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NHLBI
Global Health Strategic Plan

2012-2017

Office of Global Health
National Heart, Lung, and Blood Institute

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Transformative changes have occurred over the past century in the threats to human health. In 1900, a third of worldwide deaths were caused by pneumonia tuberculosis, and diarrhea. In 2000, half of global deaths were from heart disease, chronic lung disease and cancer — together, these accounted for <13% of deaths in 1900. What happened in the intervening century? Advancements in biomedical research led to decreases in the rates of TB, pneumonia and diarrhea — first, in the developed world, and then in the developing world. Despite the intervening global epidemic of HIV/AIDS, 80% of deaths from chronic heart and lung diseases now occur in low and middle income countries. These changes in demographics reflect unprecedented triumphs of biomedical research that, because they have been implemented on a global scale, have enormously improved public health.

With these changes have come emerging opportunities to improve both the quality and duration of life for millions of persons globally. With control — and in some instances, eradication — of infectious diseases, chronic diseases affecting those who survive into middle age have become more prominent as a cause of disability and death. The burdens imposed by cardiovascular, pulmonary and hematologic diseases those conditions that are the very reason that United States Congress created the National Heart, Lung, and Blood institute — extend well beyond life expectancy; they affect the quality of life of individuals and families, and the economic well-being of communities and nations. The uncontrolled costs, associated with the diseases themselves and with the health care efforts to treat them seriously, impede efforts to invest in all of the other areas, such as education and improved nutrition, that are necessary to ensure peace and economic stability on Earth.

In 2007-2008, the NHLBI undertook a strategic planning process to identify high priority items in heart, lung, and blood diseases. Even in the initial discussions in the process, the importance of implementing the research agenda on a global scale was recognized. Over the intervening 4 years, global issues have become even more pressing as the costs of ensuring health and treating disease have become less sustainable.

In 2010, the NHLBI established an Office of Global Health to coordinate those components of heart, lung, and blood research that could best be accomplished with global activities engaging multiple partners. The NHLBI’s global health priorities require integration of public health and medical practices, and full engagement of partners in areas that are not usually considered to be within the traditional health care sectors: economics, agriculture, transportation, anthropology, energy and climate. The intent is to focus on research that will enable persons in the developing world to benefit from gains in knowledge already implemented in the developed world, including those related to rheumatic fever, hemoglobinopathies and the safety of the blood supply. Americans are justly proud of the many contributions to science, health and improvement of life on Earth that have already come from their wise investment as taxpayers in biomedical research. And yet, we must admit that we are not without self-interest in this effort. We believe that research with international partners offers opportunities for the United States to develop creative approaches to ensuring that the broad impact of health advances can be achieved at affordable costs without compromise in quality, and thus improve the health of American citizens as well.

Susan B. Shurin, M.D.
Acting Director,
National Heart, Lung, and Blood Institute
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Introduction

The National Heart, Lung, and Blood Institute (NHLBI) Global Health Strategic Plan is intended to define a scientific framework for the Institute’s global research, training, and education programs over the next 5 to 10 years. This plan supports the NHLBI mission “to promote the prevention and treatment of heart, lung, and blood diseases and enhance the health of all individuals so that they can live longer and more fulfilling lives.” A detailed implementation plan to address the challenges identified in this plan will be developed and adapted by the NHLBI Office of Global Health, in consultation with NHLBI internal stakeholders and with representatives from the global research community and the public.

The research and training strategies outlined in this plan focus on heart, lung, and blood diseases and conditions that occur commonly across the globe and on rare diseases for which research must be conducted internationally to answer scientific and clinical questions. Many common diseases that occur globally and many diseases that are rare in the U.S. but are common elsewhere impose a disproportionate burden both on disadvantaged populations and on vulnerable groups in developed nations. In addressing both common and rare diseases, the global community faces challenges that require information sharing and collaboration. The diseases within the mandate of the NHLBI have a profound adverse effect upon global social and economic development and therefore require a global strategy to address them.

The intended audiences of the NHLBI Global Health Strategic Plan are the internal stakeholders of the NHLBI, external professional and research communities and institutions, lawmakers, global governmental agencies, advocacy groups, and the general public. The Plan is intended to help coordinate activities with all NHLBI components, other global health offices across the NIH, and key external stakeholders including the Department of Health and Human Services (HHS), other Federal agencies, multilateral agencies such as the United Nations (UN), the World Health Organization (WHO), other national governments including their public research funding agencies, national and international non-governmental organizations, and public and private corporations. The NHLBI expects to realize the goals of this plan through a wide variety of public and private partnerships and collaborations.
The NHLBI supports research on cardiovascular, pulmonary, and hematologic conditions within its research mission. Cardiovascular conditions of interest include atherothrombosis, acute coronary syndrome, myocardial infarction, heart failure, hypertension, vascular disease, arrhythmias, valvular disease (including rheumatic fever), and congenital heart disease. Pulmonary conditions of interest include asthma, chronic obstructive pulmonary disease, impaired lung development caused by inhaled toxins, and rare lung diseases. Hematologic conditions of interest include hemoglobinopathies, especially sickle cell disease and the thalassemias, other forms of anemia, and disorders of thrombosis and hemostasis. The NHLBI research mission also includes blood resource availability and safety. The genetic and environmental factors that contribute to the conditions within the NHLBI mandate and their prevention and management are all of interest, as are health disparities, health services research, and disease prevention and health promotion.

Each of the conditions within the NHLBI mandate offers unique opportunities for global health research. Among common diseases, cardiovascular and pulmonary diseases are now the leading causes of death worldwide. Iron deficiency is the most common cause of anemia and the most common nutritional deficiency worldwide. Thrombotic disorders cause extensive disability globally. Blood safety is an international public health issue. Although recognized as important health problems in the United States, sickle cell disease and the thalassemias are far more common and comprise a major public health problem in sub-Saharan Africa and in Southeast Asia. Bleeding disorders such as hemophilia are expensive to manage. Because they are rare globally, research to address those demands international collaboration.

