PERSPECTIVES FROM NHLBI gWATCH

Noncommunicable Diseases in Low- and Middle-Income Countries



A Strategic Approach to Develop a Global Implementation Research Workforce

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ABSTRACT

Globally, most of the burden from noncommunicable disease is now evident in low- and middle-income countries (LMICs). At the same time, many effective noncommunicable disease interventions are now available and recommended for implementation and scale-up across LMIC health systems—yet are not being widely implemented. Understanding optimal and sustainable implementation strategies for these interventions within the LMIC context will need locally led and conducted implementation research— a research capacity which currently is lacking. The National Institutes of Health institutes, centers, and offices work with the Fogarty International Center to support biomedical research and research training across the globe. The National Heart, Lung, and Blood Institutes' Center for Translation Research and Implementation Science has a strategic focus on implementation research in global health. The Center for Translation Research and Implementation Science is considering strategies for developing research capacity and skill sets to conduct this priority research along with National Institutes of Health institutes and centers and other key global institutions that highly value implementation research. Short-term and medium-term strategies will be needed along with building on current efforts and investments and considering new efforts to address gaps. Developing and sustaining this research workforce will present many challenges and require much effort, but the returns could be transformative in advancing the prevention, treatment, and control of noncommunicable diseases within LMICs.

RESPONDING TO THE NONCOMMUNICABLE DISEASE BURDEN IN LOW- AND MIDDLE-INCOME COUNTRIES

We have strong evidence that health is improving across the globe with declines in morbidity and mortality from noncommunicable diseases (NCDs) in high-income countries (HICs), but this is much less evident in many low- and middle-income countries (LMICs) [1]. Globally, this results in a substantial morbidity and mortality burden in LMICs where over 80% of cardiovascular and diabetes deaths and almost 90% of chronic obstructive pulmonary disease deaths occur [2,3]. These deaths are not limited to elderly populations—each year an estimated 15 million people die from NCDs between the ages of 30 and 69 years with over 80% of these premature deaths in LMICs [3].

Fortunately, many effective NCD interventions are now available and recommended for implementation and scale-up across health systems, but they are not being widely implemented in LMICs. However, to study optimal and sustainable implementation strategies for these interventions in LMICs, local implementation research capacity is needed [4]. Yet, research infrastructure and

outputs in LMICs are often insufficient, and the data from these settings are scarce [5-7]. Many globally focused institutions—including the World Health Organization (WHO) [8], World Bank [9], academia [10], US Agency for International Development [11], National Institutes of Health (NIH) [12-18], and others—appreciate the importance of locally driven in-country implementation research. Understanding and including country context challenges is critical for delivering high quality research. As the research community considers options, here we identify some challenges and opportunities ahead and propose a strategy to foster development of needed capacity and skills for implementation research—research that takes effective interventions and studies their optimal and sustainable implementation—that could be transformational in tackling NCDs within LMICs.

OPPORTUNITIES AND CHALLENGES

Implementation research conducted in LMICs offers unique opportunities to understand key barriers in the adoption, scale-up, and sustainment of evidence-based interventions in LMICs as well as in low-resource settings

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TABLE 1. WHO best buys*			
Modifiable risk factors			
Reduce tobacco use	 Increase excise taxes and prices on tobacco products Implement plain/standardized packaging and/or large graphic health warnings on all tobacco packages Enact and enforce comprehensive bans on tobacco advertising, promotion, and sponsorship Eliminate exposure to secondhand tobacco smoke in all indoor workplaces, public places, public transport Implement effective mass media campaigns that educate the public about the harms of smoking/tobacco use and secondhand smoke 		
Reduce the harmful use	Increase excise taxes on alcoholic beverages		
of alcohol	 Enact and enforce bans or comprehensive restrictions on exposure to alcohol advertising (across multiple types of media) 		
	 Enact and enforce restrictions on the physical availability of retailed alcohol (via reduced hours of sale) 		
Reduce unhealthy diet	 Reduce salt intake through the reformulation of food products to contain less salt and the setting of target levels for the amount of salt in foods and meals Reduce salt intake through the establishment of a supportive environment in public institutions, such as hospitals, schools, workplaces, and nursing homes, to enable lower sodium options to be provided Reduce salt intake through a behavior change communication and mass media campaign Reduce salt intake through the implementation of front-of pack labeling 		
Reduce physical inactivity	 Implement community-wide public education and awareness campaign for physical activity that includes a mass media campaign combined with other community-based educational, motivational, and environmental programs aimed at supporting behavioral change of physical activity levels 		
Disease management			
Manage cardiovascular disease and diabetes	• Drug therapy (including glycemic control for diabetes mellitus and control of hypertension using a total risk † approach) and counseling to individuals who have had a heart attack or stroke and to persons with high risk (\geq 30%) of a fatal and nonfatal cardiovascular event in the next 10 years		
Manage cancer	 Vaccination against human papillomavirus (2 doses) of 9- to 13-year-old girls Prevention of cervical cancer by screening women ages 30 to 49 years, either through: Visual inspection with acetic acid linked with timely treatment of precancerous lesions Pap smear (cervical cytology) every 3 to 5 years linked with timely treatment of precancerous lesions Human papillomavirus test every 5 years linked with timely treatment of precancerous lesions 		

