Report Date: May 10, 2016

Report of Consultation on Division of International Epidemiology and Population Studies (DIEPS), Fogarty International Center (FIC), NIH

Lawton Chiles International "Stone" House

April 4, 2016 – 1:00-5:00 pm

Table of contents

Executive summary

Expert consultants articulated strong support for DIEPS past and current research activities, accomplishments and unique position within Fogarty. Useful suggestions were made for maintaining strengths and criteria when choosing new research areas, while stressing the importance of aligning DIEPS activities with the Fogarty mission. DIEPS staff provided five potential future modeling and analysis research directions: 1) interactions between and among disease, 2) antimicrobial resistance, 3) implementation science, 4) economics and social science, and 5) the microbiome. The consultants agreed that DIEPS is well positioned to develop research foci in both disease interactions and antimicrobial resistance, they suggested merging the implementation science and economics/social science areas would give them another growth opportunity, and build on their expertise, and finally that the microbiome research area is important but may not yet be the best area for investment without further scoping. It was also suggested that vaccines—the potential of new ones and the effectiveness of current ones—would be a good starting point to build on existing expertise and explore new avenues. Consultants identified success of DIEPS staff members thus far as an important predictor of contributions they could make in the future.

External consultants

- Dr. Bob Bollinger, Director of the Center for Clinical Global Health Education and Professor of Infectious Diseases, Johns Hopkins University School of Medicine
- Dr. Maria Freire, President and Executive Director of the Foundation for the National Institutes (FNIH) of Health (past FIC board member)
- Dr. Bryan Grenfell, Professor of Ecology and Evolutionary Biology and Public Affairs, Woodrow Wilson School, Princeton University (DIEPS RAPIDD collaborator)
- Dr. Lee Hall, Chief, Parasitology and International Programs Branch, DMID, NIAID
- Dr. Art Reingold, Professor and Head of Epidemiology, School of Public Health, University of California, Berkeley (past Board member and previous DIEPS reviewer)

Welcome and meeting overview

Dr. Roger Glass opened the meeting by thanking the consultants for taking their time to participate in this consultation on Fogarty's Division of International Epidemiology and Population Studies (DIEPS). He

noted that this was a particularly opportune time for this consultation, in that FIC had received its first substantial budget increase in years. He also thanked Dr. Peter Kilmarx for leading the initiative and the staff for all of their support. Dr. Kilmarx echoed Dr. Glass' appreciation and reiterated the timing and purpose of the consultation noting that many current DIEPS activities are concluding in the next 12-24 months and that, with a change in DIEPS leadership, it is a good time to take stock of the division's recent accomplishments, current capabilities and capacity, and potential future contributions to the mission and goals of Fogarty and NIH.

The following objectives were reviewed:

1. Assess how current strengths of DIEPS can be harnessed to have the greatest scientific impact and contribution to FIC mission and goals.
2. Identify the most promising scientific areas of focus for DIEPS that will make the most significant contribution to global health and the FIC mission and goals.
3. Recommend approaches for future strategic partnerships within and outside of NIH and for assuring sustainability of Division activities.

Background material on DIEPS programs and activities were provided ahead of the consultation (see appendix II).

An overview of current programs, staffing and core budget was presented by DIEPS staff. DIEPS has succeeded in performing many of the valuable roles that intramural research programs fulfill within other NIH ICs. One of the major components of various programs in DIEPS is the application of modeling to develop innovative, integrative approaches in population health research, practice, and policy. DIEPS international and multidisciplinary networks foster research and training in computational biology, links between academia, NGOs, USG, bilateral and multilateral agencies, and promote informed use of models and modeling tools to guide public health practice and policy as well as decision-making during public health crises.

DIEPS personnel have a strong track record for generating high-impact results through publications, training, and capacity building. The reputation of NIH, FIC, and the division provides strong incentives for joining the team--which has facilitated the recruitment of high-quality talent to DIEPS. Resources to build concomitant capacity in new fields of study will likely generate similar results, but will require additional resources to generate similar trajectories of past and current success.

Five potential future modeling-and-analysis-related research directions were put forward by DIEPS staff: 1) disease interactions, 2) antimicrobial resistance, 3) implementation science, 4) economics and social science, and 5) the microbiome. The aim is to have disproportionate, catalytic effects on these areas, as has been done in others, and to engage substantial networks, that would then continue to grow globally and collaboratively.

Discussion by consultants:
The MISMS and RAPIDD programs were praised for having incredibly catalytic effects and convening authority in the field of modeling, building broader global networks and disseminating information. It was noted that by being a neutral partner and honest broker in the MAL-ED program, for instance, DIEPS was in a unique position to bring those partners together and bring the data together to tackle the research questions. This was similarly clear for the Household Air Pollution (HAP) program. Another unique aspect of the MAL-ED program is the positive synergy established by the partnership with FNIH.

Guidance and recommendations from consultants:
Following a dynamic discussion, a closed session with the consultants was facilitated by representatives of the FIC Division of International Scientific Policy and Program Evaluation during which several important recommendations were made. Broadly, the importance of better alignment of DIEPS activities with the Fogarty mission was stressed. Elaborating DIEPS' contributions to the capacity building mission of Fogarty was suggested and exploring concrete ways in which DIEPS could collaborate with DITR and provide training for grantees was suggested.

DIEPS modeling capabilities may also be able to contribute valuable insights into trends in disease burden and risk factors contributing to health outcomes in both communicable and non-communicable disease.

Prioritizing future scientific research directions:

- New directions should be evolutionary rather than entirely new, and should be provided with some additional resources to efficiently explore these potential areas, develop specific expertise and demonstrate proof of concept. DIEPS should not lose its infectious diseases focus, but rather build on it.
- Future scientific areas should depend on who takes over the leadership role of the division. It is important for that individual to have a strong/solid scientific foundation, and the resources and flexibility to chart a new course.
- Broad criteria for choosing any new area of research were suggested and include: 1) good/strong science; 2) defining the unmet need; 3) articulating the value added by DIEPS; and 4) articulating DIEPS' comparative advantage in the area of research.

Of the several possible new areas of research focus (1) disease interactions, 2) antimicrobial resistance, 3) implementation science, 4) economics and social science, and 5) the microbiome the consultants had the following feedback:

- DIEPS is well positioned to develop research foci in both disease interactions and antimicrobial resistance; another initial focus could be vaccines.

- Merging the implementation science and economics/social science areas would give them another growth opportunity, and build on their expertise, particularly through the use of

modeling to identify key gaps in knowledge and data to improve the outcomes of implementation science research and analyses.

- The microbiome research area is extremely important, and should be carefully watched for opportunities, but may not yet be the best area for investment without further scoping.
- Vaccines—the potential of new ones and the effectiveness of current ones—may be an ideal thread linking several of these new inter-related research areas, and would be a good starting point to build on existing expertise and explore new avenues.

One final recommendation related to finding external support for their work. It was recommended that in building their portfolio (either leveraging the current science DIEPS engages in or building a new area with an internal champion), they should develop a strong base of science prior to shopping an idea to potential partners. It was noted that FNIH can help with this.

While there was discussion about how DIEPS differed from an academic unit and whether some of the activities would be more well suited to NIAID, overall, there was strong support for DIEPS continuing their important work at Fogarty. Consultants repeatedly identified their success thus far as an important predictor of contributions they could make in the future.

Dr. Glass closed the four-hour meeting by thanking the consultants for their valuable time and guidance on the future directions of DIEPS.

Appendix I: DIEPS Consultation Questions, Agenda and Link to 2009 Review

Questions

1. Where has DIEPS had its greatest impact?
2. Building on their successes, how can DIEPS most effectively position itself to contribute to the mission of FIC in the coming 5/10 years? Conversely, how can FIC ensure that it is leveraging DIEPS scientific expertise and scientific depth to achieve its goals?
3. Thinking broadly, what recent global health landscape developments can help to inform how they further develop their scientific portfolio?
    a. Are there critical scientific gaps relevant to DIEPS expertise that are not being addressed by others?
    b. Are there areas where EPS might be able to leverage an upswing in funding and research to collaborate with others?
4. With regard to the five proposed areas of strategic opportunity:
    a. Which best contributes/supports the mission of FIC and why?
    b. Which has the most potential for cultivating fruitful collaborations (trans-FIC, trans-NIH collaboration or outside NIH)?
5. What is an ideal breadth of focus/expertise for the DIEPS portfolio? If they were to expand their expertise, should they focus on cultivating expertise in one or more than one additional scientific area?