In fact, international collaboration on all aspects of the NHLBI mission will provide the Institute — and indeed the entire global health community — with unique opportunities to address basic scientific questions, develop effective new approaches to manage and treat disease, and suggest ways to implement broad scale public health programs for disease prevention.

Scientific collaborations for health also offer the ancillary benefit of strengthening international relationships and diplomacy. The results of the work envisioned in this strategic plan will benefit the millions of Americans who experience a substantial burden from the diseases covered by it. International collaborations enable research to be conducted more efficiently and rapidly and ensure that results are broadly applicable. The diversity of investigators and environments engaged in international collaborations can be expected to develop creative approaches that are likely to be applicable in the U.S. Scientific collaborations for health also offer the ancillary benefit of strengthening international relationships and diplomacy.
Vision
The OGH, along with all of the other components of the NHLBI, is guided by the NHLBI vision statement:

“As a steward of the public investment in biomedical science, the NHLBI strives to discover and apply knowledge to improve health globally. Holding ourselves to the highest standards of excellence, and challenging those we support to do likewise, the NHLBI will expand understanding of health and of diseases affecting the heart, lungs, and blood; use the enhanced understanding to reduce the burdens of illness; and enable scientists and citizens to create a better world.”

Consistent with the Institute’s vision statement, the OGH will facilitate collaborations between NHLBI-supported U.S. investigators and international investigators that will advance discovery, facilitate research translation, and ultimately improve the health of Americans, while also benefitting global public health. Investment in education and training of U.S. investigators and international collaborators is essential to achieve this vision.

Mission
The NHLBI provides global leadership for research, training, and education programs to promote the prevention and treatment of heart, lung, and blood diseases and enhance the health of all individuals so that they can live longer and more fulfilling lives. The Institute’s overriding mission is to help reduce the burden of heart, lung, and blood diseases worldwide. The NHLBI global health research portfolio will focus on strategic international opportunities to stimulate basic discoveries about the causes of disease, enable the translation of basic discoveries into clinical practice, foster training and mentoring of emerging scientists and physicians in the U.S. and abroad, and communicate research advances to the public, with a special focus on providing evidence to support the activities of policy makers around the world.

Strategic Goals
The NHLBI Strategic Plan focuses on three primary goals. The OGH will support and facilitate research and training in international collaborative settings to help achieve each of them.

Goal 1: To increase understanding of the molecular and physiological basis of health and disease and to use that understanding to develop improved approaches to disease diagnosis, treatment, and prevention.

Goal 2: To improve understanding of the clinical mechanisms of disease and thereby enable better prevention, diagnosis, and treatment.

Goal 3: To generate an improved understanding of the processes involved in translating research into practice and use that understanding to enable improvements in public health and to stimulate further scientific discovery.
Situational Analysis

Historical Perspective

Over the past several decades, great progress has been made in addressing many of the infectious disease problems that have challenged the health of populations in less developed parts of the world. Better maternal and infant care and greater access to family planning have significantly improved health outcomes for women and their infants. As life expectancy has increased, chronic diseases have emerged as the leading causes of morbidity and mortality globally, including in very resource-poor settings. Cardiovascular diseases are now the leading cause of death worldwide, with pulmonary diseases, cancer, and diabetes close behind. The burden imposed on populations and nations by chronic noncommunicable diseases and by diseases that are rare in the U.S. but common in other nations destabilizes economies and political systems and threatens peace and overall well-being.

The NHLBI supports biomedical research and training. Studies performed in the U.S. have resulted in major public health benefits throughout the world. NHLBI-supported research defined major risk factors for cardiovascular and pulmonary diseases and enabled development of effective therapies and preventive measures for them that have been implemented globally. Although the Institute’s direct investment in international research has been modest, it does serve as a global leader in development of appropriate strategies and programs to advance research on heart, lung, and blood diseases.

The global burden of NCDs is an urgent and increasing public health concern and a strain on global economies, particularly as these diseases have become more of a factor in low- and middle-income countries.

FIC Global Health Matters Newsletter, Sept/Oct 2011
Examples include:

In 2007, the NHLBI director coauthored an article, “Grand challenges in chronic noncommunicable diseases,” in the journal Nature, which delineated 20 top global policy and research priorities for chronic diseases.

In 2009, the NHLBI joined with other public funders of biomedical research as a founding member of the Global Alliance for Chronic Diseases (GACD).

In 2009, the NHLBI joined the WHO Global Alliance for Respiratory Diseases (GARD), an alliance of national and international organizations, institutions, and agencies committed to working towards reducing the global burden of chronic respiratory diseases, focusing specifically on the needs of resource-poor settings.

In 2009, in partnership with UnitedHealth Group (UHG) the NHLBI established its Global Health Initiative—a worldwide network of Collaborating Centers of Excellence to build institutional and community capacity. The program advances the Institute’s engagement in global health issues by working to prevent and control chronic disease worldwide. The Institute’s expertise in biomedical research and training complements the UHG expertise in health systems and health care delivery.

In 2008, the NHLBI commissioned the Institute of Medicine (IOM) of the National Academies to conduct a study on the evolving global epidemic of cardiovascular disease, and to seek recommendations to improve cardiovascular control. The resulting report, “Promoting Cardiovascular Health in the Developing World,” was published in March 2010.

In 2011, the NHLBI acting director coauthored with several NIH leaders and others “Accelerating progress on noncommunicable diseases” in The Lancet, which calls for a transformation of global strategies on noncommunicable diseases and highlights the NIH’s commitment to combating these diseases.

