Summary of Research Activities by Key Approach and Resource

Epidemiological and Longitudinal Studies

In the midst of a devastating cholera outbreak in 1854, John Snow systematically mapped the distribution of deaths in the Soho neighborhood of London and pinpointed water from the now-famous Broad Street pump as the source of the disease. In addition to helping curb future outbreaks by advancing the notion that cholera is transmitted through contaminated water, Snow’s efforts helped lay the foundation for modern epidemiological studies, which collect data and test hypotheses relative to a vast range of factors that affect diseases—from genetic variability to socioeconomic status—with the ultimate goal of improving public health.

Introduction

Epidemiological studies examine the causes of health and disease in human populations using a broad range of approaches. Persons or groups can be followed over time in longitudinal studies, or a snapshot of information can be collected at a single point in time. Studies can be done retrospectively, examining outcomes that have already occurred and factors that may have contributed to health or disease, or they can be done prospectively by beginning to monitor a population of interest before a particular disease-related outcome occurs. Some epidemiological studies, such as randomized controlled clinical trials, are experiments that actively test an intervention; others, however, are observational in nature, collecting information about and comparing groups—called cohorts—made up of individuals who share a characteristic of interest (e.g., tobacco use, age, educational status).

The varied approaches to epidemiological research can be employed to answer a broad range of questions, such as:

- “What genetic and environmental factors interact to cause cancer?”
- “What environmental or behavioral factors have led to increased rates of obesity?”
- “How well does vaccination protect elderly people from influenza?”
- “Do patterns of adolescent drug use vary by geographic region?”

In order to address these questions, epidemiological research draws on expertise from a number of disciplines, including, but not limited to, epidemiology, social and behavioral sciences such as economics and demography, genetics, and public health. Although some epidemiological studies may be adequately addressed within a single discipline, collaboration among scientists with a variety of expertise is necessary to unravel the multifarious factors that contribute to a complex disease such as cancer or diabetes.

Epidemiological research—particularly the large prospective studies with longitudinal followup that are usually the most robust and informative—is time-consuming and expensive, but NIH investment in this type of research over the past half-century continues to yield invaluable results. For example, two generations of offspring born to the original subjects in the Framingham Heart Study, which was initiated in 1948 and identified high blood pressure, smoking, and other now well-known risk factors for cardiovascular disease, are now being followed to identify hereditary factors that contribute to cardiovascular disease. Moreover, repositories of data and biospecimens collected years ago in long-running epidemiological and longitudinal studies are allowing researchers to answer the research questions of today. For example, the NIH Genes, Environment, and Health Initiative is using DNA samples collected from persons who participated in past studies to systematically identify disease-related genes and gene variants. The combination of genetic and longitudinal data should help elucidate the complex gene-environment interactions that contribute to disease.
NIH is leveraging its past investments as well as its position as one of the foremost research hubs in the world to spur the next generation of truly "big science." Although technological advances are contributing to this effort, its success is even more deeply rooted in the growing number of scientists working together in a truly interdisciplinary fashion. Such a collaborative approach permits the integration of diverse data from a variety of sources to improve understanding of (a) the factors that converge to cause disease and (b) the interventions that may reduce disease risk. Equally important, this culture of cooperation is characterized by a willingness to make results publicly available in a timely manner for the benefit of the entire research enterprise.

Beyond interdisciplinary collaboration, however, NIH also recognizes the great potential of a systems approach that integrates genetics, biology, and the social sciences, as well as multilevel studies that illuminate the mechanisms linking features of societies and communities to individual behaviors and health outcomes, often on a global level. This approach often requires an understanding of economic trends and their relationships to both acute and chronic diseases, and it demands explicit consideration of the environment in which health and disease are being studied. It recognizes that factors such as public health policy and neighborhood design may be just as important as genetic variation and individual behavior, and that addressing any of these factors in isolation will result in an inadequate understanding of health and disease. One example of a systems approach to studying disease is the International Epidemiologic Databases to Evaluate AIDS (IeDEA) consortium, which is working to harmonize HIV/AIDS data from a number of sources worldwide to gain a better understanding of HIV/AIDS pathogenesis as well as the efficacy of treatment and prevention strategies within different settings and populations.

Building on its past investment, NIH currently supports numerous epidemiological and longitudinal studies to increase understanding of diseases ranging from cancer to Alzheimer's disease to influenza. Through interdisciplinary efforts and integration of data from a variety of disciplines, NIH is helping to usher in an era of personalized medicine in which the genetic, biological, and behavioral risk factors of an individual are considered within the context of the sociocultural and physical environment. The following section provides an overview of NIH-supported epidemiological and longitudinal studies, followed by “notable examples” of NIH work in this field across different disease areas. Detailed information on clinical trials, one type of experimental epidemiological study, can be found in the section on Clinical and Translational Research in Chapter 3.

**Summary of NIH Activities**

The NIH mission encompasses a broad range of activities, from the pursuit of fundamental knowledge about the nature and behavior of living systems to the application of that knowledge to extend healthy life and reduce the burdens of illness and disability. As part of this continuum from basic to applied research, epidemiological and longitudinal studies are critical for the translation of research findings to real-world application at the population level. In addition to testing hypotheses generated through basic, translational, and clinical research, these types of studies often result in the formulation of new or modified hypotheses, spurring new laboratory and clinical studies. Thus, epidemiological and longitudinal studies are essential for linking bench to bedside to population and help ensure that public investment in research delivers tangible value by providing an empirical perspective on the accrual and application of scientific knowledge. Numerous prior and ongoing NIH studies have yielded results with meaningful implications for the health of the population. This progress has been due to a variety of factors, including a longstanding and continuous investment in epidemiological and longitudinal research, a deeply entrenched culture of cooperation, and a commitment to gaining a comprehensive understanding of health and disease.

**Investments in the Past Continue to Pay Off**

NIH has been investing in epidemiological and longitudinal studies for more than 50 years. The infrastructure created and the data collected from these studies continue to advance understanding of disease and health in new and exciting ways. Prolonged followup also has enormously increased the value of these studies, and their existence helps form the foundation for extraordinary opportunities in biomedical research today. Below are
highlights of select NIH research activities that illustrate how findings from long-term population-based studies have elucidated different facets of important public health issues.

