International research collaboration: the key to combating pulmonary vascular diseases in the developing world

Pulm Circ 2015;5(3):413-414. DOI: 10.1086/682961.

Medical and scientific research in the past few years has become increasingly global, cross-national, cross-cultural, and collaborative. This is a reflection of the globalization of modern-day life and the easy communications and movement of health professionals and patients. The sheer volume of international collaborations has increased substantially during the past 20 years.¹ This increase is also seen in the number of papers internationally coauthored by researchers from the developed world (usually referred to in political jargon as the “North”) and those from developing and emerging countries (usually referred to as the “South,” e.g., India and Bangladesh, Mexico and Brazil, China and Pakistan).

Pulmonary vascular diseases (PVDs) are global conditions that are as yet neither understood nor addressed by the traditional public news media or the new “social media.” However, scientific and medical work done in the past 15 years, in particular after the advent of specific new therapies, has created a clearer picture of their distribution and prevalence in the North. Meanwhile, developing nations have various clinical conditions not prevalent in the developed world that may contribute to PVD in the South, but there are no patient-based studies to assess the prevalence of this condition. We believe that infectious diseases are among the contributors to PVDs in the South.

One example is schistosomiasis, which affects 200 million people worldwide. Africa houses 80% of global schistosomiasis patients and has far worse disease control than the rest of the world. It is well documented as a culpable cause of PVD, but at present we do not know the real incidence or prevalence of PVD associated with schistosomiasis. The most recently available data estimated that 4–16 million people globally have schistosomiasis-related PVD.^{2,3} In addition, other comorbidity complicates the picture in Africa, for example HIV, which in itself can contribute to the development of pulmonary hypertension. We do not know how much comorbidity with these two infectious diseases can enhance the clinical picture of PVD.⁴ Many other conditions that cause PVDs are seen mainly in the South, including high altitude, hemoglobinopathies, high prevalence of chronic obstructive pulmonary disease, and delayed management of cardiac conditions such as rheumatic heart diseases and congenital heart diseases.^{2,3}

PVDs in the developed world show a picture very different from that in the developing world. The number of people living in the developing world is about 6 billion, versus 1 billion in the developed world. On the basis of the speculative calculations presented here and accounting for population numbers, it seems that the prev-

alence of PVDs is 6 times per billion of the population higher in the South than in the North.³ Thus, there are more PVDs to investigate in the South; investigating them will not only help local health care but also will help the global understanding of the pathological milieu of PVDs in general.

There are various forms of collaboration in the scientific study of PVDs. The common form is short- or long-term individual collaboration. One example is a schistosomiasis–pulmonary hypertension collaboration within the Pulmonary Vascular Research Institute (PVRI) task force, which has yielded many original publications and review articles. Another form is collaboration and alliance between research organizations that share the same interest, as exemplified by the successful collaboration between many centers in the North and local institutions for the study of high-altitude PVD in Asia and South America.

Organized international collaboration, which is usually initiated by centers of excellence trying to find new research (and may be commercial), offers opportunities in a promising emerging market. We are seeing an increase in this form of collaboration, where centers of excellence in the developed countries are opening research offices to facilitate and enhance continuous collaborations. Many of the current clinical trials in PVDs involve centers from developing countries, with variable success rates with respect to recruitment, accuracy of diagnosis, adherence to protocol, and accuracy of the data.

The large, learned scientific societies are now an accepted platform of international collaborations. There is an increasing trend of establishing an equal partnership with scientists from the North and the South. For example, the need to collaborate in “pulmonary vascular disease” on a global scale prompted the formation of a virtual institute for PVDs, the PVRI (<http://www.pvri.info>), which includes an equal partnership of experts and researchers from the North and the South. Furthermore, the American Thoracic Society, as one example, attracts delegates from all over the world and has become more international than national. Other forms of collaboration are international cross-border activities such as the Global Alliance Against Chronic Respiratory Diseases (<http://www.who.int/respiratory/gard/en/>) and the Global Strategy for Asthma Management and Prevention (<http://www.ginasthma.org>).

The benefits of collaboration are not only in the interests of developed countries,^{5–7} since these efforts have helped scientists to keep abreast of international science and share expertise and resources. For example, the new policies in the United Kingdom,

which are led by primary health care, have resulted from international health policy based on the experiences of many developing countries over the past 30 years.⁷ Collaboration also helps in the building up of research capacity and has direct economic significance. Some governments are already beginning to pay premiums to become hubs in the global excellence network. It remains to be seen whether this development will produce significant changes in the world capacity for research on PVD. However, the majority of these collaborations are still disorganized efforts, and they vary according to the centers and universities from which they originate.

