobiologists for Detection of Cancer and Cancer Risk leverages the technology and expertise developed in NIH programs for translational research in cancer biomarker discovery.
- A Small Business Innovation Research (SBIR)/Small Business Technology Transfer (STTR) program funds the commercial development of innovative technologies for carbohydrate analysis.
  - For more information, see [www.ncrr.nih.gov/glycomics](http://www.ncrr.nih.gov/glycomics)
  - For more information, see [www.functionalglycomics.org](http://www.functionalglycomics.org)
  - This example also appears in *Chapter 3: Molecular Biology and Basic Sciences* and *Chapter 3: Technology Development*.
  - (E) (NCRR, NCI, NHLBI, NIGMS, NINDS)

**Preclinical Disease Models Informatics:** Preclinical research results derived from animal models are an essential element in the decisional process to determine whether a basic science discovery should be considered as a potential therapeutic approach worthy of future development. However, more effective integration of the growing number of disparate data sources is urgently needed. NIH is developing a new resource to assimilate information from diverse disease-model data repositories and to disseminate innovative and novel interpretations of these data. This will help researchers minimize the time required to search multiple data sources, while optimizing the quality and relevance of the results. Activities in this area include:

- Determined community-defined needs and next steps during a workshop held in FY 2006.
- Issued request for proposals (fall 2007) that will address the need for an electronic directory of models resources.
- Forming critical inter/intra-agency and public-private partnerships to (1) address the need for and development of extensible prototypes and (2) ensure this resource remains broadly informed and grows coincidental with relevant technology.
  - For more information, see [www.esi-bethesda.com/ncrrworkshops/navigating/index.aspx](http://www.esi-bethesda.com/ncrrworkshops/navigating/index.aspx)
  - (E) (NCRR)

**Translational Research at Primate Research Centers:** Non-human primates (NHPs) are critical components for translational research because of their close physiological similarities to humans. NHPs are widely used for both hypothesis-based and applied research directly related to human health, such as the development and testing of vaccines and therapies. The NIH-supported National Primate Research Centers and other primate resources provide investigators with the animals, facilities, specialized assays, and expertise to perform translational research using NHPs. In FY 2007, more than 1,000 research projects used NHPs from these resources. Highlights of research activities include:

- Use of the simian immunodeficiency virus for AIDS-related research, including development of novel microbicides to prevent infection by the AIDS virus and testing of AIDS vaccines
- Identification of the central role of specific genes and molecules in drug addiction and neurological conditions and diseases, studies of the biochemistry and physiology of drug and alcohol addiction, and development of stem cell-based therapies for neurodegenerative diseases.
- Sponsored scientific workshops in FY 2006 and 2007 that further defined the genetic tools necessary for translational research using NHPs.
  - For more information, see [ncrr.nih.gov/comparative%5Fmedicine/resource\\_directory/primates.asp](http://ncrr.nih.gov/comparative%5Fmedicine/resource_directory/primates.asp)
  - This example also appears in *Chapter 2: Infectious Diseases and Biodefense*.
  - (E) (NCRR)

**Medical Countermeasures Against Nuclear and Radiological Threats:** NIH is leading the HHS effort to sponsor and coordinate research to develop means to counter detrimental effects of a range of radiological threats. Most medical countermeasures to treat radiation injury are still in the early stages of development but are progressing.

NIH-funded researchers recently (1) screened more than 40,000 candidate compounds and identified 52 candidates for evaluation as protective agents against the toxic effects of ionizing radiation, (2) developed improved forms of the chelating agent diethylenetriaminepentaacetic acid (DTPA), which animal testing data suggest can effectively clear the radionuclide Americium-241 from the blood, and (3) studied 29 candidate drugs that are active against a broad range of radionuclides and might be useful in treating victims of radiological dispersion devices (“dirty bombs”).

- For more information, see <http://www3.niaid.nih.gov/research/topics/radnuc/>
- This example also appears in Chapter 2: *Infectious Diseases and Biodefense*.
- (E) (NIAID)

**Centers of Research Translation (CORT):** NIH launched its CORT program to unite basic and clinical research in a way that translates basic discoveries into diagnostic approaches and treatments. The first set of centers, focusing on lupus, orthopaedic trauma care, scleroderma, and a genetic form of rickets (a childhood disorder characterized by a softening and weakening of bones), began in FY 2006 and are funded through FY 2011.

- For more information, see [http://www.niams.nih.gov/News\\_and\\_Events/Press\\_Releases/2006/11\\_08.asp](http://www.niams.nih.gov/News_and_Events/Press_Releases/2006/11_08.asp)
- This example also appears in Chapter 2: *Minority Health and Health Disparities*.
- (E) (NIAMS)

**Quantum Program :**The NIH Quantum Grants Program has been developed to make a profound (quantum level) advance in health care by funding research, over two phases, on targeted projects that will develop new technologies for the diagnosis, treatment, or prevention of a major disease or national public health problem. The first of the Quantum Grants was to engineer stem cell-based neurovascular regenerative units in a laboratory environment, which can then be implanted into the damaged cortex of stroke patients to provide a source of neural and vascular cells that will continue to develop and differentiate and lead to the first true treatment for stroke, one of the most common causes of disability, severely affecting quality of life of patients throughout the world. Another Phase I Quantum competition was completed in September 2007, with four additional grants awarded. The Phase II Quantum competition will begin in FY 2009.

- For more information, see <http://www.nibib.nih.gov/Research/QuantumGrants>
- This example also appears in Chapter 2: *Neuroscience and Disorders of the Nervous System*.
- (E) (NIBIB)

**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 Genetic Association Information Network (GAIN), a public-private partnership between NIH and industry.

- [Mueller PW et al. \*J Am Soc Nephrol\* 2006;17:1782-90](#), PMID: 16775037
- For more information, see [http://www.idrf.org/index.cfm?fuseaction=home.viewPage&page\\_id=B9C33021-1321-C834-0382E079E7865807](http://www.idrf.org/index.cfm?fuseaction=home.viewPage&page_id=B9C33021-1321-C834-0382E079E7865807)
- This example also appears in Chapter 2: *Chronic Diseases and Organ Systems* and Chapter 3: *Genomics*
- (E) (NIDDK)

**Type 1 Diabetes-Rapid Access to Intervention Development (T1D-RAID):** Many investigators who have discovered promising therapeutic agents in the laboratory do not have the resources to ready the agents for use in human clinical trials. Therefore, NIH supports the T1D-RAID program to provide resources for preclinical development of

agents to test in clinical trials. For example, the drug lisofylline, prepared and tested by T1D-RAID, will be studied in an upcoming pancreatic islet transplantation clinical trial.

- For more information, see <http://www.t1diabetes.nih.gov/T1D-RAID/index.shtml>
- This example also appears in Chapter 2: *Autoimmune Diseases*.
- (E) (NIDDK, NCI)

**Specialized Program of Translational Research in Acute Stroke (SPOTRIAS):** The objective of the SPOTRIAS is to serve as an incubator for translational and early-phase clinical research studies. SPOTRIAS sites are located at medical centers where staff members have the capacity to evaluate and treat stroke patients very rapidly after symptom onset. NIH supports seven SPOTRIAS sites, which have made substantial progress, including impressive increases in the use of the “clot buster” tPA (tissue plasminogen activator) to treat acute stroke; the establishment of three interlinked repositories for protein and DNA tissue samples, neuroimages, and clinical data; enrollment of more than 640 individuals with acute stroke into treatment protocols; the management of 17 early-phase clinical trials; and the training of 25 research fellows.

- For more information, see <http://www.spotrias.com/>
- This example also appears in Chapter 2: *Neuroscience and Disorders of the Nervous System*.
- (E/I) (NINDS)

**Toward Better Treatment for Muscular Dystrophy:** Activities funded by NIH are pursuing multiple pathways to therapeutic development for the muscular dystrophies. NIH funds six Senator Paul D. Wellstone Muscular Dystrophy Cooperative Research Centers, designed to accelerate the translation of fundamental scientific advances to the clinic (see Chapter 4). NIH also recently funded two large-scale translational research projects in muscular dystrophy: one to develop small-molecule drugs for Duchenne and potentially other forms of muscular dystrophy and another to develop the optimal vector for vascular delivery of genes. A new NIH Government Performance and Results Act (GPRA) goal aims to advance two emerging strategies for treating muscular dystrophy to clinical trial readiness by 2013. The Muscular Dystrophy Coordinating Committee's *Action Plan for the Muscular Dystrophies* also identified therapy development goals to be pursued by NIH and the committee's partner agencies and organizations. A recent workshop convened by NIH reviewed the status of different therapeutic approaches for muscular dystrophy and discussed ways to move this research forward.

- For more information, see [http://www.ninds.nih.gov/find\\_people/groups/mdcc/MDCC\\_Action\\_Plan.pdf](http://www.ninds.nih.gov/find_people/groups/mdcc/MDCC_Action_Plan.pdf)
- For more information, see [www.wellstonemdccenters.nih.gov](http://www.wellstonemdccenters.nih.gov)
- This example also appears in Chapter 2: *Neuroscience and Disorders of the Nervous System*.
- (E) (COE) (NINDS, NIAMS, NICHD) (GPRA Goal)

**The SMA Project:** A decade ago, spinal muscular atrophy (SMA) was one of hundreds of poorly understood inherited disorders that affect the nervous system, and the outlook for developing treatments was bleak. The discovery of the gene defect causing SMA dramatically improved prospects, revealing a rational strategy to develop drugs. The SMA Project is a novel approach to pre-clinical drug development and may serve as a model for other disorders. The Project brought together expertise from industry, academia, the FDA, and NIH to generate a detailed drug development plan. A “virtual pharma organization” develops and applies the resources to carry out the plan through subcontracts to companies that serve the pharmaceutical industry. The project created a new drug through extensive modification of indoprofen, a drug with known activity in experimental settings that was not suitable for clinical application. Through repeated modification and evaluation cycles in laboratory tests, the project produced hundreds of chemical compounds related to indoprofen and has made encouraging progress. In 2007, preclinical studies began to evaluate the two best candidates for clinical readiness. The best of these will likely be ready for early stage clinical testing in 2008 or 2009. In early 2008, the project also began two new drug development projects that could yield additional drug candidates for SMA.

- For more information, see <http://www.smaproject.org/>
- This example also appears in Chapter 2: *Neuroscience and Disorders of the Nervous System*
- (E) (NINDS)

**Translational Research:** To meet the special needs of translational research across neurological disorders, NINDS developed a program to support pilot projects, full-scale collaborative teams in academia and small businesses, and training efforts. Investigator-initiated proposals are rigorously peer reviewed, with expertise and criteria tailored to translational research objectives. Funding is milestone-driven, and the program fosters collaborative research. Ongoing projects are developing drug, stem cell, or gene therapies for ALS, Batten disease, epilepsy, Huntington's disease, Duchenne and other muscular dystrophies, Parkinson's disease, tuberous sclerosis, and stroke and other disorders. In 2008 the program will expand to include molecular diagnostics, which are critical for catching disease early when intervention is most likely to succeed.