Results of large, national longitudinal studies have helped guide medical recommendations for specific populations, substantially improving their health outcomes. For example, in 1991, NIH launched the Women's Health Initiative (WHI), a national longitudinal study that included nearly 162,000 women of many racial and ethnic backgrounds—the largest and most comprehensive study of women to date. Over the next 15 years, WHI conducted clinical trials and observational studies to identify strategies for preventing heart disease, breast and colorectal cancer, and osteoporotic fractures in postmenopausal women. One of the most important discoveries of the original WHI studies was that estrogen plus progestin hormone therapy increases risk of breast cancer and may also increase risk of coronary heart disease, stroke, and pulmonary embolism\(^1\). This evidence led to a precipitous drop in use of hormone replacement therapy by postmenopausal women, which is thought to have contributed to the 6.7 percent decline in breast cancer incidence observed in the following year\(^2\). In addition to pursuing the primary study objectives of WHI, NIH encourages investigators to take advantage of the specimens and data accumulated through WHI. To date, nearly 100 ancillary studies have been funded to research myriad issues that affect older women, from domestic violence to periodontal disease. Many of these studies are carrying earlier WHI results back to the laboratory in order to explain and build upon population-level observations. One group is surveying over 1,000 proteins in specimens collected from WHI subjects with the goal of identifying a small group of proteins that will predict both risk of disease and response to hormone therapy.

Long-term longitudinal studies also can uncover health trends related to people’s social and cultural behaviors, and thus suggest new health interventions. For instance, a recent analysis of social network data collected on three generations of Framingham Heart Study subjects revealed that individuals are significantly more likely to become obese if they have a friend, sibling, or spouse who becomes obese. Interestingly, the strongest association was found between friends, not siblings, suggesting that social relationships play an even more important role in obesity than genetic background. Furthermore, the effect was not observed between neighbors who were not friends, indicating that social relationships are more important than geographic or neighborhood factors\(^3\). The observation that obesity—commonly attributed to genetic and individual behavioral factors—can also spread through social ties has implications for public health interventions and suggests the possibility of harnessing social networks to spread positive health behaviors.

Long-term population studies also have provided insight into intergenerational influences on health and behavior. For example, NIH facilitated extensive research on linkages between parental factors and child development by building on the U.S. Department of Labor National Longitudinal Survey of Youth—a longitudinal study designed to further understanding of how young Americans move into productive roles in the economy. In 1979, the U.S. Department of Labor began collecting health, income, and educational attainment information on a cohort of 14- to 22-year-olds. In 1986, NIH expanded the study and began amassing extensive information on children born to women of the 1979 cohort on a biennial basis; these children now range in age from 5 years to 20-something. The resulting intergenerational database combines cognitive, social, and physical information about the children with longitudinal information on family background, education, employment history, and economic well-being. Studies on children of the 1979 cohort have spawned over 1,000 publications on health and other outcomes, from the effects of family income on children’s health to the effects of public policy on the investment of fathers in their children.

Longitudinal studies also can be used to inform the decisions of policymakers and assess both short- and long-term effects of policies on health or health-related behaviors. In 1975, NIH launched Monitoring the Future (MTF), a

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study that tracks the beliefs, attitudes, and behaviors of adolescents and young adults. MTF surveys approximately 50,000 students in grades 8, 10, and 12 each year. Among other things, MTF gathers information on alcohol and other drug use, and its findings have been used by the Office of National Drug Control Policy to monitor progress toward national health goals. Survey results from 2007 show a 24 percent decline among the three grades combined in recent abuse (i.e., during the past month) of “any illicit drug” between 2001 and 2007. Also, during this period, marijuana abuse has decreased roughly 25 percent, and teen cigarette use has declined by a third to be the lowest point in the survey’s history. The use of ecstasy has declined by more than half, and methamphetamine use has plummeted by more than 60 percent since 2001. This translates to 860,000 fewer youth using illicit drugs, a testament to the impact of targeted drug abuse prevention efforts, which, by depicting emerging trends, such surveys help to inform.

**Culture of Cooperation**
Bridging the gap between research and application requires the contributions of numerous scientists with diverse expertise. Recognizing this, NIH fosters a culture of cooperation that has yielded consortia of scientists enthusiastic about working together in interdisciplinary teams and willing to make research results immediately and freely available for the benefit of the whole research enterprise. This emerging “big science” paradigm provides support for interdisciplinary epidemiological and longitudinal studies and also promotes the creation of resources and tools that will help the broader scientific community benefit from and build upon these studies.

NIH supports several studies that bring together expertise from multiple fields to more effectively address research questions and/or simultaneously address multiple research questions. For example, the National Longitudinal Study of Adolescent Health (Add Health) was initiated in 1994 as a joint effort of 18 NIH Institutes and Federal offices to examine how families, peers, schools, and neighborhoods influence the health-related behaviors of adolescents in grades 7 through 12. A new wave of interviews with the original Add Health cohort, now ages 24-32, will include collection of genetic data and biological markers of disease processes, in addition to basic social, individual, and behavioral data. The new design was developed by a collaborative team representing the fields of epidemiology, cardiology, psychology, sociology, behavioral genetics, nutrition, biostatistics, anthropology, medicine, molecular virology, statistics, and survey research. Working together, these diverse teams will address a broad range of research questions that collectively will yield a deeper understanding of the factors influencing the health of young people.

Other multidisciplinary endeavors at NIH have engendered collective analyses, which extend the power of these studies. As an example, the Magnetic Resonance Imaging (MRI) Study of Normal Brain Development receives contributions from several NIH Institutes and Centers, including NICHD, NIDA, NIMH, and NINDS. Researchers with expertise in child development, neuropsychology, neurology, and imaging work together to increase understanding of normal brain development. This longitudinal effort involves coordination of six Pediatric Study Centers distributed across the country, all of which use cutting-edge technology to monitor brain development in approximately 500 children from 7 days to 18 years of age. Importantly, the Centers have developed and adopted a uniform approach to collecting these images to ensure that their data can be collectively analyzed, extending the power and benefit of the study. Data collected through the study are being used to build the Nation’s first normative database of MRI images and accompanying clinical and behavioral data, all of which are being made available to the scientific community. This knowledge will be valuable for future laboratory and clinical studies examining the underlying causes of childhood disorders such as mental retardation, developmental disabilities, mental illness, drug abuse, and pediatric neurological diseases.

The MRI database is only one of the many tools NIH has created to facilitate research community access to

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emerging scientific information. These resources are particularly relevant for genomic studies. Building on recent knowledge gained through the Human Genome Project and the International HapMap Project, NIH has launched a series of consortia that combine multiple cohorts to create powerful, large-scale studies. One of these consortia, the Cancer Genetic Markers of Susceptibility (CGEMS) study, is performing genome-wide scans to identify genetic variants associated with risk for developing cancer of the breast, prostate, and colon. The Pancreatic Cancer Cohort Consortium (PanScan) is conducting an analogous scan for pancreatic cancer, and scans are under way for lung, bladder, and other cancers as well. All of the data collected through these studies will be freely available through caBIG (the Cancer Bioinformatics Grid), a bioinformatics tool being developed for the explicit purpose of transforming cancer research into a more collaborative, efficient, and effective endeavor. CGEMS researchers recently identified a common genetic variant on chromosome 8 that strongly predicts prostate cancer risk; interestingly, genetic variants in this same region also have been associated with breast and colorectal cancers. These discoveries, made through population-based epidemiological studies, are already spawning new laboratory research, allowing scientists to learn more about the molecular basis of prostate and other cancers.