Recognizing that rigorous, collaborative research undertaken in a variety of settings can increase understanding of basic disease causation and the interplay between biological, environmental, and socio-cultural contributors to public health, the NHLBI established the OGH in 2010 to coordinate internal and external activities in international biomedical research. The OGH serves as a central office with expertise in international research for NHLBI international programs and collaborations.
Organizational Roles
The OGH will collaborate with the NHLBI divisions to coordinate and leverage scientific opportunities to advance the Institute’s global research agenda and training mission. The OGH will coordinate NHLBI activities with the Fogarty International Center (FIC), other NIH Institutes and Centers (ICs), other agencies of the HHS, other federal agencies, foreign governmental agencies, nongovernmental and private organizations, and domestic and international investigators and institutions. The OGH will seek out new opportunities for collaboration to support the NHLBI’s biomedical research agenda in international settings.

The OGH will focus on leveraging global resources, expertise, and approaches to stimulate basic discoveries about the causes of disease; enabling the translation of basic discoveries into clinical practice and public health; fostering training and mentoring of emerging scientists and physicians; and communicating research advances to the public.

It will create and support an international collaborative research infrastructure in partnership with internationally focused private and public organizations to help reduce the burden of heart, lung, and blood diseases worldwide.

The OGH will support the identification of potential research partners for NHLBI activities; track existing relationships and agreements between nations and between organizations with common interests in the U.S. and abroad; facilitate connections between NHLBI staff and investigators and governmental agencies, aid communications between potential partners and the NHLBI; and represent the NHLBI in global health activities within the NIH and the HHS and with the U.S. Department of State. The OGH will have a close partnership with the FIC on behalf of the NHLBI to facilitate efficient, effective coordination and avoid redundancy of programs.

Environmental Context
In 2000, the UN General Assembly held its first high-level meeting on health, and identified eight Millennium Development Goals: eradicate extreme poverty and hunger; achieve universal primary education; promote gender equality and empower women; reduce child mortality; improve maternal health; combat HIV/AIDS, malaria and other diseases; ensure environmental sustainability; and develop a global partnership for development. Many of the specific goals focused on eradication of infectious diseases. While these goals will not be fully realized by the initial deadline of 2015, they were reaffirmed in 2011, and the attention focused by the UN on health as a contributor to peace, justice, and economic development has affected investments made by governments, non-governmental organizations, and trans-national groups.
As the world’s population ages, it becomes more vulnerable to chronic diseases that impose a substantial burden on public health and health care systems, and that threaten international economic development. Research on rare and genetic diseases requires international collaboration. Recent advances in genomics and molecular biology and the availability of accessible technologies for use in the study of genes and environment have created tremendous scientific opportunities. Inclusion of broad demographic and geographic diversity enhances the value of basic biomedical research, clinical translational sciences, and epidemiologic data. Dissemination and implementation of research discoveries is essential to achieve public health benefits; lessons learned in diverse settings often facilitate application across nations.

An environmental scan of research opportunities conducted in preparing this plan included reviews of the NHLBI Strategic Plan; the strategic plans of the FIC, HHS, and WHO; NIH research priorities; the aforementioned IOM report on cardiovascular health in the developing world; a Lancet publication on priority actions for noncommunicable diseases (NCDs); and the Moscow Declaration on Healthy Lifestyles and Noncommunicable Diseases.

Several factors inform current opportunities to advance basic science and translational research, epidemiologic studies, and train those who design and conduct research in heart, lung, and blood diseases.

“Scientific discovery knows no boundaries — and neither do chronic diseases ... which are increasingly affecting the young and the elderly, the rich and the poor, and every ethnic group in every nation.”

Dr. Elizabeth G. Nabel
President of Brigham and Women’s Hospital and Former Director, National Heart, Lung, and Blood Institute
Further understanding of the translation process itself is needed to expedite and expand the adoption of biomedical advances into clinical practice and individual health behaviors.

NHLBI Strategic Plan, Sept. 2007
common in other parts of the world. Mendelian diseases such as the hemoglobinopathies are dramatic examples of conditions in which international collaboration will permit identification of genetic and environmental modifiers of disease manifestations, answering questions that cannot be addressed in the United States. Molecular classifications of disease increase our ability to develop specific therapies, but commensurately reduce the number of affected persons eligible for each treatment. As a result, it will not be possible to conduct many such studies without global cooperation.

**Global Collaborations.**

Global collaborations among research funders are being created to coordinate implementation research in NCDs. The WHO and the UN have expressed concern that chronic genetic and acquired diseases are adversely affecting worldwide economic development and international relations. The expanded focus of the WHO and the UN in these areas provides opportunities to develop multi-sector collaborations with public health and economic benefits.

**Private Nonprofit Funding.**

Private foundation funding of global health programs has increased significantly. Private foundations are able to target investments to their specific areas of interest. By developing and maintaining public-private partnerships and leveraging its investments, the NHLBI can create a research agenda focused on public health priorities with which other funders can collaborate, thus accelerating clinical research discoveries, facilitating advances in prevention and control of chronic diseases, helping to build research and training capacity, and ensuring sustainability of programs.  

**Social, Behavioral, and Economic Factors.**

Cultural, social, behavioral, and economic factors have profound influences on the development of NCDs and on the priorities and approaches to studying genetic and other diseases. Insufficient data exist about how to implement effective interventions. Efforts to elucidate the interactions of environment and biological systems can provide an opportunity for multidisciplinary research and training between the social sciences and the health sciences. The OGH will explore opportunities for biomedical and social science researchers to engage across disciplines.