*Modified from Vázquez and Ghebreyesus [21]. Includes all effective interventions with cost-effectiveness analysis < \$1\$100 per disability-adjusted life years averted in low- and middle-income countries.

†Total risk is defined as the probability of an individual experiencing a cardiovascular disease event (for example, myocardial infarction or stroke) over a given period of time, for example, the next 10 years.

in HICs. Research that galvanizes patients, communities, nongovernmental organizations, and academia together with ministries of health and ministries of finance has the potential to find sustainable solutions tailored to local incountry context. An example of our recent National Heart, Lung, and Blood Institute (NHLBI) focus on implementation research in LMICs is our participation in the Global Alliance for Chronic Diseases [19], a global partnership of 14 leading biomedical research funders. For the Global Alliance for Chronic Diseases' next research call starting in 2018, the focus will be on implementation research to scale-up hypertension prevention and control [20].

In 2011, the World Economic Forum and WHO studied the economic toll of NCDs and the cost of scalingup a small core set of proven-effective interventions, so-called best buys (Table 1) [22]. This report was targeted to decision makers, civil society, and the private sectorkey stakeholders for adopting, implementing, and sustaining delivery of these recommended intervention. In 2013, when the World Health Assembly endorsed WHO's Global Action Plan for the Prevention and Control of NCDs

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2013-2020 [4], there was hope that this plan would facilitate achievement of the key NCD Sustainable Development Goal [23]-achieving Good Health and Well-being (Target 3.4)—and ultimately lead to universal health coverage [21]. Part of this plan included updating the best buys assessments, which WHO did in 2017 [24]. In this update, 16 of 88 effective interventions assessed were considered best buys (ie, \le International \$100/ disability-adjusted life years averted in LMICs) and recommended for implementation. Other interventions were of less value and, depending on country context, can also be considered for adoption and uptake. Updated best buys options cover the 4 key risk factors for NCDs (tobacco, harmful use of alcohol, unhealthy diet, and physical inactivity) and the 4 key disease areas (cardiovascular disease, diabetes, cancer, and chronic respiratory disease) [24]. Examples of these updated, WHO developed, best buys include the following: increasing excise and prices on tobacco and alcohol purchases; reducing salt through behavior change communication and mass media campaigns, reformulating food products, and front of package labeling; physical activity campaigns; and drug therapy and counseling for those who have had a heart attack or stroke (Table 1).

However, a major challenge ahead is understanding the best strategies to deliver these best buys and other effective interventions in the country's context. A recent systematic review of the literature on whether these best buys can be delivered with fidelity in LMICs—that is, delivered effectively—found little evidence and the investigators made calls for urgent evaluation of these best buys interventions in the local LMIC context [25]. This study also found that most NCD studies in LMICs were led by a small number investigators, published in relatively low-impact journals, and did not yield findings vital to incountry social and economic development priorities [25]. These findings point to the need for a strategic approach in developing capacity to study implementation within the local context.

THE ROLE OF NIH AND NHLBI

Global health research has historically been a high priority area at the NIH [26]. Prior to 2008, NIH global health research investment was overwhelmingly focused on human immunodeficiency virus/AIDS and other infectious diseases. In 2009, NIH leadership encouraged all institutes, centers, and offices to engage more substantially in global health and to work with the Fogarty International Center to support biomedical research and research training across the globe [26–28] (Table 2). Aligned with NIH's prioritization to tackle global health challenges, NHLBI has supported a broad spectrum of past and current global health research, training, and education in LMICs [29]. For example, during 2009 to 2015, the public-private partnership between the NHLBI and UnitedHealth Group supported the Global Health Centers of Excellence

Program, which resulted in a network of 11 LMICs country-based research centers in Asia, Africa, and Latin America. Key accomplishments of this initiative included capacity building for research and team science, conducting several smaller scale yet priority research studies, and gaining additional research funding from other funding institutions [29]. Continuing these efforts, in 2014, NHLBI created the Center for Translation Research and Implementation Science with a strategic focus on implementation research in global health [13].

