

Modeling the Impact of Policy Options during Public Health Crises

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1 Motivation for the Workshop

While many of us have been thinking about pandemic influenza lately, when we submitted our proposal three years ago, SARS was fresh in our minds. We weren't as useful to policymakers as we wanted to be during that crisis and frankly, don't believe any other modelers were either. This is not to say interesting articles weren't published, some by workshop participants, but we didn't affect the global response. We attributed our collective failure in part to few of us understanding what policymakers needed or few policymakers understanding what we had to offer. Our solution was to mix those interested in working together in a setting conducive to getting to know each other's needs and capabilities.

Five participants in this workshop were physicians, internists or pediatricians with infectious disease sub-specialties. One was a health communicator, and the rest were more or less applied mathematicians. We range from population biologists – of which there were two – to at least one pure mathematician, who fortunately for us became interested in infectious diseases. Roughly a third staffed governmental or multi-governmental agencies and two-thirds were academicians. Finally, we were joined by three normaliens, students at the Ecole normale supérieure de Cachan and civil servant trainees (i.e., they have 10-year contracts with the State, which pays their salaries).

2 How modelers can help policymakers prepare for, and facilitate sound policy decisions during foreseeable health crises

John Glasser

“Modeling contributed little to policymaking during the last crisis because few of us understand that process and even fewer policymakers understand ours. I attended several SARS workshops, one right here. One could infer – from our presentations – we believed policymakers wanted to know what \mathcal{R}_0 was and if the equilibria of arbitrary models were locally, if not globally stable. As they actually needed help deciding what to do, we contributed very little to their global response.

“My own experience began well enough: Two CDC people asked me to evaluate quarantine. I made a model, estimated the biological parameters from the initial case series in Hong Kong, fit control parameters to hospital admissions, isolations, discharges and deaths during the outbreak in Singapore, and compared final sizes with proportion quarantined – isolated before they became ill – at its estimated value and zero. As these results differed by only a handful, I concluded the impact of quarantine was small. While correct, that was not the desired answer.

“In the outbreaks in Singapore and Taiwan, only 5% of probable SARS cases were quarantined. No matter how effective an intervention, if it misses the target 95% of the time, it cannot have much impact. By showing how much impact quarantine *could* have, modelers actually contributed to the problem - a) tens of thousands quarantined, at enormous social cost, b) persistent misunderstanding - versus solution. Why?

“It was difficult to tell who had been infected before they developed symptoms, especially given uncertainty about the mode of transmission. What could authorities have done instead? Because infected people were not particularly infectious until acutely ill – common knowledge now, but Dashun deduced it from only 30 days of hospital records – 1) encouraging people with prodromal symptoms to seek care, especially if they might have been exposed to someone since diagnosed, and helping 2) clinicians to diagnose and 3) infection-control personnel to isolate them effectively, would have had much greater impact.

“In the possibly naive belief that such results would have been more valuable in real time (e.g., *before* billions were spent on quarantine), we modeled a generic respiratory disease and interventions likely to be available, and Zhilan derived the reproduction number and took its partial derivatives with respect to control parameters. She is embedding such analytical results in a Mathematica™ notebook that could be used both with initial guesstimates and increasingly reliable estimates of the biological parameters. Her objective is to develop a tool that could help policymakers decide how to respond in the next crisis. We plan to revisit the SARS outbreaks and ask our EOC staff to evaluate a prototype in a simulated EID outbreak.

“I frankly don’t know how else to demonstrate what they have to offer, but other contributors to this session, if not workshop participants, surely will have other ideas.”

David Earn

Some time ago, given that vaccine distribution policies affect the threshold for elimination of diseases such as measles and polio, David wondered how he would implement them. In 1994, the UK conducted an expensive mass vaccination campaign to forestall a predicted measles epidemic due to susceptible adolescents and young adults. It is difficult to assess the benefit, especially as measles is endemic again in the UK now. Similarly, he interviewed people involved in the 2001 foot and mouth epidemic, and had difficulty determining if modeling had an impact via suggesting new or confirming the wisdom of existing ideas.

