What Defines a Valuable Investment in Global Health Research?

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At a time in history when noncommunicable diseases (NCDs) increasingly account for worldwide deaths, morbidity, and costs, it is imperative both to invest in and to demonstrate the value of investments in global health research. This issue of *Global Heart* does just that for an investment in NCD research and capacity building in low- and middle-income countries (LMICs). In 2008, an ambitious public-private partnership between the National Heart, Lung and Blood Institute and UnitedHealth Group was launched to create a network of research Centers of Excellence (COEs) in LMICs, partnered with institutions in high-income countries. In this issue, we highlight 19 original investigations, reviews, and editorials that represent a fraction of the concrete returns and anticipated yields of this historic investment in global health research. The scope of research results presented in this issue mirrors the multipronged approach needed to decrease the burden of NCDs worldwide and attests to the value of global health investment. From among these articles, several themes emerge.

HYPERTENSION

Worldwide, hypertension accounted for 10.4 million deaths and 208.1 million disability-adjusted life-years (DALYs) lost between 1990 and 2013 [1]. Three articles in this issue tackle hypertension explicitly. The prevalence of hypertension varies widely (age-standardized prevalence, 19% to 55%) in different communities across 7 population-based cross-sectional studies in 9 LMICs [2]. Awareness and treatment vary similarly, and the data reported by Irazola et al. [2] will undoubtedly guide regional interventions. An analysis from the Peru COE identifies that several demographic, social, and environmental factors were the strongest predictors of receiving antihypertensive therapy after 1 year [3]. The Tunisia COE shows that a comprehensive community-based intervention decreased hypertension rates by 30% over 3 years, whereas in a control community, rates remained the same or were slightly higher [4]. These findings demonstrate the great gains potentially made by leveraging locally acquired data and resources.

CARDIOMETABOLIC RISK

Obesity and diabetes are increasingly prevalent worldwide, even in rural areas [5]. In an analysis of 31,118 people from LMICs, Patel et al. [6] report a high prevalence of, and variation in, general obesity (11% to 50%) across countries and an even higher prevalence of central obesity (19% to 79%). Both body mass index and waist circumference were associated with greater cardiovascular risk across populations. Interestingly, although general obesity was highest among South Asians, central obesity was highest among South Americans. In a second paper, Patel et al. [7] compare the prevalence of a phenotype, comprising dysglycemia, low high-density lipoprotein cholesterol, and high triglycerides, and found that whereas 8% to 15% of U.S. men and 1% to 2% of U.S. women from diverse ethnic groups display this phenotype, urban South Asians in India and Pakistan are 5 to 9 times more likely to do so, a finding—suggesting a unique "South Asian phenotype." Shen et al. [8] find the prevalence of diabetes and prediabetes to be alarmingly high in urban and periurban parts of Latin America, South Asia, and South Africa and note that the South Asian populations had higher diabetes prevalence at lower body mass index and younger ages than other LMIC populations. Diabetes awareness and control rates were also disturbingly low. Rosana et al. [9] examine physical activity, an important risk factor for obesity and diabetes, and find that 58% of people in Chile engaged in insufficient physical activity, and 23% were physically inactive. Women, older people, and those with higher education were more likely to be physically inactive in this population.

HEART FAILURE

Heart failure has plagued sub-Saharan Africa for decades or longer [10]. An analysis from the Kenya COE investigated the contribution of atherosclerosis to heart failure and questioned prevailing assumptions about the paucity of atherosclerosis in this region [11]. Noninvasively assessed markers of atherosclerosis were commonly found in middle-aged persons with heart failure and contribute to 25% of all cases identified in this study. More locally obtained data to uncover the current state of the epidemiologic transition in sub-Saharan Africa are needed.

OVERALL CARDIOVASCULAR RISK

Extending a previously validated tool, the network identifies "high cardiovascular risk" in 9 LMIC areas in Africa, Asia, and South America [12]. High cardiovascular risk is uncommon before age 50 years but increases 10-fold thereafter, with significant variation among sites. Another analysis finds that the association between socioeconomic factors and cardiometabolic risk factors varies depending

on the socioeconomic indicator used, a finding implying a benefit to contextualizing risk factors by socioeconomic groups in Latin American settings [13]. Building on past experience, Gaziano et al. [14] show that a non—laboratory-based cardiovascular risk score similarly ranks persons compared with 4 commonly used risk scores throughout the world. Assessing cardiovascular risk in the general populations of resource-limited settings without the inconvenience of measuring cholesterol could prove a cost-effective approach to risk prediction around the globe. Although validation against clinically meaningful endpoints is the logical next step for these studies, the findings support efforts by the World Health Organization to streamline cardiovascular risk assessment in LMICs [15].