OPEN SESSION:

13:00-13:10 – Welcome, overview – Dr. Roger Glass, FIC Director and Associate Director for International Research, NIH

13:10-13:30 – Objectives, agenda, recap of 2009 review – Dr. Peter Kilmarx, FIC Deputy Director and DIEPS Acting Director

13:30-14:00 – Review of current activities, outputs and impacts

Overview – Ms. Stacey Knobler, Senior Scientific Program Director (15 minutes)

RAPIDD – Dr. Ellis McKenzie, Senior Scientist, DIEPS (5 minutes)

MISMS – Dr. Cecile Viboud, Staff Scientist, DIEPS (5 minutes)

14:00-14:30 - Considerations for future directions – Dr. Ellis McKenzie, Dr. Cecile Viboud

CLOSED SESSION (including break):

14:30-16:00 – Discussion of consultation questions – external consultants, facilitated by Division of International Science Policy and Program Evaluation and Director, Center for Global Health Studies, FIC

OPEN SESSION:

16:00-16:30 – report out from consultants – *rapporteur TBD*

16:30-16:50 – discussion – moderator Dr. Peter Kilmarx

16:50-17:00 – wrap up/next steps – Dr. Roger Glass

Link to previous DIEPS review – 2009:
http://www.fic.nih.gov/About/Staff/Policy-Planning-Evaluation/Documents/DIEPSReview2009.pdf

Appendix II

Background material for April 4, 2016, consultation: Prospectus for the further development of Division of International Epidemiology and Population Studies (DIEPS), Fogarty International Center (FIC), NIH

March 25, 2016

Executive Summary

DIEPS has established a world-class reputation in infectious disease modeling, with significant impacts on public health policy at national and global scales. Its activities are consistent with and contribute significantly to FIC's strategic goals, and bring to FIC many of the unique advantages conferred by the formal intramural programs present at all but two of the 26 other ICs. Since 2006, DIEPS has brought in roughly $100M in outside funding, but in two years almost all of the associated programs will have concluded. There are at least five new areas of strategic opportunity across FIC – disease interactions, antimicrobial resistance, the microbiome, implementation science, and social science – which DIEPS is well positioned to exploit, in collaboration with other FIC divisions, given relatively small seed investments of increased core funding to pilot these new initiatives and establish the *bona fides* needed to seek additional outside funding partners. This additional investment from within FIC would provide "proof of concept" research and an important signal to other funders, inside and outside NIH, that the work is valued internally—and consequently worth additional, leveraged support from them. While it is recognized that it is not feasible for FIC to explore all five new research areas in parallel, priorities should be identified.

Background

FIC could support a stable, intramural equivalent that is integral to FIC's mission and oriented toward our strategic plan goals. If adequately supported, DIEPS is uniquely positioned to:

1. Carry out high-risk/high reward research that's unlikely to be funded through normal study section peer review;

2. Support orphaned areas or unique niches that are important to FIC's mission, or that require the convening power of the USG to assist in priority-setting for research and policy;

3. Keep FIC staff close to hands-on science so we have up-to-date expertise in house to inform the work of the Center;

4. Be able to respond quickly and effectively to a changing landscape or crisis, (e.g., the Ebola outbreak);

5. Train rising stars in global health, through postdoctoral fellowships and in workshops, contributing to the larger scientific and policy communities;

6. Have a greater impact on policy, as FIC in-house researchers are government employees with privileged ties to HHS and other areas of the USG, rather than academics who are primarily driven by publication recognition and not given regular access to the decision- and policy-making space of the USG and other donor organizations.

The DIEPS value proposition

The decade-long work of MISMS, RAPIDD, and other programs (see Table 1) has established DIEPS as a globally recognized center of excellence in statistical and mathematical modeling research and training.

Table 1. Current and Recent DIEPS programs. See also Figure 2 for a map of DIEPS international network of collaborators and affiliates.

RAPIDD (2008-2015):

This program aimed at improving the state of the art of mathematical modeling of infectious diseases of humans and animals. Supported by $17.3M from DHS, it focused both on developing fundamental cross-disciplinary understanding of key pathogens, and exploring control measures relevant to policy makers preparing for or responding to outbreaks. Through an extensive series of workshops, working groups and postdoctoral fellowships RAPIDD surveyed the existing state of the art of infectious disease modeling to identify key conceptual and methodological gaps. Based on these analyses, working groups focused on:

- Mathematically neglected host-pathogen interactions, notably vector-transmitted infections, emerging zoonoses and reservoir dynamics in bats and other small mammals;
- Methodological gaps, notably in spatial dynamics of pathogens and epidemic model fitting and prediction;
- Evolutionary dynamics, notably viral phylodynamics and antimicrobial resistance;
- Impact of pathogen coinfection and other immunological and environmental complexities;
- Optimizing deployment of current and putative vaccines and other control strategies against human and animal pathogens and their invertebrate vectors

RAPIDD made major progress in these and a number of other areas. It supported 85 core faculty and junior researchers, and, in particular, 13 postdoctoral fellows at the interface of

disease dynamics and policy, most of whom are now in tenure-track faculty jobs in the US.

RAPIDD organized 114 workshops, across a wide range of topics, carefully focused and planned with explicit deliverables. Successful workshops often formed a series to develop new areas. 834 additional scientists from 39 countries participated in the workshops, as did 106 US government employees. RAPIDD produced 906 peer-reviewed scientific publications that have been cited 22,243 times (as of February 25, 2016). Its workshops and publications have influenced policy for a range of governmental and other organizations.

MISMS (2001-ongoing):

MISMS is an international collaborative effort to elucidate the epidemiology and evolutionary dynamics of influenza in humans and other natural hosts, with a particular focus on mathematical and statistical modeling. Key research areas include pandemic preparedness, control strategies, transmission dynamics, and multinational disease burden studies. Until 2013 the project was supported by HHS/OGA/International Influenza Unit (now Office of Pandemic and Emergent Threats) through annual grants to fund training workshops and core research (ranging from ~$125K in 2007 to ~$800K in 2013). The program is now supported by core EPS funds. During 2007-2015, 16 MISMS workshops conducted in the Americas, Europe, Africa, Asia and Pacific regions have helped train 400+ scientists and public health experts and led to ~180 collaborative publications in high-profile journals.

Policy impacts of MISMS include: shifting the age priority groups for pandemic vaccination in the US, promoting new vaccination strategies for seasonal outbreaks to optimize direct and indirect protection for vulnerable populations, guiding the timing and composition of seasonal vaccines in tropical settings, and optimizing global surveillance for zoonotic influenza viruses with pandemic potential.

Notable scientific achievements include assessment of the burden of influenza viruses and their impact on other diseases in over 25 tropical and temperate countries on 6 continents, and estimation of the transmission potential of established and zoonotic viruses. Phylogenetic studies conducted within the MISMS network have elucidated the evolutionary dynamics of swine influenza viruses at the animal-human interface and demonstrated the importance of live swine trade in driving viral migration domestically and internationally. Further, MISMS was instrumental in evaluating the transmission dynamics of influenza viruses across time and space, especially in understudied regions such as South-East Asia and Africa. Findings demonstrate the occasional persistence of viruses in less connected populations and support a sink-source model of viral evolution focused on tropical regions. Finally, MISMS scientists uncovered uniquely detailed archival datasets informing the epidemiology of historical influenza pandemics in the Americas, Asia and Europe and

underscored the importance of virus re-cycling and prior immunity in older populations. Taken together, these findings have helped establish priorities for surveillance and control in resource-constrained settings.

MAL-ED (2008-2018):

The MAL-ED Network represents an international collaboration of investigators led by FIC and the Foundation for the National Institutes of Health (FNIH). The goal of the Network is to investigate the interactions among exposure, infection, and disease associated with enteric pathogens; diet and nutritional status; and socio economic status (SES) in relation to impacts on gut physiology; immune function and vaccine response; physical growth; and cognitive development. A prospective field, clinical, and laboratory based observational study of cohorts of neonates followed to 24 months has been established at 8 geographically diverse sites, in Bangladesh, Brazil, India, Nepal, Pakistan, Peru, South Africa, and Tanzania. The project is supported by an initial $40 million grant from the Bill & Melinda Gates Foundation, with additional supplemental funding of $5 million in 2014 and $3 million in 2015. Central questions addressed by this work include: 1) Whether specific enteric pathogens or combinations of pathogens have stronger associations with malnutrition than others; 2) Whether there is a particularly vulnerable period in infancy/early childhood during which specific enteric infections cause greater morbidity; and, 3) Whether results from one locale can be extrapolated to other populations based on common environmental and biological determinants. Epidemiologic, anthropologic, physiologic, and genomic data are being compiled at each site and in the central database for comprehensive analyses by members of the Network and, eventually, by other members of the scientific community. The findings of such analyses will be applied toward improving long-term public health at the participating sites and considered for their ability to be translated appropriately for other populations in resource-poor settings. By obtaining thorough characterization of the populations under study, and by improving the local infrastructure and capacity, these sites will be ready to test the efficacy of various intervention strategies through hypothesis-based as well as efficacy trials that are highly relevant to their respective population, disease, and social, political, and economic characteristics.