He was personally involved in the 2003 SARS outbreak in Toronto by a hospital administrator, who called and asked for help he was ill prepared to provide. He thought about why Toronto and why – once introduced – SARS spread. SARS was introduced to Toronto via travel patterns, after which it spread partly by virtue of a misdiagnosis due to co-morbidity and partly exceeding capacity of negative pressure rooms. This led him to think about the economics of surge capacity. If we knew what decisions would be required of policymakers during emergencies, we might be able to obtain the information we need to help in advance.

Fred Roberts

Fred was involved in TOPOFF3, but not as a modeler. In future exercises, modelers should design, participate and analyze. This exercise was highly controlled, without stochastic effects, flexibility in event course by virtue of choices made early on, . . . , and participants identified the infectious agent long before they would have in reality (and just happened to have appropriate materials). As information was consistent, there was no chaos.

We could model how to transport people who might be infectious, food, materials, all while providing security. The most successful portable dispensary violated the rules (i.e., dispensed to a few people who went into the community and distributed). How could we determine if centralization or de-centralization would be best, who had the necessary information and how best to communicate with them? What if primary communications were disabled? Should we use the media as a back-up? Modeling could have improved this exercise.

In reality, there will be personnel as well as technical problems. Terrorists will use primary attacks as diversions and then attack the responders. In New Jersey, a “Preparedness College” is exploring these and other issues (e.g., dealing with uncertainty, communicating risk, ···). Isn’t this exactly what video game designers do?

Simon Levin

Modelers could contribute by anticipating needs, detecting threats, designing stockpiles and infection-control wards, and exploring possible responses (e.g., quarantine and isolation). There are roles for detailed models of specific threats and generic ones that extract principles, for scenarios that lay out possible outcomes and for simulation trainers.

Agent-based models were useful in preparing for pandemic influenza (e.g., via MIDAS), but dimensionality must be reduced to make results more robust. We have put too much faith in untested assumptions. Bio-terrorism is a game (i.e., terrorists respond to our responses), so we must adapt. Actions useful early on won’t have any impact later.

Game theory is an under-exploited area, so a good way for modelers to contribute. Modelers can help to determine what information is needed, versus easily obtained, and some might be obtained in advance. Established inter-personal relations, partnerships, ··· will facilitate cooperation, but we’ll be more helpful in preparing for crises than in responding.

We could help policymakers to develop better mental models. We cannot anticipate all data needed, so must be involved during crises. But effectiveness during depends on preparation. One way of establishing relationships is to help solve routine problems (e.g., design programs for new vaccines, and monitor to ensure policy goals are being met).

3 Spatial spread of pathogens (and policy implications, opportunities)

Julien Arino: Meta-population models: theory and an example

Julien discussed meta-population models for the spread of infectious diseases, mostly from a modeling versus theoretical point of view, showing what type of problems could be described with this tool. Then he presented a project on air traffic he is conducting with colleagues at Saint Michael’s Hospital, in Toronto.

Steven Riley: Hedging against antiviral resistance during the next influenza pandemic using small stockpiles of an alternate chemotherapy

The effectiveness of single-drug interventions to reduce morbidity and mortality during the next influenza pandemic will be substantially weakened if transmissible strains emerge that are resistant to the stockpiled drugs. Steven used a multi-strain stochastic transmission model of influenza to show that the spread of antiviral drug resistance can be effectively reduced by deploying a small stockpile of a secondary drug during the early phase of local epidemics. He considered two alternative strategies for using the small secondary stockpile: early combination chemotherapy (ECC, individuals are treated with both drugs in combination while both are available); and sequential multi-drug chemotherapy (SMC, individuals are treated only with the secondary drug until exhausted and then with the primary drug). He investigated all potentially important regions of unknown parameter space and found that both ECC and SMC reduced the cumulative attack rate

and the resistant attack rate unless the probability of emergence of resistance to the primary drug was so low that resistance was unlikely to be a problem or so high that resistance emerged as soon as primary drug monotherapy began. He extended his model using flight volume data between 105 large cities to investigate the robustness of these resistance-limiting strategies on a global scale. Intriguingly, so long as populations that were the main source of resistant strains employed these strategies (SMC or ECC), those same strategies were also effective for populations far from the source even when some intermediate populations failed to control resistance (by implementing monotherapy). In essence, the interconnectedness of the global network dampened the international spread of resistant strains with its many wild-type epidemics. His results demonstrate that the augmentation of existing stockpiles of oseltamivir with smaller stockpiles of a second drug would be an effective and inexpensive epidemiological hedge.