**Limited Biomedical Research Resources.**

The level of public investment in biomedical research varies across the world. China, India, and South Korea are increasing their research investments. The economic crisis of the early 21st century has limited the ability of the United States to invest in biomedical research; a decline in spending power associated with flat budgets has been accompanied by an increase in the costs of conducting research. Pharmaceutical industry investment in research has diminished as its profits have declined. The limited resources available for support of biomedical research underscore the importance of developing collaborations and leveraging investments. The OGH will develop partnerships and collaborations that will leverage, and thereby increase, the return on NHLBI investments in global health research and training programs, contributing to sustainability and adding value in the United States and other nations. When collaborating with nations that have resources to invest, the OGH will encourage co-investment and sharing of expertise and skills by both partners.
“We know what needs to be done, but often we don’t know how to effectively implement change. The NIH focus is on the generation of evidence of the effectiveness of an intervention, and its applicability on a population-wide scale.”

Dr. Susan B. Shurin
Acting Director, National Heart, Lung, and Blood Institute

**Impact of Health Trends – Obesity and Diabetes.**

Major discoveries made over the last several decades have contributed to the decline of cardiovascular deaths in the United States, but the current epidemics of obesity and diabetes are threatening to halt or even reverse that decline. In particular, the prevalence of obesity in children and youth may cause the next generation to be less healthy than previous generations. Obesity, diabetes, and hypertension during pregnancy predispose children to early development of cardiovascular, renal, and metabolic disorders. The effects of the epidemics of obesity and diabetes will likely add to the burden of chronic disease on current and future generations.

**Domestic Impact.**

Increases in chronic diseases, including cardiovascular and pulmonary diseases, cancer, and diabetes, and the rise of obesity, are especially prevalent in vulnerable and disadvantaged groups in developed nations, including the United States. Substantial disparities exist in the health status of ethnic groups within the United States. Research conducted in global settings can provide creative and effective approaches to control chronic diseases within the United States. Improved approaches to the prevention and treatment of cardiovascular and pulmonary diseases in the stroke belt in the American South and in minority populations such as African Americans, Americans of Hispanic heritage, and Native Americans would decrease health costs.
in the United States, and improve the nation’s economic status. Research on rare diseases that afflict Americans will advance understanding and lead to new therapies of broad benefit.

**Opportunities in Cardiovascular Health**

As control of infectious diseases has improved and western lifestyles have been increasingly adopted, cardiovascular disease (CVD) has become the leading cause of death in the world, accounting for 30 percent of all deaths. Low- and middle-income countries (LMICs) are disproportionately affected: 82 percent of CVD deaths take place in LMICs and occur almost equally in men and women. The majority of worldwide CVD deaths are attributable to coronary heart disease and stroke. By 2030, an estimated 23.6 million people will die annually from CVD. The largest increase in number of deaths will occur in the South-East Asia Region.

Over 220 million people worldwide have diabetes. In 2004, an estimated 3.4 million people died from consequences of high blood sugar. Diabetic patients die of CVD mostly due to macro- and micro-vascular complications. More than 80 percent of diabetes deaths occur in LMICs. The WHO projects that diabetes deaths will double between 2005 and 2030. Healthy diet, regular physical activity, maintaining a healthy body weight, and avoiding tobacco use can prevent or delay the onset of type 2 diabetes.

In 2010, the IOM released the aforementioned NHLBI-commissioned report, “Promoting Cardiovascular Health in the Developing World” that highlighted the global burden of CVD and outlined several key challenges facing all nations. They include major demographic changes, including urbanization, changes in physical activity, changes in food quality and sources, environmental change, and economic and social upheaval. The report also noted a high rate of premature cardiovascular mortality (less than 60 years of age) in most LMICs.

**Benefits to Americans:** The rates of CVD are much greater in minority populations in the United States than in the nation as a whole. Existing research has demonstrated the power of changes in diet and physical activity to prevent the development of CVD, and the benefits of adequate control of blood pressure and cholesterol, with medications for primary and secondary prevention of CVD. Research in global settings will inform approaches to disease prevention and low-cost approaches to optimizing use of medication in areas of the United States, where it has been difficult to implement changes that improve health.
Opportunities in Lung Health

Chronic respiratory diseases (CRDs) comprise an array of diseases, many of which are preventable or treatable. CRDs affect hundreds of millions of people of all ages worldwide. In 2005, CRDs were responsible for 7 percent of all deaths and are projected to increase 17 percent over the next 10 years, while deaths from other conditions are declining. The WHO predicts that one CRD, chronic obstructive pulmonary disease (COPD), will increase by 30 percent in the next 10 years and will be the third leading cause of death worldwide by 2030.

COPD, a disease of airflow limitation, is not curable, but is largely preventable. In the more developed countries, exposure to tobacco smoke, whether direct or indirect, is the primary cause of COPD, but in certain countries, the burning of biomass fuel and air pollution are major causes, especially in women, who generally do not smoke. Asthma, a treatable CRD of variable airflow limitation, affects 300 million people of all ages and accounts for many days lost at school and work. Lack of proper treatment contributes to its social and economic burden. Other CRDs, such as occupational lung disease, sleep apnea, and pulmonary hypertension contribute to the global burden of CRDs. Many CRDs are under diagnosed, even in high-income countries, making estimates of their true burden difficult to calculate. In resource-poor settings, treatments that could lower the burden and improve productivity and quality of life are either not available or not affordable.