Pakistan (two programs, 2011-2016 and 2015-2018):

FIC/EPS is the U.S. base for two programs funded by the US-Pakistan Bioengagement and Science & Technology Projects (BEP) of the U.S. State Department.

1) Water, Sanitation, Health and Hygiene Interventions (WSHHI) in a Northern Pakistani Village: a 15-year follow-up of diarrheal disease, pneumonia, childhood growth, water quality and latrine microbiology ($465,000). This study of a population in the Gilgit-Baltistan region

of Pakistan is a collaborative effort between FIC/DIEPS, KIU, the Aga Khan University (AKU), Karachi, and the University of the Punjab, Lahore.

2) Expanding the Scope of Biosecurity and Biosafety in Pakistan: strengthening biorisk management training and capacity ($2,100,000). This series of projects focuses on the further development of Pakistan's biosecurity/ biosafety training and biorisk management capacity related to safe laboratory methods in pathogen identification, containment, and protection in both human and veterinary sciences. Activities promote responsible conduct in the life sciences and improve management of pathogens in the laboratory and community context while promoting partnerships and sustainable networks among scientists and institutions across the country. Activities are carried out in collaboration with experts from the Pakistan Biological Safety Association (PBSA), the International Council for Life Sciences (ICLS), and academic and health research institutions within Pakistan.

Household Air Pollution (2015-2020):

We have recently established a Clean Cooking Implementation Science Network (in collaboration with FIC's Center for Global Health Studies) that integrates funded projects supported by five ICs, the CDC, USAID, and the Global Alliance for Clean Cookstoves.

Current Burden of Disease estimates that over 4 million early deaths per year due to infectious and chronic conditions are due to Household Air Pollution. Our aim is to develop a comprehensive knowledge base to improve the provision, uptake, appropriate and sustained use of evidence-based clean cooking interventions to maximize public health and quality of life benefits in LMICs. Over the next five years we will synthesize and adapt analytical tools for planning and evaluating household energy interventions, develop case studies, support strategically designed and chosen studies to answer key questions, and disseminate our findings and other products as widely as possible to enhance the knowledge base and toolkit available for scaling up of clean cooking systems around the world. Because adoption and use challenges are so central to understanding how clean cooking can provide positive health effects, the Clean Cooking ISN brings together leading HAP researchers in epidemiology and exposure science along with experts in anthropology, economics, rural energy and implementation science, and policy makers and implementers in the HAP arena. Our initial funding base is a $5M award from the NIH Common Fund, and leverages a $30M Health Outcomes trial currently in competition, as well as over a dozen other projects supported by the NIH and our partners, including FIC's extramural GEOHealth program.

SMART Vaccines (2014-2017)

In collaboration with the National Vaccine Program Office (NVPO) of the US Department of

Health and Human Services, supported by $800,000 in NVPO funding, FIC/EPS collaborates on projects in support of both agencies' missions related to developing and implementing strategies for increasing the prevention of human diseases through immunization.

The prototype decision-support tool, SMART Vaccines, was delivered to NVPO and FIC/EPS by the Institute of Medicine (IOM) in early 2015. In support of the National Vaccine Action Plan, NVPO and FIC had charged the IOM with developing a tool that reflected the dynamic and complex nature of decision-making among multiple stakeholders within the vaccine decision-making space—comprising the different interests, roles, and priorities of individuals engaged in vaccine research, research funding, purchasing, immunization programs, and policy.

Specific project objectives include: 1) Evaluation and enhancing the usability of a vaccine prioritization software tool (the SMART Vaccines prototype developed by IOM) in decision making settings; 2) gather user feedback toward refining the model and enhancing the software, develop a framework for a data warehouse to support the prioritization software including the phase I and phase II vaccine candidates of domestic and global importance; 3) determine a sustainable, open-access hosting mechanism for a refined model, enhanced software, and a data warehouse 4) create a catalog of new vaccines and disease burden data sets for the open access tool.

The opportunity now exists to leverage DIEPS capabilities and proven track record, and build from the core expertise toward new opportunities that are responsive to emergent issues in global health research and well-matched to the strategic priorities of FIC and NIH. Of particular interest is the opportunity to explore how the work of DIEPS can enrich and complement the work of other FIC divisions. Contributions of DIEPS to trans-FIC programs and objectives are proposed below with a special emphasis on areas of major, growing importance in global health research that are drastically under-served by modeling and analytic approaches, and therefore ripe for new DIEPS initiatives.

Areas of strategic opportunity across FIC

- **Disease interactions:** addressing two critical areas of these relationships, the first would address the dynamic association between chronic and infectious diseases (e.g. TB-diabetes, HIV-cardiovascular diseases, early life insults and long-term health and development); another would dissect key pathogen-pathogen interactions (e.g. TB-flu, HIV-Hep C) and their effects on clinical outcomes, transmission and control policy. This would build naturally on on-going research and methodologies developed within the MISMS and RAPIDD programs.

- **Antimicrobial resistance:** high-level studies have begun to motivate top-level policy and funding, but have not yet been complemented by specific analyses that might guide changes in incentive structures and help optimize treatments. On the upstream side, strategies such as drug rotations and combinations have barely been addressed; little quantitative information exists on antibiotic stewardship, while the relative contribution of local emergence vs regional spread remains unclear. While antibiotic resistance was among the focus areas of the RAPIDD program, clearly more quantitative research is needed to address this huge global health issue. Critical research is needed at the interface of epidemiology, phylogenetic analyses, evolutionary biology and mathematical modeling, which are areas of particular strength for DIEPS.

- **The microbiome:** this is a rapidly growing area of research with vast implications across the human health spectrum. Quantitative studies in the context of global health research are very limited. A strategic investment by FIC DIEPS would likely focus on the microbiome's role as a potential mediator of non-communicable diseases, and/or potential mediator of disease interactions and antibiotic resistance. Importantly, this work could frame future investments by other parts of FIC toward expanding this research globally. Efforts to apply multi-pathogen and multi-host ecological models to study the dynamic webs of commensal populations characteristic of the microbiome are just beginning.

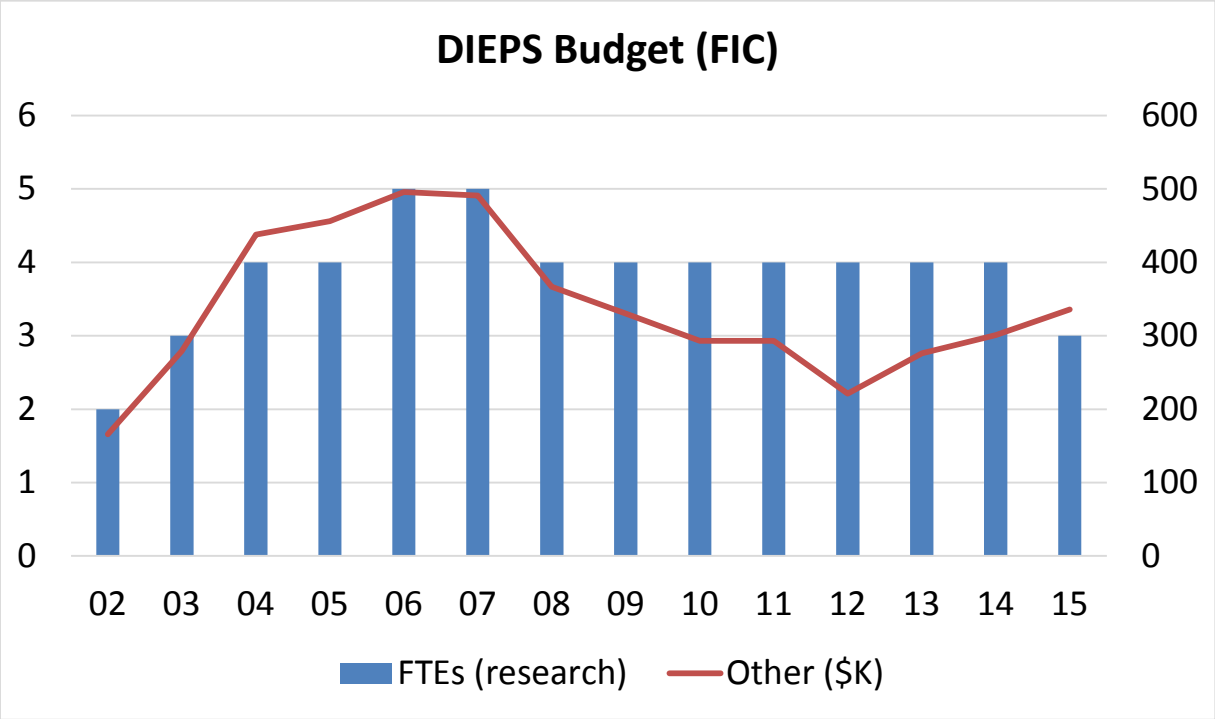
- **Implementation science:** quantitative tools from economics and operations research – for which the fundamental concern is the optimal allocation of limited resources – are greatly needed and underutilized in analyzing such challenges as vaccine/drug/blood supply chains, health-system resilience and, risk assessment. This is a particularly rich area for collaboration between DIEPS and FIC's Center for Global Health Studies.