The NIH investment in genome-wide analyses extends well beyond cancer. The Database of Genotype and Phenotype (dbGaP) was initiated in December 2006 as a platform to archive and distribute data generated by the increasing number of studies exploring the association between specific genes and disease-related traits. dbGaP already contains data from several studies, including the Age-Related Eye Diseases Study, a prospective study of the clinical course of age-related macular degeneration and cataracts, and the Parkinsonism Study, which collected genetic information on neurologically normal and Parkinson’s disease patients. This growing repository of freely available genomic data and other similar resources illustrate a staunch commitment to data-sharing that should help generate new hypotheses and spur discoveries that will eventually be translated into effective therapies.

**A Comprehensive Understanding of Disease**

NIH recognizes that efficient translation of scientific knowledge to population-level application requires a systems approach that integrates genetics, biology, and the social sciences, and also includes multilevel studies that illuminate the mechanisms linking features of societies and communities to individual behaviors and health outcomes. Performing these studies in diverse contexts, from the community to the global level, contributes to a more comprehensive understanding of health and disease. NIH supports a number of studies in the United States and worldwide aimed at uncovering how these diverse elements interact to influence patterns of disease with the goal of identifying new and effective approaches for prevention and treatment.

Numerous NIH-supported studies examine how genes, biology, behavior, and environment interact to influence disease risk. For example, the Jackson Heart Study, a prospective epidemiological study of cardiovascular disease among African Americans in the Jackson, Mississippi, metropolitan area, is assessing genetic and other risk factors that underlie cardiovascular disease. The study also is considering how sociocultural factors, such as racism, discrimination, and coping strategies, affect disease in African Americans. In another example, the National Children’s Study will track more than 100,000 children from across the United States from the prenatal period through age 21 to examine factors ranging from natural and man-made environment to biological, genetic, social, and cultural influences. Researchers will analyze how these elements interact with each other to influence health and disease in children throughout development. Plans also are under way for the NIH-wide Genes, Environment, and Health Initiative, which will use genomics, proteomics, and metabolomics to assess how genetic variance and environmental exposures influence disease.

In addition to pursuing multifactorial explanations for disease risk, NIH is examining how diverse factors converge to influence an individual’s response to interventions. In 2002, the NIH Diabetes Prevention Program revealed that individuals at high risk of type 2 diabetes could substantially lower disease occurrence through intensive lifestyle intervention. Extensive followup of the same cohort through the Diabetes Prevention Program Outcomes Study also resulted in the identification of a genetic variant that predisposes people to type 2 diabetes. Importantly,

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researchers found that people with the high-risk genetic variant benefited as much or more from intensive lifestyle intervention as did those without the variant. These types of studies are becoming increasingly important as personalized medicine becomes a tangible reality. Multilevel studies will lay the groundwork for the informed selection of preventive or therapeutic interventions according to genetic, biological, behavioral, and environmental factors.

NIH also uses longitudinal and epidemiological studies to gather information on global patterns of infectious diseases. These efforts not only will advance understanding of the causes of these diseases, but also should contribute to the development of interventions to lessen disease burden in the United States and worldwide. One illustration of this is the Multinational Influenza Seasonal Mortality Study, an NIH-led collaborative that is analyzing national and global epidemiological patterns associated with influenza virus circulation. The goals of this large-scale collaboration are to evaluate and compare public health strategies to alleviate the impact of seasonal influenza in different countries and better understand the global circulation patterns of influenza and their impact on populations. To this end, 20 countries have contributed data on mortality, virus surveillance, genomics, and influenza control strategies. A more comprehensive understanding of influenza epidemiology worldwide will result in the development of better vaccines as well as other types of strategies to avoid future influenza pandemics.

A global perspective is also being acquired through the International Epidemiological Databases to Evaluate AIDS (IeDEA). This regional collaborative of centers on five continents is focused on the harmonization and integration of data in order to pursue population-level research questions about HIV/AIDS that cannot be addressed in single cohorts. Topics of research will include 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.

**Conclusions**

Epidemiological and longitudinal studies are essential to NIH efforts in bridging the results of basic, translational, and clinical studies to applications in the general population. In addition to testing hypotheses at the population level, observations gathered through these studies help optimize existing interventions and stimulate novel laboratory and clinical research. Many NIH epidemiological and longitudinal studies have had substantial influence on public health. This success is due to a number of factors, including investment in long-term studies, promotion of a culture of cooperation, and pursuit of a comprehensive view of disease. The studies presented here represent only a fraction of NIH efforts in this area. Although still not comprehensive, additional notable examples of NIH-supported epidemiological and longitudinal studies, as well as further information about the activities mentioned above, are found in the following section.

**Notable Examples of NIH Activity**

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<thead>
<tr>
<th>Key for Bulleted Items:</th>
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<tr>
<td>E = Supported through Extramural research</td>
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<tr>
<td>I = Supported through Intramural research</td>
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<tr>
<td>O = Other (e.g., policy, planning, and communication)</td>
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<tr>
<td>COE = Supported through a congressionally mandated Center of Excellence program</td>
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<td>GPRA Goal = Concerns progress tracked under the Government Performance and Results Act</td>
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**Investments in the Past Continue to Pay Off**
Framingham SNP-Health Association Resource (SHARE): The Framingham SHARE is a comprehensive new effort by NIH and the Boston University School of Medicine to pinpoint genes underlying cardiovascular and other chronic diseases. The program builds on the Framingham Heart Study (FHS), which was begun in 1948 to identify factors that contribute to cardiovascular disease, and on other NIH-funded research demonstrating that common but minute variations in human DNA, called single nucleotide polymorphisms (SNPs), can be used to identify genetic contributors to common diseases. The initiative will examine over 500,000 genetic variants in 9,000 study subjects across three generations. NIH will develop a database to make the data available to researchers around the world. The database will help researchers to integrate the wealth of information collected over the years in the FHS with the new genetic data, resulting in an increased understanding of genetic influences on disease risk, manifestation, and progression. Because of its uniqueness in including three generations of subjects with comparable data obtained from each generation at the same age, the FHS is the first study to be included in the SHARE initiative. NIH is currently considering expansion of SHARE to include other large longitudinal studies such as the Jackson Heart Study and the new Hispanic Community Health Study.

