A Global Health Strategy to Capitalize on Proven-Effective Interventions for Heart, Lung, and Blood Diseases

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Global health research has historically been a high priority endeavor at the National Institutes of Health (NIH) and currently represents 1 of the 5 priorities of the NIH director [1]. Recognizing that science and disease have no national borders, NIH has encouraged its institutes, centers, and offices to work with the Fogarty International Center to support biomedical research and research training across the globe [2,3]. In this effort, many institutes including the National Institute of Allergy and Infectious Disease, National Cancer Institute, National Eye Institute, National Institute of Environmental Health Sciences, and others have established or expanded their global health programs. More recently, the U.S. Council on Foreign Relations produced a report calling for a more robust U.S. engagement in global health, especially for noncommunicable diseases (NCD) [4,5]. In the report, a task force commissioned by Council on Foreign Relations analyzed the case for increased U.S. focus on NCD by examining countries that received significant U.S. health assistance and found that the premature burden of death and disability in many of these countries was heavily NCD-related [5]. The Council on Foreign Relations finds 2 compelling global health interests that justify increasing the U.S. engagement with NCD. First, NCD undermine the effectiveness of existing U.S. global health investments. Second, NCD represent an opportunity for the U.S. government to build on existing U.S. global health platforms that can achieve sustainable reductions in premature death and disability that disproportionately affect the poor.

In support of these calls for prioritizing global health, the National Heart, Lung, and Blood Institute (NHLBI) has championed a broad spectrum of biomedical research, training, and education programs, especially in low- and middle-income countries [6]. These NHLBI investments span the full spectrum from basic fundamental discoveries to population health research in alignment with the 3 goals of the NHLBI Global Health Strategic Plan [6]. The majority of these funded research activities focus on basic, clinical, and population science research that emphasize fundamental discoveries and early stages (T1 to T3) of the translational science roadmap [6]. Some highlights of these global health activities include (Table 1):

- NHLBI/UnitedHealth Group Collaborating Centers of Excellence in low- and middle-income countries with formation of 11 centers of excellence focused on heart and lung research and training [7];
- Global Alliance for Chronic Diseases, 10 of the world's largest public funders partnered to support biomedical

research, which to date has invested a research portfolio for hypertension prevention and control, diabetes, and cardiovascular disease [8];

- Global Alliance for Clean Cookstoves, a public private foundation hosted by the UN Foundation, focused on reducing chronic lung disease among vulnerable women and children exposed routinely to indoor burning of solid biomass fuels [9]; and
- Medical Education Partnership Initiative in sub-Saharan Africa focused on medical education and building research capacity for human immunodeficiency virus/ acquired immunodeficiency syndrome but also included NHLBI-funded linked awards focused on cardiovascular diseases in Uganda and Zimbabwe [10].

These global health efforts have primarily focused on epidemiology and intervention efficacy studies. However, training and experience with T4 research — late-stage translation research — that is, research that will take proven-effective interventions and study their broad implementation across populations — has been minimal or lacking altogether. Yet, these skill sets are urgently needed in order to capitalize on the large pool of proven effective interventions that are available for uptake in the global health arena [12]. Specific skills that will be needed include experience in T4 research methods and metrics, partnership building for testing multilevel, multifaceted interventions, and grant writing.

The recent establishment of the Center for Translation Research and Implementation Science (CTRIS) within NHLBI, provides a unique opportunity to build on NHLBI's biomedical research investments within its global health efforts with a focus on T4 research [13]. Other leading global institutions, such as the World Bank are now calling for more T4 research within global health efforts [14]. CTRIS is charged with providing T4 research leadership for heart, lung, and blood diseases and sleep disorders in the global health arena while it partners with all the NHLBI divisions, centers, and offices to advance the institute's research mission in the earlier T1 to T3 stages of the translational science roadmap. In addition, CTRIS is teaming up with the Fogarty International Center [15] and other key NIH partner institutes and centers to build on past global efforts and develop new collaborations working on T4 research.

Today, a vast array of proven-effective heart, lung, and blood diseases and sleep disorders disease interventions are available. A recent World Economic Forum and World Health Organization collaboration developed a report

TABLE 1. Examples of global health projects, their funding partners, and participating countries by World Bank country income per capita categories*