- For more information, see <http://www.ninds.nih.gov/funding/research/translational/index.htm>
- This example also appears in Chapter 2: *Neuroscience and Disorders of the Nervous System*.
- (E) (NINDS)

**The NIH Rapid Access to Intervention Development (RAID) Pilot Program:** The NIH-RAID Pilot program makes available, on a competitive basis and at no cost to investigators, certain critical resources needed to develop new small-molecule drugs, including not only laboratory services but also expertise in the regulatory process. The program directly addresses roadblocks to moving from bench to bedside. Among the projects approved are drugs for hepatic fibrosis, the blood diseases beta thalassemia and sickle cell anemia, brain tumors, and the neurological disorders Friedreich's ataxia and Alzheimer's. The NIH-RAID Pilot is part of the NIH Roadmap for Medical Research.

- For more information, see <http://nihroadmap.nih.gov/raid/index.aspx>
- This example also appears in Chapter 2: *Neuroscience and Disorders of the Nervous System*.
- (E) (Roadmap—all ICs participate)

**Translational Research on Alzheimer's Disease (AD):** To move basic research on AD and associated disorders into translational research and drug testing in clinical trials, this initiative includes drug discovery, preclinical development, and a program of toxicology services for academic and small business investigators who lack the resources to perform the required toxicology studies on promising therapeutic compounds. In order to closely monitor the progress of the translational projects, provide guidance, and foster interactions among investigators involved in translational research funded by these programs, NIH staff held the First Annual Investigators Meeting for Translational Research in September 2007.

- For more information, see <http://grants.nih.gov/grants/guide/pa-files/PAR-07-048.html>
- This example also appears in Chapter 2: *Neuroscience and Disorders of the Nervous System*
- (E/I) (NIA)

**Potential Therapy for Children Afflicted With Progeria Syndrome:** Hutchinson-Gilford progeria syndrome (HGPS) is a genetic disorder of accelerated aging. In addition to other symptoms of aging, HGPS patients suffer from accelerated cardiovascular disease and often die in their teen or even pre-teen years from heart-related illnesses. No treatments are currently available for HGPS; however, recent work led by NHGRI researchers indicates that farnesyltransferase inhibitors (FTIs), a class of drugs originally developed to treat cancer by blocking the growth of tumor cells, are capable of reversing the effects of the defective HGPS protein, lamin A. Ongoing studies in a mouse model have validated the results of preliminary experiments, and a clinical trial of FTIs in children with progeria began in 2007. In FY 2008, researchers plan on expanding the study to investigate whether FTIs are capable of reversing the detrimental effects after progression of the cardiovascular anomalies that are seen in the mouse model. The development of biological assays to assess the effects of FTI treatment on the patients' cells is

in progress to monitor potential beneficial effects of the clinical trial. In addition, it has been demonstrated that the progerin protein is present in small amounts in normal aging tissues. The investigation of this phenomenon is being pursued as a contributory factor to the normal aging process.

- [Cao K, et al. \*Proc Natl Acad Sci U S A\* 2007;104:4949-54](#), PMID: 17360355
- [Capell BC, et al. \*Proc Natl Acad Sci U S A\* 2005;102:12879-84](#), PMID: 16129833
- For more information, see <http://www.genome.gov/10000608>
- For more information, see <http://www.genome.gov/15515061>
- This example also appears in Chapter 3: *Genomics* and Chapter 2: *Life Stages, Human Development, and Rehabilitation*.
- (I) (NHGRI)

**Trans-NIH Initiative for Translational Research in Immunology, Autoimmunity, and Inflammation:** A new, trans-NIH initiative is being developed by the intramural research program to facilitate the translation of advances in basic immunology to improved therapies and clinical care for immune-mediated diseases. The translation of basic immunology to the clinic has been impeded by separations between basic immunologists, physicians, and epidemiologists and by barriers among clinicians who address diseases that share pathophysiologic mechanisms but are historically separated in different specialty practices. The new program will integrate research efforts not only across the basic, clinical, and population sciences but also across conventional medical subspecialties. Research will focus on a variety of autoimmune diseases, congenital and acquired immunodeficiency syndromes, processes in which inflammation or altered immunity has a pathogenic role, and malignant diseases influenced by the immune system. Studies will address the underlying role of the immune system and the similarities and differences of the inflammatory response in many seemingly unrelated immune-mediated diseases. The initiative is expected to advance understanding of the causes of the diseases and to promote the development of new therapies. It also is expected to serve as a model for future trans-NIH translational research efforts to facilitate more rapid development and testing of new therapies and enhance interdisciplinary training.

- This example also appears in Chapter 2: *Autoimmune Diseases*
- (I) (NHLBI, NIAID, NIAMS, NIDDK)

## Clinical Research: Learning Which Interventions Work

**New Medical Adhesive Boasts Unique Wet-Dry Abilities:** One day, tissue engineering will make it possible to regenerate lost facial components. Until then, victims of massive craniofacial trauma or extensive surgeries due to cancer often must depend on maxillofacial prosthetics to provide the form and function needed to resume their day-to-day lives. Current adhesives are not always retentive over long periods or changing conditions. The loss of retention can result in visible margins or even dislodgement of the prosthesis. Now NIH-supported scientists report they have merged two of nature's most elegant strategies for wet and dry adhesion. As reported in *Nature*, the scientists designed a synthetic material that starts with the dry adhesive properties of the gecko lizard and supplements it with the underwater adhesive properties of a mussel. The hybrid material, which they call a geckel nanoadhesive, proved in initial testing to be adherent under dry and wet conditions, and also adhered much longer under both extremes than previous gecko-based synthetic adhesives, a major issue in this area of research. According to the authors, their findings mark the first time that two polar opposite adhesion strategies in nature have been merged into a man-made reversible adhesive. It is envisioned that the new adhesive will be used for many medical applications including enhancing the retention of oral/maxillofacial prosthetics.

- [Lee H, et al. \*Nature\* 2007;448:338-41](#), PMID: 17637666
- For more information, see <http://www.nidcr.nih.gov/Research/ResearchResults/NewsReleases/ArchivedNewsReleases/NRY2007/PR07182007.htm>
- This example also appears in Chapter 2: *Life Stages, Human Development, and Rehabilitation* and Chapter 3: *Technology Development*.
- (E) (NIDCR)

**Diabetes Prevention Program Outcomes Study (DPPOS):** The landmark NIH Diabetes Prevention Program clinical

trial showed that lifestyle change or treatment with the drug metformin significantly delayed development of type 2 diabetes in people at high risk. The DPPOS is a long-term followup study of the 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, as 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) while the metformin treatment had progressively less impact with increasing age.

- [Florez JC, et al. \*N Engl J Med\* 2006;355:241-50](#), PMID: 16855264
- For more information, see <http://tinyurl.com/24okog>
- For more information, see <http://tinyurl.com/295h4l>
- This example also appears in Chapter 2: *Chronic Diseases and Organ Systems* and Chapter 3: *Epidemiological and Longitudinal Studies*
- (E) (NIDDK, CDC, IHS, NCMHD, NEI, NHLBI, NIA, NICHD, ORWH)

**Clinical Research and Trials in Neurological Disease:** NINDS provides extramural funding for more than 1,000 clinical research studies. Nearly 1 million people participate in these projects, and it is essential to assess the return on this investment in improving quality of life. NINDS contracted an independent evaluation of the costs and benefits of its Phase III clinical trials. Investigators found that while the total cost of clinical trials in the study was \$335 million, the cumulative benefits over a 10-year period exceeded \$15 billion and added 470,000 healthy years of life to people in the United States. NINDS is extending this evaluation approach by developing a computer model that will estimate the public health impact of any given clinical trial in neurology or neurosurgery. This model will be publicly available for use by researchers and the Institute to facilitate decision-making. NINDS is also assessing ways to further improve its trials. To this end, the Institute has funded a Neurological Emergencies Treatment Trials (NETT) Network to facilitate high-quality clinical trials in acute neurological disorders and accelerate the implementation of new therapies into practice in emergency departments.

- [Johnston SC, et al. \*Lancet\* 2006;367:1319-27](#), PMID: 16631910
- For more information, see <http://www.nett.umich.edu/nett/welcome>
- This example also appears in Chapter 2: *Neuroscience and Disorders of the Nervous System*.
- (E) (NINDS)

**Multiple Sclerosis (MS):** While the exact cause of MS is unknown, research suggests a strong genetic component. NIH funds a number of studies to determine the underlying genetic causes of MS, including a project to identify regions of the genome containing MS susceptibility genes using a large familial dataset and genomic analysis tools. NIH also funds clinical trials to test therapies for MS, including the CombiRx trial, a randomized, controlled clinical trial comparing the efficacy of treatment combining interferon-beta (IFN) and glatiramer acetate (GA) versus treatment with a single agent for relapsing forms of MS. A study conducted in conjunction with CombiRx by NIH intramural researchers (BioMS) is assessing MS biomarkers using genomic and proteomic technology and relating the information obtained back to clinical and MRI data generated by the CombiRx clinical trial.

- [Gregory SG, et al. \*Nat Genet\* 2007;39:1083-91](#), PMID: 17660817
- [International Multiple Sclerosis Genetics Consortium, et al. \*N Engl J Med\* 2007;357:851-62](#), PMID: 17660530
- This example also appears in Chapter 2: *Autoimmune Diseases* and Chapter 2: *Neuroscience and Disorders of the Nervous System*
- (E/I) (NINDS)

**Toward Better Treatment for Muscular Dystrophy:** Activities funded by NIH are pursuing multiple pathways to therapeutic development for the muscular dystrophies. NIH funds six Senator Paul D. Wellstone Muscular Dystrophy Cooperative Research Centers, designed to accelerate the translation of fundamental scientific

advances to the clinic (see Chapter 4). NIH also recently funded two large-scale translational research projects in MD: one to develop small molecule drugs for Duchenne and potentially other forms of MD and another to develop the optimal vector for vascular delivery of genes. A new NIH GPRA goal aims to advance two emerging strategies for treating MD to clinical trial readiness by 2013. The Muscular Dystrophy Coordinating Committee's (MDCC) *Action Plan for the Muscular Dystrophies* also identified therapy development goals to be pursued by NIH and its MDCC partner agencies and organizations. A recent workshop convened by NIH reviewed the status of different therapeutic approaches for MD and discussed ways to move this research forward.

- For more information, see [http://www.ninds.nih.gov/find\\_people/groups/mdcc/MDCC\\_Action\\_Plan.pdf](http://www.ninds.nih.gov/find_people/groups/mdcc/MDCC_Action_Plan.pdf)
- For more information, see [www.wellstonemdcenters.nih.gov](http://www.wellstonemdcenters.nih.gov)
- This example also appears in Chapter 2: *Neuroscience and Disorders of the Nervous System*
- (E) (NINDS, NIAMS, NICHD)

**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 multi site trials—involving over 10,000 subjects at over 200 sites—has forged efficient, effective, and collaborative relationships between scientists and clinicians throughout the country. In order 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 between 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>
- For more information, see <http://www.nimh.nih.gov/healthinformation/stard.cfm>
- For more information, see <http://www.nimh.nih.gov/healthinformation/stepbd.cfm>
- This example also appears in Chapter 2: *Neuroscience and Disorders of the Nervous System* and Chapter 2: *Chronic Diseases and Organ Systems*
- (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 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 interdisciplinary investigations employing molecular, physiological, biochemical, immunological, genetic, behavioral, and social science approaches. This work is beginning to shed light on many facets of the 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 effect in the relationship between patient and health care provider.