Benefits to Americans:

Significant health disparities exist in the rates and outcomes of COPD and asthma within the United States. African Americans are at particularly high risk for pulmonary diseases. Better understanding of genetic and environmental contributors to the disparities, and approaches to primary and secondary prevention, will require research in international settings. The results of that research will directly benefit U.S. citizens.
Opportunities in Blood Diseases and Blood Safety

Dramatic changes have occurred in the clinical course of hemoglobinopathies (primarily sickle cell disease and the thalassemias) in the developed world over the past four decades. While death in childhood is now rare for children with sickle cell disease in the United States and the European Union, over 95 percent of children in sub-Saharan Africa who are born with sickle cell disease die before their fifth birthdays. Births of children with thalassemias are now rare in Italy and Greece, but the burden of thalassemias in Southeast Asia remains high. The total costs associated with proving proper care for persons with hemoglobinopathies and bleeding disorders exceed the resources of many of the nations where the diseases are common. The WHO has issued resolutions to urge that the burden of hemoglobinopathies be addressed. The NHLBI has supported research on hemoglobinopathies since its inception in 1948, and has supported all of the studies that have improved the outcome for patients in developed countries. Two major opportunities for international research efforts exist that would have important benefits in the United States and abroad. Research among sub-Saharan African and Southeast Asian populations could lead to an improved understanding of the genetic modifiers of monogenic diseases and facilitate development of improved methods of management and detection of complications of hemoglobinopathies.

A safe and available blood supply is critical to the millions of patients who rely on transfusion therapies including surgery patients, critically ill patients with anemia, patients with non-malignant hematologic disorders such as hemoglobinopathies and hemophilia, cancer patients, and trauma victims. Transmissible agents in the blood supply now pose an international threat because air travel has erased borders that formerly limited transmission. NHLBI-supported programs have provided evidence that has increased the benefits and reduced the risks of transfusions in the United States and in other countries. The impact of existing infectious agents (e.g., HIV/AIDS, hepatitis B and C), new and emerging agents, and opportunities for evidence-based implementation of blood safety measures in diverse and vulnerable populations, are important priorities for research to inform policy and practice.

Benefits to Americans: Many basic scientific and clinical questions in blood diseases can be answered only with international research studies, because the diseases, though imposing significant health burdens in the United States, are relatively rare here. Some blood diseases are common in other parts of the world, whereas others, such as the hemophilias, are rare everywhere. They are very expensive to manage and impose high burdens of suffering on patients and costs to their families and communities. Essential advances in understanding and managing blood diseases will require coordinated international efforts to reduce both the burdens they impose and their associated costs.
Justification

Defining the Need
Dramatic changes in communication, education, economics, culture, and travel have made the world more interconnected than ever before. Economic development, public health policies, and advances in scientific knowledge and medical care have all contributed to improvements in health. Yet vast disparities exist in the extent to which improvements in health have been realized across the globe, with those in resource-poor settings experiencing major disruptions associated with epidemiological transitions that have contributed to their disparate health gains. Improved health is both necessary for, and a consequence of, economic development in the poorest nations. With a more global economy, geographic borders are no longer effective in limiting the spread of diseases, and they should no longer limit access to therapies.

Collaboration between U.S. and international scientists will accelerate research progress in two important ways. First, it will facilitate efforts to gain an improved understanding of fundamental biology, including genomics, proteomics, metabolomics, and systems biology by providing access to diverse populations and environments. Second, it will enable development of new approaches to prevention and treatment of diseases that affect Americans and citizens of other nations. For many rare diseases, research is virtually impossible without the cooperation of international partners. For more common diseases, including many of those that impose great public health burdens, international cooperation will increase the overall level of resources focused on developing better approaches to prevent and manage these diseases, thereby benefiting both the United States and its international research partners. For most of the diseases within the NHLBI mandate, international collaboration will both ensure continued progress toward reducing disease burden in the United States and enhance the international stature of the United States by contributing to improvements in global public health.

“There are crucial basic science questions that will help us get a better handle on the mechanisms of disease causation and design more targeted and effective interventions adapted to local demographics, culture and environments.

We need more research to guide the economic and public policy changes that need to be made.”

Dr. Susan B. Shurin
Acting Director, National Heart, Lung, and Blood Institute
Program Impact
The NHLBI Strategic Plan enunciates broad goals for research in heart, lung, and blood diseases and conditions. The Institute’s investments in training and research programs will create partnerships between U.S. scientists and institutions and their counterparts in other nations, which will promote collaborative efforts toward shared scientific goals. Such goals include advancing understanding of gene-environment interactions and the determinants of health and disease from a life-course perspective; facilitating development of new therapies for rare diseases with global applications; and building an extensive evidence base for prevention and management of chronic diseases. The evidence base should encompass data on medications, policy interventions, and information from partnerships with multiple sectors and industries, including energy, transportation, defense, housing, urban development, and agriculture.

Achieving the goals of the NHLBI Strategic Plan will be possible only if adequate biomedical research capacity is available both in the United States and abroad. While highly skilled teams of investigators currently exist in many developed and developing nations, further training of investigators and of the many support professionals needed to conduct research is needed in many resource-poor settings to ensure that research is conducted according to current ethical standards and in a fiscally responsible manner.

Benefits to Americans: The benefits of the NHLBI investment in international collaborations are expected to be extensive. Advances in scientific understanding will lead to new therapies and to improvements in public health. Better prevention and treatment approaches will open new markets to U.S. companies in areas such as information technology, mobile health, agriculture, transportation, and education. The insights gained will improve health care management, which will also benefit U.S. citizens.
Strategic Goals

“America’s scientific and technical capabilities support our foreign policy by addressing challenging problems facing the world. In addition, scientists speak a common language that transcends political systems and cultures, which can create channels of communication even when governmental relations are difficult. This “science diplomacy” can be of enormous benefit, especially when opportunities emerge for improved political relations.”