Michael Johansson: Spatio-temporal dynamics of dengue

When and where will outbreaks happen? Periodicity may be due to weather, host immunity, interaction among serotypes (e.g., replacement), or viral evolution. In Thailand, population centers are supposed to drive multi-annual periodicity, whereas it seems to be weather in Puerto Rico (e.g., temperature in rainy areas and rainfall in dry ones). What data are needed and how should we analyze them (e.g., Morlet wavelets)?

Pauline van den Driessche: Spatial heterogeneity: meta-population disease models

Pauline motivated modeling spatial phenomena and focused on mathematics for discrete spaces, meta-population SEIR models in particular. She derived some mathematical results, added biological details as needed for specific problems and considered their implications.

4 Mathematical epidemiology for policymakers (what they need to know to understand the literature, collaborate with modelers)

Fred Brauer

Fred gave a brief description of the MITACS-PIMS summer schools on modeling of infectious diseases in Banff (2004), Toronto (2006), and Edmonton (2008). The goals of these schools were to introduce mathematical modeling of infectious diseases to mixed groups of students from mathematical and health sciences with the hope of encouraging epidemiologists to appreciate modeling. A central part of these programs is the development and study of models by mixed groups, with some students trained in mathematics and others epidemiology. The material in the schools was quite mathematical, using calculus and qualitative properties of ordinary differential equations.

Christophe Fraser

The Imperial College course is designed for a widening array of public health practitioners. We introduce the simple models, show how they relate to more complex ones, and emphasize parameter estimation and case studies. Our goal is to make students intelligent collaborators and consumers of models. We developed the “MRC Centre for Outbreak Analysis and Modeling” to formalize ad hoc work begun with former students. PhD students and post-docs trained in biology are the best teachers because they concentrate on ‘why’ versus ‘how.’

Linda Gao

Linda described challenges of communicating to her college emergency response committee and county ER coordinator how models can help with decision-making in times of crisis.

5 Other crises (dengue, malaria, polio, global warming)

Jim Alexander: Residual issues in polio eradication that might be amenable to modeling

Achieving and maintaining elimination despite outbreaks of wild or vaccine-derived strains are the main issues. OPV and IPV both have roles in polio eradication.

Ellis McKenzie: Malaria models and intervention policies: history and prospects

In the century since Ross published the first mathematical model of malaria, models developed to inform research and intervention programs have met with varying degrees of success. The modeling enterprise has grown from relatively simple analytic systems to vast individual-based simulations, but basic questions remain about how biological knowledge can be incorporated and biological unknowns addressed at appropriate, useful scales. These questions will be increasingly critical as models begin to encompass operational, economic and other factors, to become multi-disciplinary tools meant to inform policy decisions and to guide investment in and implementation of interventions. Lessons from past experience, and from a recent example, can help modelers address these challenges.

6 Heterogeneous transmission by setting (e.g., households) or activity (e.g., age groups) and intervention targeting

Frank Ball: Vaccination and intervention strategies for epidemics among a population of households

Frank gave a brief introduction to models for epidemics among a population of households, then spoke about vaccination schemes that are implemented in advance of outbreaks, deriving optimal such schemes, and finally described some more recent work in which vaccination (and other intervention strategies) takes place in response to detected cases in households.

Christophe Fraser: Modeling household transmission for historical and future epidemics

Households play an important role in disease transmission and should be considered when designing public health responses. Christophe described some historical models, mathematical and mechanical, used to simulate epidemics in populations of households. He derived some methods for estimating household reproduction numbers in emerging infections, and showed some applications to influenza. He also introduced some inequalities that help determine the magnitude of biases in simple models that ignore household heterogeneities.