In 2016, NHLBI completed a Strategic Vision process that engaged diverse domestic and global stakeholders [30]. Of 8 objectives, 1 has elements focused on global health and 1 is focused on training, including (1) optimizing clinical and implementation research to improve health and reduce disease—both domestically and globally, and (2) developing a diverse and sustainable scientific workforce capable of accomplishing the NHLBI mission. Specific research priorities were identified within the Strategic Vision's Compelling Questions and Critical Challenges [31]. Within the Center for Translation Research and Implementation Science, this led to development of a "6-C" approach to global health that includes (1) prioritizing Critical challenges; (2) focusing on Compelling questions; (3) Customizing initiatives to the country per capita income level; (4) using Context-specific approaches aligned with local capabilities, needs, and environment; (5) targeting Country-driven priority health issues; and finally, (6) focusing on Capacity building and research training. This approach has led to development of an agenda and portfolio of LMIC implementation research programs [32,33] and training efforts [34] with special emphasis on capacity building, skills development, and workforce development. This approach also fosters leveraging platforms and activities from other past and ongoing efforts.

KEY STRATEGIC OPTIONS

Implementation research embraces team science and, equipped with the best-buy types of interventions, can focus on leveraging expertise in disease prevention, treatment, and control and in epidemiology, biostatistics, health services research, economics, and health promotion. In order to foster a pipeline of global researchers with these implementation research skills, global biomedical funding institutions may consider investing in both HIC investigators as well as investigators from LMICs to meet this urgent need for several reasons, including the following: maximizing the pool of potentially qualified researchers from HIC and LMIC sources; fostering global engagement and multidirectional learning across countries; understanding the socioeconomic context in LMICs that local researchers bring—an understanding critical to conducting impactful implementation research; providing leadership to identify priority issues with local scientists who will efficient work execution and effective

TABLE 2. Examples of recent and ongoing global health research training opportunities at NIH

Name	Purpose	NIH Institute(s) and Center(s)	Open Duration	Link
Emerging Global Leader Award	To provide research support and protected time for LMIC early career research scientists who have junior faculty positions within LMIC academic or research institutions (individual awards).	FIC, NCI, NHGRI, NIDCR, NIEHS, NIMH, NINDS, ORWH	November 2016 to December 2018	https://grants.nih.gov/ grants/guide/pa-files/ PAR-17-001.html
Global Infectious Disease Research Training Program	To support applications for the Global Infectious Disease Research Training Program from US and LMIC institutions (institutional awards).	FIC, NIAID	June 2016 to July 2019	https://grants.nih.gov/ grants/guide/pa-files/ PAR-17-057.html
nternational Research Scientist Development Award—Independent Clinical Trial Not Allowed	To support protected time for postdoctoral US research scientists and recently appointed US junior faculty for mentored research career development experiences in LMICs (individual awards).	NCI	February 2018 to March 2020	https://grants.nih.gov/ grants/guide/pa-files/ PAR-18-539.html
nternational Research Scientist Development Award—Independent Clinical Trial Required	To support protected time for postdoctoral US research scientists and recently appointed US junior faculty for mentored research career development experiences in LMICs (individual awards).	FIC, NCI	February 2018 to March 2020	https://grants.nih.gov/ grants/guide/pa-files/ PAR-18-540.html
nternational Bioethics Research Training Program	To support the development of a sustainable critical mass of bioethics scholars in LMIC research institutions (institutional awards).	FIC, NHGRI	April 2018 to May 2018	https://grants.nih.gov/ grants/guide/pa-files/ PAR-18-716.html
Fogarty HIV Research Training Program for Low-and Middle-Income Country Institutions (Clinical Trial Optional)	To support research training programs to strengthen the scientific capacity of institutions in LMICs to conduct HIV research (institutional awards)	FIC, NCI, NIAAA, NIDA, NIMH	July 2018 to August 2018	https://grants.nih.gov/ grants/guide/pa-files/ PAR-18-717.html

FIC, Fogarty International Center; HIV, human immunodeficiency virus; LMIC, low- and middle-income country; NCI, National Cancer Institute; NHGRI, National Human Genome Research Institute; NIAAA, National Institute on Alcohol Abuse and Alcoholism; NIAID, National Institute of Allergy and Infectious Disease; NIDA, National Institute on Drug Abuse; NIDCR, National Institute of Dental and Craniofacial Research; NIEHS, National Institute of Environmental Health Sciences; NIH, National Institutes of Health; NIMH, National Institute of Mental Health; NINDS, National Institute of Neurological Disorders and Stroke; ORWH, Office of Research on Women's Health.

134 GLOBAL HEART, VOL. 13, NO. 2, 2018 communication of results; and finally, within the global health community, recognizing that investing in local research capacity—where the research is to be conducted—is broadly supported.