- [Zubieta JK, et al. \*J Neurosci\* 2005;25:7754-62](#), PMID: 16120776
- This example also appears in Chapter 2: *Chronic Diseases and Organ Systems* and Chapter 2: *Neuroscience and Disorders of the Nervous System*.
- (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 contribute 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: *Chronic Diseases and Organ Systems* and Chapter 2: *Neuroscience and Disorders of the Nervous System*
- (E) (NCCAM)

**Gene Therapy for Leber's Congenital Amaurosis (LCA):** LCA is a rare, inherited retinal degenerative disease that causes severe vision loss in infancy and early childhood. Although currently untreatable, NIH-funded investigators have restored vision in dogs with LCA 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 2: *Chronic Diseases and Organ Systems*.
- (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 often requiring 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 severe uveitis.

- For more information, see <http://www.musttrial.org/>
- This example also appears in Chapter 2: *Chronic Diseases and Organ Systems*.
- (E) (NEI)

**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 sickle cell disease patients who have pulmonary hypertension. A randomized, double-blind, placebo-controlled Phase II clinical trial is testing the drug's safety and its 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>
- This example also appears in Chapter 2: *Chronic Diseases and Organ Systems* and Chapter 2: *Minority Health and Health Disparities*.
- (E/I) (NHLBI)

**Maternal Oral Health and Obstetric Outcomes:** In recent years evidence has suggested that a pregnant woman with periodontal (gum) disease might be at increased risk for premature birth. Two similar but not identical NIH-supported trials evaluate this possibility. Conducting more than one large clinical trial on this important public health question will cast a wide enough investigational net to determine which, if any, women are at risk. One study, called the *Obstetrics and Periodontal Therapy Trial (OPT)* recently concluded that periodontal treatment during pregnancy is safe for mother and baby but does not significantly lower preterm birth risk. The *Maternal Oral Therapy to Reduce Obstetric Risk (MOTOR)* study is ongoing.

- For more information, see <http://www.nidcr.nih.gov/Research/ResearchResults/NewsReleases/ArchivedNewsReleases/NRY2006/PR11012006.htm>
- For more information, see <http://www.nidcr.nih.gov/Research/ResearchResults/InterviewsOHR/TIS072005.htm>
- This example also appears in Chapter 2: *Life Stages, Human Development, and Rehabilitation*.

- (E) (NIDCR)

**The PCOS Twin Study:** The PCOS (Polycystic Ovarian Syndrome) Twin Study is sponsored by NIH. NIH researchers are studying polycystic ovary syndrome in twins to find out if it is caused by genetics or the environment or a combination of both. Once scientists know more about the causes of PCOS, then health care professionals can then treat it more effectively or possibly lower the chance that a woman will develop it.

- For more information, see <http://www.niehs.nih.gov/pcos/index.htm>
- (I) (NIEHS)

**Salivary Gene Transfer and Therapeutics:** Gene transfer may be an ideal strategy to boost salivary production for cancer patients whose salivary glands were damaged during radiation therapy. While radiation therapy kills cancerous cells, it frequently also destroys the acinar (fluid-producing) salivary gland cells that lie within the salivary gland in grape-like clusters. Patients are unable to produce adequate saliva and suffer a host of long-term problems such as recurrent oral infections and difficulties with swallowing, speech, and taste. Unlike acinar cells, ductal cells in the salivary gland (which can be thought of as the “stems” on the grapes) often survive irradiation. But they cannot make or secrete saliva. NIH scientists used gene transfer techniques to insert an aquaporin protein gene into the ductal cells; aquaporins are a family of proteins that form pores in cell membranes, through which fluid can pass. Their insertion “plumps up” the stems and allows the flow of fluid into the mouth again. The scientific team has collaboratively and methodically moved this promising idea through the research process, benefiting greatly from the wealth of scientific expertise on the NIH campus. This year, FDA approved the first clinical trial of gene transfer into the salivary glands for cancer patients with dry mouth. Although the outcome of clinical trials is always hard to predict, the preclinical data have been extremely promising.

- This example also appears in Chapter 2: *Cancer*.
- (I) (NIDCR)

**Long-Term Oxygen Treatment Trial (LOTT):** Although oxygen therapy is known to benefit patients who have chronic obstructive pulmonary disease (COPD) and 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 management of such patients and to provide a basis for Medicare coverage decisions. LOTT is the focus of a new NIH Government Performance and Results Act (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.nhlbi.nih.gov/new/press/06-11-20.htm>
- This example also appears in Chapter 2: *Chronic Diseases and Organ Systems*.
- (E) (NHLBI) (GPRA Goal)

**HIV/AIDS Epidemiological and Long-Term Cohort Studies:** NIH supports epidemiological HIV research through a wide range of cohort studies that contribute to our understanding of risk factors that lead to HIV transmission and disease progression. Established in 2005, the International Epidemiologic Databases to Evaluate AIDS (IeDEA) compiles data from NIH-funded international HIV research to answer population-level questions about HIV variants and resistance, HIV pathogenesis in different settings, success of antiretroviral therapy, treatment history of HIV in different populations, success of prevention strategies, and vaccines. The Pediatric HIV/AIDS Cohort Study (PHACS), established in 2005, addresses two critical pediatric HIV research questions: the long-term safety of fetal and infant exposure to prophylactic antiretroviral chemotherapy and the effects of perinatally acquired HIV infection in adolescents. The Women's Interagency HIV Study (WIHS) and the Multicenter AIDS Cohort Study (MACS) are the two largest observational studies of HIV/AIDS in women and homosexual or bisexual men,

respectively, in the United States. These studies exceed standard clinical care diagnostics and laboratory analysis on both HIV-infected, and, importantly, HIV-negative controls, which allows for novel research on how HIV spreads, how the disease progresses, and how it can best be treated. The studies focus on contemporary questions such as the interactions among HIV infection, aging, and long-term treatment; cardiovascular disease; and host genetics and their influence on susceptibility to infection, disease progression, and response to therapy.

- For more information, see <http://www3.niaid.nih.gov/news/newsreleases/2007/ctu07.htm>
- This example also appears in Chapter 3: *Epidemiological and Longitudinal Studies* and Chapter 2: *Infectious Diseases and Biodefense*
- (E) (NIAID) (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.

- [The Look AHEAD Research Group. \*Diabetes Care\* 2007;30:1374-83](#), PMID: 17363746
- For more information, see <http://tinyurl.com/2xaypk>
- This example also appears in Chapter 2: *Chronic Diseases and Organ Systems* and Chapter 2: *Minority Health and Health Disparities*.
- (E/I) (NIDDK, CDC, NCMHD, NHLBI, NINR, ORWH) (GPRA Goal)

**Interventions and Services for Youth With Mental Illness Who Are Transitioning to Adulthood:** The transition to adulthood for youth with mental illness is often a period in which care is compromised, with a host of negative outcomes. In 2006, NIH launched an initiative to stimulate research on refining and testing interventions in service delivery models for youth transitioning to adulthood. Four applications were funded.

- For more information, see <http://grants.nih.gov/grants/guide/rfa-files/RFA-MH-07-050.html>
- <http://www.nimh.nih.gov/science-news/2007/new-research-to-help-youth-with-mental-disorders-transition-to-adulthood.shtml>
- This example also appears in Chapter 2: *Life Stages, Human Development, and Rehabilitation*.
- (E) (NIMH)

**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 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://www.areds2.org/>
- This example also appears in Chapter 2: *Chronic Diseases and Organ Systems* and Chapter 2: *Neuroscience and Disorders of the Nervous System*.
- (E) (NEI, NIA)

**Improved Management of Antiretroviral Therapy for Adults and Children:** Two recent NIH studies transformed the management of antiretroviral therapy (ART) by extending survival of adults and children with HIV/AIDS. Results from the Strategies for Management of Antiretroviral Therapy (SMART) study, one of the largest HIV/AIDS treatment trials ever conducted, showed that episodic use of ART based on CD4+ cell levels is inferior to use of

continuous therapy for treatment-experienced patients and that deliberately interrupting antiretroviral therapy more than doubles the risk of developing AIDS or dying from any cause. The Children with HIV Early Antiretroviral Therapy (CHER) Study examined early ART in South African children. Interim data showed a 96 percent increase in survival among infants who received immediate ART compared to infants who received therapy later.

- [SMART Study Group et al. \*N Engl J Med\* 2006;355:2283-96](#), PMID: 17135583
- For more information, see <http://www3.niaid.nih.gov/news/newsreleases/2006/smart06.htm>
- This example also appears in Chapter 2: *Infectious Diseases and Biodefense*.
- (E) (NIAID)

**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 under three. 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.

- For more information see <http://www3.niaid.nih.gov/topics/allergicDiseases/researchActivities.htm>
- This example also appears in Chapter 2: *Chronic Diseases and Organ Systems* and Chapter 3: *Epidemiological and Longitudinal Studies*
- (E) (NIAID)

**Therapies to Treat and Prevent Food Allergies:** The NIH Consortium of Food Allergy Research is developing immune-based approaches to treat food allergy, rather than to simply avoid food allergens. Basic studies are ongoing using mouse models to study how modified forms of peanut allergens protect against peanut-induced anaphylaxis. The five clinical sites of the Consortium are developing treatment and prevention strategies for food allergy, and they work to educate parents and health care providers regarding food allergies. An ongoing observational study is examining immune mechanisms, genetic factors, and environmental factors associated with the development of new food allergy to peanut and the loss of egg allergy to high-risk children. An interventional study aims to determine the safety and immunologic effects of giving egg by mouth to egg-allergic children, with the goal of inducing immunological tolerance. Phase I clinical trials are assessing the safety of treating peanut-allergic subjects with either a modified form of peanut allergen or small amounts of peanut allergen under the tongue.

- For more information, see <http://www3.niaid.nih.gov/topics/foodAllergy/default.htm>
- This example also appears in Chapter 3: *Epidemiological and Longitudinal Studies*.
- (E) (NIAID)

**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 joint and muscle (TMJ) 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 TMJ disorders and advance virtually all aspects of understanding and caring for these disorders.

- For more information, see

<http://www.nidcr.nih.gov/Research/ResearchResults/NewsReleases/ArchivedNewsReleases/NRY2005/PR12052005.htm>

- For more information, see <http://www.nidcr.nih.gov/Research/ResearchResults/InterviewsOHR/TIS012006.htm>
- This example also appears in Chapter 2: *Chronic Diseases and Organ Systems* and Chapter 3: *Epidemiological and Longitudinal Studies*.
- (E) (NIDCR)

**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 additionally 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: *Chronic Diseases and Organ Systems* and Chapter 2: *Life Stages, Human Development, and Rehabilitation*.
- (E) (NIDDK, ORWH)

**Polycystic Kidney Disease (PKD):** The Consortium for Radiologic Imaging Studies of PKD (CRISP) showed that magnetic resonance imaging could accurately track structural changes in the kidneys in 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 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.

- [Grantham JJ, et al. \*N Engl J Med\* 2006;354:2122-30, PMID: 16707749](#)
- For more information, see <http://tinyurl.com/2qu94j>
- For more information, see <http://www.pkd.wustl.edu/pkd-tn/>
- This example also appears in Chapter 2: *Chronic Diseases and Organ Systems* 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.

