Princeton Global Network on Infectious Disease Epidemiology

A global collaborative network bridging tropical field epidemiology with advanced epidemiological and policy analysis

Supported by Santander Bank

Principal Investigators

Prof Bryan Grenfell
Princeton University, Princeton, NJ

Prof Guy Thwaites
University of Oxford, Oxford, UK
Oxford University Clinical Research Unit, Vietnam

Dr Ramanan Laxminarayan
Center for Disease Dynamics, Economics, and Policy, Washington DC and New Delhi

Dr Maciej Boni ’99
University of Oxford, Oxford, UK
Oxford University Clinical Research Unit, Vietnam

Executive Summary

Developing countries around the world face common challenges in combatting communicable and non-communicable disease. Over the past several years, Princeton has successfully partnered with leading institutions in Asia, Africa and Latin America to conduct interdisciplinary faculty, postdoctoral and student research on a broad range of infectious disease topics. Recent projects have investigated global health topics through the lens of economics, policy, biology, anthropology and politics.

A key element of many of the successful collaborations has been to the combination of partner institutions’ field expertise with Princeton’s multidisciplinary analytical expertise. Investigations of the dynamics of infectious disease demands a field site in which to conduct hands-on research. Princeton depends on its partners for a clinical research infrastructure in the target settings – typically hubs of infectious disease activity and research. Field partners, in contrast, benefit from Princeton’s broad base of academic and research capacities that add a critical interdisciplinary lens to their clinical research.

Two major partners in Princeton’s recent collaborative research are regional and national hubs in Asia: the Oxford University Clinical Research Unit (OUCRU), based in Vietnam and carrying out a wide slate of clinical research projects throughout various Asian countries; and the Center for Disease Dynamics, Economics and Policy (CDDEP), located in India with headquarters in Washington, DC, which is housed within and works closely with the Public Health Foundation of India (PHFI). Past projects conducted with OUCRU have examined topics such as rural influenza transmission, mapping of Typhoid, and mathematical modeling of the HIV and Hepatitis C epidemics among injecting drug users. Research carried out with
CDDEP has addressed vaccine coverage in urban and rural settings, antibiotic resistance, tuberculosis, and public health policy and communications.

We propose to establish the Princeton Global Network on Infectious Disease Epidemiology, a global collaborative network that converges our partners’ tropical field epidemiology and with Princeton’s advanced epidemiological and policy analysis. The network will engage OUCRU in Vietnam and CDDEP in India in global health research and teaching exchanges. It will leverage, sustain and expand a highly successful and multi-faceted collaboration that has been growing steadily since 2010. It will also act as a bridge and focus on the transfer of expertise between Southeast and South Asia. Over the long term the network will expand to include other partners working on similar topics around the world, with Princeton serving as a hub for interdisciplinary infectious disease research.

We request funding for a three-year period that will cover initial individual-level exchanges and research, seed grants for joint institutional projects, an international conference convening network partners for cross-fertilization of ideas and methodologies, and hosting partners’ graduate students for semester-long visits at Princeton. During this initial period we will pursue long-term funding to sustain and expand the research network well into the future.

**Rationale for network joining field expertise with analytical expertise**

Field epidemiological and clinical studies in tropical disease are the definitive way to improve understanding of the drivers of infectious disease burden in tropical countries and to plan for potential for public health interventions. Both local and international research centers play a critical role in connecting patients and health services in tropical countries with the research community, and in turn this relationship permits the researchers to provide medical and public health services in the communities they operate. These successful relationships have generated years – in some cases decades – of clinical data on tropical disease. Unfortunately, the analytical capacity to interpret large amounts of data was not built in to the original collaborations. For this reason, it is critical to establish and maintain collaborations that build a bridge between centers of academic excellence (analytical expertise) and locally-rooted clinical research institutes (clinical and epidemiological expertise).