- Consideration could also be given to a **social science** component, modeling social and economic behavior in health systems: this could connect with related work at other ICs which already includes modeling (e.g. of obesity, tobacco use, and adherence to drug therapies), and could contribute to the indoor-air-pollution project already being conducted collaboratively between DIEPS and CGHS. This would also leverage use of mobile technologies to obtain baseline indicators of population behavior and detect dynamical changes.

These new areas of research would provide exciting opportunities for collaboration with DISPPE/CGHS and DITR, particularly as they relate to implementation science, use of mobile technologies in data collection and data networks, and the NCD-ID nexus. Informal discussions have already identified specific ways in which we could work together in these areas with additional seed funding. These new initiatives would build upon DIEPS' strong track record in linking mechanism, epidemiology and policy, through world-class modeling and analysis, and extend FIC's reputation for developing and catalyzing "integrative global public health."

Importantly, such work would also facilitate connections with other ICs, not only in modeling behavior and operations (as noted above), but also, for instance, with the microbiome – an area of intense interest across many ICs. As noted in Derek Yach's recent editorial, Fogarty remains underutilized as "the face of US excellence in health sciences globally." The ability to use integrative modeling approaches to better identify and coordinate key global health research opportunities across the NIH campus can support this critical component of the FIC mission.

Figure 1. DIEPS budget ($1,000s) and FTE history.



DIEPS could use additional core operating funds to support additional research staff and activities that will develop new areas of opportunity across the Center, tied to seeding 2-3 new areas of research with the necessary resources. In addition to 2-3 additional research scientists and 4-5 postdoctoral fellows, the new funding would go to support senior researchers visiting on sabbaticals each year, and to catalyze a "mini-RAPIDD" program – a series of focused workshops with specific deliverables targeted at identifying key research gaps and public health questions amenable to modeling as well as junior/mid-career scientists working in the new research areas proposed here. Previous experience with RAPIDD and MISMS indicates that such activities can have disproportionately galvanic effects on research and its interface with policy.

These new initiatives will allow for further connections for FIC within NIH and beyond, to organizations such as IHME, the Wellcome Trust, the Skoll Foundation, the Gates Foundation and others with aligned interests that might provide substantial funding once DIEPS has established expanded areas of expertise. The additional investment from within FIC will provide

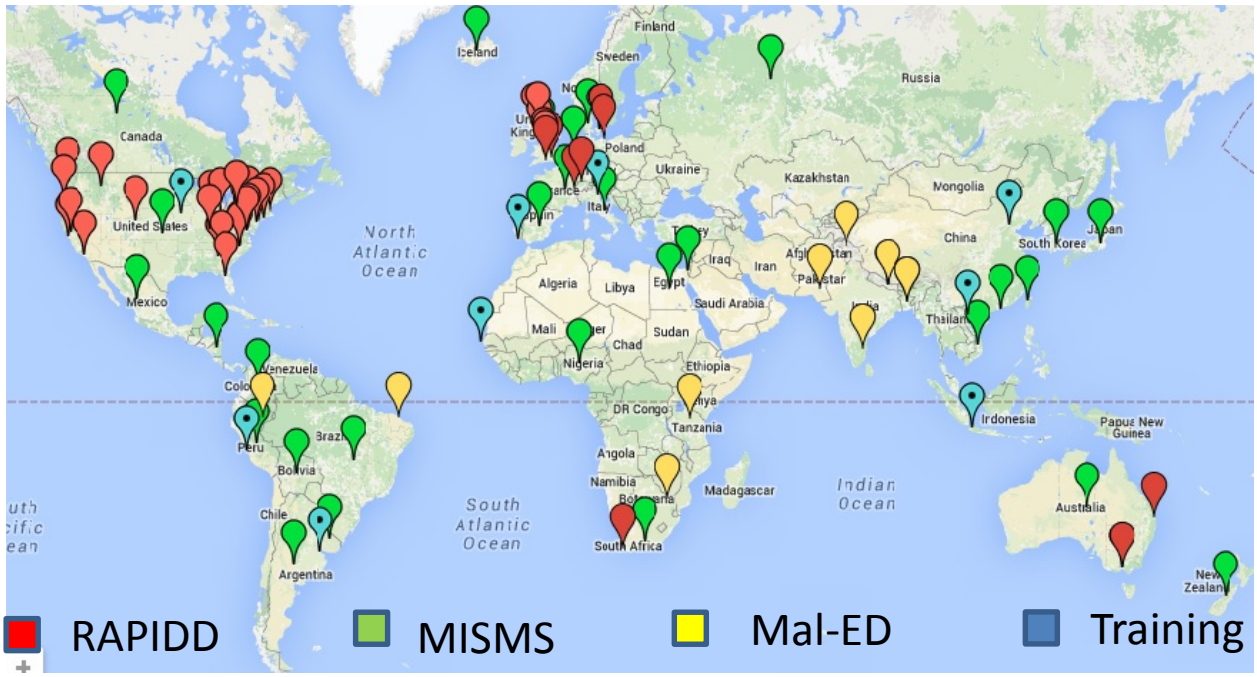
"proof of concept" research as well as an important signal to other funders that the work is valued internally—and consequently worth additional, leveraged support from them.

Value to FIC:

DIEPS is prepared to build on the strengths of its small but solid, world-class core, to extend into new areas of opportunity – with the prospect of attracting outside funds, once sufficiently established – and to continue its unique contributions as the "intramural" part of FIC. All Institutes and every other Center that supports research and training at the NIH has an intramural program that helps provide a scientific identity to the IC. Identity is of additional import in providing prestige to the unit as a scientific organization and to enhancing the morale of its staff members and grantees: strengthening the "intramural" role of DIEPS can only strengthen FIC as a whole. This important effort can be achieved with modest new investments that have the potential for considerable return across the whole of the Center.

Fig 2: Building on DIEPS international network of collaborators and affiliates. DIEPS promotes:

- **Research, data access, methods, and training in computational biology**
- **Strong links between academia and USG**
- **Informed use of models to guide policy during public health crises**



Appendix III: DIEPS Presentation

Review of DIEPS current activities, outputs and impacts

- Stacey Knobler, Overview of Current Activities and Capabilities
- Ellis McKenzie, RAPIDD Program
- Cecile Viboud, MISMS Research Network

Role of intramural research programs

25 of 27 NIH ICs conduct intramural research

- High risk/high reward research or orphaned areas
- Rapid response and agility to address emergent issues
- Strong science in-house to
  - support decision-making
  - attract and train new talent
- Enhanced impact on policy, through privileged ties to USG policy leaders.