- [Albo ME et al. \*N Engl J Med\* 2007;356:2143-55, PMID: 17517855](#)
- For more information, see <http://www.nih.gov/news/pr/may2007/niddk-21.htm>
- This example also appears in Chapter 2: *Chronic Diseases and Organ Systems*.
- (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 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>

- For more information, see <http://www.searchfordiabetes.org/>
- This example also appears in Chapter 2: *Chronic Diseases and Organ Systems*, Chapter 3: *Epidemiological and Longitudinal Studies*, and Chapter 2: *Life Stages, Human Development, and Rehabilitation*.
- (E) (NIDDK, CDC)

**Centers on Suicide Prevention:** In response to the 2002 Institute of Medicine Report, “Reducing Suicide: A National Imperative,” NIH issued a request for applications and funded three centers focused on intervention and prevention of suicide. Now in their third year of support, the centers have conducted pilot intervention studies with patients suffering from mental and substance use disorders.

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

**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, firefighters, police, and rescue workers.

- For more information, see <http://grants.nih.gov/grants/guide/rfa-files/RFA-MH-08-010.html>
- This example also appears in Chapter 2: *Chronic Diseases and Organ Systems* and Chapter 2: *Neuroscience and Disorders of the Nervous System*.
- (E) (NIMH)

**ClinicalTrials.gov:** Established in 2000 in response to congressional mandate (Pub. L. No. 105-115), [ClinicalTrials.gov](http://ClinicalTrials.gov) has grown to become the largest clinical trial registry in the world with information on clinical research studies for hundreds of diseases and conditions conducted in 148 countries. At the end of September 2007, it contained more than 47,000 registered trials—more than double the number of entries 2 years earlier. Legislation enacted in September 2007, the Food and Drug Administration Amendments Act of 2007 (Pub. L. No. 110-85), expanded the scope of trials to be registered with [ClinicalTrials.gov](http://ClinicalTrials.gov) and the registration information to be provided. It also mandates the inclusion of specified results information beginning in September 2008.

- [Drazen JM, et al. \*N Engl J Med\* 2007;356:184-5](#), PMID: 17215537
- [Zarin DA, et al. \*N Engl J Med\* 2005;353:2779-87](#), PMID: 16382064
- For more information, see <http://clinicaltrials.gov>
- This example also appears in Chapter 3: *Disease Registries, Databases, and Biomedical Information Systems*.
- (I) (NLM)

**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.

- [Manheimer E, et al. \*Acupunct Med\* 2006;24:S7-14](#), PMID: 17308513
- This example also appears in Chapter 2: *Chronic Diseases and Organ Systems* and Chapter 2: *Neuroscience and Disorders of the Nervous System*.
- (E) (NCCAM)

**Research on Popular Dietary Supplements:** A significant body of research on complementary and alternative medical 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 1200 IU/day for 2 years had no effect on serum concentrations of total, LDL, or HDL cholesterol.
- [Clegg DO, et al. \*N Engl J Med\* 2006;354:795-808](#), PMID: 16495392
- [Singh U, et al. \*Clin Chem\* 2007;53:525-8](#), PMID: 17234730
- This example also appears in Chapter 2: *Chronic Diseases and Organ Systems*.
- (E) (NCCAM, NIAMS, ODS)

**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 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.

- [Habashi JP, et al. \*Science\* 2006;312:117-21](#), PMID: 16601194
- For more information, see <http://clinicaltrials.gov/show/NCT00429364>
- For more information, see <http://www.pediatricheartnetwork.org/>
- This example also appears in Chapter 2: *Chronic Diseases and Organ Systems* and Chapter 3: *Molecular Biology and Basic Sciences*.
- (E) (NHLBI)

**Hepatitis C Antiviral Long-Term Treatment Against Cirrhosis (HALT-C) Trial:** The HALT-C trial studies whether long-term antiviral therapy can prevent liver disease progression 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 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.haltctrial.org/> .
- This example also appears in Chapter 2: *Chronic Diseases and Organ Systems*
- (E) (NIDDK, NCI, NIAID)

**Compliance With the NIH Policy on the Inclusion of Women and Minorities as Subjects in Clinical Research:** NIH works to ensure compliance with the NIH Policy for the Inclusion of Women and Minorities as Subjects in Clinical Research by convening a trans-NIH committee that addresses consistency in inclusion policy implementation and population data reporting. Over the last 2 years, a more streamlined method of reporting minority participation in

NIH-funded clinical research has been developed; the most recent Federal standards for reporting race and ethnicity have been clarified; and new methodologies for collecting and reporting more reliable population data from investigators have been implemented. In 2007, ORWH collaborated with OER in providing training sessions for grants management, review, and program staff on implementation of the NIH inclusion policy. These mandatory training sessions, “Sex/Gender, Race and Ethnicity Inclusion in Clinical Research,” were designed to help participants better understand congressionally mandated inclusion policies and how to implement them, reemphasized the vital role and responsibilities of NIH staff members in the management of grants, contracts, and cooperative agreements that involve human subjects research, and also highlighted the role of NIH staff, peer reviewers, and investigators in meeting inclusion policy requirements. In addition to these activities, NIH prepared the annual aggregate comprehensive reports: Monitoring Adherence to the NIH Policy on the Inclusion of Women and Minorities as Subjects in Clinical Research (see Appendix E) as well as the 2007 Biennial Report Certifying IC Compliance with the Inclusion Guidelines based upon IC Advisory Council reviews, as required by statute.

- For more information, see <http://orwh.od.nih.gov/inclusion.html>
- (E, I) (ORWH, OER)

**Developing Pediatric Drug Data:** Clinicians prescribing pharmaceuticals for sick infants and children face major gaps in the scientific data on safety and efficacy of pharmaceuticals for their young patients. Obtaining available data from drug trials in adults is often problematic because of important differences in the ways that drugs act in the bodies of adults and children. Furthermore, data from adults cannot be used to characterize the effects of drugs on children's development and health over time. To respond to this concern, Congress passed the Best Pharmaceuticals for Children Act (BPCA) to support the additional research needed to test the effect of pharmaceuticals specifically for children. NIH, in collaboration with FDA and private-sector experts and organizations, maintains an extensive program for identifying priority drugs used “off label” in children—that is, prescribed without safety and efficacy data that would be required for FDA to approve or label them for use in children. This program involves requests to industry for needed pediatric research on priority “off-patent” drugs and conducting studies of priority drugs that industry declines to undertake. Under NICHD leadership, NIH Institutes participate in the ongoing BPCA program, including its funding.

- For more information, see <http://bpca.nichd.nih.gov/index.cfm>
- (E/I) (NICHD)

**Web-Based Instruction on the Science of Sex and Gender in Human Health:** NIH, in collaboration with the Office of Women's Health, U.S. Food and Drug Administration (FDA), developed a Web-based course in 2006 to create a permanent foundation for sex and gender accountability in medical research and treatment. The course provides uniform instruction for physicians and scientists to meet the NIH and FDA requirements for inclusion, and the implications of sex and gender differences for policy, research, and health care. The course addresses the scientific basis of known sex and gender differences and explores the influence of sex and gender differences on health outcomes and illness. Each lesson is interactive and includes seminal references on topics such as developmental biology and pharmacogenomics.

- For more information see <http://sexandgendercourse.od.nih.gov/>
- (E) ORWH, NICHD, NHLBI, FDA, AHRQ

## Putting Clinical Research Results Into Practice

**Success in Treating Drug Addiction Internationally:** International efforts to disseminate effective drug abuse treatments have seen success in countries with epidemic opiate addiction/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, 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.

- [Mazlan M, Schottenfeld RS, Chawarski MC. \*Drug Alcohol Rev\* 2006;25:473-8](#), PMID: 16939945
- This example also appears in Chapter 2: *Chronic Diseases and Organ Systems* and Chapter 2: *Infectious Diseases and Biodefense*.
- (E) (NIDA, NIAID)

**Value of Early HIV Screening, Testing, and Counseling:** HIV/AIDS disproportionately affects several minority groups, particularly African Americans. Although adult and adolescent African Americans make up ~13 percent of the population, they accounted for half of the new HIV/AIDS diagnoses in 2001-2005. This disparity is particularly striking because African Americans do not have higher rates of addiction or intravenous drug use than Whites. One contributing factor is that African Americans are often diagnosed with HIV infection at a later point in the illness, increasing their likelihood of progressing to AIDS and of transmitting the disease. As part of efforts to prevent late diagnosis and HIV spread, NIH is working to identify and address the cultural barriers to making HIV screening more acceptable and to strengthen the link between education, testing and counseling, and treatment within all ethnic groups. Indeed, NIH-supported modeling research has shown that routine HIV screening, even among populations with prevalence rates as low as 1 percent, is as cost-effective as screening for other conditions such as breast cancer and high blood pressure. These findings have important public health implications, recognized by the Centers for Disease Control and Prevention (CDC), which has called for increased HIV screening as part of its recommended guidelines. NIH is eager to advance new HIV rapid-screen technologies and counseling in community drug treatment programs and in criminal justice settings.

- For more information, see <http://www.drugabuse.gov/ResearchReports/hiv/hiv.html>
- For more information, see <http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5514a1.htm>
- This example also appears in Chapter 2: *Infectious Diseases and Biodefense* and Chapter 2: *Minority Health and Health Disparities*.
- (E) (NIDA)

**Diagnostic Genetic Test Translation From the Research Laboratory to the Clinic:** Because the majority of rare diseases are genetic disorders, genetic testing is an essential part of diagnosis and treatment. Few incentives exist for translating research findings into clinical tests that are available to the public. To address this gap, NIH created the Collaboration, Education and Test Translation (CETT) for Rare Genetic Diseases pilot program. The CETT pilot program brings new genetic and diagnostic tests to patients, encourages clinical laboratory and research collaborations, and stimulates dialogue with patient advocacy groups. Goals include developing models for information on clinical uses of the test; how the test results will be interpreted for clinical care providers, patients, and their families; methods to collect and store in publicly accessible databases the clinical information on each sample necessary to interpretation, while at the same time respecting confidentiality; and methods to collect and store test result information in publicly accessible databases. Since February/March 2006, 21 tests have been reviewed and 19 have been approved. The CETT pilot program has seen the successful development of 10 clinical tests for Cornelia de Lange syndrome, Joubert syndrome, cherubism, X-linked chondrodysplasia punctata, Kallmann syndrome, progressive familial intrahepatic cholestasis, Russell Silver syndrome, MPS VI, Niemann Pick disease A/B, and X-linked periventricular nodular heterotopia. These tests address more than 18 conditions and 13 genes. Tests for primary ciliary dyskinesia, infantile neuroaxonal dystrophy, and arginase deficiency will be

released later this year and more tests are under development.

- For more information, see <http://www.cettprogram.org>
- (E/I) (ODP/ORD, NLM)

**Advances in Oral Cancer Detection:** The first product of a current NIH-funded research project to integrate new technologies into a reliable clinical protocol to improve oral cancer detection and survival has reached the market. Researchers report success using a customized optical device that allows dentists to visualize in a completely new way whether a patient might have a developing oral cancer. The simple, handheld device emits a cone of light into the mouth that excites molecules within our cells, causing them to absorb the light energy and re-emit it as visible fluorescence. Remove the light, and the fluorescence disappears. Changes in the natural fluorescence of healthy tissue can indicate light-scattering changes caused by developing tumor cells. Health care providers shine a light onto a suspicious sore in the mouth, look through an attached eyepiece, and check for changes in color. Normal oral tissue emits a pale green fluorescence, while early tumor cells appear dark green to black. The instrument is an effective screening adjunct and is useful for helping surgeons determine how far to extend the surgical borders when removing tissue for biopsies.