- For more information, see [http://www.nhlbi.nih.gov/new/press/06-02-06.htm](http://www.nhlbi.nih.gov/new/press/06-02-06.htm)
- This example also appears in Chapter 2: *Chronic Diseases and Organ Systems* and Chapter 3: *Genomics*.
- (E) [NHLBI, NLM](http://www.grc.nia.nih.gov/branches/blsa/blsanew.htm)

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

- This example also appears in Chapter 2: *Chronic Diseases and Organ Systems* and Chapter 3: *Genomics*.
- (E) [NHLBI](http://www.nhlbi.nih.gov/new/press/06-02-06.htm)

Baltimore Longitudinal Study of Aging (BLSA): In 2008, NIA will celebrate the 50th anniversary of the BLSA, America’s longest running scientific study of human aging. More than 1,400 men and women ranging in age from their twenties to their nineties have been study volunteers. The BLSA has generated significant findings to elucidate the normal course of aging and disentangle the effects of disease from the normal aging process.

- For more information, see [http://www.grc.nia.nih.gov/branches/blsa/blsanew.htm](http://www.grc.nia.nih.gov/branches/blsa/blsanew.htm)
- This example also appears in Chapter 2: *Life Stages, Human Development, and Rehabilitation*.
- (I) [NIA](http://www.niams.nih.gov/News_and_Events/Advisory_Council_Minutes/2006/sum01_06.asp)

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

- For more information, see [www.niams.nih.gov/News_and_Events/Advisory_Council_Minutes/2006/sum01_06.asp](http://www.niams.nih.gov/News_and_Events/Advisory_Council_Minutes/2006/sum01_06.asp) (Section VII - Study of Osteoporotic Fractures)
- This example also appears in Chapter 2: *Chronic Diseases and Organ Systems*. 
Population Research: Given the Nation’s increasing diversity and changing demographics, it is critical to understand how trends in such areas as immigration, fertility, marriage patterns, and family formation affect the well-being of children and families. NIH research in these areas allows policymakers and program planners to better address public health needs. For instance:

- The Fragile Families and Child Well-Being Study follows children born to unmarried parents to assess how economic resources, father involvement, and parenting practices affect children’s development.
- The New Immigrant Survey follows the first nationally representative sample of legal immigrants to the United States, providing accurate data on legal immigrants’ employment, lifestyles, health, and schooling before and after entering the country.
- The National Longitudinal Survey of Youth (1979 cohort) continues to assess the work, educational, and family experiences of a nationally representative cohort of young men and women who were 14-22 years old when they were first studied in 1979. The study also follows children born to female subjects up through age 20, creating the opportunity to study intergenerational influences on child development, health behaviors, and educational attainment.

  - For more information, see [http://www. fragilefamilies.princeton.edu/index.asp](http://www. fragilefamilies.princeton.edu/index.asp)
  - For more information, see [http://nis.princeton.edu/](http://nis.princeton.edu/)
  - For more information, see [http://www.bls.gov/nls/lhsy79ch.htm](http://www.bls.gov/nls/lhsy79ch.htm)
  - This example also appears in Chapter 2: *Life Stages, Human Development, and Rehabilitation*.
  - (E) (NICHD, NCI, NCMHD, NIA, NIAAA, NIAID, NIDA, NIDCD, NINR, OAR, OBSSR, ORWH)

A Look at Drug Abuse Trends: Local to International: Several major systems of data collection are helping to identify substance abuse trends locally, nationally, and internationally: Monitoring the Future Survey (MTF), the Community Epidemiology Work Group (CEWG), and the Border Epidemiology Work Group (BEWG). All help to surface emerging drug abuse trends among adolescents and other populations, and guide responsive national and global prevention efforts. The MTF project, begun in 1975, has many purposes, the primary one being to track trends in substance use, attitudes, and beliefs among adolescents and young adults. The survey findings are also used by the President’s Office of National Drug Control Policy to monitor progress towards national health goals. The MTF project includes both cross-sectional and longitudinal formats—the former given annually to 8th, 10th, and 12th graders to see how answers change over time, and the latter given biennially, or every 2 years (until age 30, then every 5 years) to follow up on a randomly selected sample from each senior class. CEWG, established in 1976, provides both national and international information about drug abuse trends through a network of researchers from different geographic areas. Regular meetings feature presentations on selected topics, as well as those offering international perspectives on drug abuse patterns and trends. A recently established Border Epidemiology Work Group represents a collaboration of researchers from both sides of the U.S.-Mexico border. Of special interest are drug abuse patterns and problems in geographically proximal sister cities/areas. Development of a Latin American Epidemiology Network is under way. NIH has also provided technical consultation for the planning and establishment of an Asian multi-city epidemiological network on drug abuse.

  - For more information, see [http://www.monitoringthefuture.org/](http://www.monitoringthefuture.org/)
  - For more information, see [http://www.drugabuse.gov/about/organization/CEWG/CEWGHome.html](http://www.drugabuse.gov/about/organization/CEWG/CEWGHome.html)
  - This example also appears in Chapter 3: *Disease Registries, Databases, and Biomedical Information Systems, and Chapter 2: Minority Health and Health Disparities*.
  - (E) (NIDA)

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

- This example also appears in Chapter 2: *Chronic Diseases and Organ Systems* and Chapter 2: * Minority Health and Health Disparities.*
- (I) (NIDDK)

**The Role of Development in Drug Abuse Vulnerability:** NIH supports a number of longitudinal studies at various stages of development, following cohorts over extended timeframes. Information is gathered on children’s cognitive and emotional development, as well as their vulnerability to addiction later in life. These studies have been critical to estimate, for example, the contribution of in utero drug exposure to emotional and cognitive development, vulnerability to substance abuse, and other mental disorders. This knowledge, together with animal studies that provide complementary and validating information while minimizing the confounding factors that are likely to play a role in prenatal effects of drug exposure in humans, will help us to mitigate the deleterious impact of substance abuse on the developing fetus. With regard to later developmental stages, the application of modern brain imaging technologies has generated unprecedented structural and functional views of the dynamic changes occurring in the developing brain (from childhood to early adulthood). The discovery of these changes has been critical to understanding the role of brain development in decision-making processes and responses to stimuli, including early exposure to drugs. Such studies have suggested, for example, that an unbalanced communication between volitional control and emotional circuits may explain some of the impulsive reactions typical of adolescents, who tend to engage in risky behaviors, and are at heightened risk for developing addictions. Collectively, these longitudinal studies, using new imaging and genetics tools, promise a greatly enhanced ability to interpret the effects of myriad environmental variables (e.g., quality of parenting, drug exposure, socioeconomic status, and neighborhood characteristics) on brain development and behavior.