DIEPS has performed well in all areas

Current and recent programs in DIEPS

MAL-ED (2008-2018)

Pakistan Research & Capacity Building Activities (2010-2015 and 2014-2018)

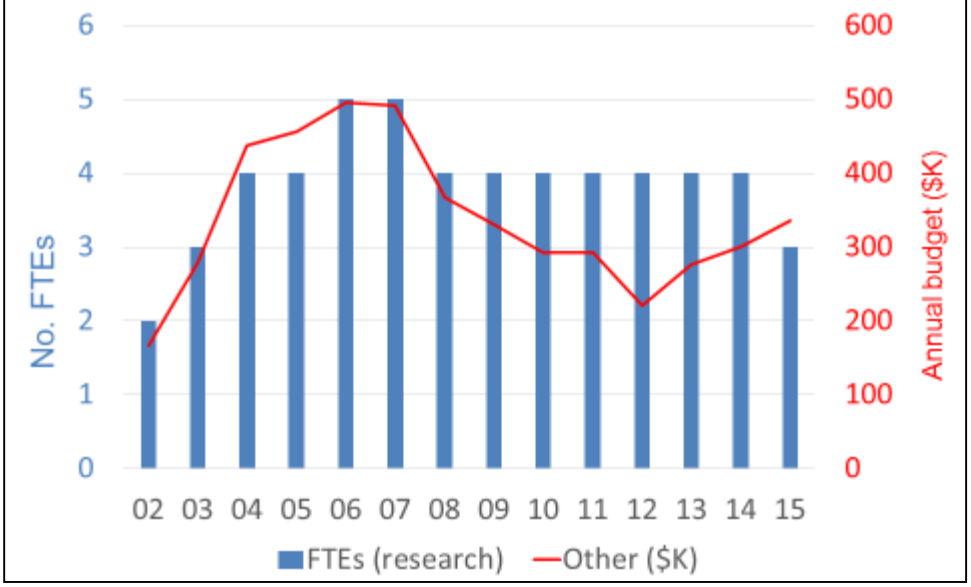
Household Air Pollution (2015-2020)

SMART Vaccines (2013-2018)

RAPIDD (2008-2015)

MISMS (2001-)

DIEPS Staff and Core Budget

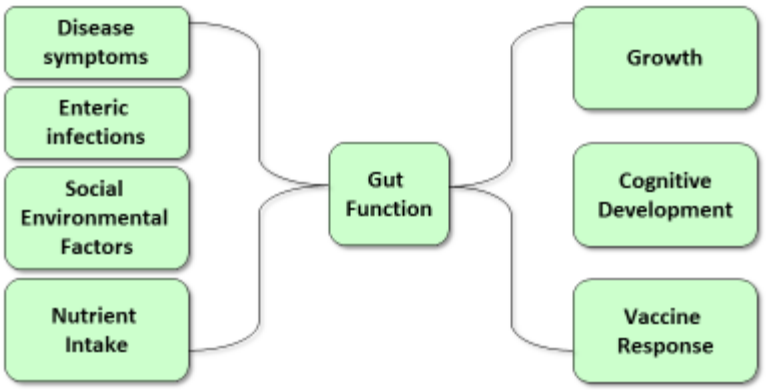


Application of Modeling for Innovation in Population Health Research, Practice, and Policy

- Identifying and addressing the complexities of
  - Disease systems
  - Health/Intervention Delivery systems
  - Decision-making processes

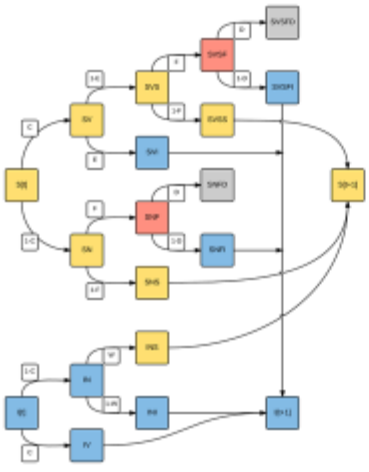
Disease Systems: MAL-ED

How do various environmental exposures early in life conspire to affect subsequent growth and development outcomes?



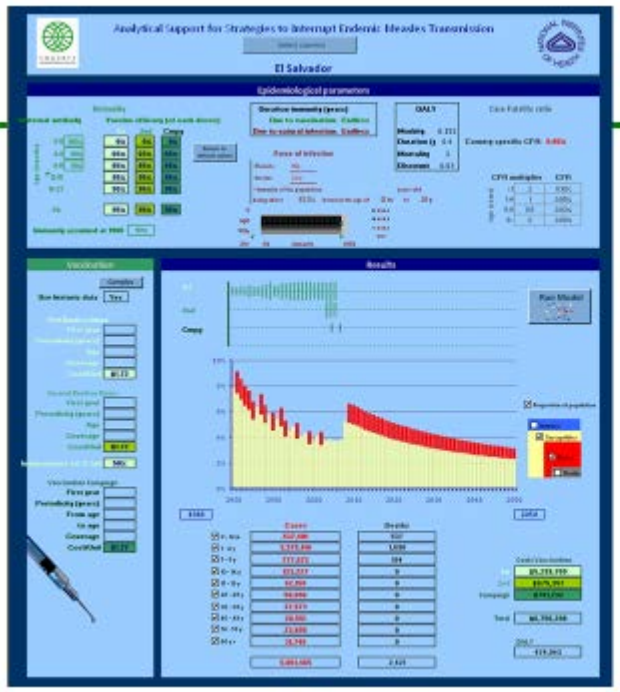
Health/Intervention Delivery Systems: Household Air Pollution (HAP)

Health/Intervention Delivery Systems: A framework for modeling the impact of alternative immunization strategies



Enables integrating population- and individual-based modeling approaches into single structure.

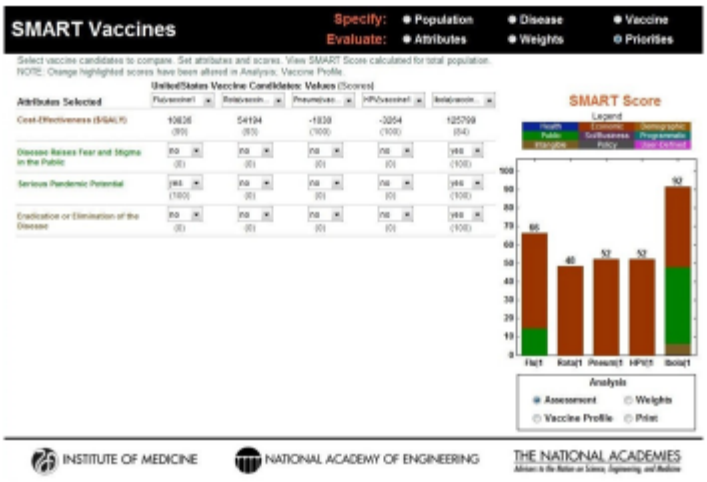
Uses matrices as multidimensional databases where events (immunization or infection history), parameters (case fatality rates, waning immunity), and states (infected, immune, susceptible, dead) associated with all population strata can be tracked.



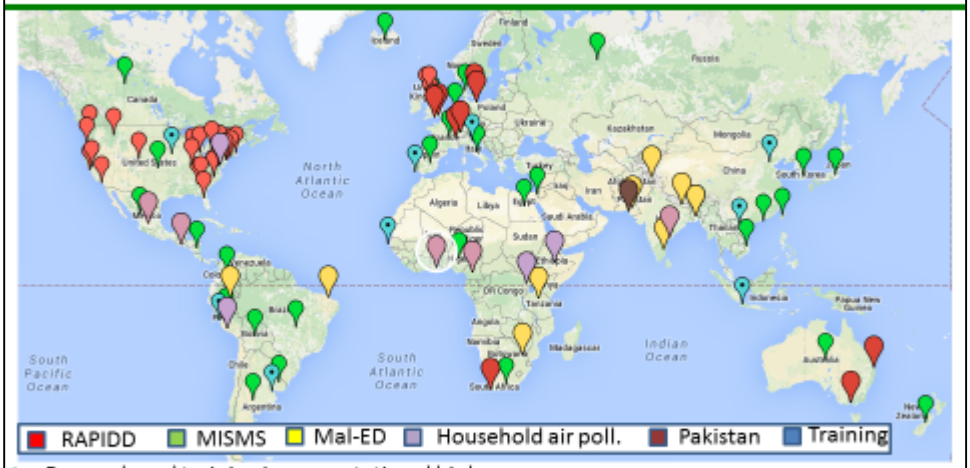
As a by-product, we developed a software that was made available to the WHO

The software can be adapted to simulate immunization scenarios for other vaccine preventable diseases

Decision-making processes: SMART Vaccines…beyond cost-effectiveness



DIEPS international & multidisciplinary network



- Research and training in computational biology
- Fosters links between academia, NGOs, bi-lateral & multilateral agencies, and USG
- Promotes informed use of models and modeling tools to guide both public health practice and policy as well as decision-making during public health crises