- For more information, see <http://clincancerres.aacrjournals.org/cgi/content/full/12/22/6716>
- This example also appears in Chapter 2: *Cancer* and Chapter 3: *Technology Development*.
- (E) (NIDCR)

**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 NCMHD and others cofunds the HEAL Project (Head Off Environmental Asthma in Louisiana) to assess the impact on asthma in New Orleans children of environmental health conditions that were caused and exacerbated by Hurricane Katrina, as well as to implement an intervention program to address these problems. The project's three main goals are to conduct an extensive epidemiology study to assess the nature of the environmental and psychological impacts of Hurricane Katrina and subsequent flooding on children in New Orleans; to examine the genetic and environmental risk factors for asthma, including genetic susceptibility to mold toxins, and gene interactions; and 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 outcome, as well as for receiving input from the community.

- For more information, see <http://heal.niehs.nih.gov/>
- This example also appears in Chapter 2: *Chronic Diseases and Organ Systems* and Chapter 2: *Minority Health and Health Disparities*
- (I) (NIEHS, NCMHD)

**The Report on Carcinogens, Eleventh Edition:** More than 80,000 chemicals are registered for use in the United States. Each year, an estimated 2,000 new ones are introduced for use in such everyday items as foods, personal care products, prescription drugs, and household cleaners. In response to concerns about the relationship between environment and cancer, the National Toxicology Program (NTP), an interagency program led by NIEHS, produces the Report on Carcinogens (RoC) biennially. The RoC is an informational scientific and public health document that identifies and discusses agents, mixtures, or exposure circumstances that may pose a hazard to health by virtue of their carcinogenicity. It includes data on the carcinogenicity, genotoxicity, and biologic mechanisms of the listed substances in humans and/or animals, the potential for human exposure to these substances, and Federal regulations to limit exposures.

- For more information, see [http://ntp.niehs.nih.gov/files/11thROC\\_factsheet\\_1-31-05.pdf](http://ntp.niehs.nih.gov/files/11thROC_factsheet_1-31-05.pdf)
- For more information, see <http://ntp.niehs.nih.gov/go/roc>

- (O) (NIEHS)

**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 trained to implement them. This work is occurring through the National Drug Abuse Treatment Clinical Trials Network (CTN) at NIH, which involves practitioners from community treatment programs (CTPs) 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 CTPs 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/>
- For more information, see <http://www.cjdats.org/>
- For more information, see <http://www.drugabuse.gov/Blending/>
- This example also appears in Chapter 2: *Chronic Diseases and Organ Systems*, Chapter 3: *Health Communication and Information Campaigns and Clearinghouses*, and Chapter 2: *Neuroscience and Disorders of the Nervous System*.
- (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, etc. and (2) Motivational Incentives for Enhanced Drug Abuse Recovery, a cost-effective incentive method for cocaine and methamphetamine addiction, 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>
- For more information, see <http://www.drugabuse.gov/Testimony/6-28-06Testimony.html>
- This example also appears in Chapter 2: *Chronic Diseases and Organ Systems* and Chapter 2: *Neuroscience and Disorders of the Nervous System*.
- (E) (NIDA)

**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 (PAR) 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 PAR serves as the basis for a GPRA Goal as well. 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>
- (E/I) (NIMH, NCI, NIAAA, NICHD, NIDA, NIDCD, NIDCR, NINR) (GPRA Goal)

**Science of Dissemination and Implementation:** Relatively little is known about how to ensure that the lessons learned from research inform and improve the quality of health and human services in the population at large. The goals of the program announcement, *Dissemination and Implementation Research in Health, and conference, Building the Science of Dissemination and Implementation in the Service of Public Health* (September 2007), are to support innovative approaches to identifying, understanding, and overcoming barriers to the adoption, adaptation, implementation, and maintenance of evidence-based practices by health providers, insurers, policymakers, and the public.

- For more information, see <http://grants.nih.gov/grants/guide/pa-files/PAR-07-086.html>
- For more information, see <http://obssr.od.nih.gov/di2007/index.html>
- This example also appears in Chapter 3: *Health Communication and Information Campaigns and Clearinghouses*.
- (E) (NCI, NHLBI, NIAAA, NICHD, NIDA, NIDCD, NIDCR, NIMH, NINR, OBSSR, ODS)

**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 <http://grants.nih.gov/grants/guide/pa-files/PAR-06-532.html>
- This example also appears in Chapter 2: *Chronic Diseases and Organ Systems* and Chapter 2: *Minority Health and Health Disparities*.
- (E) (NIDDK)

**Comprehensive Review of Meditation Research:** A recent comprehensive literature review on meditation research included over 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>
- This example also appears in Chapter 2: *Chronic Diseases and Organ Systems*.
- (E) (NCCAM)

**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 discectomy is generally effective in relieving pain from herniated discs, but—if their pain is tolerable—their symptoms will likely 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.

- [Weinstein JN, et al. JAMA 2006;296:2441-50](#), PMID: 17119140
- [Weinstein JN, et al. JAMA 2006;296:2451-9](#), PMID: 17119141

- [Weinstein JN, et al. \*N Engl J Med\* 2007;356:2257-70](#), PMID: 17538085
- For more information, see [http://www.niams.nih.gov/News\\_and\\_Events/Spotlight\\_on\\_Research/2006/backpain\\_surgery.asp](http://www.niams.nih.gov/News_and_Events/Spotlight_on_Research/2006/backpain_surgery.asp)
- For more information, see [http://www.niams.nih.gov/News\\_and\\_Events/Press\\_Releases/2007/06\\_28.asp](http://www.niams.nih.gov/News_and_Events/Press_Releases/2007/06_28.asp)
- This example also appears in Chapter 2: *Chronic Diseases and Organ Systems*.
- (E) (NIAMS, NIOSH, ORWH)

**Neonatal Onset Multisystem Inflammatory Disease (NOMID):** For children and young adults who suffer from a rare and debilitating disorder called NOMID, the arthritis drug anakinra brings marked improvement in both symptoms and the inflammation underlying the disease.

- [Goldbach-Mansky R, et al. \*Arthritis Rheum\* 2007;56:2099-101; author reply 2101-2](#), PMID: 17530657
- For more information, see [http://www.niams.nih.gov/News\\_and\\_Events/Press\\_Releases/2006/08\\_09.asp](http://www.niams.nih.gov/News_and_Events/Press_Releases/2006/08_09.asp)
- (I) (NIAMS)

## Bolstering the Research Continuum

**Clinical Trials Education:** Materials represent a collection of over 20 resources developed to increase awareness and participation in cancer prevention and treatment clinical trials. These materials include workbooks, a guide for community outreach, a trainer's guide, online courses for health professionals, DVDs, and slide sets to assist in education programs.

- For more information, see <http://cancer.gov/publications>
- This example also appears in Chapter 2: *Cancer* and Chapter 3: *Health Communication and Information Campaigns and Clearinghouses*.
- (E/I) (NCI)

**Health Care Delivery Consortia To Facilitate Discovery and Improve Quality of Cancer:** NIH supports several research consortia that are designed to enhance understanding of cancer control across the continuum of prevention, screening, and treatment within the context of health care delivery.

- The most comprehensive of these initiatives, the **Cancer Research Network (CRN)**, seeks to improve the effectiveness of preventive, curative, and supportive interventions for major and rare tumors. The CRN consists of the research programs, enrolled populations, and data systems of 13 health maintenance organizations covering care for over 9 million enrollees, or 3 percent of the U.S. population. This initiative uses a consortium of delivery systems to conduct research on cancer prevention, early detection, treatment, long-term care, and surveillance. Given its large and diverse populations, the CRN is uniquely positioned to study the quality of cancer care in community-based settings and to explore rare conditions. Seminal research includes, for example, CRN research documenting specific gaps in implementing effective tobacco cessation services among clinicians, reasons for late diagnosis of breast and cervical cancer, more rapid uptake in the use of aromatase inhibitors in comparison to tamoxifen in treatment for breast cancer, and examination of the role of a number of common drugs and cancer outcomes using its large and automated pharmaceutical databases.
- In the area of the evaluation of cancer screening in clinical care, the **Breast Cancer Surveillance Consortium (BCSC)** is a collaborative network of mammography registries linked to tumor and/or pathology registries designed to assess the delivery and quality of breast cancer screening and related patient outcomes in the United States. Because of the vast size and continually updated clinical information in this research initiative, the BCSC is responsible for research that for the first time documented the falling incidence of hormone replacement therapy among screened women, quantified the extent of difference in the association of breast density with breast cancer risk among pre- and postmenopausal women, and identified that although biopsy rates are twice as high in the United States in comparison to the United Kingdom, cancer detection rates are very similar in the two countries.

- In an effort to address how characteristics of patients, providers, and care delivery systems affect the cancer management and treatment services that patients receive, as well as the relationship between cancer-related clinical practices and outcomes, including patient-centered outcomes, such as symptom control and quality of life, the **Cancer Care and Outcomes Research Surveillance Consortium (CanCORS)** was established. It supports prospective cohort studies on 10,000 patients with newly diagnosed lung or colorectal cancers across geographically diverse populations and health care systems and examines issues related to health outcomes, costs, and patient-centered issues such as symptom control and quality of life.
  - For more information, see <http://crn.cancer.gov/>
  - For more information, see <http://breastscreening.cancer.gov>
  - For more information, see <http://healthservices.cancer.gov/cancors/>
  - This example also appears in Chapter 2: *Cancer*, Chapter 3: *Disease Registries, Databases, and Biomedical Information Systems*, and Chapter 3: *Epidemiological and Longitudinal Studies*.
  - (I) (NCI)

**Clinical and Translational Science Award (CTSA) Program Progress:** Since the inception of the CTSA program, NIH has made significant progress in building a national consortium for clinical and translational research. The first CTSA awards were made in September 2006 to 12 academic health centers (AHCs) throughout the country, along with 52 planning grants to help institutions prepare to join the Consortium in the future. To meet the goal of 60 CTSA sites by 2012, NIH has developed and released annual funding opportunity announcements, which will provide AHCs, including those with General Clinical Research Centers (GCRCs), an opportunity to build on their existing resources and transform into this new integrated program. The CTSA infrastructure will not only enhance the research capacity already developed through the GCRC program, but will also create an integrated home for clinical and translational research and training. During the transition to the CTSA program, NIH is continuing to work closely with GCRCs and is allowing them flexibility on a case-by-case basis to plan and apply for a CTSA award.

- For more information, see <http://www.ctsaweb.org/>
- (E) (NCRR)

**Clinical Research Networks:** Clinical research is essential for translating laboratory findings into evidence-based interventions targeting an array of public health concerns. Many research programs involve collaborative networks, drawing scientists together to bring the benefits of clinical research to high-risk populations, hard-to-reach communities, and individuals with rare or understudied conditions. Among such networks that have generated significant findings to advance medical practice and improve public health are the Maternal and Fetal Medicine Network, Neonatal Research Network, Obstetric Pharmacology Research Network, Pediatric Critical Care Research Network, Pelvic Floor Disorders Network, Traumatic Brain Injury Clinical Trials Network, and Global Network for Women's and Children's Health Research.

