International Clinics on Infectious Disease Dynamics and Data (ICI3D) Program

Mathematics and simulation are essential tools in infectious disease control, enabling decision-makers to explore control policies before implementing them, interpret trends, and predict emerging threats. The ICI3D Program, a collaboration between the UF Emerging Pathogens Institute and the South African Centre for Epidemiological Modelling and Analysis (SACEMA), provides intensive training in these methods to students and researchers from Africa and North America and aims to cultivate an international network of researchers from diverse backgrounds. The program comprises two distinct but overlapping International Clinics on Infectious Disease Dynamics and Data and a complementary research scholars exchange program.

The annual Clinic on the Meaningful Modeling of Epidemiological Data (MMED), which is held in South Africa, exposes participants to a diverse set of modeling approaches that will allow them to engage with real-world questions about infectious disease dynamics by integrating mathematical models with epidemiological data. We teach participants to use data to inform the construction of clear and concise models appropriate to answer a given question, rather than developing complex mathematical models unrelated to data. The Clinic consists of two tracks, one that targets quantitative scientists, including mathematicians, statisticians, and computer scientists, and a second that targets classically trained infectious disease epidemiologists. In the second week of the Clinic, participants collaborate on research projects, working in interdisciplinary groups.

The Clinic on Dynamic Approaches to Infectious Disease Data (DAIDD), which is held annually in Florida, targets public health researchers and population biologists interested in studying infectious diseases. Instruction focuses on identification of infectious disease research questions that can be usefully addressed using mechanistic models and construction of models tailored to these questions. Participants develop written research proposals for their systems of interest and receive guidance in seeking out the resources necessary for carrying out their proposed research.

The International Disease Dynamics and Data Research Scholars Exchange Program (I3D) allows selected Clinic participants to engage further with Clinic faculty. The program funds scholars to spend a minimum of six weeks working on an approved research project at the faculty member's home institution. I3D scholars from Africa work with faculty at North American institutions, and American I3D scholars work with faculty at African institutions. The I3D scholars program complements the two annual clinics to provide a near-continuous flow of collaborative research between the two continents.

The ICI3D program has been funded through a Research Education grant from the National Institute for General Medical Sciences (NIGMS/NIH grant R25GM102149) since 2012. Over this time, we have provided training to 134 participants based at African and North American institutions and established pipelines to train and recruit talented young researchers to join our program's faculty. The following pages detail the program's outcomes, as measured by scientific products (publications and presentations) and research exchanges. For more information on the ICI3D program, please visit ici3d.org or contact the program director.

Presentations and Publications Resulting from the ICI3D Program

(Includes work funded by the current ICI3D program grant and products from MMED 2010-2012, which predated the current funding.)

Key: ICI3D participant = <u>underlined</u>, ICI3D faculty = **bolded**, Graduate Student = [g], Post-Doctoral Researcher = [p], Undergraduate = [u]

Refereed publications with participants as authors

<u>Sempa, JB</u> [g], **J Dushoff**, MJ Daniels, M Nieuwoudt, and **SE Bellan** [p]. (In press) Reevaluating cumulative HIV-1 viral load as a prognostic predictor: predicting opportunistic infection incidence and mortality in a Ugandan cohort. *American Journal of Epidemiology*.

<u>Ying, R</u> [g], RM Granich, S Gupta, and **BG Williams**. (2016) CD4 cell count: Declining value for antiretroviral therapy eligibility. *Clinical Infectious Diseases*. Published online ahead of print: January 29, 2016. doi: 10.1093/cid/civ1224

Brook, CE [g], R Beauclair [g], O Ngwenya, L Worden, M Ndeffo-Mbah, TM Lietman, SK Satpathy, AP Galvani, and **TC Porco**. (2015) Spatial heterogeneity in projected leprosy trends in India. *Parasites and Vectors* 8:542-552. doi:10.1186/s13071-015-1124-7

Enanoria WTA, L Worden, F Liu [p], D Gao [p], <u>S Ackley</u> [g], **JC Scott**, M Deiner, <u>E Mwebaze</u> [p], W Ip, TM Lietman, and **TC Porco**. (2015) Evaluating subcriticality during the Ebola epidemic in West Africa. **PLOS ONE** 10(10): e0140651. doi:10.1371/journal.pone.0140651

Hargrove, JW and SF Ackley [g]. (2015) Mortality estimates from ovarian age distributions of the tsetse fly Glossina pallidipes Austen sampled in Zimbabwe suggest the need for new analytical approaches. **Bulletin of Entomological Research** 105(3): 294-304.

