Correction

The editors note that four authors' names appeared incorrectly. Eric Lofgren should instead appear as Eric T. Lofgren, C. M. Rivers should instead appear as Caitlin M. Rivers, J. M. Drake should instead appear as John M. Drake, and M. C. Eisenberg should instead appear as Marisa C. Eisenberg.

The authors also note that affiliation [a] should instead appear as [a]Virginia Bioinformatics Institute, Virginia Tech, Blacksburg, VA 24061.

The authors also note that two affiliations should be listed for M. Elizabeth Halloran. The affiliations should be Department of Biostatistics and Fred Hutchinson Cancer Research Center, University of Washington.

The corrected author and affiliation lines appear below. The online version has been corrected.

Eric T. Lofgren[a,1], M. Elizabeth Halloran[b], Caitlin M. Rivers[a], John M. Drake[c], Travis C. Porco[d], Bryan Lewis[a], Wan Yang[e], Alessandro Vespignani[f], Jeffrey Shaman[e], Joseph N. S. Eisenberg[g], Marisa C. Eisenberg[g], Madhav Marathe[a,h], Samuel V. Scarpino[i], Kathleen A. Alexander[j], Rafael Meza[g], Matthew J. Ferrari[k], James M. Hyman[l], Lauren A. Meyers[m], and Stephen Eubank[a]

[h]Department of Computer Science, [j]Department of Fish and Wildlife Conservation, [a]Virginia Bioinformatics Institute, Virginia Tech, Blacksburg, VA 24061; [b]Department of Biostatistics and Fred Hutchinson Cancer Research Center, University of Washington, Seattle, WA 98195; [c]Odum School of Ecology, University of Georgia, Athens, GA 30602; [d]Francis I. Proctor Foundation, University of California, San Francisco, CA 94143; [e]Department of Environmental Health Sciences, Mailman School of Public Health, Columbia University, New York, NY 10032; [f]Department of Physics, Northeastern University, Boston, MA 02115; [g]Department of Epidemiology, University of Michigan, Ann Arbor, MI 48109; [i]Santa Fe Institute, Santa Fe, NM 87501; [k]Department of Biology, Pennsylvania State University, University Park, PA 16802; [l]Department of Mathematics, Tulane University, New Orleans, LA 70118; and [m]Department of Integrative Biology, The University of Texas at Austin, Austin, TX 78712

OPINION

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Opinion: Mathematical models: A key tool for outbreak response

Eric T. Lofgren[a,1], M. Elizabeth Halloran[b], Caitlin M. Rivers[a], John M. Drake[c], Travis C. Porco[d], Bryan Lewis[a], Wan Yang[e], Alessandro Vespignani[f], Jeffrey Shaman[e], Joseph N. S. Eisenberg[g], Marisa C. Eisenberg[g], Madhav Marathe[a,h], Samuel V. Scarpino[i], Kathleen A. Alexander[j], Rafael Meza[g], Matthew J. Ferrari[k], James M. Hyman[l], Lauren A. Meyers[m], and Stephen Eubank[a]

[h]Department of Computer Science, [i]Department of Fish and Wildlife Conservation, [a]Virginia Bioinformatics Institute, Virginia Tech, Blacksburg, VA 24061; [b]Department of Biostatistics and Fred Hutchinson Cancer Research Center, University of Washington, Seattle, WA 98195; [c]Odum School of Ecology, University of Georgia, Athens, GA 30602; [d]Francis I. Proctor Foundation, University of California, San Francisco, CA 94143; [e]Department of Environmental Health Sciences, Mailman School of Public Health, Columbia University, New York, NY 10032; [f]Department of Physics, Northeastern University, Boston, MA 02115; [g]Department of Epidemiology, University of Michigan, Ann Arbor, MI 48109; [i]Santa Fe Institute, Santa Fe, NM 87501; [k]Department of Biology, Pennsylvania State University, University Park, PA 16802; [l]Department of Mathematics, Tulane University, New Orleans, LA 70118; and [m]Department of Integrative Biology, The University of Texas at Austin, Austin, TX 78712

The 2014 outbreak of Ebola in West Africa is unprecedented in its size and geographic range, and demands swift, effective action from the international community. Understanding the dynamics and spread of Ebola is critical for directing interventions and extinguishing the epidemic; however, observational studies of local conditions have been incomplete and limited by the urgent need to direct resources to patient care.

Mathematical and computational models can help address this deficiency through work with sparse observations, inference on missing data, and incorporation of the latest information. These models can clarify how the disease is spreading and provide timely guidance to policymakers. However, the use of models in public health often meets resistance (1), from doubts in peer review about the utility of such analyses to public skepticism that models can contribute when the means to control an epidemic are already known (2). Even when they are discussed in a positive light, models are often portrayed as arcane and largely inaccessible thought experiments (3). However, the role of models is crucial: they can be used to quantify the effect of mitigation efforts, provide guidance on the scale of interventions required to achieve containment, and identify factors that fundamentally influence the course of an outbreak.