- For more information, see [http://www.drugabuse.gov/NIDA_notes/NNvol19N3/Conference.html](http://www.drugabuse.gov/NIDA_notes/NNvol19N3/Conference.html)
- This example also appears in Chapter 2: *Life Stages, Human Development, and Rehabilitation* and Chapter 2: *Neuroscience and Disorders of the Nervous System*
- (E) (NIDA, NICHD) (GPRA Goal)

**The Carolina Lupus Study:** Since 1997, NIH supported the Carolina Lupus Study, the first population-based epidemiologic study to examine the influence of hormonal and occupational exposures, in addition to genetic factors affecting immune function and metabolism, on systemic lupus erythematosus (SLE). SLE is a severe, disabling autoimmune disease that can lead to morbidity and mortality from renal and cardiovascular disease. African Americans are two to three times more likely than whites to develop the disease for reasons unknown. The study included 265 patients and 355 people without lupus living in 60 counties in North and South Carolina. The results for analysis of occupational exposure to silica dust in relation to risk for SLE were striking. Other associations were seen with self-reported occupational exposure to mercury, in mixing pesticides for agricultural work and among dental workers. Weaker associations were seen between SLE and shift work and among health care workers with patient contact.

- For more information, see [http://www.niehs.nih.gov/research/atniehs/labs/epi/studies/cls/index.cfm](http://www.niehs.nih.gov/research/atniehs/labs/epi/studies/cls/index.cfm)
- This example also appears in Chapter 2: *Autoimmune Diseases.*
- (I) (NIEHS)

**Culture of Cooperation**

**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 premenopausal 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: Clinical and Translational Research, and Chapter 3: Disease Registries, Databases, and Biomedical Information Systems.
- (f) (NCI)

**Database of Genotype and Phenotype (dbGaP):** Research on the connection between genetics and human health and disease has grown exponentially since completion of the Human Genome Project in 2003, generating high volumes of data. Building on its established research resources in genetics, genomics, and other scientific data, NIH established dbGaP to house this growing body of information, particularly the results of genome-wide association studies (GWAS), which examine genetic data of subjects with and without a disease or specific trait to identify potentially causative genes. By the end of 2007, dbGaP included results from more than a dozen GWAS, including genetic analyses added to the landmark Framingham Heart Study and trials conducted under the Genetic Association Information Network. dbGaP is to become the central repository for many NIH-funded GWAS in order to provide for rapid and widespread distribution of such data to researchers and accelerate the advance of personalized medicine.
• For more information, see http://view.ncbi.nlm.nih.gov/dbgap
• This example also appears in Chapter 3: Disease Registries, Databases, and Biomedical Information Systems and Chapter 3: Genomics.
• (I) (NLM)

NIH Collaborative Psychiatric Epidemiology Surveys (CPES): Through cooperative agreements, NIH supports the National Co-morbidity Survey-Replication (NCS-R), the National Latino and Asian American Study (NLAAS), and the National Survey of American Life (NSAL). These studies are large, nationally representative surveys assessing the prevalence and correlates of mental health disorders. The NLAAS provides national information on the similarities and differences in mental illness and service use of Latinos and Asian Americans. The objectives of the NSAL are to investigate the nature, severity, and impairment of mental disorders among national samples of the African American and non-Hispanic white populations in the United States.

• For more information, see http://www.hcp.med.harvard.edu/ncs/
• For more information, see http://www.multiculturalmentalhealth.org/nlaas.asp
• For more information, see http://www.rcgd.isr.umich.edu/prba/nsal.htm
• This example also appears in Chapter 2: Minority Health and Health Disparities.
• (E) (NIHM)

Genome-Wide Association Studies of Cancer Risk: Beginning with the Cancer Genetic Markers of Susceptibility (CGEMS) initiative for breast and prostate cancer, NIH has capitalized on its long-term investment in intramural/extramural consortia by creating strategic partnerships to accelerate knowledge about the genetic and environmental components of cancer induction and progression. Using powerful new technology capable of scanning the entire human genome, these efforts have recently identified unsuspected genetic variants associated with increased risk for developing cancers of the prostate, breast, and colon. Additional scans, either planned or under way, will be directed at cancers of the pancreas, bladder, lung, and other organs. The results of these genome-wide studies, together with the follow-on studies planned to narrow the search for causal gene variants, promise to provide novel clinical strategies for early detection, prevention, and therapy. To expand upon these emerging opportunities, a new Laboratory of Translational Genomics (LTG) has been established to further characterize genetic regions associated with cancer susceptibility, and to identify gene-gene and gene-environment interactions. The LTG will create opportunities for collaboration and data-sharing in order to accelerate the translation of genomic findings into clinical interventions.

• For more information, see http://cgems.cancer.gov/
• For more information, see http://epi.grants.cancer.gov/BPC3/cohorts.html
• For more information, see http://cgems.cancer.gov/index.asp
• For more information, see http://epi.grants.cancer.gov/PanScan/
• This example also appears in Chapter 2: Cancer and Chapter 3: Genomics.
• (E/I) (NCI)

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

• For more information, see http://www.nhlbi.nih.gov/new/press/06-10-12.htm
• This example also appears in Chapter 2: Chronic Diseases and Organ Systems and Chapter 2: Minority Health and Health
The Rapid Response Program: In April 2002, the Task Force on College Drinking released its seminal report A Call to Action: Changing the Culture of Drinking at U.S. Colleges. As part of its college focus, NIH initiated support of collaborations between university personnel who have responsibility for alcohol programs on various campuses and established college drinking researchers to implement and evaluate programs to reduce underage alcohol use and its consequences.

- Dec. 2002 - RFA AA-03-008: “Research Partnership Awards for Rapid Response to College Drinking Problems.” Five U01 (cooperative agreement) 5-year grants were awarded.
- June 2003 - PAR-03-133: “Rapid Response to College Drinking Problems.” Fifteen 3-year grants were awarded.
  - This rapid funding mechanism (U18, cooperative agreement) supports timely research on interventions to prevent or reduce alcohol-related problems among college students. It was intended to support studies of services or interventions that could capitalize on “natural experiments” (e.g., unanticipated adverse events, policy changes, new media campaigns, campus-community coalitions)
  - Each U18 grantee was required to partner with a U01 grantee. Together, these pairs, working with NIH Scientific Staff Collaborators, jointly design, develop, implement, and evaluate college drinking projects on their campuses.

- This example also appears in Chapter 2: Chronic Diseases and Organ Systems, Chapter 3: Health Communication and Information Campaigns and Clearinghouses, and Chapter 2: Life Stages, Human Development, and Rehabilitation.
- (E) (NIAAA)

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.

- 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: Clinical and Translational Research.
- (E) (NIDDK)

Health and Retirement Study (HRS): The HRS is the leading source of combined data on health and financial circumstances of Americans older than age 50 and a valuable resource to follow and predict trends and help inform policies for an aging America. Now in its 14th year, the study follows more than 20,000 people at 2-year intervals and provides researchers with an invaluable, growing body of multidisciplinary data on the physical and mental health of older Americans, insurance coverage, finances, family support systems, work status, and retirement planning. Managed under a cooperative agreement between NIH and the University of Michigan, the study was expanded in 2006 to include additional key constructs in cognitive aging. A substudy will provide the first estimates of cognitive impairment and dementia based on nationally representative data and validation of survey measures. HRS staff will also assemble information on sample and questionnaire design, computer-assisted interview programming, interviewer performance, and data dissemination to improve the quality of data collected and provide an incentive for international partners to follow a harmonized design that will maximize the potential...
for cross-national behavioral and social research on aging.