Gabriela Gomes (discussion of the utility of GripNet for influenza modeling)

Jamie Lloyd-Smith: Disease invasion dynamics in spatially heterogeneous populations

Spatial structure in human and animal populations often can be represented by subpopulations or patches with individuals moving among them. Typically there is some degree of heterogeneity among patches that may influence transmission dynamics. Jamie discussed stochastic models addressing the influence of spatial structure and heterogeneity on the invasion of infectious diseases, focusing on between-patch movement rates.

Lorenzo Pellis: SIR epidemics in socially structured populations - presence of households and workplaces

Lorenzo presented a stochastic model for the spread of an SIR disease in a fully susceptible population with a social structure characterized by the presence of households and workplaces. He recalled a previously defined threshold parameter, and defined a new household-to-household reproduction number, R_H . Among other properties, it is related to a secure vaccination coverage (i.e., proportion of households whose vaccination reduces R_H and other reproduction numbers at least to 1, if not below).

James Watmough (discussion of impact of detail included in infectious disease models on our advice to decision-makers)

7 Engaging policymakers (what they really want from modelers)

Jen-Hsiang Chuang: Engaging policymakers - what they really want from modelers

At the Center for Disease Control in Taiwan, we increasingly desire transmission models constructed for emerging infections such as pandemic influenza, re-emerging infections such as HIV/AIDS, tuberculosis, dengue fever and enterovirus, and vaccine-preventable diseases such as chickenpox and seasonal influenza. We want models constructed using our observations 1) to evaluate or simulate the impact of certain policies in Taiwan (such as harm reduction strategies and needle exchange programs for intravenous drug users to reduce HIV transmission), 2) to predict the impact of epidemics (such as the peak size of enterovirus epidemics and estimating the number of patients with severe complications) on the healthcare system, and 3) to simulate the impacts of different control policies for newly emerging diseases (such as school or class closure policies for enterovirus or vaccinating children against enterovirus 71 should a vaccine become available).

It is important for policymakers to understand modelers' approaches and key assumptions. Yet modelers typically publish complex and possibly irrelevant information, or simply "black boxes", without explaining their main ideas. To facilitate policymakers' understanding of modelers' approaches and findings, a set of general guidelines (e.g., a publication requirements checklist) should be formulated as a universal reference for modeling publications. This would ensure consistently high standards in the practice of infectious disease modeling and allow policymakers to make better use of modelers' findings.

In addition, policymakers may not be able to determine the quality and validity of a modeling paper after reading through it. Therefore, an evaluation methodology should be developed to aid in assessing modeling papers. Evidence-based medicine (EBM) has been adopted by major international medical journals, which applying strict criteria to determine the quality and validity of clinical research. In studies using EBM strategies, the key details are summarized in a concise yet informative abstract accompanied by expert commentary on the clinical applications of the studies. The EBM approach could be used to assess modeling papers to help policymakers determine the quality and validity of such studies.

Lastly, a registry for documenting mathematical epidemiology studies would provide a comprehensive collection accessible to all involved in public health decision-making at the click of a mouse. Thus, it is useful to set up a database that can be searched systematically to allow policymakers to find studies most relevant to their interests.

Richard Hatchett: Inexact science and the development of public health emergency preparedness policy

In February of 2007, the US Centers for Disease Control and Prevention (CDC) released its Interim Pandemic Planning Guidance: Community Strategy for Pandemic Influenza Mitigation in the United States - Early, Targeted, Layered Use of Nonpharmaceutical Interventions, culminating a year-long policy development process that incorporated insights derived from computational models, close scrutiny of historical data, and inductive reasoning from incomplete observational data about the "microdynamics" of pandemic and seasonal influenza. Richard coordinated computational modeling of various pandemic influenza mitigation strategies by National Institute of General Medical Sciences grantees, as recently described (PNAS 2008;105:4639-44), and analyzed the efficacy of non-pharmaceutical interventions in selected U.S. cities during the 1918 influenza pandemic (PNAS 2007;104:7582-7). This analytical work was augmented by an extensive survey of the scientific literature concerning the epidemiology and population dynamics of influenza, interviews with influenza experts, and socialization of the proposed response strategy through a variety of outreach and focus group meetings. The development of the community mitigation strategy for pandemic influenza illustrates how insights about the population dynamics of a contagious pathogen may inform the development of emergency preparedness and response plans and more generally, how scientific data and hypotheses must be balanced against other considerations in the development of public policy.