Project Name	Funding Partners Country/Location	Countries Participating by World Bank Income/Capita Categories Level*	Comments
NHLBI/UnitedHealth Group Collaborating Centers of Excellence [7]	United States — NHLBI and United Health Group	Low income: Bangladesh, Kenya Lower-middle income: Guatemala, India (2 sites) Upper-middle income: Argentina, China, Mexico, Peru, South Africa, Tunisia	2010-2014 11 countries Focused on heart and lung disease research and training. Project completion and evaluation is underway.
Global Alliance for Chronic Diseases [8]	Australia, Canada, China, European Union, India, Mexico, South Africa, Thailand, United Kingdom, United States (NHLBI)	Low income: Kenya, Nigeria, Rwanda, Tanzania, Uganda Lower-middle income: Ghana, India (4 sites), Samoa Upper-middle income: Argentina, China, Fiji, Malaysia, Peru, South Africa (2 sites) High income: Canada (aboriginal population)	2007 - ongoing 15 countries Focused on prevention and control of blood pressure for first proposal call, diabetes on second call, and household air pollution on third call.
Global Alliance for Clean Cookstoves [9]†	Canada, Denmark, Germany, Ireland, Malta, Netherlands, Norway, Spain, Sweden, United Kingdom, United States Supported by grants and investments from governments, corporations, foundations, civil society, investors, and individuals	Low income: Bangladesh, Kenya, Uganda Lower-middle income: Ghana, Guatemala, India, Nigeria Upper-middle income: China	Public-private partnership with U.N. Foundation: goals are to save lives, empower women, and creating global market for clean household cooking solutions 8 focus countries. Phase 1 (2010-2014) — focused on enhancing demand for clean cookstoves and fuels; strengthening the supply of clean cookstoves and fuels; and fostering the enabling environment for a thriving market for clean cooking solutions. Phase 2 (2015-2017) — focused on adoption of clean cookstoves and fuels
Medical Education Partnership Initiate [10]	Office of the U.S. Global AIDS Coordinator, using largely U.S. President's Emergency Plan for AIDS Relief funds; jointly administered by the Fogarty International Center of the National Institutes of Health and the HIV/AIDS Bureau of the U.S. Health Resources and Services Administration along with funds from 8 NIH office/centers/ institutes (including NHLBI)	Low income: Botswana, Ethiopia, Kenya, Malawi, Mozambique, Tanzania, Uganda, Zimbabwe Lower-middle income: Ghana, Nigeria, Zambia Upper-middle income: South Africa	Phase 1: 2010-2015 - focused on medical education and capacity building for HIV/AIDS with linked awards for other disease areas - NHLBI supported 2 linked awards for CVD research (Uganda and Zimbabwe). Phase 2: 2015-2020 - focused on mentored research and will again have linked awards.

AID, acquired immunodeficiency syndrome; CVD, cardiovascular disease; HIV, human immunodeficiency virus; NHLBI, National Heart, Lung, and Blood Institute; NIH, National Institutes of Health; U.N., United Nations.

*See reference [11] and http://data.worldbank.org/about/country-and-lending-groups.

†Global Alliance for Chronic Diseases has 48 partner countries total. The participating countries are focus countries.

TABLE 2. 2015 World Bank country classification to low-, lower-middle, and upper-middle income by gross national income per capita using the atlas method*

Low-Income Countries (US$1,045 or less): 34

Afghanistan	Gambia, The	Nepal
Bangladesh	Guinea	Niger
Benin	Guinea-Bissau	Rwanda
Burkina Faso	Haiti	Sierra Leone
Burundi	Kenya	Somalia
Cambodia	Korea, Democratic Republic	Tajikistan
Central African Republic	Liberia	Tanzania
Chad	Madagascar	Togo
Comoros	Malawi	Uganda
Congo, Democratic Republic	Mali	Zimbabwe
Eritrea	Mozambique	
Ethiopia	Myanmar	

Lower-Middle-Income Countries (US$1,046 to $4,125): 50

Armenia	Kiribati	São Tomé and Principe
Bhutan	Kosovo	Senegal
Bolivia	Kyrgyz Republic	Solomon Islands
Cameroon	Lao People's Democratic Republic	South Sudan
Cabo Verde	Lesotho	Sri Lanka
Congo, Republic	Mauritania	Sudan
Côte d'Ivoire	Micronesia, Federated States	Swaziland
Djibouti	Moldova	Syrian Arab Republic
Egypt, Arab Republic	Mongolia	Timor-Leste
El Salvador	Morocco	Ukraine
Georgia	Nicaragua	Uzbekistan
Ghana	Nigeria	Vanuatu
Guatemala	Pakistan	Vietnam
Guyana	Papua New Guinea	West Bank and Gaza
Honduras	Paraguay	Yemen, Republic
Indonesia	Philippines	Zambia
India	Samoa	