- For more information, see [http://hrsonline.isr.umich.edu/](http://hrsonline.isr.umich.edu/)
- This example also appears in Chapter 2: Life Stages, Human Development, and Rehabilitation.
- (E) (NIA)

Magnetic Resonance Imaging (MRI) Study of Normal Brain Development: Understanding healthy brain development is essential to finding the causes of many childhood disorders, including those related to mental retardation, developmental disabilities, mental illness, drug abuse, and pediatric neurological diseases. NIH is creating the Nation’s first database of MRI measurements and analytical tools, and clinical and behavioral data to understand normal brain development in approximately 500 children from across the Nation. This large-scale longitudinal study uses several state-of-the-art brain-imaging technologies. The data will be disseminated as a Web-based, user-friendly resource to the scientific community.

- For more information, see [http://www.bic.mni.mcgill.ca/nihpd/info/index.html](http://www.bic.mni.mcgill.ca/nihpd/info/index.html)
- This example also appears in Chapter 2: Life Stages, Human Development, and Rehabilitation and Chapter 2: Neuroscience and Disorders of the Nervous Systems
- (E/I) (NICHD, NIDA, NIMH, NINDS)

National Longitudinal Study of Adolescent Health (Add Health): Several NIH Institutes are supporting this study, which integrates biomedical, behavioral, and social science data to discover the pathways that lead to health and/or disease in adulthood. NIH initially funded Add Health in 1994 as a social science study of the causes of adolescent health problems and health-related behaviors. As the cohort of adolescents has moved into early adulthood, the study’s focus has shifted to the environmental, behavioral, and biological pathways that lead to the development of adult chronic disease. The study initially incorporated measurements of social environments—peer groups, families, schools, and neighborhoods—that could affect health and also incorporated a sibling-pair design that facilitated quantitative genetic studies. Most recently, in collaboration with other Federal offices, NIH funded a new wave of interviews that will include collection of genetic data and biological markers of disease processes, as well as basic social, individual, and behavioral data. The new design was developed by a collaborative team representing the fields of epidemiology, cardiology, psychology, sociology, behavioral genetics, nutrition, biostatistics, anthropology, medicine, molecular virology, statistics, and survey research.

- For more information, see [http://www.cpc.unc.edu/addhealth](http://www.cpc.unc.edu/addhealth)
- This example also appears in Chapter 2: Life Stages, Human Development, and Rehabilitation.
- (E) (NICHD, NCI, NCMHD, NIA, NIAAA, NIAID, NIDA, NIDCD, NINR, OAR, OBSSR, ORWH)

Study of Normal Brain Development: The NIH Intramural Research Program is conducting studies to explore brain development in healthy children and adolescents using magnetic resonance imaging. Recent studies have addressed brain structure differences related to risk for Alzheimer’s disease and sex differences in brain development trajectories.

- This example also appears in Chapter 2: Life Stages, Human Development, and Rehabilitation and Chapter 2: Neuroscience and Disorders of the Nervous System
- (I) (NIMH)

A Comprehensive Understanding of Disease

National Health and Nutrition Examination Survey (NHANES): CDC uses rigorous surveys such as NHANES to collect health information and disease burden statistics representative of the entire U.S. population. Surveys also
provide insight on health-seeking behaviors, as well as quality of life experiences and priorities. NIH and CDC collaborate to generate stable national estimates of vision impairment. A recent analysis of vision data indicated that 11 million of the estimated 14 million Americans with vision impairment could have their vision improved to normal levels if they had appropriate refractive correction (e.g., glasses or contact lens), including 9 percent of all young adults ages 12-19.

- For more information, see http://www.cdc.gov/nchs/nhanes.htm
- For more information, see http://www.cdc.gov/nchs/nhis.htm
- (E) (NEI)

**Ocular Epidemiology Panel Report:** The broad aim of National Eye Institute (NEI)-sponsored epidemiology research is to reduce the burden of visual impairment through research into the causes, diagnosis, prevention, treatment, and rehabilitation of the most prevalent blinding diseases. The ability to apply genetic and molecular tools in the context of populations, in connection with behavioral, environmental, and social factors, has transformed the potential contribution of epidemiology to the goal of controlling the major blinding diseases. NEI recently convened an expert panel to assess the unique needs and opportunities in ocular epidemiology that result from these new tools and to make recommendations for their application in future research. The panel’s recommendations are contained in its report *Epidemiological Research: From Populations through Interventions to Translation*.

- For more information, see http://www.nei.nih.gov/funding/nprp.asp
- (E/I) (NEI)

**Multi-Ethnic Study of Atherosclerosis (MESA):** In an ancillary study to the NHLBI-sponsored MESA, retinal disease was assessed in more than 6,000 African American, Hispanic, White, and Asian subjects in this large population-based study of cardiovascular health. Eyes of African American and Hispanic study subjects are more likely to have signs indicative of diabetic eye disease whereas the eyes of White and Chinese subjects are more likely to show signs of age-related macular degeneration. Other analyses demonstrate racial/ethnic differences in the relative size and characteristics of the blood vessels lining the back of the eye, which are associated with various cardiovascular profiles. Future analyses will expand on these results and will consider the impact of genes, alone and in combination with differential exposure to environmental factors, such as cigarette smoke and air pollution, on retinal health.

- For more information, see http://www.mesa-nhlbi.org/default.aspx
- This example also appears in Chapter 2: *Minority Health and Health Disparities*.
- (E/I) (NHLBI, NEI)

**Chronic Kidney Disease (CKD) and End-Stage Renal Disease (ESRD):** The Chronic Renal Insufficiency Cohort (CRIC) study is investigating the relationship between CKD and cardiovascular disease. With approximately 3,000 subjects, this is the largest cohort study of CKD undertaken to date. The Chronic Kidney Disease in Children Study (C-KiD) is a cohort study of 540 children. It aims to identify novel and traditional kidney disease risk factors for the progression of CKD, and to characterize the impact of a decline in kidney function on neurodevelopment, cognitive abilities, and behavior. The U.S. Renal Data System is a national data system that collects, analyzes, and distributes information about CKD and ESRD in the United States.

- For more information see http://tinyurl.com/39nk3x
- For more information, see http://www.statepi.jhsph.edu/ckid/
- For more information, see http://www.usrds.org/
- (E) (NIDDK, NICHD)

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

- For more information, see http://www.bsc.gwu.edu/bsc/studies/edic.html
- This example also appears in Chapter 2: Autoimmune Diseases and Chapter 2: Chronic Diseases and Organ Systems.
- (E) (NIDDK, NICHD)

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.