Advances in data analysis have moved by leaps and bounds over the past two decades, with computing power increasing 100-fold, genetics moving into genomics, and basic epidemiological principles now being supported by a vast literature of tested epidemiological theory. Of these, epidemiological theory in particular (sometimes referred to as mathematical modeling or epidemiological modeling) has made a significant shift from model development to field testing over the past decade. The main bottleneck in this academic shift has been the availability of and accessibility to high-quality, interpretable, epidemiological data. Our proposed collaboration will link the most advanced analytical methods to the highest quality data sets, with the resulting interpretation producing academic, clinical, and public health benefits to all partners.

Princeton fills a special niche as a research partner by providing multidisciplinary expertise that spans natural science, social science, public policy, operations research, and engineering. Health and disease cannot be studied in a vacuum: effective solutions required an examination of the social, political and
environmental factors that influence the spread and persistence of any given illness or ailment. Joint investigations by Princeton and its field research partners enable a multidisciplinary and comprehensive approach to research that is essential for addressing complex infectious disease challenges.

Princeton can play an important role in furthering field-based infectious disease research by deploying its advanced analytical methodologies and policy expertise – most of which has not yet made it into the front lines of field studies. The majority of the world’s universities focusing on public and global health are insufficiently equipped to deal with the multidisciplinarity and complex nuances of cutting-edge science, making Princeton’s contribution unique and essential.

**Background**

Since the introduction of its interdisciplinary global health program in 2007, Princeton has an excellent track record for collaboration and exchanges with various institutions around the world – including research institutes, policy organizations and health care facilities. Faculty, researchers and students have worked in over 20 countries on topics spanning the natural and social sciences, engineering and the humanities.

Highlights of collaborations to date led by faculty that engaged postdoctoral fellows, graduate students and undergraduates include:

- “Common Property Problems in Health” – This interdisciplinary project led by Simon Levin (EEB) and Ramanan Laxminarayan (Princeton Environmental Institute) examined the challenge of drug resistance within the broader context of common-property problems in infectious disease. Institutional partners included: the Public Health Foundation of India (PHFI); the Center for Disease Dynamics, Economics and Policy (CDDEP), with offices in in India and the U.S.; and the U.S. Centers for Disease Control and Prevention.

- “Health as an Ecosystem Service Around Tanzanian Lakes and National Parks” – Andrew Dobson (EEB) is leading a project that project investigates the dynamics and control of zoonotic and vector-borne disease in East Africa and the ‘ecosystem service’ that biodiversity plays in buffering and reducing disease outbreaks. The primary institutional partner is Tanzania’s National Institute for Medical Research.

- “Demanding the Right to Health in Courts: AIDS Treatment Access, Drug Markets, and Citizenship in Brazil Today” – In this multi-site, interdisciplinary project, Joao Biehl (Anthropology) and his Princeton students collaborated with local Brazilian university students studying social science, law, and medicine to understand the impact of judicial claims for access to high-cost pharmaceutical products in the Brazilian health care system. Partners included Human Rights Watch in the U.S., and Hospital de Clínicas de Porto Alegre and Universidade Federal do Rio Grande do Sul in Brazil.

The global health program’s Health Grand Challenge initiative has been the central body supporting international collaborations over the past six years, and it has developed a set of best practices for working
effectively with partner institutions and networks. We intend to build on our successful exchanges to date and to establish a more formal network that bridges our relationships across regions. The proposal below constitutes the first step in a long-term plan for international global health partnerships.

Oxford University Clinical Research Unit (OUCRU)

The Health Grand Challenge has an ongoing partnership with the Oxford University Clinical Research Unit (OUCRU) in Vietnam. OUCRU aims to have a positive and significant impact on global health and, in particular, the prevention, diagnosis and treatment of infectious diseases. Its key areas of research are: Dengue fever; malaria; tuberculosis; influenza; enterics; HIV and HIV coinfection; central nervous system infections; animal health and zoonoses; pharmacology; and statistics, bioinformatics, modeling, and mapping.