Dr. E. William Colglazier
Science and Technology Adviser to the Secretary of State

Program-Specific Goals and Priorities

The NHLBI Strategic Plan consists of a set of goals that reflects the successive movement of scientific discovery from “form to function” (Goal 1), “function to causes” (Goal 2), and “causes to cures” (Goal 3), with research challenges identified for each of the goals along with a set of strategies to be used to address the plan as a whole. The goals of the NHLBI global health program are derived from and are designed to fulfill the opportunities identified in the NHLBI Strategic Plan.

Form to Function

Goal 1: To increase understanding of the molecular and physiological basis of health and disease and to use that understanding to develop improved approaches to disease diagnosis, treatment, and prevention.

The NHLBI global health scientific questions focus on enhancing understanding of the cellular and tissue effects of environmental factors, including heavy metals, indoor air pollutants, and infectious agents; nutritional deficiencies; metabolic alterations; physical activity levels; and sleep deprivation on the development and function of the cardiovascular, pulmonary, hematopoietic, and immune systems.
To accomplish this goal, mechanisms must be delineated that relate molecular events to health and disease. Some of the challenges in Goal 1 that can be significantly advanced through international collaborations are:

**Challenge 1.1: Develop a detailed understanding of the molecular, cellular, and physiological mechanisms that maintain health from embryonic development to the end of the human lifespan.**

All chronic diseases, whether complex or monogenic, must be viewed from a life-course perspective. The effects of prenatal and early-life nutritional status and exposures to toxins, indoor air pollution, infectious experiences, and stress are long lasting; they interact with genetic factors and affect cardiovascular, pulmonary, and renal function. Infections in childhood influence the manifestations of hemoglobinopathies modify the effects of environmental exposures (including indoor and outdoor air pollution and tobacco smoke) on the development of cardiovascular and pulmonary disease, and can lead to unusually severe clinical phenotypes, e.g., rheumatic carditis in sub-Saharan Africa. The fundamental biologic processes underlying such phenotypes are not well understood.

Cardiovascular and pulmonary health in adulthood is affected by early-life events that have long-term effects. Neither their mechanism of action nor their modifiability is well understood.
Challenge 1.2: Determine key genetic variants that are associated with specific diseases and delineate the molecular mechanisms that account for susceptibility or resistance to disease.

The phenotypic variability of hemoglobinopathies is striking considering that they are monogenic diseases. The benefits for patients with hemoglobinopathies from modifying genomic and environmental factors appear to be significant, but the effects of individual factors are poorly understood. The genetic background of persons of African heritage in the United States is much more variable than that of persons in Africa. The opportunity to work with other countries to study hemoglobinopathies will advance understanding of them much more rapidly than would be possible by studies conducted solely in the United States.

Challenge 1.3: Define molecular, cellular, and organ-specific responses to environmental challenges and the mechanisms by which heritable and non-genetic factors interact in disease initiation and progression and in therapeutic response.

Unique features of disease phenotypes are seen in some geographic locations, the biologic bases of which are not well understood. Included among them are right-sided heart failure in Kenya; the unusually rapid progression and severity of rheumatic heart disease across sub-Saharan Africa; the early age of onset of atherothrombosis in the Indian subcontinent; the underlying reasons for patterns of development of vascular disease in China; and the susceptibility of aboriginal peoples to development of metabolic syndrome and type 2 diabetes. Investigations focused on unique disease manifestations can provide great insight into disease mechanisms that underlie more common disease manifestations.

“Given the changing nature of the global health landscape, we must act now to broaden our vision even further. First, we need to apply the power of scientific innovation to more health problems. Secondly, we need to recognize that developed nations are not the only source of such innovation.”

Dr. Francis S. Collins
Director, National Institutes of Health
**Challenge 1.4:** Discover biomarkers that differentiate clinically relevant disease subtypes and that identify new molecular targets for application to prevention and diagnosis.

CVDs, such as right-sided heart failure, are relatively common in middle-age women in Africa, so studies conducted in collaboration with African investigators may enable discovery of biomarkers for differential diagnoses of clinical subtypes and identification of new targets for therapeutic intervention. In addition, comparative studies to identify biomarkers or molecular determinants, such as ApoA-1 Milano, which is known to be associated with low risk of coronary artery disease or heart failure including systolic or diastolic dysfunction in older adults, may be a research focus for geographic locations where rates of cardiovascular diseases are very low.

**Challenge 1.5:** Identify molecular signatures that allow complex disease phenotypes to be stratified into clinically relevant categories.

As molecular signatures are developed, international collaborations will enable them to be validated in diverse global populations and, then used to develop treatments that are tailored to distinct populations.
Function to Cause
Goal 2: To improve understanding of the clinical mechanisms of disease and thereby enable better prevention, diagnosis, and treatment.

Intensified efforts are needed to translate basic research findings into clinical studies to accelerate realization of the benefits of scientific advances both in the United States and throughout the world. Translation of clinical research findings back to the laboratory can further improve public health by stimulating acquisition of additional basic biomedical knowledge. Conditions that affect many countries, including the United States, can be studied in larger populations through collaborative efforts. For example, the most common CVDs in Africa include dilated cardiomyopathy, peri-partum cardiomyopathy, and, to a lesser extent, hypertrophic cardiomyopathy and arrhythmogenic RV dysplasia. Rheumatic carditis, now far less common in the United States than in the past, is common in African populations and has an aggressive course. These are all conditions seen in the United States, so global collaborations will enable studies of adequate size to provide direct benefit to the health of Americans.