- For more information, see http://tinyurl.com/24okqop
- For more information, see http://tinyurl.com/29sh4l
- This example also appears in Chapter 2: Chronic Diseases and Organ Systems and Chapter 3: Clinical and Translational Research.
- (E) (NIDDK, CDC, IHS, NCMHD, NEI, NHLBI, NIA, NICHD, ORWH)

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

- For more information, see http://pubs.niaaa.nih.gov/publications/arh29-2/toc29-2.htm
- This example also appears in Chapter 2: Chronic Diseases and Organ Systems, Chapter 2: Life Stages, Human Development, and Rehabilitation, and Chapter 2: Minority Health and Health Disparities.
- (E/I) (NIAAA, NIDA)

Boston Area Community Health Study (BACH) Survey: Interstitial cystitis/painful bladder syndrome (IC/PBS) is a urologic condition whose prevalence is uncertain and which remains difficult to diagnose and treat. The Boston Area Community Health (BACH) Survey is a population-based study of urologic conditions, including IC/PBS, in over 5,500 adults in Boston. Results emerging from BACH about IC/PBS prevalence by demographic group, the role of
comorbid conditions, and the impact of IC/PBS on quality of life are providing a clearer picture of the IC/PBS burden in the population and will inform research efforts to reverse this burden.

- For more information, see http://tinyurl.com/35limz
- For more information, see http://tinyurl.com/363842
- (E) (NIDDK)

**Multinational Influenza Seasonal Mortality Study**: NIH is leading an international collaborative effort to analyze national and global epidemiological patterns associated with influenza virus circulation. Twenty countries have contributed data on mortality, virus surveillance, genomics, and control strategies. The goals of this large-scale collaboration are to evaluate and compare public health strategies to alleviate the impact of seasonal influenza in different countries, and understand the global circulation patterns of influenza and their impact on populations. A better understanding of influenza epidemiology worldwide can inform vaccine strain selection and strategies to mitigate future influenza pandemics.

- For more information, see http://origem.info/misms/
- This example also appears in Chapter 2: Infectious Diseases and Biodefense.
- (O) (FIC)

**Screening Infants for Congenital CMV Infection**: “By 2013, develop and evaluate the efficacy of neonatal screening for congenital cytomegalovirus (CMV) infection to permit identification of infants who will develop CMV-induced hearing loss in the first years of life.” Approximately 1 percent of newborns, or about 40,000 infants each year, are born infected with CMV. As much as 20 to 30 percent of childhood hearing loss is caused by CMV, the most common virus that is passed from a mother to her unborn child. However, 90 percent of CMV-infected children show no symptoms at birth. Due to the compelling but limited data on congenital CMV infection and hearing loss in infants, NIH funded a research contract to the University of Alabama School of Medicine, Birmingham (UAB). The contract funds UAB to lead a multicenter longitudinal study entitled “CMV and Hearing Multicenter Screening” (CHIMES) Study, on the role of congenital CMV in the development of hearing loss in children. A major focus of this research is identifying asymptomatic children and following their progress to determine whether hearing loss develops. The CHIMES study is one of the largest studies of its kind with approximately 100,000 children to be screened at birth for CMV infection. Those who test positive for CMV will undergo followup diagnostic hearing testing to determine the onset, severity, and progression of hearing loss. NIH-supported scientists are combining screening newborns for CMV infection with newborn hearing screening to improve our ability to detect and predict hearing loss in children.

- (E) (NIDCD) (GPRA Goal)

**International Training and Research Program in Population and Health**: This program supports U.S. universities that provide training to scientists from developing countries in population studies or reproductive biology. Objectives of this program include enhancing population research programs and international collaborative studies on (a) reproductive processes and contraceptive development and (b) demographic processes, including aging, mortality, morbidity, fertility, migration, and linkages between health and economic development; strengthening the ability of scientists from developing nations to contribute to global population research efforts and advance knowledge in support of population policies appropriate for their home countries; and developing and strengthening centers of research excellence in population-related sciences in developing countries.

- For more information, see http://www.fic.nih.gov/programs/training_grants/itrph/index.htm
- This example also appears in Chapter 3: Research Training and Career Development
Jackson Heart Study: The Jackson Heart Study, a large epidemiological study of cardiovascular disease (CVD) among over 5,300 African American residents of Mississippi, has been renewed through FY 2013. The project is exploring genetic, biological, and environmental factors that influence the development and course of CVD in African Americans. It is also seeking to expand minority participation in public health and epidemiological research by providing classes and hands-on training to interested undergraduate students. Moreover, a community health education component is using data derived from the study cohort to develop and disseminate up-to-date information on reduction of risk factors, practice of healthy lifestyles, and adherence to proven risk-reducing therapies.

- For more information, see http://jhs.jsums.edu/jhsinfo/
- This example also appears in Chapter 2: *Chronic Diseases and Organ Systems* and Chapter 2: *Minority Health and Health Disparities*.
- (E) (FIC, NICH, ODS)

Retrovirus Epidemiology Donor Study (REDS): REDS was begun by NIH in 1989 to determine the prevalence and incidence of HIV infection among blood donors and the risks of transmitting HIV and other viruses via transfusions. In 2004, NIH launched REDS-II to monitor the appearance of newly discovered infectious agents in the blood supply, evaluate the characteristics and behaviors of voluntary blood donors, determine the causes of transfusion reactions of unknown etiology, assess the results of new donor screening methods, assess the effects of new blood banking technologies, and evaluate the donation process. In 2005, an international component was added to REDS-II to conduct research on blood donors in selected countries seriously affected by the AIDS epidemic to ensure the safety and availability of blood for transfusion.

- For more information, see http://clinicaltrials.gov/ct/show/NCT0097006?sessionid=7A9763F65A8C734DA771CD85210D4877?order=7
- This example also appears in Chapter 2: *Infectious Diseases and Biodefense*.
- (E) (NHLBI)

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.

- This example also appears in Chapter 2: *Chronic Diseases and Organ Systems* and Chapter 3: *Clinical and Translational Research*.
- (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 intervention
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: Clinical and Translational Research
- (E) (NIAID)

**Prenatal Alcohol, Sudden Infant Death Syndrome (SIDS), and Stillbirth (PASS) Research Network:** Following a 3-year feasibility study, NIH established this multidisciplinary consortium in order to determine the role of prenatal alcohol exposure and other maternal risk factors in the incidence and etiology of SIDS, stillbirth, and fetal alcohol syndrome, all of which are devastating pregnancy outcomes. The PASS study will follow 12,000 pregnant high-risk American Indian and South African women and their infants prospectively until the infants are 12 months old. Maternal, fetal, and infant measures and tissues will be obtained for analysis.

