Global Health Research

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> "The future is already here — it's just not evenly distributed".
>
> William Gibson
>
> The Economist, December 4, 2003

The most recent data from the Global Burden of Diseases, Injuries, and Risk Factor Study (GBD, 2013) suggest that, in the aggregate, global health is improving [1]. From 1990 to 2013, life expectancy at birth increased by 6.2 years, from 65.3 years in 1990 to 71.5 years in 2013. Concordant with this improvement, age-standardized disability-adjusted life years (DALYs) per 100,000 people fell by 26.7%, and healthy life expectancy increased [1]. In its *World Health Statistics* report, the World Health Organization (WHO) [2] demonstrated that in 2014, both men and women were living longer. An even more optimistic future was recently painted by a Lancet Commission report that highlighted the "possibility of achieving dramatic gains in global health by 2035" and offered good reasons "to be optimistic about seeing the global health landscape utterly transformed … within our lifetimes" [3].

Although these global data on improving global health represent good news, they mask important regional, national, and subnational findings on health. For example, the dramatic declines in cardiovascular mortality rates seen in high-income countries have not been matched by similar declines in most low- or middle-income countries (LMICs) [4-7]. In fact, although age-standardized coronary heart disease mortality rate has declined by more than 50% in many high-income countries, the rate trend has been flat or has increased in several LMICs [4-7]. Additionally, in most LMICs in particular, population growth and aging, coupled with epidemiological, nutritional, and other health transitions, are creating a rising burden of cardiovascular diseases and other noncommunicable diseases (NCDs) that threaten health, well-being, and economic development [1,8,9]. Marked inequities in health also remain pervasive by sex, income level, educational status, geography, race, and ethnicity in most regions of the world, including many high-income countries [2,10,11]. The drivers of these inequities and trends remain incompletely understood. Most importantly, safe, effective, and affordable drugs, devices, and interventions for reducing preventable morbidity and mortality remain suboptimally employed in many countries, especially among high-risk and high-burden subnational population groups. Additionally, the skilled scientific workforce and infrastructure needed to undertake rigorous research to address locally relevant health challenges remain suboptimal.

The National Institutes of Health (NIH) is the leading public source of funding for biomedical research in the world and remains committed to advancing global health research, training, and education. In this endeavor, we embrace the challenges embodied in the United Nations agenda to reduce premature cardiovascular disease mortality by 25% by 2025 and transform our world by 2030 [12,13]. The articles in this issue of *Global Heart* attest to commitment of the National Heart, Lung, and Blood Institute (NHLBI) over the last decade to contribute to this effort. In this article, we first summarize the major NHLBI global health research investments over the last decade and then highlight current strategies to support research training, education, and capacity building for implementation research in LMICs, with special attention to high-burden diseases and risk factors such as hypertension, diabetes complications, and household air pollution. We then discuss how the Institute is envisioning our global health research agenda over the next decade. We conclude with selected examples of current research funding opportunities.

BACKGROUND

Since its inception in 1948 as the National Heart Institute, the NHLBI has always valued support for global health research [14,15]. Consistent with its mission to provide global leadership in research, research training, and health education to promote the prevention and treatment of heart, lung, and blood diseases and sleep disorders, the NHLBI has worked in collaboration with other NIH institutes and offices, other U.S. government agencies, and major funders of biomedical research in both the public and private sector to advance global health. The Institute's investments in basic, clinical, and population science research over the past decade include funded investigations in more than 3 dozen countries [16,17]. The NHLBI is proud of the strong international research relationships and networks it has helped foster, the quality of the scientific research investigators have conducted, and importantly, the substantial research capacity NHLBI has helped build in LMICs. Three such activities are discussed here as examples of NHLBI investments in global health research over the last decade.

NATIONAL HEART, LUNG, AND BLOOD INSTITUTE GLOBAL HEALTH RESEARCH INVESTMENTS OVER THE LAST DECADE

In partnership with the UnitedHealth Group in 2009, the NHLBI established 11 Collaborating Centers of Excellence

The author reports no relationships that could be construed as a conflict of interest.
The views expressed in this article do not necessarily represent the views of the National Institutes of Health or the United States Department of Health and Human Services.
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GLOBAL HEART

VOL. 11, NO. 1, 2016
ISSN 2211-8160/$36.00.
http://dx.doi.org/10.1016/j.gheart.2016.01.005

TABLE 1. Examples of research funding opportunities at the National Institutes of Health addressing heart, lung, blood, and sleep disorders and other chronic noncommunicable diseases