Personnel & Expertise

- DIEPS personnel have a strong track-record for generating high-impact results through publications, training, and capacity building
- The reputation of NIH, FIC, and the division provide strong incentives for joining the team--which has facilitated the recruitment of high-quality talent to DIEPS
- Resources to build concomitant capacity in new fields of study will likely generate similar results, but will require additional resources to generate similar trajectories of past and current success

RAPIDD

Research and Policy for Infectious Disease Dynamics
2008-2015

- Improve state-of-the-art of infectious disease modeling
- Strong links to data and applications
- Model development, comparison, validation
- Focus on dynamics and control of:
  - Foreign animal diseases
  - Zoonoses and emerging infections
  - Human diseases as modeling case studies

13 RAPIDD Postdoctoral Fellows:

Prof. Shweta Bansal	Georgetown University
Prof. Joel Miller	Monash University
Prof. Virginia Pitzer	Yale University
Prof. Juliet Pulliam	University of Florida
Prof. Angie Luis	University of Montana
Dr. Seth Blumberg	UC San Francisco
Dr. Kim Pepin	USDA/APHIS
Dr. Jonathan Zelner	Columbia University
Dr. Tiffany Bogich	Standard Analytics IO
Prof. Alex Perkins	Notre Dame
Prof. Robert Reiner	Indiana University
Dr. Michael Buhnerkempe	UCLA
Dr. David Kennedy	Penn State

4 RAPIDD core working groups

Emerging Infectious Diseases

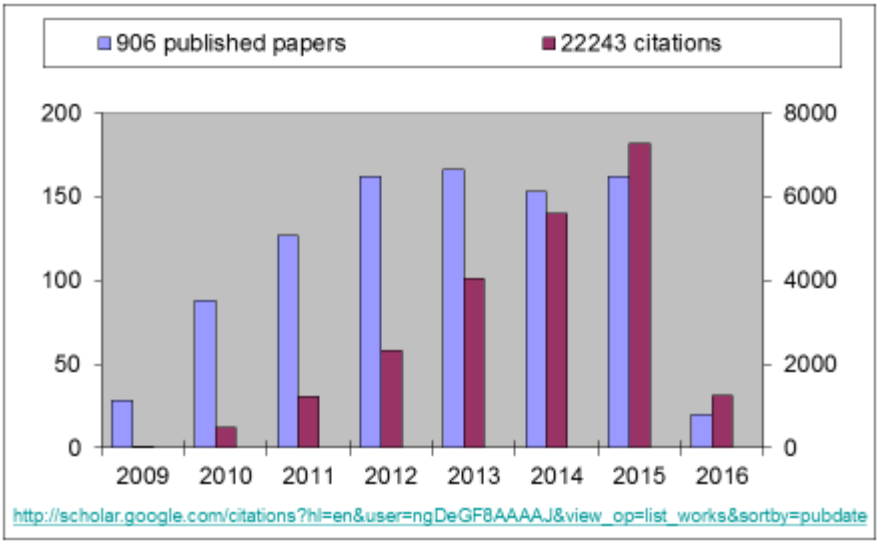
Small Mammal Reservoirs

Mosquito-borne infections

Model hierarchies

114 RAPIDD workshops

RAPIDD scientific publications & citations

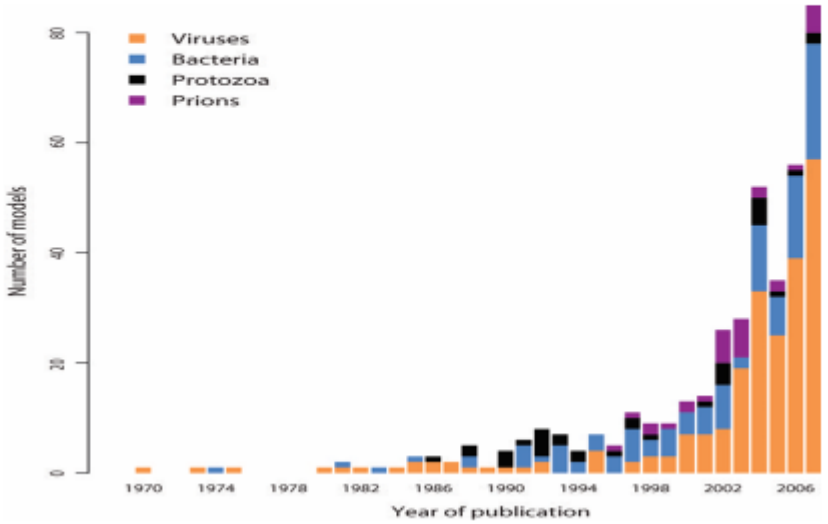


h-index = 70; i10-index = 513

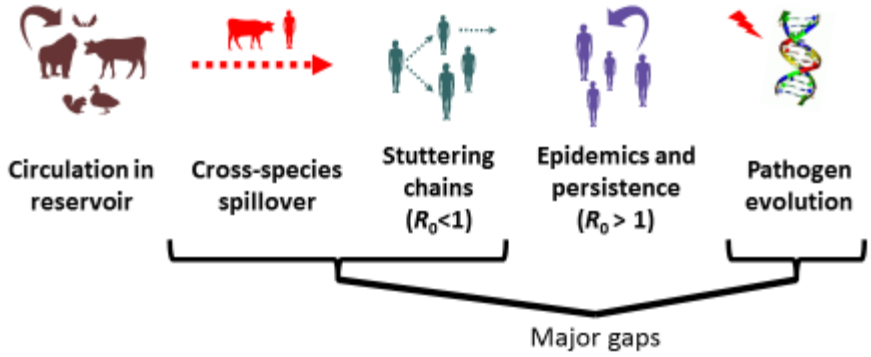
February 25, 2016

Epidemic dynamics at the human-animal interface

Lloyd-Smith et al. 2009 (Science 326: 1362-1367)



Key processes in zoonotic dynamics



Research themes

- Dynamics of cross-species spillover transmission and stuttering chains of weak transmission in the new host.
- Evolutionary causes and consequences of cross-species emergence.
  - adaptation to enable emergence
  - evolution of virulence following emergence

Bats and rodents as zoonotic reservoirs

A COMPARISON OF BATS AND RODENTS AS DISEASE HOSTS

Are bats special?

Zoonotic virus species/ species: bats ~2X rodents

Overlapping species ranges, higher-density roosts, regional migration, long-lived, small litters, etc.

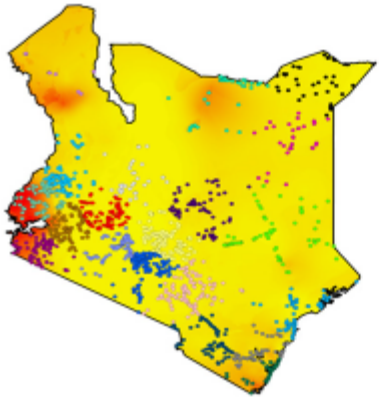
Luis et al. Proc Roy Soc B 280: e20122753, Ecology Letters 18: 1153-1162

A framework for the study of zoonotic disease emergence and its drivers: spillover of bat pathogens as a case study

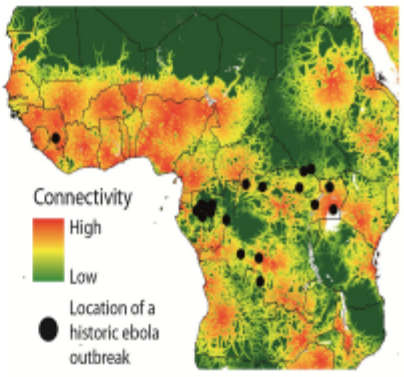
Wood et al. 2012 Phil Trans Roy Soc B 367: 2881-2892

Improving surveillance and response

Spatio-temporal dynamics of human density/movement via cell phone data, satellite night-lights imagery, etc.