Situational Awareness, Intervention Planning, and Projections

During the 2014 Ebola outbreak, governments and nongovernment organizations have used models to forecast the size of the epidemic (4–8) and to predict the risk of importation of cases from Africa (7), an area of increasing concern. Model forecasts have been used heavily to communicate the severity of the epidemic if left unchecked (4–8). As with all forecasts, there are qualifications associated with such predictions. Precisely because they can be used to quantify the severity of a situation to policymakers, models early in the epidemic may predict a more severe epidemic than comes to pass not because they are wrong, but because they helped prompt a strong response. Despite the limitations inherent to forecasting a social system, formal models benefit from explicitly laying out their assumptions and invite users to examine and even alter them.

Models can also be used to explore areas of uncertainty in the epidemic. They can examine parameters where there is disagreement about a particular value or a range of

A woman has her temperature taken at the October Canton Fair in Guangdong province in China, a front line in preventing the Ebola virus from entering the country. Image courtesy of Shutterstock/plavevski.

possible values (5). By comparing different models (4–8) to uncover the source of their disagreement, modelers can work with decision makers and public health professionals to identify key data that are critical to resolving these differences and solidifying our understanding of the epidemic. Stochastic models can incorporate uncertainty caused by chance and statistical variation (6, 7), resulting in a range of projections for epidemic progression that presents policymakers with optimistic and pessimistic scenarios. Appropriate responses to previous outbreaks, such as the A/H1N1 influenza outbreak, have benefitted from ensembles of potential scenarios to consider (9–11). These two types of uncertainty, one that may be improved by more information and one that is inherent to the system, are both important and both capable of being explored using modeling (12).

The forecasts that models provide are valuable not only for quantifying how an epidemic might spread if left unchecked, but also in evaluating the effectiveness of interventions. These forcasts provide a baseline for measuring success against, and may quantify how effective an intervention need be to achieve containment. The most basic of these analyses is the estimation of the effective reproductive number (R_E), which is the number of secondary cases caused by each current case. If R_E falls below one following an intervention, this indicates that the disease lacks further epidemic potential and the incidence should decrease in time. Models may also examine practical logistical questions, such as travel bans or the placement of new treatment centers that are not easily addressed by other study designs.

Epidemiological Explanations

Beyond asking, "How many and for how long?" policymakers are asking, "Why here and now?" Prior Ebola outbreaks have been geographically confined to Central Africa, occurred mainly in small rural communities, and have been relatively small. Why has this outbreak emerged in Western Africa, in urban settings, and why has it spread unchecked?

Model-based risk assessment of emerging pathogens can assess the potential for a major epidemic, even in the absence of prior outbreaks. In the case of Ebola, models analyzing data from previous outbreaks (13) showed the disease had the potential for epidemic spread, and parameters from earlier outbreaks have been found to be capable of generating larger outbreaks in simulation (14). This finding suggests both that there

may not be anything inherently different about this Ebola outbreak, and that emerging diseases should be considered for their epidemic potential, even in the absence of historical precedent.

The use of models for this sort of deductive reasoning is in contrast to the inductive approach traditionally used in epidemiology. The analysis of an outbreak begins with a causal argument (the model itself), which is checked against observed data to see if it is capable of producing the observed results. Of course, consistency of the observed data with the model does not imply that the model is correct but it does provide the context for a structured discussion of potential transmission mechanisms. The ability of model predictions to be tested—and falsified—lies at the heart of science (15).

Models as Structured Reasoning

Models provide a means of incorporating data from diverse sources to create a coherent picture of disease dynamics. Some of this information is familiar to epidemiologists: transmission chains, genomic data, or the geographical and temporal distribution of cases. However, the data required extends well beyond the traditional domain of epidemiology and public health. Cultural practices, social networks, formal and informal transportation networks (16), and the interface between human and animal populations may all prove essential to fully understand the epidemic.

It is this aspect of models, where implicit assumptions are made explicit and gaps in knowledge brought to light, that provides the

greatest opportunity for strengthening partnerships among modelers, policymakers, and public health workers. Models show what remains unknown, revealing targets for future empirical research. This research, in turn, improves the models. Finally, models allow for exploration of counterfactual scenarios; they provide a record of "what might have been," allowing public health authorities to guard against accusations of either not taking an epidemic seriously (when interventions fail to contain the epidemic) or reacting too strongly (when successful interventions readily bring the epidemic under control).

Models of infectious disease spread are important, not despite our lack of data, but precisely because of our lack of data; they are powerful tools to control infectious diseases as they emerge and to prepare for the future. For models to reach their potential, modelers, those on the ground, and policymakers must work in partnership to ensure that models are answering policy-relevant questions and that the data necessary to do so is accessible. Initiatives that encourage and facilitate these partnerships—for example, the National Institutes of Health/National Institute of General Medical Sciences Models of Infectious Disease Agent Study program—must be strengthened and supported so that disease outbreak models work as a tool that helps save lives.

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