The NHLBI expects to address several challenges through global research collaborations that will contribute to the development of an enhanced evidence base for use in guiding practice and policy. They include collaborations to:

Challenge 2.1: Increase understanding of the interactions between genetic and environmental factors that influence disease development and progression, and response to therapy.
Opportunities exist for global efforts to learn about risk factors for noncommunicable diseases and especially about genes and their interaction with behavioral and environmental factors. Studies of the effects of prenatal and early-life environments on the development of heart, lung, and blood disorders require large numbers of participants with a wide range of prenatal experiences that can best be accrued through international collaborations. Partnering with the President's Global Health Initiative on women's health would provide an opportunity for the NHLBI to support and conduct research to develop evidence on the effectiveness of interventions to improve the health of adolescent girls. Abundant evidence suggests that the health and educational levels of girls during adolescence comprise a key determinant of the health of their children.
Challenge 2.2: Integrate, analyze, and share genotypic and phenotypic data to elucidate the basis of phenotype variability in both complex and single-gene disorders.
Understanding the different phenotypic manifestations of a disorder will help elucidate and develop early detection and effective interventions. Conditions known to have markedly different phenotypes include hypertension, early-onset atherothrombosis, rheumatic carditis, chronic heart failure, COPD, sickle cell disease, the thalassemias, the hemophilias, and thrombotic disorders. Access to data from the markedly greater number of individuals available through international collaborations will substantially expand knowledge of various possible manifestations of disease.

Challenge 2.3: Identify and predict disease risk by early and accurate risk stratification, diagnosis of cardiovascular, lung, and blood disorders, and correlation with biomarkers.
Models to estimate the risk of CRD attributable to environmental factors are needed to determine individual susceptibility and to guide industrial and policy interventions to lessen that risk.

Challenge 2.4: Develop new and targeted therapies that come from basic research, as well as improved approaches to known problems.
The development of cost-effective and affordable interventions and therapies is of great importance given the increasing number of people who are suffering from cardiovascular, lung, and blood disorders. Rigorous, scientifically based behavioral and lifestyle interventions need to be tested, for example, to control abnormal lipids and hypertension, increase physical activity (considering the built environment), stop primary and secondary smoking, and reduce exposure to toxic gases and particles from alternative cooking and heating sources.

Therapeutic modalities that increase the adherence of patients to medications need to be developed and tested to insure better control of risk factors and prevention of clinical disease.
Causes to Cures
Goal 3: To generate an improved understanding of the processes involved in translating research into practice and use that understanding to enable improvements in public health and to stimulate further scientific discovery.

Gaps in knowledge, gaps in knowledge implementation, and priorities for research on translating results into practice have to be identified so that the evidence needed to improve clinical practice and inform policy interventions can be developed. Collaborations with organizations such as the GARD and the WHO are essential for obtaining the evidence needed to assess the effects of policies on the determinants of, risk factors for, and consequences of heart, lung, and blood diseases; and to provide models of effective, evidence-based policy-making.

Identifying effective implementation strategies to address the main shared and modifiable risk factors for chronic cardio-respiratory diseases (i.e., hypertension, tobacco use, indoor and outdoor air pollution, and occupational exposures) is critical to reducing their collective public health burden. Collaborations with organizations such as the GACD and other multilateral agencies, such as the WHO and the World Bank, should be helpful in identifying the most effective methods in a wide range of settings.

The challenges identified in Goal 3 that align with those in the NHLBI Strategic Plan will be major topics of research in international settings. They apply broadly across the spectrum from common to rare diseases within the NHLBI mission, and are listed below as they appear in the NHLBI Strategic Plan:
**Challenge 3.1:** Complement bench discoveries and clinical trial results with focused behavioral and social science research. (NHLBI Challenge 3.1)

Develop and evaluate policy, environmental, and other approaches for use in community settings to encourage and support lifestyle changes. (3.1.b)

**Challenge 3.2:** Identify cost-effective approaches for prevention, diagnosis, and treatment. (NHLBI Challenge 3.2)

Develop research designs, outcome measures, and analytical methods to assess prevention and treatment programs in community and health care settings across populations and lifespan. (3.2.b)

**Challenge 3.3:** Promote the development and implementation of evidence-based guidelines in partnership with individuals, professional and patient communities, and health care systems, and communicate research advances effectively to the public. (NHLBI Challenge 3.3)

Develop personalized and community- and healthcare systems-oriented approaches to increase the use of evidence-based guidelines by individuals, communities, health care providers, public institutions, and, especially, by populations that experience a disproportionate disease burden. (3.3.b)
Strategies
Implementation of this plan will require diverse approaches to address the global scientific challenges previously discussed. This section presents the strategies that the NHLBI intends to employ to facilitate research; enhance interdisciplinary work; speed early stage translation of basic discoveries; ensure cross-fertilization of basic, clinical, and epidemiologic discoveries; and maximize the resultant public health benefit. The global health strategies listed here correspond to the strategies identified in the NHLBI Strategic Plan.

Strategy A (NHLBI Strategy 1): Develop and facilitate access to scientific research resources.
Encourage development and sharing of transnational tissue and animal repositories, databases, and information systems dedicated to the support of biomedical research.

Support the development of data standards and phenotype definitions that can be employed globally, especially in resource-poor settings, for heart, lung, and blood disorders. This consistency will facilitate sharing among global partners.

Provide technical expertise to encourage the development of data systems, including vital registration, surveillance, and registries to enable research on heart, lung, and blood disorders.

Strategy B (NHLBI Strategy 2): Develop new technologies, tools, and resources.
Encourage international research collaborations that develop innovative technologies and research tools (e.g., unique animal models, mobile health technologies, and improved imaging modalities), share unique resources (e.g., registries, cohorts, databases,
and electronic health records), and provide evidence of effective interventions for prevention and/or treatment approaches to clinicians, health systems, and local and national decision makers.

**Strategy C (NHLBI Strategy 4): Establish and expand collaborative resources for clinical research.**

Exploit existing healthcare and public health systems to develop stronger research agendas, partnering with national and international organizations and leveraging their existing infrastructure created around infectious disease and maternal child health to implement heart, lung, and blood disease prevention and control strategies.