TRAINING AND CAPACITY BUILDING
The yields from the network most likely to reap future benefit are the structure and cohesion of the collaborative network itself and the persons who receive mentored research training. Dianis et al. [16] quantify the interconnectedness of the COEs using social network analysis demonstrating a yield in terms of ongoing collaboration beyond the initial funding period. Furthermore, an analysis profiles the methodology used to create and sustain a research training program across the COEs and frames what is needed to sustain this type of program to create future opportunities [17].

Gains in NCD control have been observed in many high-income countries [18]. Yet, many LMICs are juxtaposed between increasing rates of NCDs [19] and insufficient locally actionable information on which to act. Translating these gains to LMICs requires a multipronged strategy that includes an investment in research to understand the unique, as well as and common, attributes (e.g., epidemiology, phenotypes, environment, genetics, social context) that affect global health in disparate settings. In this context, an important strategy will be to recognize, and tap into, the extraordinary resilience and resourcefulness of people who work to improve health in disparate settings; thereby creating a more robust global community that will share the collective future of promoting health by using emerging population health systems [20].

Lessons from the COE network are instructive for the next phase of global health research investment. Effective programs will focus on capacity building and training early-stage investigators while investing in mentors as well. Effective networks will consist of partners from high-income countries and from LMICs with equitable leadership and scientific opportunities. Future networks should also be good stewards of existing global health infrastructure (e.g., GRANDSouth collaborators, Red de Instituciones de Investigación en Enfermedades Crónicas, United States Agency for International Development [USAID], Global human immunodeficiency virus [HIV]/acquired immunodeficiency syndrome [AIDS] networks) and leverage local expertise. An inclusive but innovative

research agenda is warranted to attract a breadth of expertise across the basic, clinical, biomedical, behavioral, prevention, population, health services, operations, and implementation sciences. In deploying future research agendas, paced and tailored approaches will be critical for achieving success. For instance, countries or regions with limited capacity or research infrastructure may require longer lead time as well as larger initial efforts for planning, training, and execution [21].

Although >70% of CVD deaths occur in LMICs [22], <20% of the cardiovascular research emanates from these countries [23], with the lowest proportion coming from sub-Saharan Africa [24]. Reversing this trend is not only possible, but also imperative. With the vital experience of the COE network, we have the tools to do so. At a time when globalization is creating an interconnected world, and when science and its fruits should be borderless, we call on the global health community to demonstrate the will to invest in global NCD research. All countries, both rich and poor, will benefit from it. Above all, we stand at the threshold of making huge progress in controlling NCDs, just as we have managed to affect HIV/AIDS and child mortality through global collaboration and collective investment in research and action.

Postscript. The categorization of country income levels (low, middle) in several of the papers reflects the situation at the start of the Global Health Centers of Excellence Program, and the editors and authors are aware that some countries that were low-income have progressed into the middle-income category.

REFERENCES
1. GBD Risk Factors Collaborators, Forouzanfar MH, Alexander L, et al. Global, regional, and national comparative risk assessment of 79 behavioural, environmental and occupational, and metabolic risks or clusters of risks in 188 countries, 1990—2013: a systematic analysis for the Global Burden of Disease Study 2013. Lancet 2015;386:2287—323.
2. Irazola VE, Gutierrez L, Bloomfield G, et al. Hypertension prevalence, awareness, treatment, and control in selected LMIC communities: results from the NHLBI/UHG network of Centers of Excellence for chronic diseases. Glob Heart 2016;11:47—59.
3. Zavalla-Loayza JA, Benziger CP, Cardenas MK, et al. Characteristics associated with antihypertensive treatment and blood pressure control: a population-based follow-up study in Peru. Glob Heart 2016;11:109—19.
4. Sahil J, Maatoug J, Harrabi I, Fredj SB, Dendana E, Ghannem H. Effectiveness of a community-based intervention program to reduce hypertension prevalence among adults: results of a quasiexperimental study with control group in the region of Sousse, Tunisia. Glob Heart 2016;11:131—7.
5. GBD DALYs and HALE Collaborators, Murray CJ, Barber RM, et al. Global, regional, and national disability-adjusted life years (DALYs) for 306 diseases and injuries and healthy life expectancy (HALE) for 188 countries, 1990—2013: quantifying the epidemiological transition. Lancet 2015;386:2145—91.
6. Patel SA, Ali MK, Alam D, et al. Obesity and its relation with diabetes and hypertension: a cross-sectional study across 4 geographical regions. Glob Heart 2016;11:71—9.
7. Patel SA, Shivashankar R, Ali MK, et al. Is the "South Asian phenotype" unique to South Asians? Comparing cardiometabolic risk