8 Compartmental vs. network or individual-based modeling (indications for each approach)

Gerardo Chowell: Signatures of non-homogeneous mixing in disease outbreaks

Despite its simplifying assumptions, SEIR-type models continue to provide useful insights and predictive capability. However, non-homogeneous mixing models such as those for social networks are often assumed to provide better predictions of the benefits of various mitigation strategies such as isolation or vaccination. In practice, it is rarely known to what extent SEIR-type models will adequately describe a given population. Gerardo's goal was to evaluate possible retrospective signatures of non-homogeneous mixing. Each signature evaluated the goodness of fit of SEIR-type model predictions to actual epidemics. For example, the extent of agreement between the observed and predicted final outbreak sizes based on reproduction number estimates arising from fitting various portions of the epidemic curve are possible signatures. On the basis of simulated outbreaks, he concluded that such signatures could detect non-SEIR-type behavior in some but not all social structures considered.

Markus Schwehm: Integration of compartmental and individual-based models

At ExploSYS, we have implemented two models for pandemic influenza. InFluSim is a compartmental model used by several health care agencies worldwide for pandemic influenza preparedness planning. SimFlu is an individual- and network-based model with more detailed intervention options. Both models have different purposes - while the compartmental model can evaluate general interventions like treatment and social distancing, the individual-based model can evaluate containment strategies at the beginning of an outbreak. In this contribution, we will present an integrated approach. Consider a large sub-population like the employees of a company or soldiers in a military unit. The subgroup will inevitably have contact with the pandemic ongoing in the outside population. To optimally protect them from the pandemic, it is possible to execute individually targeted interventions within the subgroup. The resulting model consists of a compartmental model for the outside population and an individual- and network-based model within the subgroup.

Da-Wei Wang: Efficiently implementing programs for individual-based models

Da-Wei discussed an approach to individual-based modeling with he has attained performance via desktop computers exceeding that attained via super-computers elsewhere.

Ping Yan: Unifying statistical inference and mathematical compartment models

Among mathematical models of infectious disease, compartment models account for biological and environmental as well as clinical aspects. The number of parameters tends to be large and all may not be identifiable from the same data. Therefore, parameters are often assigned based on other studies. To be mathematically tractable, many models implicitly assume time durations between pairs of successive events in the system are exponentially distributed. Models with non-exponential distributions are more realistic, but involve systems of Volterra renewal type integro-differential equations. Not only do they introduce more parameters that make fitting models to data even more challenging, but also involve convolution terms that increase the difficulty of assessing parameters statistically. On the other hand, statistical models are designed from observations of the system. They have fewer parameters. They tend to focus on one or few specific aspects of the system instead of the whole system with the focus on fitting models to data and short term predictions. Parameters also may be detached from any biological meaning.

These two approaches are regarded by many as different paradigms rather than a continuous modeling spectrum. Ping presented some ideas of using statistical inferences to build compartment models and then estimate the parameters in a single analysis based on data from a typical outbreak. He used some past experience from the SARS outbreaks to highlight data typically collected at the beginning and during outbreaks. A key difficulty to unifying statistical inference and compartment models is the gap between what are usually observable (i.e., incubation period, clinical serial interval) in statistical inferences and what are usually not

observable in compartment models, durations based on infectiousness (e.g., latent and infectious periods). To overcome this difficulty, one needs to break down the observable time intervals, such as the incubation period into the latent period and a portion of the infectious period. This involves the de-convolution of terms in the integro-differential equations.

Ping demonstrated successful application to a mumps outbreak that took place in a post-secondary institution in eastern Canada between February 2007 and 2008. The model structure and disease transmission parameters are determined from statistical inferences. Sensitivity analyses are conducted for the environment, such as (i) the initial proportion of infected individuals in the population and (ii) the average number of new susceptible people joining the “currently” susceptible population per time unit.