Bellan, SE [g], <u>K Fiorella</u> [g], <u>D Melesse</u> [g], W Getz, **BG Williams**, and **J Dushoff**. (2012) Extra-couple HIV transmission in sub-Saharan Africa: a mathematical modelling study of survey data. *The Lancet* 381(9877): 1561-1569. doi:10.1016/S0140-6736(12)61960-6.

Submitted manuscripts with participants as authors

Means, A [g], K Risher [g], E Ujeneza [g], I Maposa, J Nondi, SE Bellan [p]. Impact of age and sex on CD4+cell count trajectories following treatment initiation: an analysis of the Tanzanian HIV treatment database.

Ying, R [g], PD Williams [p], N Dorratoltaj [g], JB Sempa [g], L Lourens [u], F Liu [p], T Gebre, B Ayele, N Dube [g], Z Zhou, PM Emerson, TM Lietman and **TC Porco**. A mathematical model for the prospects of trachoma elimination through mass treatment targeted at children.

Conference presentations given by participants

(Includes only presentations for which conference travel was directly supported by ICI3D funds.)

<u>Borchering, RK</u> [g], **SE Bellan** [p], JM Flynn [g], **JRC Pulliam**, and SA McKinley. Effects of resource density on encounter rates and disease outcomes. Epidemics 5, Florida, USA, December 2015. [poster]

<u>Williams, PD</u> [p], <u>R Ying</u> [g], <u>N Dorratoltaj</u> [g], <u>L Lourens</u> [u], F Liu [p], <u>JB Sempa</u>, T Gebre, B Ayele, Z Zhou, PM Emerson, TM Leitman, and **TC Porco**. Prospects for trachoma elimination through mass treatment targeted at children. Epidemics 4, Amsterdam, Netherlands, November 2014. [poster]

Faculty collaborations incorporated into the ICI3D curriculum

Pulliam, JRC, SE Bellan [p], M Gambhir, LA Meyers, and J Dushoff. (2015) Evaluating Ebola vaccine trials: insights from simulation. *The Lancet Infectious Diseases* 15(10): 1134. doi:10.1016/S1473-3099(15)00303-5

Bellan, SE [p], **JRC Pulliam**, CAB Pearson [p], D Champredon [g], SJ Fox [g], L Skrip [p], AP Galvani, M Gambhir, BA Lopman, **TC Porco**, LA Meyers, and **J Dushoff**. (2015) Statistical power and validity of Ebola vaccine trials in Sierra Leone: a simulation study of trial design and analysis. *The Lancet Infectious Diseases* 15(6): 703-710. doi: 10.1016/S1473-3099(15)70139-8.

Bellan, SE [p], **J Dushoff**, AP Galvani, LA Meyers. (2015) Reassessment of HIV-1 acute phase infectivity: accounting for heterogeneity and study design with simulated cohorts. *PLOS Medicine* 12(3): e1001801. doi: 10.1371/journal.pmed.1001801

Bellan, SE [p], JRC Pulliam, J Dushoff, and LA Meyers. (2014) Ebola control: effect of asymptomatic infection and acquired immunity. *The Lancet* 384(9953): 1499-1500. doi: 10.1016/S01406736(14)618390

Bellan, SE [p], **JRC Pulliam**, **J Dushoff**, and LA Meyers. (2014) Ebola vaccine trials: the ethical mandate for a therapeutic safety net. **The British Medical Journal** 349: g7518. doi: http://dx.doi.org/10.1136/bmj.g7518

Refereed publications on instructional approaches

Bellan, SE [g], **JRC Pulliam**, **JC Scott**, **J Dushoff**, and the MMED Organizing Committee. (2012) How to make epidemiological training infectious. **PLoS Biology** 10(4): e1001295. doi:10.1371/journal.pbio.1001295

Conference presentations and invited seminars on instructional approaches

Pulliam, JRC, A Welte, SE Bellan [p], AG Hitchcock, J Dushoff, and the ICI3D Faculty. Creating a Model World: An active-learning approach to teaching dynamic modeling. *Ecology and Evolution of Infectious Diseases annual meeting*. Athens, GA, May 2015.