factors in the CARRS and NHANES studies. Glob Heart 2016;11:89–96.

8. Shen J, Kondal D, Rubinstein A, et al. A multiethnic study of prediabetes and diabetes in LMIC. Glob Heart 2016;11:61–70.

9. Poggio R, Serón P, Calandrelli M, et al. Prevalence, patterns, and correlates of physical activity among the adult population in Latin America: cross-sectional results from the CESCAS I study. Glob Heart 2016;11:81–8.

10. Opie LH, Mayosi BM. Cardiovascular disease in sub-Saharan Africa. Circulation 2005;112:3536–40.

11. Bloomfield GS, DeLong AK, Akwanalo CO, et al. Markers of atherosclerosis, clinical characteristics, and treatment patterns in heart failure: a case-control study of middle-aged adult heart failure patients in rural Kenya. Glob Heart 2016;11:97–107.

12. Carrillo-Larco R, Miranda JJ, Li X, et al. Prevalence of pragmatically-defined high CV risk and its correlates in 10 low- and middle-income areas in Africa, Asia, and South America. Glob Heart 2016;11:27–36.

13. Quispe R, Benziger CP, Bazo-Alvarez JC, et al. The relationship between socioeconomic status and CV risk factors: the CRONICAS cohort study of Peruvian adults. Glob Heart 2016;11:121–30.

14. Gaziano TA, Abrahams-Gessel S, Alam S, et al. Comparison of non-blood-based and blood-based total CV risk scores in global populations. Glob Heart 2016;11:37–46.

15. World Health Organization (WHO). Prevention of Cardiovascular Disease: Guidelines for Assessment and Management of Total Cardiovascular Risk. Geneva, Switzerland: WHO; 2007.

16. Dianis NL, Wolbach TL, Spiegelman M. The NHLBI-UnitedHealth Global Health Centers of Excellence Program: assessment of impact of federal funding through a social network analysis. Glob Heart 2016;11:145–8.

17. Bloomfield GS, Xavier D, Belis D, et al. Training and capacity building in LMICs for research in heart and lung diseases: the NHLBI-UnitedHealth Global Health Centers of Excellence Program. Glob Heart 2016;11:17–25.

18. Mirzaei M, Truswell AS, Taylor R, Leeder SR. Coronary heart disease epidemics: not all the same. Heart 2009;95:740–6.

19. GBD 2013 Mortality and Causes of Death Collaborators. Global, regional, and national age-sex specific all-cause and cause-specific mortality for 240 causes of death, 1990—2013: a systematic analysis for the Global Burden of Disease study 2013. Lancet 2015;385:117–71.

20. Gibbons GH, Sampson UK, Cook NL, Mensah GA. NHLBI perspectives on the growth of heart, lung, blood and sleep conditions in Africa: global and domestic insights, challenges and opportunities. Cardiovasc J Afr 2015;26(Suppl 1):S18–20.

21. Engelgau MM, Peprah E, Sampson UK, Mensah GA. A global health strategy to capitalize on proven-effective interventions for heart, lung, and blood diseases. Glob Heart 2015;10:87–91.

22. Roth GA, Huffman MD, Moran AE, et al. Global and regional patterns in cardiovascular mortality from 1990 to 2013. Circulation 2015;132:1667–78.

23. Huffman MD, Baldridge A, Bloomfield GS, et al. Global cardiovascular research output, citations, and collaborations: a time-trend, bibliometric analysis (1999—2008). PLoS One 2013;8:e83440.

24. Bloomfield GS, Baldridge A, Agarwal A, et al. Disparities in cardiovascular research output and citations from 52 African countries: a time-trend, bibliometric analysis (1999—2008). J Am Heart Assoc 2015;4:e001606.