Work with local, national, and international health organizations (e.g., CDC, FDA, WHO, GACD, Wellcome Trust) the European Union, and other governments to establish and strengthen administrative processes and evidence to help establish plans for the prevention and control of heart, lung, and blood diseases.

**Strategy D (NHLBI Strategy 7): Develop and retain human capital.**

Partner with U.S. and international universities, professional schools, and research institutes to assist in the development of mechanisms to train health researchers.

**Strategy E (NHLBI Strategy 8): Bridge the gap between research and practice through knowledge networks.**

Facilitate and support a global network of national, regional, and international networks and programs such as the WHO regional networks for noncommunicable disease prevention and control.
Assumptions and Constraints

Assumptions

International activities will be conducted primarily as scientific and organizational partnerships.

*All NHLBI international programs will engage U.S. investigators and institutions.*

*The NHLBI will co-design and implement programs with national authorities of its international partners.*

Strategic coordination and integration with other programs will be encouraged.

Shared funding of programs will encourage country ownership and capacity building. Programs will be designed to strengthen the capacity of U.S. investigators and institutions, key multilaterals, and other partners.

International partners will contribute funding or in-kind investments as they are able. Countries with emerging economies will be expected to support development of their own infrastructure and to assume long-term responsibility for programs.

Joint programs will be developed with partners and with other funders through the GACD.

All programs will emphasize metrics, monitoring, and evaluation.

Practical Considerations

Legal constraints: Programs run jointly with or co-funded by non-U.S. governmental entities will provide full transparency of funding and will not co-mingle funds with other projects.

Fiscal constraints: The state of the global economy will limit investment by the NHLBI and by public and private partners. The economic impact of the diseases within the NHLBI mission is such that research continues to be a good investment for the NHLBI and international partners.

Logistical constraints: Obstacles are likely to be encountered in identifying strategies and resources to achieve goals; developing tools for monitoring and evaluation; engaging and negotiating with partners; aligning the visions of multiple organizations with missions that overlap but are not fully concurrent; and assessing the return on investment of funded international activities.
Benefits to America and Prospects for the Future

The mission of the NIH is to seek and disseminate knowledge to enhance health, lengthen life, and reduce the burdens of illness and disability. Through the implementation of this strategic plan for global health, the NHLBI will accelerate understanding, preventing, managing, and minimizing the burden of heart, lung, and blood diseases and conditions. Through NHLBI global health activities, U.S. scientists and organizations will be afforded new opportunities to develop collaborations with scientists and institutions in other countries. Establishing such international collaborations will enable scientific progress by developing research capacity; facilitating the establishment of infrastructure needed to conduct global health research; training and supporting the next generation of investigators; sharing information and expertise; and realizing the promise of science to improve the well-being of the citizens of the world.

While short-term benefits are expected — and they have been highlighted throughout the text — it is over the long term that the greatest returns from efforts to implement this plan will be realized. The investments of the NHLBI will be leveraged and complemented by international investments — both intellectual and financial, and both public and private — and thereby greatly expand the resources directed at mitigating the global burden of noncommunicable diseases.

Through careful planning and implementation, the NHLBI can use its leadership and innovation in biomedical research to ensure that its investment in global health will result not only in improved health internationally but also pronounced health and economic benefits for all Americans.

“Rather than seeing biomedical innovation as something that flows from developed nations to low-income nations, we need to start viewing innovation as a two-way street from which the entire world stands to benefit. As global health advocate Lord Nigel Crisp so aptly puts it: ‘Innovation is happening everywhere.’”

Dr. Francis S. Collins
Director, National Institutes of Health
Appendix - References

The following documents are referenced in this document.

Grand challenges in chronic noncommunicable diseases

WHO Fact sheet N°317: Cardiovascular diseases (CVDs)

WHO Fact sheet N°312: Diabetes

Promoting Cardiovascular Health in the Developing World

Accelerating progress on non-communicable diseases


United Nations Sixty-sixth Session General assembly, agenda Item Agenda Item 117: Political Declaration of the High-level Meeting of the General Assembly on the Prevention and Control of Non-communicable Diseases

NHLBI Strategic Plan

FIC Strategic Plan 2008-2012

The Global Health Strategy of the U.S. Department of Health and Human Services

WHO 2008-2013 Action plan for the global strategy for the prevention and control of noncommunicable diseases
Opportunities for Research and NIH

Priority actions for the noncommunicable disease crisis

Moscow Declaration on Healthy Lifestyles and Noncommunicable Disease Control

WHO Fact Sheet N° 315: Chronic obstructive pulmonary disease (COPD)

WHO—GARD— Global Surveillance, prevention and control of chronic respiratory diseases: a comprehensive approach

NHLBI New Obesity Data on US Adults and Children

NIDDK National Diabetes Statistics 2011 Fact Sheets

The WHO Fifty-Ninth World Health Assembly. Provisional agenda item 11.4: Sickle-cell anemia

The WHO Executive Board (EB117), Resolution: EB117/R3: Sickle-cell anemia

The WHO Executive Board, 118th Session. Resolution EB118.R1: Thalassaemia and other haemoglobinopathies
The following table provides a key for abbreviations used throughout this document.

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Full Name</th>
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<tbody>
<tr>
<td>CDC</td>
<td>Centers for Disease Control and Prevention</td>
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<td>COE</td>
<td>Collaborating Centers of Excellence</td>
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<td>COPD</td>
<td>Chronic Obstructive Pulmonary Disease</td>
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<td>CRD</td>
<td>Chronic Respiratory Disease</td>
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<td>Cardiovascular Disease</td>
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<td>Global Alliance for Chronic Diseases</td>
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<td>Institute of Medicine of the National Academics</td>
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<td>World Health Organization</td>
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