The OUCRU-Princeton collaboration began when Jeremy Farrar, a world leader in infectious disease research and training, was appointed as a Princeton Global Scholar in 2010. At the time Farrar was the Director of OUCRU, and his multi-year appointment to Princeton included recurring and extended visits to the University, cooperation with faculty on teaching and research, and mentorship of students on campus and abroad. In 2013, Farrar was named as the new director of the Wellcome Trust, the world's second largest philanthropy for global health and biomedical research. Although his term as a Princeton Global Scholar has concluded, Princeton will continue its collaborations with OUCRU, with the hope of attracting additional research funding from the Wellcome Trust.

Over 20 projects have been carried out through Princeton-OUCRU collaborations since 2010. The five projects listed below are the longer-collaborations that are still ongoing:

- Modeling the impact of methadone maintenance scale-up on the epidemiology and burden of HIV and HCV among people who inject drugs in Ho Chi Minh City, Vietnam
- The impact of anti-helmintic treatment on the incidence of diarrheal disease in Vietnamese school children
- The role of artemisinin in reducing malaria incidence in southern Vietnam, 1990-2010
- EV71 dynamics in Japan and Vietnam
- Spatiotemporal mapping and modeling of hospitalized diarrhoeal infections in children resident in Ho Chi Minh City, Vietnam

Center for Disease Dynamics, Economics and Policy (CDDEP)

The Health Grand Challenge has been working with the Center for Disease Dynamics, Economics and Policy (CDDEP) since 2009. CDDEP produces independent, multidisciplinary research to advance the health and wellbeing of human populations in the United States and around the world. The organization was founded with the objective of using research to support better decision-making in health policy, and the CDDEP team employs a range of expertise—including economics, epidemiology, disease modeling, risk analysis, and statistics—to produce actionable, policy-
oriented studies on malaria, antibiotic resistance, disease control priorities, environmental health, alcohol and tobacco, and various other diseases.

CDDEP works closely with and is housed within the Public Health Foundation of India (PHFI), a public-private initiative that has collaboratively evolved through consultations with multiple constituencies including Indian and international academia, state and central governments, multi & bi-lateral agencies and civil society groups. It focuses on broad dimensions of public health that encompass health promotion, preventive and therapeutic services, many of which are frequently lost sight of in policy planning as well as in popular understanding.

The central link between institutions is Ramanan Laxminarayan, a Princeton Research Scholar and Lecturer who serves as the Director of CDDEP.

Princeton’s collaboration with CDDEP has yielded over 10 projects since 2009. Two major research projects supported by the Health Grand Challenge, both of which have enlisted faculty and students, are:

- Common Property Problems in Health – PIs: Ramanan Laxminarayan (PEI) and Simon Levin (EEB)
- Informational Structure of Infectious Diseases – PIs: Ramanan Laxminarayan (PEI) and Simon Levin (EEB)

As highlighted above, outputs of Princeton partnerships with OUCRU and CDDEP have included undergraduate internships and theses, as well as collaborative research projects among graduate students, postdoctoral fellows, and faculty members at both institutions. Other activities include expert conferences, special lectures on global health and infectious disease, and exchanges of faculty and researchers. Thanks to these linkages, Princeton students and researchers who have worked with OUCRU and CDDEP have participated in long-term research projects, won prestigious fellowships, and attained significant professional and educational advancement.

The next level of the collaboration will be the internationalization of Princeton’s infectious disease research efforts through OUCRU’s and CDDEP’s respective partner networks in clinical research and health policy, and through Princeton’s international profile as an elite academic institution.