- For more information, see <http://www.bsc.gwu.edu/mfmu/>, <https://neonatal.rti.org>
- For more information, see <http://www.nichd.nih.gov/about/org/crmc/opp/index.cfm>
- For more information, see <http://www.cpccrn.org/>, <http://www.pfdnetwork.org/>
- For more information, see <http://www.nichd.nih.gov/research/supported/TBI.cfm>
- For more information, see <http://www.nichd.nih.gov/publications/pubs/upload/GlobalNetwork.pdf>
- (E) (NICHD, FIC, NCCAM, NCI, NIDCR, NIDDK, ORWH)

**Centers of Excellence for Research on CAM (CERC), Developmental Centers for Research on CAM (DCRCs), and International Centers for Research on CAM:** These Centers bring cutting-edge scientific technology to programs of research on the usefulness, safety, and mechanisms of action of various CAM interventions. Based in collaborations between established biomedical research scientists and experts in CAM or traditional medicine, these programs are also aimed at enhancing the global state of research capacity on CAM. For example, the CERCs are led by scientists with outstanding research records who direct teams of investigators with both CAM and conventional scientific expertise. During the first 3 years of the CERC program, awardees have made sentinel

advances in our understanding of the scientific basis for the effects of acupuncture through the use of modern brain imaging, and they have explored innovative approaches to the treatment of asthma with antioxidants and approaches based on traditional Chinese medicine (TCM). Other CERCs are focusing on (1) the study of acupuncture and TCM herbal treatments of arthritis, (2) the effects of mindfulness meditation on the progression of HIV/AIDS, and (3) the mechanisms of action of millimeter wave therapy (use of low-intensity millimeter wavelength electromagnetic waves) for a variety of chronic conditions. NIH will fund additional CERCs in late FY 2007.

- For more information, see <http://nccam.nih.gov/training/centers/>
- This example also appears in Chapter 3: *Molecular Biology and Basic Sciences*.
- (E) (NCCAM)

**Resuscitation Outcomes Consortium:** Recognizing the critical importance of early intervention for victims of cardiopulmonary arrest and traumatic injury, in FY 2004 NIH and its U.S. and Canadian partners initiated the Resuscitation Outcomes Consortium, a large-scale network to conduct clinical trials of promising approaches to improving outcomes. During FY 2006-2007, two Consortium clinical trials began enrolling patients—one to compare the efficacy of three fluids for initial resuscitation of hypotensive or brain-injured patients, and the other to test two strategies for increasing blood flow during cardiopulmonary resuscitation. The Consortium also established a pre-hospital Cardiac Arrest and Trauma Registry across the United States and Canada. In addition, emergency medicine fellowship training programs established at several study sites are enhancing training in resuscitation medicine.

- For more information, see <https://roc.uwctc.org/>
- This example also appears in Chapter 3: *Disease Registries, Databases, and Biomedical Information Systems*.
- (E) (NHLBI, NINDS)

**Alzheimer's Disease Cooperative Study (ADCS):** Much of the AD-related clinical research supported by NIH takes place through the ADCS. The study involves a consortium of centers in the United States and Canada where clinical trials are carried out on promising new therapies that may preempt the onset of AD or predict the disease's development in vulnerable people. To date, approximately 4,600 people have participated in the trials. In FY 2007, new studies included a trial to demonstrate whether intravenous immunoglobulin (IVIg) is clinically useful for treating AD and a trial to examine whether treatment with docosahexaenoic acid (DHA), an omega-3 fatty acid, will slow cognitive decline in patients with AD.

- For more information, see <http://www.nia.nih.gov/NewsandEvents/PressReleases/PR20061017ADCS.htm>
- This example also appears in Chapter 2: *Neuroscience and Disorders of the Nervous System*.
- (E) (NIA)

**The Immune Tolerance Network:** In 2007, NIH renewed support for the Immune Tolerance Network (ITN), a consortium of over 80 investigators in the United States, Canada, Europe, and Australia. The ITN studies and tests new drugs and therapies for autoimmune diseases, asthma and allergies, and rejection of transplanted organs, tissues, and cells. ITN studies are based on stimulating immunological tolerance, the mechanism by which the immune system naturally avoids damage to self. Immune tolerance approaches aim to “reeducate” the immune system to eliminate harmful immune responses and graft rejection while preserving protective immunity against infectious agents. The ITN has established state-of-the-art core laboratory facilities to study the underlying mechanisms of candidate therapies and to monitor tolerance. In 2006, the ITN reported that a novel DNA-based ragweed allergy therapy could achieve long-lasting symptom reduction after only 6 weeks of therapy, compared to current methods that require years of biweekly injections. Current ITN studies include pancreatic islet transplantation for type 1 diabetes; approaches to slow or reverse progression of autoimmune diseases; approaches to treat and prevent asthma and allergic disorders such as food allergy; and therapies to prevent liver and kidney transplant rejection without causing harmful suppression of immunity.

- For more information, see <http://www.immunetolerance.org/>
- For more information, see <http://content.nejm.org/cgi/content/abstract/355/14/1445>
- This example also appears in Chapter 2: *Autoimmune Diseases* and Chapter 3: *Molecular Biology and Basic Sciences*
- (E) (NIAID)

**A Multidisciplinary Approach to Nicotine Addiction:** Nicotine addiction is the number one preventable public health threat, with enormous associated morbidity, mortality, and economic costs. NIH-supported research has generated new knowledge to support the development of more effective prevention messages and treatment approaches. Several notable examples characterize NIH's multidisciplinary approach to targeting the best treatment (or combination of treatments) for nicotine addiction. Genomic studies have recently uncovered a series of genes associated with nicotine addiction that could provide new targets for medications development and for the optimization of treatment selection. Pharmacologic studies, critical to understanding the basis of nicotine's mode of action, have recently revealed that its addictiveness may hinge upon its ability to slowly shut down or desensitize the brain's response to nicotine. A recent imaging study indicated that a part of the brain called the insula may play an important role in regulating conscious craving. This exciting finding provides a new target for research into the neurobiology of drug craving and for development of potentially more effective smoking cessation and other addiction treatments. Results of a Phase II clinical trial strongly suggest that a nicotine vaccine, which works by preventing nicotine from ever reaching the brain, may be a particularly useful tool for cessation programs in the not-too-distant future.

- For more information, see <http://www.drugabuse.gov/ResearchReports/Nicotine/Nicotine.html>
- This example also appears in Chapter 3: *Genomics*, Chapter 2: *Cancer*, and Chapter 2: *Neuroscience and Disorders of the Nervous System*
- (E) (NIDA, NCI) (GPRA Goal)

**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 the 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.”

- For more information, see <http://grants.nih.gov/grants/guide/rfa-files/RFA-HL-04-029.html>
- This example also appears in Chapter 2: *Chronic Diseases and Organ Systems* and Chapter 3: *Molecular Biology and Basic Sciences*.
- (E) (NHLBI, NIAID) (GPRA Goal)

**Programs to Accelerate Medications 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 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: *Chronic Diseases and Organ Systems* and Chapter 2: *Neuroscience and Disorders of the Nervous System*.
- (E/I) (NIAAA) (GPRA Goal)

**Antimicrobial Resistance Research:** Antimicrobial resistance, caused by factors such as overuse of antibiotics, is severely jeopardizing the utility of many “first line” antimicrobials and has emerged as a major public health threat. NIH supports a robust basic research portfolio on antimicrobial resistance, including studies of how bacteria develop and share resistance genes. For example, clinical studies are testing interventions for community-acquired multidrug-resistant *Staphylococcus aureus* (CA-MRSA) infection and to evaluate the efficacy of off-patent antimicrobials. A clinical study is evaluating the efficacy of antimicrobials in young children with acute ear infections through the comparison of symptom resolution in children receiving antimicrobial therapy versus placebo. Research initiatives such as “Sepsis and CAP [Community-Acquired Pneumonia]: Partnerships for Diagnostics Development” and “Partnerships to Improve Diagnosis and Treatment of Selected Drug-Resistant Healthcare-Associated Infections” are supporting the development of new diagnostics to facilitate the optimization of antimicrobial therapy and eliminate the overuse of broad-spectrum antimicrobials. NIH will continue to address high-priority research questions regarding resistance to help public health officials hold the line against drug-resistant microbes.

- For more information, see <http://www3.niaid.nih.gov/topics/AntimicrobialResistance/default.htm>.
- For more information, see <http://www3.niaid.nih.gov/topics/AntimicrobialResistance/research/default.htm>
- This example also appears in Chapter 2: *Infectious Diseases and Biodefense*
- (E/I) (NIAID) (GPRA Goal)

**Improving Transplantation Outcomes:** Organ transplantation prolongs survival and improves quality of life for children and adults suffering from 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 2: *Chronic Diseases and Organ Systems*.
- (E) (NIAID, NHLBI) (GPRA Goal)

**Clinical, Operational, and Health Services Research Training (noncommunicable diseases):** To successfully develop and implement health interventions in the developing world, a well-trained cadre of scientists is needed to plan, design, and conduct clinical, operational, health services, and prevention science investigations. NIH funds research training in these disciplines, which supports the development and implementation of evidence-based interventions for non-communicable disorders/diseases in low- to middle-income countries. Projects funded by this program require collaboration between U.S. and foreign institutions and include epidemiology, health services, and genetics research on major psychiatric disorders in India; a study examining the impact of institutionalization on children in Turkey; and multidisciplinary training in substance abuse research in Eastern Europe.

- For more information, see [http://www.fic.nih.gov/programs/training\\_grants/icohrta/index.htm](http://www.fic.nih.gov/programs/training_grants/icohrta/index.htm)
- This example also appears in Chapter 3: *Research Training and Career Development*.

- (E) (FIC, NIA, NIDA, NIDCR, NIMH, NINDS, ODS)

**HIV Research Training Programs:** The AIDS International Training and Research Program (AITRP) builds institutional, national, and regional HIV research capacity in low- and middle-income countries. Over the past 19 years, this program has been responsible for many of the first generation of research scientists from these countries, with many more in the pipeline. The program offers multidisciplinary biomedical, behavioral, and social science research training to a wide range of professionals. Building on the AITRP, the Clinical, Operational and Health Services Research Training Program for HIV/AIDS and TB (ICOHRTA AIDS/TB) began in 2002 to strengthen the capacity for clinical, operational, and health services research in low- and middle-income countries where AIDS, TB, or both are significant problems. Through training health professionals who reach across the spectrum of clinical and public health research, this program is strengthening the capacity of scientists, program managers and policymakers to evaluate and better implement large-scale prevention, treatment, and care interventions that are locally relevant and effective. Many local leaders of programs supported by the President's Emergency Plan for AIDS Relief have received or are receiving their research training through the AITRP and the ICOHRTA AIDS/TB programs.