9 Evolution in response to host defenses, newly available hosts

In this session, we discussed questions relating to the challenges for public health of pathogen adaptation to host interventions. In particular, we focused on the evolution of antimicrobial resistance in response to treatment, consequences for the control of influenza and pandemic planning, and the evolutionary response of pathogens to large scale vaccination programs. We discussed what the most urgent research questions that can be approached using mathematical modeling were and what modeling approaches and techniques might be needed.

Troy Day: Evolution in response to public health interventions

Troy discussed a few of the best-available examples of pathogen evolution in response to vaccination, and highlighted some of the unanswered empirical question involved. He then considered how one might model the evolutionary consequences of interventions more generally, both for endemic diseases and for newly emerging pathogens. This latter part focused on influenza, and highlighted many of the challenges, both from a modeling standpoint, and from the standpoint of connecting such models to data.

Zhilan Feng: Effects of antiviral use on epidemics of influenza and resistance

To explore influenza medication strategies (prophylaxis, post-exposure medication and treatment at successive clinical stages) that may affect evolution of resistance (select for resistant strains or facilitate their subsequent spread), Zhilan elaborated a published transmission model. Then she derived the reproduction numbers of sensitive and resistant strains, peak and final sizes, and time to peak. These analytical results permit her to a) deduce the consequences vis--vis resistance evolution of planned medication strategies and b) explore others that might better attain policy goals (i.e., without compromising the future effectiveness of anti-viral medications).

She described the published model briefly and our elaboration in detail, highlighting features that explain why important results differ. While reproduction numbers are very complex expressions in models with multiple infectious stages, she described hers intuitively. And then she demonstrated Mathematica notebooks that illustrate these and other analytical results. Before using those tools to explore the implications vis--vis control and resistance of various medication strategies, she wishes to consult subject matter experts and policymakers to ensure she has represented the biology correctly and understands the policy issues.

Gabriela Gomes (Variant surface antigen repertoires of *Plasmodium falciparum* shaped by within-host competition and between-host transmission)

Mirjam Kretzschmar: Effects of long term vaccination and adaptation of pathogens: the example of pertussis

Mirjam described a model of the Dutch hypothesis for the resurgence of pertussis throughout the developed world, but particularly in the Netherlands, namely selection by vaccination for strains against which the vaccine is ineffective.

Rongsong Liu: Control strategies in a two-strain influenza model

Rongsong considered optimal medication strategies (fraction treated, timing of treatment given a fixed amount of drugs) in a model with drug sensitive and resistant strains.

Jamie Lloyd-Smith: Challenges in modeling pathogen adaptation

In this talk, Jamie aimed to raise general questions about how to incorporate adaptive evolution into models of pathogen transmission dynamics, such as: “How should we think about ‘fitness landscapes’ for pathogens in the context of transmission models? “How can we cope with the multiple scales of pathogen fitness that are relevant? “What data do we need to construct, parameterize and validate these models?”

Dashun Xu: An age-structured influenza model with a resistant strain

Dashun derived the reproduction numbers of sensitive and resistant strains in an age-structured model with prophylaxis, post-exposure medication, and treatment, and considered the impact of medication timing on control and evolution of resistance.

10 Adapting modeling approaches to problems

Mac Hyman

Mac related an experience in which solving a practical public health problem required increasingly complex models. But he began with a simple model and added complexity only as indicated by comparison of predictions and observations. This was refreshing in view of the extremely complex and untested, if testable individual-based models used for problems that could be addressed via simpler models.

11 Game theory and applications to decision-making about health

Simon Levin: Games and more

Simon argued that theories of games and human behavior will play an increasing role in disease modeling. Tightening feedback via local control can enhance cooperation (and coexistence), or foster greed and selfish behavior. Social norms are needed to reinforce collectively beneficial human behavior vis-à-vis health-care, including in emergency situations. Health-care involves games between physicians, patients, hospitals, HMOs and insurers, pharmaceutical companies, and multiple social systems. There are n-player games (e.g., anti-biotic resistance, hospital size and prevalence of nosocomial infections) and public goods games (individuals acting in their self-interest without accounting for social costs).

Eun-ha Shim: Antiviral intervention during pandemic influenza

Eunha studied the optimal level of drug use from individual and community perspectives. As these differ, she investigated the possible role of individual perception. She found that people overestimate the risk of infection, underestimate the efficacy of antiviral drugs for prophylaxis and treatment, and overestimate the risk of developing resistance. These discrepancies can be reduced by education.