**Network basis, structure and administration**

This global collaborative network will leverage synergies build on the successful track record of Princeton’s prior relationships with both institutions. Bryan Grenfell (EEB/WWS) is a long-time collaborator with OUCRU researchers, and he currently chairs the OUCRU Scientific Advisory Board. OUCRU’s previous director Jeremy Farrar was a Princeton Global Scholar from 2010-2013, and this appointment formed the basis of expanded institutional collaborations throughout Southeast Asia that have engaged postdoctoral fellows, graduate students and undergraduates. Scientific leadership at OUCRU for identifying collaborative strengths of all three institutions and defining research projects will come from the new OUCRU Director Guy Thwaites and Maciej Boni (Princeton Class of ’99, Princeton Postdoc 2007-2008), who has been collaborating with Princeton researchers and hosting Princeton students in his lab at OUCRU.
since 2010. Ramanan Laxminarayan (PEI) is a Princeton Research Scholar and Lecturer who serves as the Director of CDDEP and as PHFI’s Vice President for Research and Policy.

The network will exploit different complementarities within each partnership. Whereas Princeton and OUCRU have a multi-level and highly integrated collaboration centered on clinical research, joint research with CDDEP has been focused more on policy and public health. Bringing the three institutions together will facilitate cross-regional sharing—both in terms of overlapping infectious disease challenges (e.g., similar disease threats facing Southeast and South Asia) and of complementary areas of expertise.

The network will be housed in the Center for Health and Wellbeing and run under the umbrella of Princeton’s Health Grand Challenge, the program on which our proposed structure is modeled. The lead PI will be Health Grand Challenge Director Bryan Grenfell (EEB/WWS), with network administration managed by Kristina Graff, Director of Global Health Programs. The Health Grand Challenge currently supports comprehensive and integrated global health research and teaching initiatives across any array of departments. Partner institution PIs are: Guy Thwaites, Director of OUCRU; Maciej Boni, Head of Mathematical Modeling at OUCRU; and Ramanan Laxminarayan, Research Scholar and Lecturer at Princeton, Director of CDDEP and PHFI’s Vice President for Research and Policy.

Following the successful prototype that has been developed in recent years, Princeton researchers will partner with colleagues at OUCRU in Southeast Asia and CDDEP in India to address significant infectious disease challenges in an interdisciplinary manner. Faculty PIs at all three institutions will oversee the projects with a central role played by postdoctoral fellows, who in turn mentor the graduate and undergraduate students assisting in the research. The projects will feed directly into participating faculty’s current global health courses such as Disease Ecology, Economics, and Policy (ENV/ECO/EEB/WWS); Infection: Biology, Burden, Policy (MOL/WWS); and Global Challenges of Infection, Burden & Control (WWS). They will also provide pathways for senior thesis and dissertation research.

The network builds upon exchanges and joint projects that have included faculty, postdoctoral researchers, and graduate and undergraduate students. It leverages past successful collaborations by expanding its current partnerships and establishing new linkages with and between the participating institutions. Whereas previously Princeton currently has dyadic projects with each of the partner institutions, it will now lay the groundwork for long-term cross-fertilization of ideas and trans-regional cooperation—whereby two regions facing similar challenges can seek to apply each other’s methodologies to common infectious disease challenges.

A key theme of the network will be reciprocal exchanges, in which students, researchers and faculty flow between all of the participating institutions. Princeton has a history of sending its students to partners’ research sites for global health projects, but it has done proportionately less hosting of visitors on this end. With this network we seek to improve the balance between sending and receiving institutions by hosting faculty, postdoctoral fellows and graduate students for extended time periods.

The defining elements of the network are as follows:

- **An international conference convening network partners.** In the first year of the network we will hold a conference that brings participants from both institutions to discuss different approaches to specific infectious disease research topics. The goal will be to foster new and
innovative methodologies across regions, and to lay the groundwork for trans-regional collaborative projects. Following the conference, we will leverage Princeton’s communication technologies such as videoconferencing to maintain inter-visibility among the partners, and network funds will subsidize travel for individual-level collaborative activities.

- **Exchanges of faculty, postdoctoral fellows and graduate students between Princeton and the two network partners: OUCRU and CDDEP.** This aspect of the project provides research benefits for faculty and postdoctoral fellows, and it offers academic benefits for graduate students. Network partners’ postdoctoral fellows and faculty will make short-term visits to Princeton to collaborate on research, guest-lecture in courses, and lead seminars or workshops. Princeton faculty and students will conduct field-based research at partner institutions.