Capacity building in this context can be accomplished in a variety of ways. One strategic approach is to mount a short-term track (6 to 24 months) that can align with programs that are already established and running and can be adapted to accommodate general implementation research training and a middle-term track (2 to 4 years) that allows for tailored development of training opportunities that currently are not available. An emphasis on regional capacity building, rather than on specific countries, will foster neighboring country peer-to-peer engagement and address the challenge of moving all forwardincluding countries who are further along in developing their research workforce along with countries who are still in more formative stages. This approach is already underway within current NHLBI initiatives that have substantial components for training and capacity development [32,33] and with other funders who have traditionally recognized the importance of implementation research in LMICs [8,9,19,35-38].

Another short-term track to consider is building on other global health training and capacity-building efforts across those that are already in place. At NIH, the Fogarty International Center is an international leader in both global health research and training and has a strong focus on implementation science [12] (Table 2). These efforts could also align with current and future ongoing initiatives at NIH, as noted earlier, that have expanded to include training and capacity-building components [32,33]. Added value to this approach is that LMIC implementation researchers can also align and synergize training efforts within several country contexts [29].

Considering a medium-term training and capacitybuilding strategy, tailored training and capacity-building initiatives for specific priority areas not addressed with the shorter-term efforts, will be needed. Options can include building repositories of training resources to drive in-country training, leveraging country-based research that fosters local ownership and value, and providing a track where trainees can apply for funding and foresee opportunities for implementation research careers. For both short-term and medium-term strategies, there are many opportunities for partnerships with organizations and institutions that support training in implementation research. One example is a Fogarty International Center program where LMIC investigators lead in-country research and the project is twinned at onset with a linked grant to HIC investigators for training in-country researchers [39].

THE GOOD NEWS

Progress has been made in some training areas in global health and here we highlight some successes. As noted

earlier, the NHLBI-UnitedHealth Collaborating Centers of Excellence initiative (2010-2016) addressed NCD research for heart and lung disease in 11 centers around the world, and it included a training program for early stage investigators (from both LMICs and HICs)-something rarely found in global initiatives [40]. This training was tailored for people to conduct and direct research projects, yet also extended to included elements of how to facilitate changes within institutions and promote policy changes within countries to reduce the burden of NCDwhile extending beyond intra- and interinstitutional collaboration to include local, regional, and national agencies such as the Ministry of Health and other key stakeholders. An added value to this approach was development of in-country mentor pools equipped to continue this training pipeline. Finally, some lessons learned from the Centers of Excellence network provide guidance for future initiative such the investment in both capacity building and training for early stage investigators while investing in mentors as well [41].

The Global Alliance for Chronic Diseases Hypertension Program (2011-2017), also noted earlier, created a network of researchers from 19 countries across the globe. Through the annual scientific meetings, the research teams developed into a global research community that resulted in strengthening each research project. Capacity development workshops on implementation science were a key portion of the annual meetings [42]. Finally, in 2010, the Medical Education Partnership Initiative, a partnership among the President's Emergency Plan for AIDS Relief, the US National Institutes of Health, and the US Health Research and Services Administration, supported 13 African medical school and included training to deliver serves for patients with human immunodeficiency virus/AIDS along with a strategy to retain graduates within the environment in which they were trained [43,44]. Three overarching themes include increasing capacity and enhancement in quantity and quality of medical education including faculty training and support, retention of both faculty and graduates with their respective countries, and finally, developing the capacity and conducting regionally relevant research—very grounded toward improving service delivery.

THE WAY FORWARD

LMICs face major challenges in tackling their evolving burdens of disease—for both communicable and NCDs—although some progress has been made [45]. For example, globally, between 1990 and 2016, healthy life expectancy at birth increased for males in 160 countries and for females in 167 countries. For males, the largest increase occurred in Ethiopia, rising from 39.3 years in 1990 to 57.2 years in 2016. A lower burden of disability adjusted life years has also been noted across sub-Saharan Africa (eg, in The Gambia, Senegal, Liberia, Ethiopia, Rwanda) and other regions [45]. All these gains, largely from

communicable diseases and maternal-child health, will be critically important as the development investments made by global institutions shift to include human capital as a measure of the wealth of countries [46].

At the same time, a tremendous opportunity is at hand, given WHO's updated suite of highly effective and economically efficient best buys and other effective interventions for NCDs. However, capitalizing on this opportunity will require locally driven, high-priority implementation research with local capacity and skill sets to carry out this critical research agenda. To be successful, this will require a concerted effort across biomedical funding institutions aligned with key stakeholders (eg, ministries of health, ministries of finance, ministries of education, other government ministries, health care systems, providers, health financiers, and other key implementers) who will be able to use these research findings within their programs and policies. Developing and sustaining this research workforce will present many challenges and require much effort and investment, but the returns could be transformative in advancing the prevention, treatment, and control of NCDs within LMICs.

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