Announcement #	Title and Funding Opportunity Purpose	Application Open Date	Application Due Date
RFA-HL-17-006	Sickle Cell Disease in Sub-Saharan Africa: Collaborative Consortium (U24) http://grants.nih.gov/grants/guide/rfa-files/RFA-HL-17-006.html The purpose of this FOA is to solicit applications that propose to develop a Sickle Cell Disease (SCD) in Sub-Saharan Africa (SSA) Collaborative Consortium. The Collaborative Consortium will be responsible for developing an infrastructure on which a future SCD in SSA Research Network can be built.	01-26-2016	02-26-2016
RFA-HL-17-007	Sickle Cell Disease in Sub-Saharan Africa: Data Coordinating Center (U24) http://grants.nih.gov/grants/guide/rfa-files/RFA-HL-17-007.html The purpose of this FOA is to solicit applications that propose to develop a Sickle Cell Disease (SCD) in Sub-Saharan Africa (SSA) Data Coordinating Center (DCC) that will support the activities of the SCD in SSA Collaborative Consortium (RFA-HL-17-006).	01-26-2016	02-26-2016
RFA-HL-17-004	Pediatric Heart Network Clinical Research Centers (UG1) http://grants.nih.gov/grants/guide/rfa-files/RFA-HL-17-004.html This FOA invites applications from qualified institutions willing to participate with NHLBI in the Pediatric Heart Network (PHN) as Clinical Research Centers (CRCs). These CRCs will support and conduct research to improve the health and quality of life for children and adults with congenital heart disease and for children with acquired heart disease through multicenter collaborative clinical research.	02-02-2016	03-02-2016
RFA-HL-17-002	The Role of the Human Virome in Heart, Lung, and Blood Health and Resilience (R61/R33) http://grants.nih.gov/grants/guide/rfa-files/RFA-HL-17-002.html The purpose of this FOA is to support research to identify and evaluate the basic underlying molecular and physiological mechanisms by which the virome may influence heart, lung, and blood health and resilience. Research applications that can leverage cohorts or populations from other programs including global initiatives such as international sickle cell disease programs as well as global AIDS programs are encouraged.	05-24-2016	06-24-2016
RFA-CA-15-007	Planning for Regional Centers of Research Excellence in NCDs in LMICs (P20) http://grants.nih.gov/grants/guide/rfa-files/RFA-CA-15-007.html The goal of this FOA is to facilitate the planning, designing, and initial research focus of Regional Centers of Research Excellence (RCRE) for NCDs, including cancer, in LMICs.	12-10-2015	08-23-2016
PAR-16-052	Global Non-communicable Diseases and Injury Across the Lifespan: Exploratory Research (R21) http://grants.nih.gov/grants/guide/pa-files/PAR-16-052.html This FOA supports planning, design and initial pilots for locally relevant and catalytic research on NCDs or injury in LMICs. Research addressing multiple NCDs and their risk factors and research addressing NCDs as comorbidities for/with infectious diseases including HIV/AIDS is encouraged.	02-24-2016	02-24-2016 02-22-2017
PAR-15-291	Emerging Global Leader Award (K43) http://grants.nih.gov/grants/guide/pa-files/PAR-15-292.html The purpose of the Fogarty Emerging Global Leader Award is to provide research support and protected time to a research scientist from an LMIC with a junior faculty position at an LMIC academic or research institution.	11-16-2015	12-16-2015 12-14-2016 12-14-2017

(continued)

TABLE 1–*continued*. Examples of research funding opportunities at the National Institutes of Health addressing heart, lung, blood, and sleep disorders and other chronic noncommunicable diseases