Bellan, SE [g], **JRC Pulliam**, **JC Scott**, and **J Dushoff**. Muizenberg Fever: Instructive outbreaks of a novel agent. **NSF/NIH Ecology and Evolution of Infectious Disases annual PI meeting**. Berkeley, CA, March 2012. [poster]

Pulliam, JRC, SE Bellan [g], **JC Scott**, and **J Dushoff**. Muizenberg Fever: Instructive outbreaks of a novel agent. *Center for Infectious Disease Dynamics Seminar Series, Pennsylvania State University*. State College, PA, February 2012.

Pulliam, JRC, SE Bellan [g], TC Porco, JC Scott, BG Williams, JW Hargrove, and J Dushoff. Training an international community of applied infectious disease modelers in Africa. *Modeling for Public Health Action: From epidemiology to operations, Centers for Disease Control and Prevention*. Atlanta, GA, December 2010.

I3D Exchange Visits

Visits from North America to Africa

Sarah Ackley (2014), PhD student in Epidemiology at University of California – San Francisco (UCSF)

- Host institution: SACEMA
- I3D faculty mentor: Prof. John Hargrove
- Project: estimating tsetse fly mortality from entomological surveillance data

Roger Ying (2015), MD/PhD student at University of Washington

- Host institution: SACEMA
- I3D faculty mentor: Prof. Brian Williams
- Project: developing improved modeling tools for use by public health officials to inform decisionmaking for HIV-related policies

Florian Marx, MD (2016), postdoctoral researcher, Division of Global Health Equity, Brigham and Women's Hospital and Harvard Medical School

- Host institution: SACEMA
- I3D faculty mentor: Prof. Brian Williams
- Project: assessing the cost effectiveness of two TB interventions in high-risk populations: isoniazid preventive therapy and targeted active case finding

Avery McIntosh (2016), PhD student in Biostatistics at Boston University

- · Host institution: SACEMA
- I3D faculty mentor: Prof. Alex Welte
- Project: developing tools and integrating mehtods for HIV incidence estimation

Visits from Africa to North America

Joseph Sempa (2014), researcher at Infectious Diseases Institute, Uganda (IDI) *

- Host institution: University of Texas at Austin
- I3D faculty mentor: Dr. Steve Bellan
- Project: evaluating cumulative viral load as a predictor of opportunistic infection and mortality in HIV patients

Ernest Mwebaze (2014), PhD student at Makerere University in Uganda

- Host institution: University of California San Francisco (UCSF)
- I3D faculty mentor: Prof. Travis Porco
- Project: using partially observed Markov Processes as an inference tool for infectious disease dynamics, with applications to trachoma and leprosy

Welile Sikhondze (2015), PhD student at University of Cape Town supported through a SACEMA bursary

- Host institution: University of California San Francisco (UCSF)
- I3D faculty mentor: Prof. Travis Porco
- Project: modeling the impact of novel diagnostic methods on TB incidence

Joseph Nondi (2015), researcher at the Ministry of Health and Social Welfare, Tanzania

- Host institution: McMaster University
- I3D faculty mentor: Prof. Jonathan Dushoff
- Project: evaluating care and treatment of pediatric HIV in Tanzania

Roxanne Beauclair (2016 - in progress), PhD student at SACEMA

- Host institution: McMaster University
- I3D faculty mentor: Prof. Jonathan Dushoff
- Project: evaluating the effect of age-mixing patterns on HIV transmission in Malawi

List of Core Faculty

Steve Bellan, postdoctoral researcher, University of Texas at Austin
Jonathan Dushoff, associate professor, McMaster University
John Hargrove, senior research fellow, SACEMA
Travis Porco, professor, University of California - San Francisco
Juliet Pulliam, assistant professor, University of Florida
Jim Scott, associate professor, Colby College
Alex Welte, director of SACEMA and associate professor, Stellenbosch University
Brian Williams, visiting senior research fellow, SACEMA

^{*} Since completing the exchange, Joseph has received a PhD bursary from SACEMA, and his dissertation will continue this work, in collaboration with several ICI3D faculty members.