12 Immunoepidemiology (how disparate individual immune responses affect epidemiological patterns)

Jonathan Dushoff: Immuno-epidemiology and policy

Jonathan discussed epidemiological models (e.g., dose-response, partial immunity, and cross-immunity), thresholds for disease elimination, and the relationship between acquired immunity and tendency to oscillate. In conceptual modeling, we start with assumptions, construct formal models, and analyze them, possibly deriving insights (e.g., if sub-populations are relatively isolated and have high risks of infection, disease will be harder to eliminate unless we focus on most vulnerable populations). But we must interpret them biologically. If we cannot explain conceptual results in simple terms, we should mistrust our models. Can acquired immunity lead to backward bifurcations and, if so, what are the implications for malaria endemism and eradication? It depends on whether asymptomatic cases spread more or less than symptomatic ones. Does chemotherapy (which prevents development of immunity) change this? If so, on what time-scale might a changeover occur?

Christophe Fraser: Transmission of influenza in households during the 1918 pandemic

Christophe described several household models fitted to newly unearthed data from the 1918 pandemic in Maryland. Two striking features of the best fitting model are absence of asymptomatic infections and prior immunity (22%) decreased final attack rate from 60 to the observed 25%. Estimates of the infectiousness of influenza that do not account for prior immunity are too low. However, his analyses do not account for age or under-reporting.

Jamie Lloyd-Smith: The influence of heterogeneity in host immune competence on pathogen emergence

Hosts with weakened immune systems are often posited to act as stepping stones for pathogen emergence. Such hosts have increased susceptibility to infection and altered clinical courses of disease, often showing higher viral loads or prolonged infections. Jamie presented theoretical work exploring the influence of heterogeneous host immunocompetence on the evolutionary emergence of novel pathogens. He addressed the idea that immunocompromised hosts with prolonged infections can act as incubators for viral diversity, and discuss implications of these models for pathogen surveillance and control.

13 Policy needs (how modelers can assist in meeting institutional obligations)

Lance Rodewald (CDC)

Lance described some of the many opportunities for modeling in our routine work (e.g., strengthening ACIP recommendations, deciding how much vaccine to stockpile, assessing the economic value of public health programs, and the impact of school laws).

Diane Simpson (CDC)

Diane explored our obligations to various constituencies. Health authorities want help projecting the time-course of crises, identifying critical triggers and gates, and determining their need for resources and extraordinary authority. They may also want recommendations for allocating pharmaceuticals or implementing non-pharmaceutical interventions (e.g., quarantine, school closures, . . .). Political leaders want help understanding crises, determining their seriousness, deciding how to allocate resources, and if and when to request help or use extraordinary measures. Medical practitioners want to know how patient care will be affected and what prevention and treatment to recommend. The media want accurate and timely information and credible viewpoints (they might juxtapose to create controversy). The public wants to be kept informed about likely outbreak size, how fast it may spread and where resources are best located. They expect health authorities to

use those resources proactively. Likely challenges are competing modelers and other experts, and fixation on quantitative versus qualitative predictions (i.e., policymakers don't want confidence intervals).

Richard Hatchet (NIH)

This workshop is a model for how to engage policymakers. 1) Market and frame results. Some people can enjoy symphonies on paper, but most need to hear them played. 2) Engage and sustain relationships with policymakers, who will be interested in infectious disease dynamics insofar as insights are translated into possible actions. If you reach out (i.e., convince them that modeling can provide insights), they will listen. Offer diverse solutions to the problems confronting them. 3) Consider feasibility constraints, be an engineer versus scientist. The logistics may not be fascinating intellectually, but they are essential for the formulation of sound policy. The wind is in your sails.

Lara Wolfson (WHO): Modelers and modeling in global public health - present and future

Lara described models that have been used for various purposes at the WHO and some of the trade-offs between requirements of more complex models, the accuracy of readily available data, and the cost of better data, if indeed they could be collected. She also described why we need to learn to admit errors and to represent our results as educated guesses versus truth.