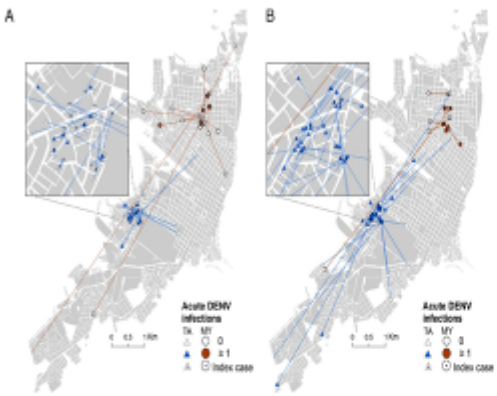


Quantifying the Impact of Human Mobility on Malaria. Wesolowski et al. 2012 Science 338: 267-270



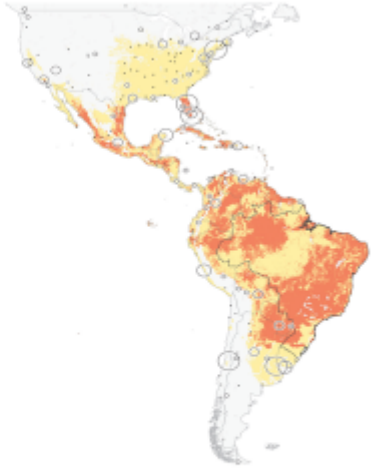
Containing the Ebola Outbreak – the Potential and Challenge of Mobile Network Data. Wesolowski et al. 2014 PLoS Currents Outbreaks 10.1371

Arbovirus transmission, household and continent scale



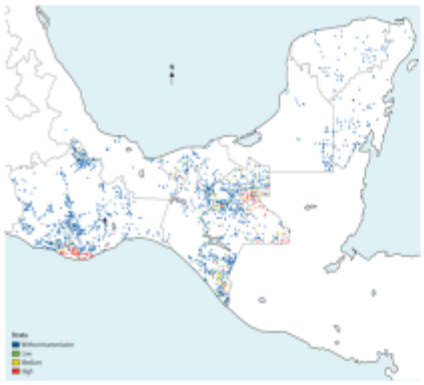
Iquitos, Peru: cluster investigations

House-to-house human movement drives dengue virus transmission. Stoddard et al. 2013 PNAS 110: 994-999



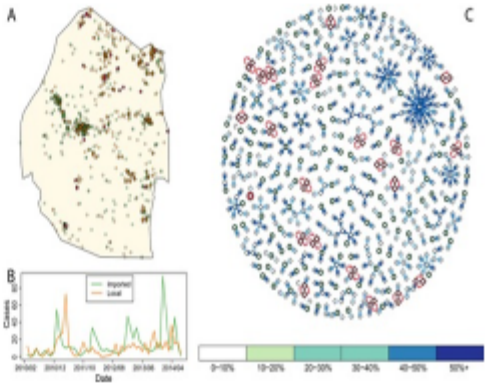
Anticipating the international spread of Zika virus from Brazil Bogoch et al. 2016, Lancet 387: 335-336.

Moving toward the "end game" in malaria



Residual malaria transmission foci in Oaxaca and Chiapas, Mexico

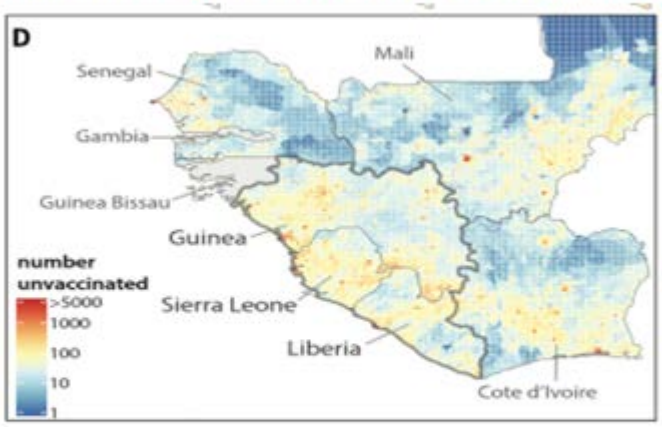
Operational strategies to achieve and maintain malaria elimination. Moonen et al. 2010. Lancet 376: 1592–1603.



Swaziland: consensus network plot of causal links, imported (green) and local cases (orange).

Mapping residual transmission for malaria elimination. Reiner et al. 2015. eLife 4: 1–21.

Indirect effects of the West Africa Ebola outbreak



Reduced vaccination and the risk of measles and other childhood infections post-Ebola

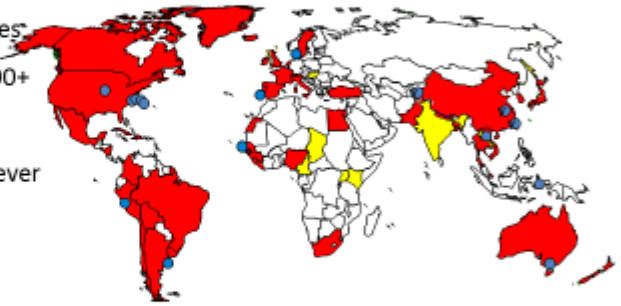
Takahashi et al. 2015 Science 47: 1240-1242

MISMS: epidemiology and evolutionary dynamics of influenza viruses

- International collaborative program established in 2001
- Research, data sharing, and training
- Funding:
  - 2001-2006, 2014-onward: core FIC funds
  - 2007-2013: HHS/OGA office of pandemic and emergent threats

Core Capacities and Scientific Outputs

- Network of 350+ collaborators in >50 countries
- 17 regional workshops; 400+ investigators trained
- First influenza workshop ever in Africa
- Strong links with NIH and other areas of USG
- 228 publications, h-index 52

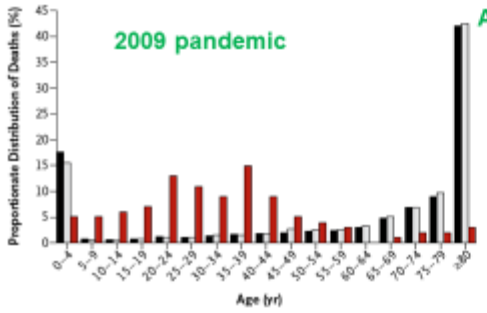


MISMS regional workshops
Genomic or epidemiologic data analyzed or ongoing data collection
In development