- For more information, see [http://www.fic.nih.gov/programs/training\\_grants/aitrp/index.htm](http://www.fic.nih.gov/programs/training_grants/aitrp/index.htm)
- For more information, see [http://www.fic.nih.gov/programs/training\\_grants/icohrta/aids\\_tb.htm](http://www.fic.nih.gov/programs/training_grants/icohrta/aids_tb.htm)
- This example also appears in Chapter 3: *Research Training and Career Development* and Chapter 2: *Infectious Diseases and Biodefense*.
- (E) (FIC, NCI, NIAID, NHLBI, NIDA, NIDCR, NIMH, NINDS, NINR, OAR, ORWH)

**Clinical Trials Networks:** These networks are part of the infrastructure that allows patients and community physicians access to national studies, facilitating the ability to put successful regimens into practice:

- The Community Clinical Oncology Program (CCOP) is a network for conducting cancer prevention and treatment clinical trials. In 23 years of CCOPs, over 200,000 people have enrolled in treatment and prevention trials. An example is the Study of Tamoxifen and Raloxifene trial (STAR), which compares the effectiveness of these two drugs for reducing the incidence of breast cancer in postmenopausal women at increased risk of the disease. Initial results indicate that raloxifene is as effective as tamoxifen with fewer side effects.
- Cooperative Group Trials consist of researchers, Cancer Centers, and community doctors who investigate new cancer treatment, prevention, early detection, quality of life, and rehabilitation. They involve more than 1,700 institutions, thousands of individual investigators, and more than 22,000 patients each year. These trials are testing therapies that demonstrate improvement to overall patient survival. For example, the [Bevacizumab](#) with Platin-Based Chemotherapy study showed that when the monoclonal antibody bevacizumab is added to a paclitaxel-carboplatin chemotherapy regimen for patients with non-small cell lung cancer (NSCLC), their overall survival, progression-free survival, and response rates significantly increased.
- The NCI Community Cancer Centers Program (NCCCP) is a 3-year pilot program to test the concept of a national network of community cancer centers to alleviate inadequate care delivery. NCCCP will develop and evaluate programs on community-based cancer care and identify ways to facilitate their broader engagement in cancer research.
  - For more information, see <http://www.cancer.gov/STAR>
  - For more information, see <http://dcp.cancer.gov/programs-resources/programs/ccop>
  - For more information, see <http://ctep.cancer.gov/>
  - For more information, see <http://ncccp.cancer.gov/>
  - This example also appears in Chapter 2: *Cancer*.
  - (E) (NCI)

**The Radiation Research Program (RRP):** The RRP establishes priorities, allocates resources, and evaluates the effectiveness of radiation research and coordinates with other Federal radiation research programs. RRP has established guidelines for studying proton radiation therapy. Major trials are evaluating radiation dose escalation,

as well as novel combinations of chemotherapy with concomitant boost radiation therapy, in non-small cell lung cancer.

- [Bonner JA, et al. \*N Engl J Med\* 2006;354:567-78](#), PMID: 16467544
- [Bao S, et al. \*Nature\* 2006;444:756-60](#), PMID: 17051156
- This example also appears in Chapter 2: *Cancer*.
- (I) (NCI)

**The NCI Vaccine Program:** The Vaccine Program develops novel vaccines for cancer immunotherapy and prevention, and HIV. The program encourages collaborations, identifies organizational and reagent needs for the community, and develops the optimal infrastructure for vaccine development and novel clinical trial approaches. Gardasil, the first vaccine to prevent cervical cancer induced by HPV, is now available to potentially save over 5,000 U.S. women's lives each year. This FDA-approved vaccine resulted from the basic research performed at NIH producing a prototype vaccine and the observation that linked the human papillomavirus (HPV) and cervical cancer.

- This example also appears in Chapter 2: *Cancer* and Chapter 2: *Infectious Diseases and Biodefense*.
- (E/I) (NCI)

**Career Development for Veterinarians in Translational Biomedical Research:** Two recent reports from the National Academies, *National Need and Priorities for Veterinarians in Biomedical Research* and *Critical Needs for Research in Veterinary Science*, have confirmed the shortage of veterinarians involved in biomedical research. To address the shortage, NIH provides career development awards in biomedical research specifically for veterinarians and veterinary students. Mentored Career Development Awards to veterinarians serve as a bridge for postdoctoral fellows to become independent investigators. In FY 2006, 25 career development awards were made to young veterinary investigators to increase the number of researchers in this field. Additionally, an initiative that began in FY 2007 encourages the specialization of veterinarians in clinical medicine at NIH-supported primate centers to address the shortage of clinical veterinary support for research primate colonies.

- For more information, see <http://grants.nih.gov/grants/guide/rfa-files/RFA-RR-06-006.html>
- For more information, see [http://www.ncrr.nih.gov/career\\_development\\_opportunities/individual\\_training\\_grants/](http://www.ncrr.nih.gov/career_development_opportunities/individual_training_grants/)
- National Need and Priorities for Veterinarians in Biomedical Research: [http://books.nap.edu/catalog.php?record\\_id=10878](http://books.nap.edu/catalog.php?record_id=10878)
- Critical Needs for Research in Veterinary Science: [http://books.nap.edu/catalog.php?record\\_id=11366](http://books.nap.edu/catalog.php?record_id=11366)
- (E) (NCRR)

**Collaborative Community-Based Research:** NIH is focusing on strategies and best practices for conducting collaborative community-based clinical and translational research, particularly in minority communities and other medically underserved communities where health disparities persist. The Institutional Development Award (IDeA) and Research Centers in Minority Institutions (RCMI) programs are encouraging efforts to build and strengthen partnerships among Government agencies and academic and private-sector organizations that are also working to improve community health outcomes. Translational, community-based research funded in several IDeA states and RCMI-supported Centers, in both urban and rural settings, is focusing on:

- Enhancing recruitment and retention of research subjects through community buy-in
- Implementing practical and effective research protocols in community health care settings
- Developing versatile and sustainable core research infrastructure to encourage community participation and leverage existing resources In addition, in FY 2007 NIH conducted two workshops to gather specific recommendations from the community that will help shape future initiatives to enhance clinical and translational research in minority and other medically underserved communities ([www.esi-bethesda.com/ncrrworkshops/Fostering/index.aspx](http://www.esi-bethesda.com/ncrrworkshops/Fostering/index.aspx)). Workshop subjects included other HHS-agencies, such

as AHRQ, CDC, the Indian Health Service, and HRSA.

- For more information, see [www.ncrr.nih.gov/research\\_infrastructure](http://www.ncrr.nih.gov/research_infrastructure)
- This example also appears in Chapter 3: *Clinical and Translational Research*.
- (E) (NCRR)

**Institutional Development Award (IDeA) Program:** The NIH IDeA program fosters health-related research and improves the competitiveness of investigators in 23 states and Puerto Rico that historically have not received significant levels of competitive research funding from NIH. The IDeA program supports multidisciplinary centers and statewide collaborative partnerships that increase institutions' capacity to conduct cutting-edge biomedical research. IDeA supports faculty development and enhancement of research infrastructure at institutions and also promotes collaborative community-based research, particularly in minority communities and other medically underserved communities where health disparities persist. The IDeA program supports the IDeANet initiative, which is expanding access to high-performance computational resources for data-intensive science applications and providing bioinformatics software tools and training to investigators. IDeANet began with Lariat, a pilot program that has enabled connectivity in six States (Alaska, Hawaii, Idaho, Montana, Nevada, and Wyoming). IDeANet ultimately will enable all institutions in the IDeA program, as well as participants in NIH's Research Centers in Minority Institutions program, to engage in national and international collaborations.

- For more information, see [http://www.ncrr.nih.gov/research\\_infrastructure/institutional\\_development\\_award](http://www.ncrr.nih.gov/research_infrastructure/institutional_development_award)
- For more information, see IDeA program evaluation GPRA Goal 8.4.
- This example also appears in Chapter 2: *Minority Health and Health Disparities*.
- (E) (NCRR) (GPRA Goal)

**Research Centers in Minority Institutions (RCMI):** The Research Centers in Minority Institutions (RCMI) Program began in 1985 in response to congressional report language (House Report 98-911 on the Labor, Health and Human Services, and Education and Related Agencies Appropriation Bill for FY 1985 [July 26, 1984, pages 78-79] directing funds to “establish research centers in those predominantly minority institutions which offer doctoral degrees in the health professions or the sciences related to health.” RCMI support includes funds to recruit established and promising researchers, acquire advanced instrumentation, modify laboratories for competitive research, and fund core research facilities and other research support. Because many investigators at RCMI institutions study diseases that disproportionately affect minorities, NCRR support serves the dual purpose of bringing more minority scientists into mainstream research and enhancing studies of minority health. The next step in increasing the research capacity of the RCMI is to link each of them together.

- For more information, see [http://www.ncrr.nih.gov/research\\_infrastructure/research\\_centers\\_in\\_minority\\_institutions/](http://www.ncrr.nih.gov/research_infrastructure/research_centers_in_minority_institutions/)
- This example also appears in Chapter 2: *Minority Health and Health Disparities*.
- (E) (NCRR, NCMHD, NHLBI, NIA, NIAID, NIAMS, NICHD, NIDA, NIDDK, NIMH)

**Shared Instrumentation Grant and High-End Instrumentation Programs:** The goal of the NIH instrumentation programs is to provide new-generation technologies to groups of NIH-supported investigators for a broad array of basic, translational, and clinical research. These programs provide essential instruments that are too expensive to be obtained through regular research grants. The Shared Instrumentation Grant (SIG) program funds equipment in the \$100,000-\$500,000 range, while the High-End Instrumentation (HEI) program funds instrumentation in the \$750,000-\$2 million range. New research technologies supported by these programs enable novel modes of inquiry, which in turn lead to increases in knowledge and ultimately have the potential for improving human health. To increase cost-effectiveness, the instruments are located on core facilities with trained technical staff to assist in protocol development and to facilitate integration of new technologies into basic and translational research. In FY 2006 and 2007 the SIG program funded a total of 264 grants for \$95.2 million; the HEI funded a total of 39 awards for \$55.9 million.

- For more information, see [http://www.ncrr.nih.gov/biomedical\\_technology/shared\\_instrumentation/](http://www.ncrr.nih.gov/biomedical_technology/shared_instrumentation/)
- This example also appears in Chapter 3: *Molecular Biology and Basic Sciences* and Chapter 3: *Technology Development*.
- (E) (NCRR)

**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, 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>
- This example also appears in Chapter 2: *Chronic Diseases and Organ Systems*.
- (E) (NEI)

**Retinal Neurodegeneration Program:** This new multidisciplinary intramural research program combines basic, preclinical, and translational research to develop and test therapeutic interventions in several retinal degenerative diseases. These interventions include gene therapy, small molecules, neurotrophic factors, and cell-based systems, in combination with a variety of treatment delivery technologies.

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

**Multiplex Initiative:** With the completion of sequencing 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 followup 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>
- This example also appears in Chapter 2: *Chronic Diseases and Organ Systems* and Chapter 3: *Genomics*.
- (I) (NHGRI)

**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 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 sickle cell patients. Ten centers are funded through

FY 2007, and the program will be renewed in FY 2008.

- For more information, see <http://grants.nih.gov/grants/guide/rfa-files/RFA-HL-06-008.html>
- For more information, see <http://www.sicklecell-info.org/>
- This example also appears in Chapter 2: *Chronic Diseases and Organ Systems* and Chapter 2: *Minority Health and Health Disparities*.
- (E) (NHLBI)

**Dental Practice-Based Research Networks:** NIH has established three regional dental practice-based research networks (PBRNs) to perform clinical research in areas that are not well suited for the academic or laboratory setting. Each PBRN involves 100 or more research-trained dentists and dental hygienists who will propose and conduct studies across a range of patient and clinical conditions. The PBRNs also will collect information to generate data on disease, treatment trends, and the prevalence of less common oral conditions. The success of the PBRNs will be rooted in their focus on real-world clinical issues and their ability to generate information that will be of immediate value to practitioners and patients alike. For example, all three networks are collaborating to expand the evidence base on an emerging public health question: a suspected increased risk of a serious condition known as osteonecrosis of the jaw for individuals who have received therapy with a kind of drug known as bisphosphonates. Dental PBRNs have the potential to generate a body of high-quality clinical research data in a relatively short period of time. Most importantly, their research will substantially enhance the evidence base that clinicians use to inform treatment decisions, translate newer information into daily practice, and directly affect and improve care.