Announcement #	Title and Funding Opportunity Purpose	Application Open Date	Application Due Date
PAR-15-292	International Research Scientist Development Award (IRSDA) (K01) http://grants.nih.gov/grants/guide/pa-files/PAR-15-291.html Foreign components, as defined in the NIH Grants Policy Statement, are allowed. See more at: http://grants.nih.gov/grants/guide/pa-files/PAR-15-291.html#sthash.HMU8LAgh.dpuf The purpose of the IRSDA is to provide support and protected time (3 to 5 years) to advanced postdoctoral U.S. research scientists and recently appointed U.S. junior faculty (at least 2 years beyond conferral of doctoral degree) for an intensive, mentored research career development experience in an LMIC that leads to an independently funded research career focused on global health.	02-02-2016	03-02-2017 03-02-2018
PAR-16-021	NHLBI TOPMed: Omics Phenotypes of Heart, Lung, and Blood Disorders (X01) https://grants.nih.gov/grants/guide/pa-files/PAR-16-021.html This FOA invites applications to use NIH-funded omics capacity to carry out studies of the genetic basis and/or omics signatures of common, complex heart, lung, and blood disorders. Successful applicants will provide biospecimens for whole genome sequencing or other omics assays.	12-19-2015	01-19-2016 01-19-2017 01-19-2018 01-19-2019
PAR-15-292	Fogarty Emerging Global Leader Award (K43) http://grants.nih.gov/grants/guide/pa-files/PAR-15-292.html The purpose of this award is to provide research support and protected time to a research scientist from an LMIC with a junior faculty position at an LMIC academic or research institution. This intensive, mentored research career development experience is expected to lead to an independently funded research career. This FOA invites applications from LMIC scientists from any health-related discipline that propose career development activities and a research project that is relevant to the health priorities of their country.	11-16-2015	12-16-2015 12-14-2016 12-14-2017
NOT-HL-15-267	Notice of Intent to Publish a Funding Opportunity Announcement for T4 Translation Research Capacity Building Initiative in Low Income Countries (TREIN) (U24) https://grants.nih.gov/grants/guide/notice-files/NOT-HL-15-267.html NHLBI intends to publish a FOA to solicit applications for skills development, needs assessments, and capacity building for T4 translation research (T4TR) in low-income countries as defined by the 2016 Country and Lending Groups categories from the World Bank.	NA	NA

AIDS, acquired immunodeficiency syndrome; FOA, Funding Opportunity Announcement; HIV, human immunodeficiency virus; LMIC, low- or middle-income country; NA, not applicable; NCD, noncommunicable disease; NHLBI, National Heart, Lung, and Blood Institute; NIH, National Institutes of Health.
From NIH Funding Opportunities and Notices. https://grants.nih.gov/grants/guide/.

to enable the development of research and training infrastructure to advance the prevention and control of chronic cardiovascular and lung diseases in LMICs [18]. The Collaborating Centers of Excellence were charged with the mission to help tackle the rising burden of NCDs in LMICs through enabling the development of relevant in-country research and training capacity [18]. Formal evaluation is currently under way through NHLBI funding support. However, the publications in this issue of *Global Heart* provide an early glimpse of what the Collaborating Centers of Excellence have been able to accomplish.

In 2009, the NHLBI orchestrated the NIH's role as a founding member of the Global Alliance for Chronic Diseases (GACD), an alliance that now represents more than 80% of public funding for biomedical research and focusses on coordinated support for NCD research on a

global scale [16,17]. Through the GACD, the NHLBI has provided funding for 4 high-quality research proposals addressing implementation research in hypertension and blood pressure control in Kenya, Peru, Argentina, and Ghana [17]. The NHLBI also participated in the second GACD funding opportunity for type 2 diabetes by supporting a transdisciplinary implementation research approach to address the challenge of reducing cardiovascular disease risk in low-resource settings in Kenya [19]. The NHLBI is currently seeking meritorious applications in response to the GACD third funding call on research proposals to address lung diseases resulting from environmental exposure to household air pollution through clean cooking interventions and, when applicable, interventions to reduce second-hand cigarette smoke exposure [20].

In addition to the foregoing biomedical research programs, the NHLBI has championed a broad spectrum of training and educational programs, especially in LMICs. In partnership with the Fogarty International Center and other institutes and centers at the NIH, the NHLBI has supported the Fogarty Clinical Scholars and Fellows Program and the Medical Education Partnership Initiative (MEPI) [21]. Initiated in 2010, the MEPI is funded by the U.S. President's Emergency Plan for AIDS [acquired immunodeficiency syndrome] Relief (PEPFAR) and the NIH. In this initiative, the NHLBI has supported linked research awards in Uganda and Zimbabwe [21]. By all accounts, investments in programs such as MEPI are transforming and revitalizing medical education in sub-Saharan Africa [22]. In Zimbabwe, for example, medical student and postgraduate enrollment has nearly doubled, from 260 in 2010 to 513 in 2013, and the Ministry of Higher Education has committed additional financial support to sustain this progress [22].