Published papers resulting from international collaboration appear in higher-impact journals and are cited more often than papers that are the outcome of local research.⁸ The majority of collaborations are between the North and the South, with only one-fifth being South-South collaborations (collaborations between developing countries).⁵ At *Pulmonary Circulation*, we specifically encourage submissions from developing countries, in particular papers resulting from collaborations between the North and the South.

Finally, we need to consider potential difficulties of the North-South collaborative. The ethical issues are a very complex area (reviewed by Varmus and Satche⁸ and others^{5,9}). The potential for clinical research to exploit populations has raised much concern. It is advisable that collaborators enter into a partnership, which means that researchers must engage the population in the development of, evaluation of, and benefits arising from the research. This can be partly handled by strengthening the international regulations and guidelines of the declaration of Helsinki, the *International Ethical Guidelines for Biomedical Research Involving Human Subjects*, the guidelines of Good Clinical Practice, and the guidelines of the International Conference of Harmonisation (<http://www.ich.org/>). There are also specific guidelines regarding certain diseases or conditions, such as epidemiological studies, genetics, and biomedical and pharmaceutical trials, but we do not yet have these for PVD trials.

While minimum research capacity may exist in many developing countries, the fact that lead institutions, as well as study countries, are concentrated in a handful of centers attests to great disparities in research capacity. Mechanisms must be introduced to ensure investment in research capacity, particularly infrastructure research capacity, such as research nurses and research associates.¹⁰ Funding is a big issue that must be considered seriously, considering that more than 90% of the world's "potential years of life lost" belong to the developing world, but those countries attract less than 10% of global research funds.¹¹

Careful consideration of the cultural, social, and intellectual properties of the developing countries has played a part in maintaining

successful research partnerships. Patenting of biological materials, such as genetic materials, made in the developing countries is becoming a key issue of contention between multinational corporations and healthcare and other campaigners (usually referred to by the negative term "biopiracy").¹²

In conclusion, research collaboration in PVDs is an enormously powerful tool that provides mutual benefits to all parties. North-South collaborations can be strengthened by promoting further involvement by more advanced countries and agencies. Finally, the developing countries must be empowered to participate in debate and decision making about priority setting for research collaboration. A good starting point for this is for countries in a specific region to begin to collaborate to tackle common regional health problems in their area, for example, the PVRI initiative in Central Asia.

Ghazwan Butrous, Senior Associate Editor

REFERENCES

1. Smeby JC, Trondal J. Globalisation or Europeanisation? international contact among university staff. *Higher Educ* 2005;49(4):449–466.
2. Butrous G, Ghofrani HA, Grimminger F. Pulmonary vascular disease in the developing world. *Circulation* 2008;118(17):1758–1766.
3. Butrous G. The global challenge of pulmonary vascular diseases and its forgotten impact in the developing world. *Adv Pulm Hypertens* 2012;11(3):117–118.
4. Butrous G. Human immunodeficiency virus-associated pulmonary arterial hypertension: considerations for pulmonary vascular diseases in the developing world. *Circulation* 2015;131(15):1361–1370.
5. González Block MA. The state of international collaboration for health systems research: what do publications tell? *Health Res Policy Syst* 2006; 4:7. doi:10.1186/1478-4505-4-7.
6. Mari JJ, Lozano JM, Duley L. Erasing the global divide in health research. *BMJ* 1997;314(7078):390.
7. Johnstone P, McConnan I. Primary health care led NHS learning from developing countries. *BMJ* 1995;311(7010):891–892.
8. Varmus H, Satcher D. Ethical complexities of conducting research in developing countries. *N Engl J Med* 1997;337(14):1003–1005.
9. Tan-Torres Edejer T. North-South research partnerships: the ethics of carrying out research in developing countries. *BMJ* 1999;319(7207): 438–441.
10. Anderson G, Metcalfe A. Calling for international collaborative research in nursing, genetics and genomics: a discussion paper. *Int J Nurs Stud* 2008;45(2):323–328.
11. Bui TD, Markle WH. The global burden of disease. In: Markle W, Fisher MA, Smego RA Jr., eds. *Understanding global health*. McGraw-Hill, Pittsburgh, 2007:19–36.
12. McKee M, Gilmore AB, Schwalbe N. International cooperation and health, Part I: issues and concepts. *J Epidemiol Community Health* 2005; 59(8):628–631.