- For more information, see http://www.nichd.nih.gov/research/supported/pass.cfm
- This example also appears in Chapter 2: Life Stages, Human Development, and Rehabilitation and Chapter 2: Neuroscience and Disorders of the Nervous System.
- (E) (NICHD, NIAAA)

**Oral Facial 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: Clinical and Translational Research.
- (E) (NIDCR)

**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: Clinical and Translational Research, and Chapter 2: Life Stages, Human Development, and Rehabilitation.
- (E) (NIDDK, CDC)

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

- For more information, see [http://teddy.epi.usf.edu/](http://teddy.epi.usf.edu/)
- This example also appears in Chapter 2: *Chronic Diseases and Organ Systems* and Chapter 2: *Life Stages, Human Development, and Rehabilitation.*
- (E) (NIDDK, CDC, NIAID, NIEHS)

**The Sister Study:** The Sister Study is a major NIH initiative to study environmental and genetic risk factors for breast cancer in a cohort of 50,000 sisters of women who have had breast cancer. The asymptomatic women are being followed over time with periodic health updates. The women who develop breast cancer during the followup period will be compared with those who remained healthy to identify factors associated with increased cancer risk.

- For more information, see [http://www.sisterstudy.org/English/index1.htm](http://www.sisterstudy.org/English/index1.htm)
- This example also appears in Chapter 2: *Cancer.*
- (I) (NIEHS)

**Cognitive and Emotional Health Project:** The Healthy Brain: The purpose of this initiative is to assess the state of longitudinal and epidemiologic research on determinants of cognitive and emotional health in aging adults. The project has completed a comprehensive review of measures that have been (or could be) used in epidemiological research. To help NIH learn what epidemiological data exist on the cognitive and emotional health of adults in the United States, the project polled investigators who are conducting these types of studies and created an online database. In addition, a Critical Evaluation Study Committee conducted an analysis and published a summary of the existing scientific literature pertaining to factors involved in the maintenance of cognitive and emotional health in adults. NIH is discussing new initiatives to expand this project, including promoting the use of existing datasets and developing ancillary studies to examine how cognitive and emotional health influence each other.

- For more information, see [http://trans.nih.gov/cehp/](http://trans.nih.gov/cehp/)
- This example also appears in Chapter 2: *Neuroscience and Disorders of the Nervous System*
- (E) (NINDS, NIA, NIMH)

**HIV/AIDS Epidemiological and Long-term Cohort Studies:** NIH supports epidemiologic 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 between HIV infection, aging, and long-term treatment; cardiovascular disease; and host genetics and its influence on susceptibility to infection, disease progression, and response to therapy.

- For more information, see [www3.niaid.nih.gov/about/organization/daids/daidsepi.htm](http://www3.niaid.nih.gov/about/organization/daids/daidsepi.htm)
- This example also appears in Chapter 2: *Infectious Diseases and Biodefense* and Chapter 2: *Life Stages, Human Development,*
and Rehabilitation.

- (E) (NIAID, NICH)

The National Children’s Study (NCS): The NCS promises to be one of the richest information resources available for answering questions related to children’s health and development and will form the basis of child health guidance, interventions, and policy for generations to come. The landmark study will examine the effects of environmental influences on the health and development of more than 100,000 children across the United States, following them from before birth until age 21. This extensive research effort will examine factors ranging from those in the natural and man-made environments to basic biological, genetic, social, and cultural influences. By studying children through their different phases of growth and development, researchers will be better able to understand the role of these factors in both health and disease. Specifically, the NCS will identify factors underlying conditions ranging from prematurity to developmental disabilities, asthma, autism, obesity, and more. The study is led by a consortium of Federal agencies including NICH and NIEHS at NIH, CDC, and EPA.

- For more information, see http://www.nationalchildrensstudy.gov/
- This example also appears in Chapter 2: Life Stages, Human Development, and Rehabilitation.
- (I) (NICH, NIEHS)

Environmental Health of Mothers and Babies: The Norwegian Mother and Child Cohort Study: NIH is participating in the Norwegian Mother and Child Cohort Study, which provides a valuable opportunity to assess the role of environmental exposures in the health of women and their children. The Norwegian Mother and Child Cohort Study or MoBa (den norske Mor & barn-undersøkelsen) is an ongoing long-term prospective cohort study of 100,000 pregnant Norwegian women and their children. In collaboration with the Norwegian National Public Health Institute (NIPH), NIH is supporting the collection of additional biologic specimens from the pregnant women. These specimens will be used for the measurement of environmental exposures. A variety of exposure and health variables on babies, mothers, and fathers are collected. Records from the cohort study will also be linked to routine national health registries.

- For more information, see http://www.fhi.no/eway/default.aspx?pid=238&trg=MainArea_5811/MainArea_5811=5903:0:15,3046:1:0:0:::0:0
- For more information, see http://www.niehs.nih.gov/research/atniehs/labs/epi/studies/moba/index.cfm
- This example also appears in Chapter 2: Life Stages, Human Development, and Rehabilitation.
- (I) (NIEHS)

Databases for Cervical Cancer Research: NIH has developed data analysis and image recognition tools for studying biomedical images of human papillomavirus (HPV) infection and cervical neoplasia. Image data include 100,000 cervicographs (high-definition cervical photograph), Pap test, and histology images. Tools allow the exploration of visual aspects of HPV and cervical cancer, for research, training, and teaching.

- This example also appears in Chapter 3: Disease Registries, Databases, and Biomedical Information Systems, and Chapter 2: Cancer.
- (I) (NLM, NCI)

U.S.-Born Children of Immigrants May Have Higher Risk for Mental Disorders Than Parents: In the first studies to examine the effects of immigration and years of residence on the mental health of Caribbean Black, Latino, and Asian populations in the United States, NIH-funded researchers found that immigrants in general appear to have lower rates of mental disorders than their U.S.-born counterparts.

- For more information, see http://www.nimh.nih.gov/press/immigrant_mentalhealth.cfm
- This example also appears in Chapter 2: Minority Health and Health Disparities.
Retinopathy Occurs in Middle-aged Adults Even Without Diabetes: Signs of retinopathy are common in the eyes of the elderly, particularly in those with diabetes. In the Atherosclerosis Risk in Communities (ARIC) Study, African American subjects were significantly more likely to have signs of retinopathy (13 percent) compared to White subjects (5.5 percent). Among persons with diabetes, 27 percent had signs of retinopathy. Unexpectedly, retinopathy signs were also observed in 4.3 percent of people who did not have frank diabetes but tended to have elevated blood pressure. Future studies will examine whether these signs of retinopathy result from high blood pressure and whether they indicate an increased risk of systemic cardiovascular disease or predict a subsequent diagnosis of diabetes.

- For more information, see http://www.csc.uc.edu/aric
- This example also appears in Chapter 2: Chronic Diseases and Organ Systems and Chapter 2: Minority Health and Health Disparities.
- (E/I) (NHLBI, NEI)