CURRENT STRATEGIES TO SUPPORT GLOBAL HEALTH RESEARCH

To build on our legacy of global health research accomplishments, the NHLBI is guided by a set of enduring principles that apply equally to research funded domestically in the United States as it does to research funded abroad. At the core of these principles is the commitment to support the most promising scientific investigations. Important questions whose answers have the potential to transform clinical and public health practice remain a priority. Similarly, research to identify novel strategies to overcome the critical barriers in global health research also remains a priority. The NHLBI particularly values investigator-initiated research in domains that span fundamental discovery science through early and late translational research and implementation science that empowers patients and enables partners to improve the health of all people locally, regionally, and globally.

The NHLBI supports both fundamental discovery and translational science research through our intramural and extramural programs. Many of these research activities have important implications for advancing global health. Recognizing that a "one size fits all" approach is not likely to be successful in the global arena because of important differences in local in-country research capacity and institutional capabilities, the NHLBI–initiated research opportunities take a tailored approach in the development of funding opportunities. Table 1 shows selected examples of NIH funding opportunities for research, as well as for research training and career development. The Institutes are interested in supporting a broad range of research activities including those that address implementation research in LMICs with special attention to high-burden diseases and risk factors and research that helps advance health equity.

ENVISIONING NATIONAL HEART, LUNG, AND BLOOD INSTITUTE GLOBAL HEALTH RESEARCH PRIORITIES OVER THE NEXT DECADE

In the fall of 2014, the NHLBI engaged its scientific community in an elaborate, open, and inclusive process to shape scientific priorities that will inform and guide the Institute's activities over the coming decade [23]. More than 1,000 persons including researchers, practicing clinicians, patients, advocacy groups, and other participants from 42 countries and the United States comprised the robust response received. The strategic priorities from this exercise will be published in early 2016 and will help identify compelling scientific endeavors that will form the focus of Institute-solicited research. It is anticipated that the strategic priorities from the strategic visioning exercise will also inform research conducted in the United States and abroad to advance global health.

In the interim, the NHLBI will continue to value investigator-initiated fundamental discovery science at the same time as it works to maintain a balanced, cross-disciplinary portfolio of basic, translational, clinical, population science research. Providing funding to support training of a diverse new generation of leaders in global health research will remain a priority. In addition, the NHLBI will support implementation science that empowers patients and enables partners to improve the health of all nations. For example, in our first round of funding as a founding member of the GACD, the NHLBI supported implementation research involving a single risk factor: hypertension. The fruits of that effort are now being realized, as demonstrated in some of the reports published in this issue of *Global Heart*. Other research efforts have provided evidence of "best buys" [3,4] that are now ready for scale-up and spread in collaboration with strategic partners in LMICs.

As we make progress and lay the groundwork for fulfilling the NHLBI mission, we recognize many important questions and challenges in the global health research arena. For example, how do we identify the best strategies for scale-up and spread to have significant population

health impact? What are the primary drivers behind the changing patterns of exposure to NCD risk factors and disease burden in LMICs? What are the context-specific, culturally appropriate implementation science analogues of landmark NHLBI-supported studies conducted in United States, and what is their clinical and public health relevance outside the United States? How may interventions from such studies be appropriately adapted and scaled as effective community-level strategies to reduce cardiovascular disease, diabetes, and obesity-related morbidity and mortality outside the United States? How do we best share lessons learned from our strategic transformation of epidemiology to leverage new data science opportunities and nurture broad research and training partnerships as recommended by our Advisory Council and Board of External Experts [24]? These questions and challenges present unique opportunities as we work collectively with our partners and investigator community to create the NHLBI of 2025.

CONCLUSIONS

The NHLBI is proud of the accomplishments of the investigators whose research results are published in this issue of *Global Heart*. The Institute remains committed to advancing global health research, training, and education as we work collectively with our other public and private partners to tackle the burden of NCDs, especially in LMICs. We recognize that many challenges persist, but there are also many opportunities [25] for U.S. investigators and researchers worldwide. We look forward to playing our part in advancing the globalization of science and the translation of the fruits of scientific discovery to maximize global health impact. We welcome our colleagues worldwide to work with us to chart the path to a world capable of "achieving dramatic gains in global health by 2035" and to "transform our world within our lifetimes."

ACKNOWLEDGMENTS

The author thanks his colleagues Drs. Nakela Cook, Stacey Adams, and K.M. Venkat Narayan for providing helpful background materials; Drs. Helena Mishoe and Emmanuel Peprah for their help with Table 1; and Drs. Michael Engelgau and Helena Mishoe, who provided constructive comments on an earlier version of the document.

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