- For more information, see <http://www.nidcr.nih.gov/Research/ResearchResults/InterviewsOHR/TIS062005>
- For more information, see <http://www.nidcr.nih.gov/Research/ResearchResults/NewsReleases/ArchivedNewsReleases/NRY2005/PR03312005.htm>
- (E) (NIDCR)

**Oral Health Disparities Centers Initiative:** In May 2007, NIH announced plans to fund a competing renewal of the *Oral Health Disparities Centers Initiative* due to the promising achievements of currently funded centers, and the magnitude of the need for scientific advancement to eliminate disparities. Despite the remarkable improvement in the Nation's oral health over the years, not all Americans have benefited equally. *Oral, dental, and craniofacial conditions remain among the most common health problems for low-income, disadvantaged, and institutionalized Americans.* Unfortunately, there is no easy, one-size-fits-all solution. Much remains to be learned about the complex array of cultural, economic, genetic, and other contributory factors to these disparities and how best to overcome them. The five currently supported Centers have devised innovative, low-cost approaches to address severe early childhood caries, oral cancer, poor diet, and malocclusion.

- For more information, see <http://grants1.nih.gov/grants/guide/rfa-files/RFA-DE-08-008.html>
- This example also appears in Chapter 2: *Minority Health and Health Disparities*.
- (E) (NIDCR)

**Dialysis Access Consortium:** Arteriovenous (AV) 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 anticlotting reagents in preventing early failure in AV fistulas and AV grafts. The AV Fistula Trial is evaluating the ability of clopidogrel to maintain access patency, while the AV Graft Trial is evaluating the ability of aspirin/extended-release dipyridamole to maintain access patency.

- [Dember LM et al. \*Clin Trials\* 2005;2:413-22](#), PMID: 16317810
- [Dixon BS et al. \*Clin Trials\* 2005;2:400-12](#), PMID: 16317809
- For more information, see <http://www.niddk.nih.gov/patient/dac/DAC.htm>
- This example also appears in Chapter 2: *Chronic Diseases and Organ Systems*.

- (E) (NIDDK)

**Community-Based Participatory Research (CBPR):** CBPR is scientific inquiry conducted in communities and in partnership with researchers. Persons affected by the health condition or issue under study, or other key stakeholders in the community's health, fully participate in each phase of the work. This input offers CBPR the potential to generate better informed hypotheses, develop more effective interventions, and enhance the translation of research results into practice. The Program Announcement *Community Participation in Research* supports CBPR on health promotion, disease prevention, and health disparities. CBPR is also the theme of the annual *NIH Research on Social Work Interventions and Health Summer Institute* (July 2007).

- For more information, see <http://grants.nih.gov/grants/guide/pa-files/PA-07-283.html>
- For more information, see <http://obssr.od.nih.gov/summerinstitute2007/index.html>
- This example also appears in Chapter 2: *Minority Health and Health Disparities*
- (E) (OBSSR, AHRQ, NCI, NHLBI, NIA, NIAAA, NICHD, NIDA, NIDCD, NIDCR, NIEHS, NIMH, NINR, NIOSH)

**Critical Issues in eHealth Research Conference:** Toward Quality Patient Centered Care (September 2006): This second of two eHealth conferences served three purposes: (1) to highlight research methodologies that intersect across information technology, health communications, behavioral science, medical science, and patient care research, (2) to showcase existing and emerging technologies relevant to communications among patients and their health care teams, and (3) to discuss conceptual issues related to patient-centered eHealth research.

- [Atienza AA, et al. Am J Prev Med 2007;32:S71-4](#), PMID: 17466821
- This example also appears in Chapter 3: *Technology Development*.
- (E) (OBSSR, NCI, ODP/ORD)

**Research on Social Work Practice and Concepts in Health:** Social workers focus on the creation of physical and mental health prevention and treatment interventions in order for individuals to become more productive members of society. As providers of front-line services in such areas as aging, teen pregnancy, child abuse, and substance abuse, particularly in underserved communities, they are in a unique position to provide valuable information on these complex social concerns. This initiative aims to incorporate unique social work concepts and perspectives into the NIH research portfolio and to build the scientific base for use by allied health professionals.

- For more information, see <http://grants.nih.gov/grants/guide/pa-files/PA-07-292.html>
- (E) (OBSSR, NCI, NHLBI, NIA, NIAAA, NICHD, NIDA, NIMH, NINR, ODP/ORD, ORWH)

**Understanding and Promoting Health Literacy:** The HHS Healthy People 2010 initiative established a national health objective to improve health literacy by the decade's end. While many diseases and conditions can be prevented or controlled, too often people with the greatest health burdens have few fact-finding skills, the least access to health information, and least effective communication with health care providers. This program announcement supports research that increases our understanding of the health literacy problem and its relationship to health disparities as well as the development of interventions to overcome the adverse consequences of low health literacy.

- For more information, see <http://grants.nih.gov/grants/guide/pa-files/PA-07-020.html>
- This example also appears in Chapter 3: *Health Communication and Information Campaigns and Clearinghouses* and Chapter 2: *Minority Health and Health Disparities*
- (E) (OBSSR, AHRQ, NCI, NHLBI, NIA, NIBIB, NICHD, NIDCD, NIDCR, NIEHS, NIMH, NINR, NLM)

**SBIR/STTR Management Redesign:** The NIH Small Business Research programs, SBIR and STTR, serve to foster and encourage innovative research with the goal of transferring technologies and processes into commercial applications that will improve the health of the Nation. By March 2007, NIH established a working group (Trans-

NIH SBIR/STTR Think Tank Working Group) to develop an agency-wide strategy that aligns the SBIR/STTR program with crosscutting NIH program goals (e.g., the NIH Roadmap for Medical Research) and advances the agency's vision for translating scientific discoveries into commercial products and services by using SBIR/STTR strategically. Future efforts will include the development and implementation of a pilot SBIR/STTR initiative that would meet these objectives, foster effective public-private partnerships, and ensure a stronger, more integrated technology program.

- For more information, see <http://grants.nih.gov/grants/funding/sbir.htm>
- (O) (OD/OER)

**Clinical and Translational Science Award (CTSA) Consortium:** To remove barriers to clinical (including pediatric) research identified by research communities, NIH launched the Clinical and Translational Science Award (CTSA) program in September 2006. The program will more rapidly and efficiently facilitate the transfer of discoveries made in the laboratory into new strategies to prevent or treat disease. Through the CTSA, academic health centers are forming a national consortium with interdisciplinary teams that cover the complete spectrum of biomedical research—from basic molecular biology to clinical medicine. The CTSA Consortium will design clinical research informatics tools, forge new partnerships with private and public health care organizations, expand outreach to minority and medically underserved communities, develop better designs for clinical trials, and train the next generations of clinical and translational researchers. Working together, the Consortium will adopt and disseminate best practices, policies, procedures, and other measures to advance collaborative clinical and translational research. The CTSA Consortium is the primary initiative for addressing the NIH Roadmap for Medical Research theme to Re-Engineer the Clinical Research Enterprise.

- For more information, see <http://www.ctsaweb.org/>
- (E) (Roadmap—all ICs participate)

**Training Activities of the Clinical and Translational Science Award Program:** Comparing new disease treatments and prevention strategies against those in current use requires dedicated clinical and translational research teams that include physicians, basic scientists, statisticians, and informatics experts, among others. Clinical research requires unique skills in addition to those needed to care for patients, so academic health centers must equip promising individuals with the special training they need to succeed in research careers. To address this need, NIH has expanded its clinical research training programs, first through the Roadmap T32 and K12 programs and, more recently, through Clinical and Translational Science Awards (CTSAs). Each program is based on placing the trainees in a mentored environment, where they learn the skills needed to cultivate multidisciplinary research team collaborations and design research projects to successfully compete for funding. The CTSA program will grow through 2012 to serve about 60 academic sites, providing research training and career development opportunities to a combined total of more than 1,200 trainees and new investigators covering multiple individual disciplines.

As mandated in Section 106 of the National Institutes of Health Reform Act (Pub. L. No. 109-482), NIH will conduct an evaluation and comparison of the outcomes and effectiveness of the CTSA training programs. This evaluation will be part of a much larger comprehensive evaluation of the CTSA program as a whole. Each individual CTSA is expected to include their training activities in their own evaluation. To coordinate and share information, including results of training activity evaluations, there is a CTSA Education/Career Development Steering Committee which provides a forum for the advancement of integrated and interdisciplinary education, training, and career development in the clinical and translational sciences and serves as a clearinghouse for clinical research training. Since the CTSA program was only recently initiated (September 2006), significant evidence of the long-term impact of the CTSA program is more likely to be measurable after 7 or more years. However, short-term process milestones and intermediate outcomes are expected in 1 to 7 years.

- For more information, see [nihroadmap.nih.gov/clinicalresearch/overview-training.asp](http://nihroadmap.nih.gov/clinicalresearch/overview-training.asp)
- For more information, see <http://www.ctsaweb.org/>
- This example also appears in Chapter 3: *Research Training and Career Development*

- (E) (Roadmap—all ICs participate)

**Reports of Clinical Trials Working Group (CTWG) and Translational Research Working Group (TRWG):** Recognizing the importance of translational and clinical research, two major reports of comprehensive evaluations were recently released that will lead to more rapid progress in translating important research findings into new, effective interventions. The CTWG and TRWG were constituted as broad and inclusive panels (memberships comprised experts from academia, the pharmaceutical industry, advocacy groups, NIH, and other governmental agencies) to review and evaluate the current portfolio of research being done in that area and identify ways to synergize, integrate, and coordinate efforts.

- For more information, see <http://www.cancer.gov/trwg>
- For more information, see <http://integratedtrials.nci.nih.gov/>
- This example also appears in Chapter 2: *Cancer*.
- (E/I) (NCI)

**Clinical and Translational Science Award (CTSA) Program Evaluation:** Given the ambitious goals of the CTSA program to transform the practice of clinical and translational science, NIH recognizes that rigorous attention must be given to evaluate the program's effectiveness in meeting those goals. NIH must ensure that program findings and outcomes are disseminated to stakeholders, including researchers, advocacy groups, Congress, and especially the patients who stand to benefit most from new prevention strategies and treatments reaching them faster. Therefore, NIH has launched a comprehensive evaluation of the CTSA program that will assess the impact of the CTSA Consortium on transforming translational and clinical research. The CTSA evaluation will proceed at both a national and an institutional level, allowing NIH to assess national, Consortium-wide goals while providing flexibility for the individual CTSA's to evaluate components unique to their specific CTSA.

- For more information, see <http://www.ctsaweb.org/>
- (E) (NCRN)

**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 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 in traditional Chinese medicine, experienced significant augmentation in levels of immunity to the virus that causes shingles following 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.

- [Irwin MR, et al. \*J Am Geriatr Soc\* 2007;55:511-7](#), PMID: 17397428
- [Yeh GY, et al. \*Am J Med\* 2004;117:541-8](#), PMID: 15465501
- This example also appears in Chapter 2: *Chronic Diseases and Organ Systems* and Chapter 3: *Molecular Biology and Basic Sciences*.
- (E) (NCCAM)