- **Research grants for faculty, postdoctoral fellows, graduate students and undergraduates.** These funds will help to support individual joint interdisciplinary projects between Princeton and each of its network partners. The projects may later be scaled up into externally funded research projects, doctoral dissertations or senior theses. They will also cover undergraduate internships that enlist students in larger research projects.

- **Joint research projects conducted by Princeton and partner institutions.** These will engage faculty, postdoctoral fellows, and graduate and undergrad students. Sample areas of inquiry include: integrating health economics into clinical and field research, social dynamics and disease modeling, logistical and policy challenges to vaccine implementation, understanding the effects of population-level infectious disease policy on changes in specific disease epidemiology and evolution.

- **Visiting student research collaborators at Princeton.** This aspect of the project serves academic purposes, and it improves reciprocity by enhancing educational opportunities for students at partner institutions. We will use the Visiting Student Research Collaborator (VSRC) program to support visiting graduate students for semester-long visits at Princeton. We will host at least two graduate students from network partner institutions per year. The students will sit in on global health courses and participate in Princeton-based research projects.

The three key research areas that we will grow across the three institutions are malaria, typhoid, and health economics.

**Educational benefits**

One of the network’s defining characteristics will be its contributions to formal and informal training of students, researchers and faculty. This will be a multi-directional benefit, with Princeton, OUCRU and CDDEP simultaneously building each other’s capacities in complementary areas of expertise. Below are selected examples of training activities that will be key components of the network. The long-term outcome is that current and future generations of research scientists, public health practitioners and policy leaders will be equipped to analyze and address some of the world’s leading infectious disease threats through an interdisciplinary lens.
Sample training activities:

- Training Princeton undergraduates in methods of interpreting epidemiological field data
- Training OUCRU students in advanced methods of epidemiological analysis, and advanced mathematical model-fitting techniques
- Training CDDEP researchers in new quantitative approaches in health economics and mathematical epidemiology
- Training Princeton PhD students by integrating them into field sites (India, Vietnam) and developing parts of their early careers as field epidemiologists – thereby establishing long-term research collaborations

Contributions to network partners

**OUCRU – Vietnam**

OUCRU is already linked to VN government institutes, to the WHO, and to international global health efforts led by the Gates Foundation, the Wellcome Trust, and the US and UK governments. In fact, OUCRU’s history in helping developing the world’s best antimalarial therapy (1990s) and helping push for worldwide adoption (2000s) through the WHO and the medical/malaria research communities, makes it the perfect partner for an international health collaboration that will be linked in to a broader program of communication and advocacy in global health. OUCRU’s local links with hospitals, clinics, field sites, and other research institutes in Vietnam make it the ideal partner for research that is locally rooted and globally relevant.

The experience of leading health research in the face of public health crises has been tested over the past 15 years in Vietnam with the global malaria disaster of the 1990s, the SARS epidemic of 2002-2003, and the frequent outbreaks of avian influenza (H5N1 and H7N9) that have kept us on the precipice of a possible public health catastrophe. OUCRU’s response to these challenges has been to initiate early studies, build integrated health and research networks, and be on the forefront of clinical research for these types of scenarios. OUCRU has been on the leading edge of internationalizing open-access research protocols, developing treatment guidelines for many of the tropics’ more severe diseases, and public health planning for artemisinin-resistance containment, dengue vaccine distribution, and other global health needs.

The research and laboratory environment at OUCRU Vietnam is well-developed and trains internationally competitive scientists and clinical researchers. However, the analytical capacity for epidemiological modeling, health economics, and bioinformatics at OUCRU is limited to a small group of researchers, who would benefit from regular interactions with an internationally recognized core of academics at Princeton.