Upper-Middle-Income Countries (US$4,126 to $12,745): 55

Angola	Fiji	Palau
Albania	Gabon	Panama
Algeria	Grenada	Peru
American Samoa	Hungary	Romania
Argentina	Iran, Islamic Republic	Serbia
Azerbaijan	Iraq	Seychelles
Belarus	Jamaica	South Africa
Belize	Jordan	St. Lucia
Bosnia and Herzegovina	Kazakhstan	St. Vincent and the Grenadines
Botswana	Lebanon	Suriname
Brazil	Libya	Thailand
Bulgaria	Macedonia, Former Yugoslav Republic	Tonga
China	Malaysia	Tunisia
Colombia	Maldives	Turkey
Costa Rica	Marshall Islands	Turkmenistan
Cuba	Mauritius	Tuvalu
Dominica	Mexico	Venezuela, Bolivarian Republic
Dominican Republic	Montenegro	
Ecuador	Namibia	

*See reference [16].

addressing current information gaps in our understanding of how to mitigate the social costs of NCD and the resource needs for managing these conditions [12]. Targeted at decision makers, civil society, and the private sector, this report provides assessments of the economic impact of NCD and costs of scaling up a core of proven-effective interventions within low- and middle income counties. These interventions, referred to as "best buys," should be feasible within the current country context. However, successfully delivering best buys within a country's context requires locally developed knowledge bases for effective and sustainable dissemination and implementation that is context specific. The specificity of local knowledge needed to understand how adoption, acceptability, appropriateness, cost, feasibility, fidelity, penetration, and sustainability are critical for implementing intervention strategies in low-resource settings provide a compelling reason to prioritize efforts on T4 translation research. In crafting a strategic way forward and to operationalize NHLBI's Global Health Strategic Plan [6], we held a Global Health Think Tank in September 2014 to obtain input from experts in global health. A panel made up of invited members of the institute's National Advisory Council and its Board of External Experts along with global health experts and key stakeholder partners was tasked with providing expert and ongoing advice on compelling scientific questions for T4 research that could inform and guide NHLBI global health research priorities including:

- Catalyzing T4 translation research in heart, lung, and blood diseases and sleep disorders in low- and lower-middle and upper-middle income countries;
- Developing T4 translation research infrastructure for global health research that leverages previous NHLBI global investments; and
- Training and mentoring for the next generation of global health researchers for rigorous T4 translation.

Globally, a huge variation in country-level resources and capacity is evident. The World Bank, using established methods [16], categorizes counties into strata by their gross national income per capita [11] (Table 2). These strata are then used to tailor World Bank development efforts and loan packages best suited to each country's current context. Moving from low-income (<US$1,045 per capita), to lower middle income (>US$1,045 to US$4,125 per capita), and to upper-middle-income countries (US$4,126 to US$12,745 per capita) finds a huge range from low-income countries with only minimal resources and capacity to well-established health care delivery systems and research infrastructure within some upper-middle-income countries. Overall, many panelists from the Global Health Think Tank supported strategically focused global health research efforts using tailored support strategies that align with the country's infrastructure, capacity, and context. This approach will ensure that goals are feasible and achievable.

Furthermore, paced and tailored strategies across low-income, lower-middle-income, and upper-middle-income countries for engaging country-driven T4 research for local priority health issues are needed. Where capacity is very limited (low- and lower-middle-income countries), larger upfront efforts for planning, organizing, and training will be the need. Whereas in upper-middle-income countries, where capacity for non-T4 research is already established, less-intensive efforts will be needed to support T4 research capacity.

Strategic partnerships are a critical success factor with global health T4 research efforts. Panel membership for the NHLBI Global Health Think Tank included heart, lung, and blood disease global health experts, NIH institute experts with global health portfolios from National Cancer Institute, National Institute for Neurologic Diseases and Stroke, National Institute for Mental Health, and the Fogarty International Center, U.S. federal agency experts from Health and Human Services Office of Global Affairs, U.S. Agency of International Development, the Agency for Healthcare Research and Quality, and the Centers for Disease Control and Prevention, and finally, less traditional partners for NIH—World Health Organization and World Bank experts.

The time is ripe for NHLBI-supported strategic efforts in research for global health. As the Institute of Medicine recently affirmed, reducing the burden of cardiovascular and other chronic diseases worldwide — especially in low- and middle-income countries — is an achievable goal [17]. However, it will require identifying strategies to link up specifically with the Fogarty International Center, other key NIH institutes and centers, along with other key stakeholders working on heart, lung, and blood diseases and sleep disorder research within global health settings. In addition to expanding our global health knowledge base, efforts in T4 research, which NHLBI has made high priority, should lead to increased adoption, adaptation, dissemination, and scaling up of the National Economic Forum's and World Health Organization's best buys — effective, affordable interventions for specific real-world settings guided by country-driven health priorities [17−19]. NHLBI's current global health strategic plan and now the ongoing strategic visioning process are providing a sound direction for this future research agenda [20].

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