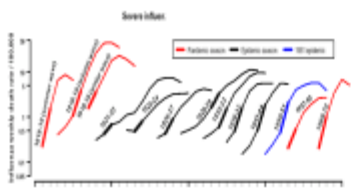
http://www.origem.info/misms

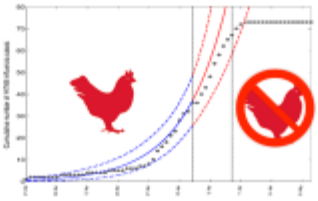
28

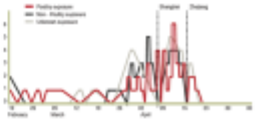
Pandemic Risk and Transmission Dynamics



Historic outbreaks

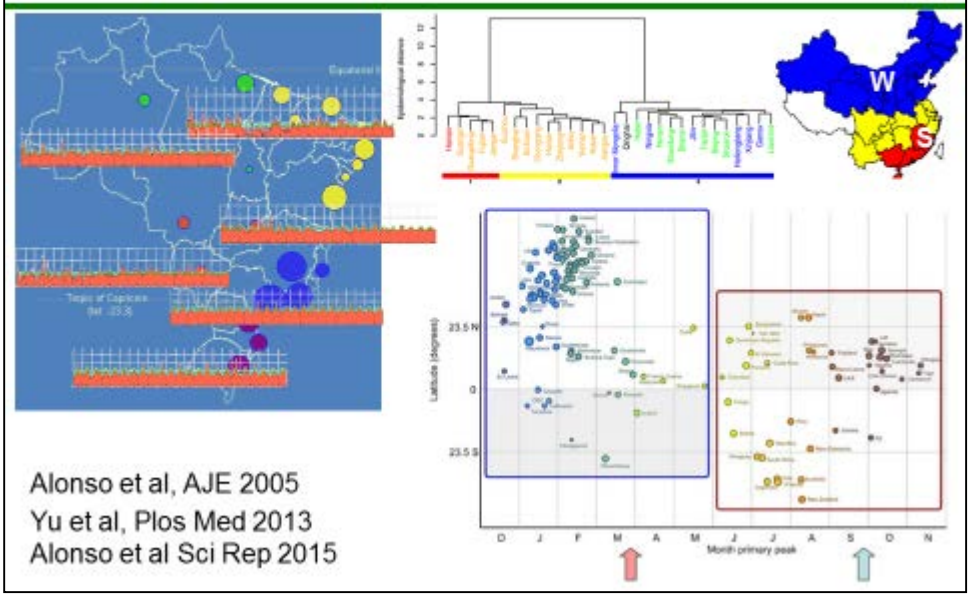






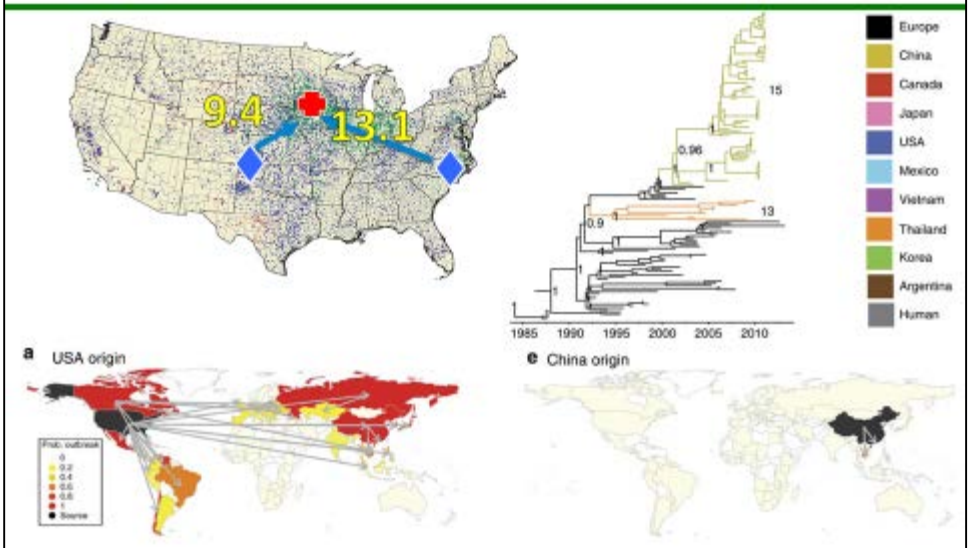
Chowell et al BMC Med 2013
Viboud et al EID 2007
Chowell et al, NEJM 2009

Guiding influenza vaccination strategies



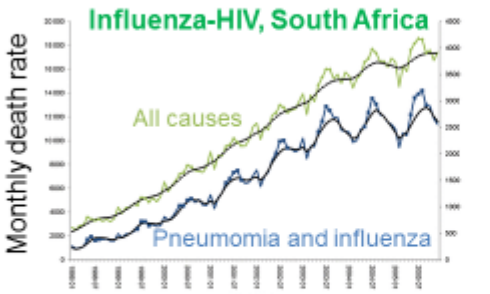
Alonso et al, AJE 2005
Yu et al, Plos Med 2013
Alonso et al Sci Rep 2015

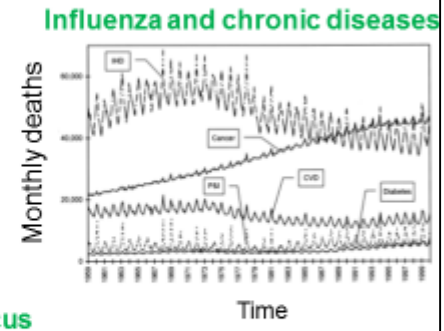
Animal human-interface: Targeting swine influenza surveillance

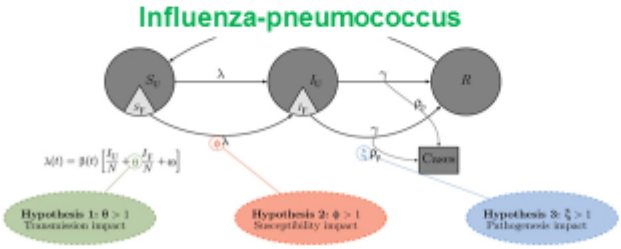


Nelson, M et al, Plos Pathogens 2011; Nelson, M et al Nat. Comm 2015

Disease interactions





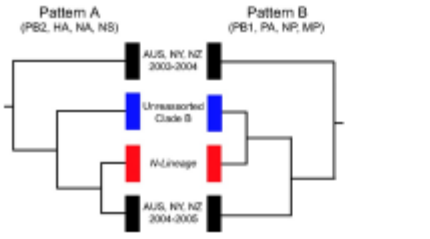


Cohen et al, CID 2013

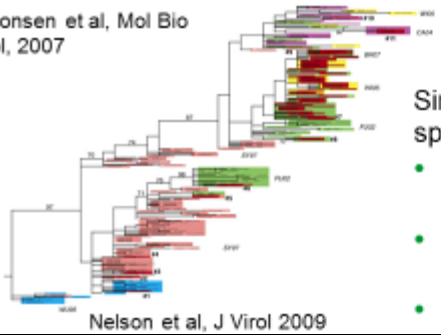
Reichert et al, AJE 2004

Shresta et al Sci Trans Med 2014

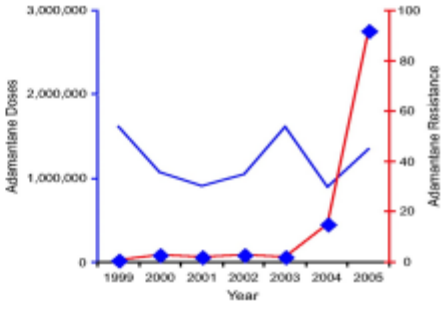
Emergence of antiviral resistance



Simonsen et al, Mol Bio Evol, 2007



Nelson et al, J Virol 2009

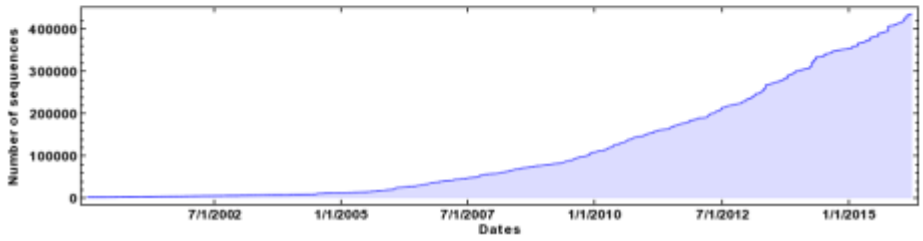


Single mutations conferring resistance spread via:

- Reassortment and hitch-hiking with antigenic novelty (adamantane)
- Additional permissive mutations (oseltamivir)
- Spatial context

Catalytic role: influenza full-genome sequencing and data sharing

- Trans-NIH (NCBI, NIAID, FIC) and JCVI collaborative effort, 2004-present
- Sparked by DIEPS white paper in 2004
- MISMS network basis to identify virus collections, further sequencing, and immediate posting on Genbank
- >400K flu sequences available on Genbank



Training and capacity building




- Aubree Gordon, PhD, Assistant Professor, School of Public Health, University of Michigan
- Dan Weinberger, PhD, Assistant Professor, School of Public Health, Yale University
- Caterina Rizzo, MD, Epidemiology and Modelling Unit, Istituto Superiore di Sanità, Italy
- Cheryl Cohen, MD-PhD, Centre for Respiratory Diseases and Meningitis, National Center for Infectious Diseases, South Africa

FUTURE DIRECTIONS:
Proposed new areas of strategic opportunity

- Important across FIC, NIH and beyond
- Under-served by modeling
- Build on DIEPS strengths

- 5 areas, but not an exhaustive list
- Need prioritizing, both between and within areas

Disease interactions

- Pathogen-pathogen interactions
  - Tuberculosis-influenza
  - HIV-Hepatitis C
- Link between infectious and chronic diseases
  - TB-diabetes
  - HIV-cardiovascular diseases
  - Early life insults and long-term health and development
- Impact on clinical outcomes, transmission dynamics and control policy

Antimicrobial resistance

- Analyses to guide changes in incentive structures and help optimize treatments
- Drug rotations and combinations
- Contribution of local emergence vs regional spread

The microbiome

Complex, poorly-characterized ecology, ripe for quantitative studies

- Mediator of non-communicable diseases
- Subject to nutritional and environmental drivers and multiple ecological interactions
- Mediator of disease interactions and antibiotic resistance

Implementation science

- Tools from economics and operations research
- Optimal allocation of limited resources
- Ripe for study of:
  - vaccine/drug/blood supply chains
  - health-system resilience, and risk assessment

Economics and Social Sciences

- Bring global health expertise to related work at other ICs that includes modeling (e.g. of obesity, tobacco use, and adherence to drug therapies, vaccine financing)
- Enhance DIEPS/CGHS collaboration on indoor-air-pollution

Proposed new areas of strategic opportunity

- Aim is to have disproportionate, catalytic effects on these areas, as we have on others
- Engage our substantial networks to continue to grow these areas globally, collaboratively

- 5 areas, but not an exhaustive list
- Need prioritizing, both between and within areas