**CDDEP – India**

CDDEP’s work dovetails with Princeton’s Health Grand Challenge program due to its emphasis on multidisciplinary research geared towards policy applications, addressing a broad range of global health challenges with a strong emphasis on infectious disease. Participation in the network will benefit CDDEP by providing more formal pathways and resources for collaboration with Princeton at multiple levels (e.g,
faculty, postdoctoral fellow and student exchanges; small research grants). Princeton has a history of linkages with CDDEP. Moreover, Maciei Boni at OUCRU was a post-doctoral researcher at CDDEP and thereby provides further connectivity between the three institutions.

CDDEP has a significant presence in India where it maintains an office. Work on antibiotic resistance at CDDEP India is part of the Global Antibiotic Resistance Partnership. The Global Antibiotic Resistance Partnership (GARP) was started in 2009 to create a platform for developing actionable policy proposals on antibiotic resistance in low-income and middle-income countries. During the first three years, Phase 1 of GARP established national working groups in four countries: India, Kenya, South Africa and Vietnam. Those working groups—multidisciplinary, with representatives from all sectors, dealing with both human and animal antibiotic use—have become national resources for their expertise and linkages to the current global research and policy advocacy activities on antibiotic resistance. Field based research at CDDEP India is focused on dissemination of antibiotic resistance genes in the environment and farm animals.

CDDEP researchers are also building large-scale models of disease transmission and health systems in the Indian context. Recent studies have estimated the long-term effects of the following risk factors in developing countries: malnutrition, infection and maternal depression. Under this work, researchers are synthesizing the evidence on the effects of childhood risks across the developing world. CDDEP has a strong research environment that relies on a combination of field-based research and access to large scale datasets on health systems, antibiotic use and resistance. CDDEP is located within a larger institution, the Public Health Foundation of India, which works on a range of public health research with significant laboratory and field research capacity.

Princeton University – U.S.

Thanks to sustained relationships and complementary strengths, Princeton faculty, researchers and students gain expanded opportunity to examine cutting-edge topics – applying critical skills and approaches in a field research setting. These collaborations achieve several Princeton research and educational aims among multiple levels of constituents, ranging from students to faculty.

Key benefits that will be achieved via the network include: field-based projects for graduate and undergraduate students, links with the University of Oxford’s Tropical Disease Network and Nuffield Department of Clinical Medicine, laboratory and field access at OUCRU (including BSL3 facilities, high-throughput serology and other facilities not available in Princeton laboratories), valuable linkages for faculty working on related projects that require a field site with clinical and/or public health research capacity.

Most important, a sound, locally-based infrastructure is essential for Princeton’s infectious disease research projects in the developing world. These partnerships enable Princeton faculty, researchers and students to concentrate their energies on the content of their projects because their logistical and practical needs are handled through the field sites’ administrative offices.
International Impact

Beyond the individual benefits that the network will confer to its institutional members, there are broader global gains it will achieve. Princeton University has made internationalization a strategic priority, and the Health Grand Challenge has carved out a niche in an interdisciplinary approach to global health that prioritizes hands-on learning. While many universities have global health programs, these are heavily concentrated in medical schools with a focus on clinical interventions and on training U.S. physicians. By contrast, this network takes a broader view of the drivers of infectious disease and global health, and it trains students who will work in a cross-section of fields that connect to health – including but not limited to medicine. Finally, Princeton is unique in its desire to bring partner institutions’ students and researchers to the U.S. so that they can benefit from its education, research community and resources.

This network connects Princeton to partners whose activities are international in scope. OUCRU is a world leader in infectious disease research with projects throughout South and Southeast Asia. CDDEP is headquartered in the U.S. with a hub in India, and its projects extend to other nations in the global South. The network will serve to strengthen the University’s international connections and profile in the infectious disease and global health arena.

Conclusion

The network created by this grant will be unique in bringing together Princeton’s tradition of excellence and scholarship, Princeton’s role among the world’s best universities in leading scientific innovation, CDDEP’s experience in translational health sciences work and applied health policy, and OUCRU’s expertise in clinical research, patient-centered science, and large-scale field epidemiology. This collaboration will push information from patient, to field, to analytics, to policy – covering the essential links that translate health data to health policy.