GOING VIRAL: MODELING EBOLA

In the midst of the Ebola epidemic, modelers tried to predict its spread, with some success. Now they’re reflecting on the lessons learned.

The worst case scenarios were frightening: At the peak of the West African Ebola epidemic of 2014, estimates of the potential death toll ranged from several hundred thousand to more than a million. Experts believe that those dire predictions spurred the international response that helped limit the death toll to fewer than 12,000 to date.

In fact, the estimates themselves were the result of an international response by computational epidemiologists who swung into action as Ebola surged across Guinea, Liberia, and Sierra Leone. Even their simpler models showed that the initial Ebola outbreak wasn’t winding down as expected. Other increasingly complex models predicted how the disease might spread, forecast the number of cases that could arise, and simulated possible interventions to help policy makers and public health officials respond effectively to the crisis.

In the end, the models tended to be most reliable when they were used to look two to three weeks ahead. Over longer time spans (e.g., two to three months), the accuracy of the models (with a few exceptions) declined precipitously. This was a good thing for humanity, as the huge death tolls the models foretold were thankfully averted—partly because of policymakers’ responses to the modelers’ nightmare scenarios, and partly because of gradual changes in the behavior of people on the ground in Africa.

Today, the same modelers are still sorting out exactly what brought the epidemic to a halt, in hopes of developing strategies for the future. In that sense, they learned from the epidemic—most notably, that it is difficult to build accurate, well-fed models when human behavior is a key parameter, the situation on the ground is messy, and information is hard to come by. “It’s a challenge to model behavior,” says Madhav Marathe, PhD, director of the Network Dynamics and Simulation Science Laboratory in the Biocomplexity Institute at Virginia Tech. “It’s an even bigger challenge to model it in a place where it is very hard to get data.”

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Ebola’s Surprising Virulence

Epidemiologist David Fisman, MD, MPH, at the University of Toronto, initially assumed that the first outbreak in Guinea would swiftly peter out, as Ebola incidents have in the past. When it didn’t, he employed a mathematical model that he first developed for SARS to illustrate just how quickly the disease appeared to be spreading.

Fisman’s model, called IDEA (for Incidence Decay and Exponential
Adjustment), was inspired by financial models that use a so-called discount factor to compensate for the decline in value of money over time. A similar discount factor can be used to predict the course of epidemics, which typically show rapid initial growth followed by similarly rapid decline. When Fisman fit IDEA to the case counts coming out of West Africa, however, he saw what looked like exponential growth tempered by a disturbingly tiny discount factor.

The good news was that Fisman’s analysis, which appeared in *PLoS Current Outbreaks* in September 2014, indicated that even a small increase in the discount factor could save tens of thousands of lives. The bad news was that because the model was so simple, it couldn’t reveal much about what was driving the epidemic—or what steps might stop it.

Other researchers, however, were using more complex models to generate those kinds of insights.

### Gauging Interventions

At Yale University, a group led by Alison Galvani, PhD, director of the Center for Infectious Disease Modeling and Analysis (CIDMA), focused on producing forecasts that could provide timely guidance to international policy makers and local authorities. But they did not have much data to work with, says Ndeffo, who co-authored several papers describing the team’s efforts. So they began with a model based on differential equations that could be run relatively quickly with limited parameters.

The model allowed individuals to move from one epidemiological category (e.g., susceptible, exposed, infectious, recovered) to another as they interacted in various settings, including hospitals and funerals—both hotspots for Ebola transmission. According to Abhishek Pandey, PhD, postdoctoral associate in epidemiology at Yale University, the model also used probabilistic methods to mimic the uncertainty in the numbers of people who might move from one category or setting to another.

The team used this stochastic model to gauge the potential impact of various interventions, from building more treatment units to distributing personal protective kits and performing sanitary burials. The takeaway was clear: combining more than one response would be far more helpful than just focusing on any single one, no matter how effective it was. (Using a different model that drew on previous efforts to simulate HIV and influenza transmission, Ndeffo and Dan Yamin, PhD, also predicted that treating the most severely ill patients within five days of showing symptoms would do the most to halt the spread of the disease—a result that jibed well with what health workers were finding on the ground.) But individual findings were sometimes counterintuitive, like the prediction that distributing protective gear would only have a significant effect once treatment centers were already at capacity. “That was a bit surprising,” says Ndeffo, adding that it was “the kind of insight you could only get from a model.”

### Networked Epidemiology

Marathe and his colleagues also began modeling the initial outbreak using differential equations. By October 2014, however, they had shifted gears and developed a multiscale agent-based model to predict the course of what had become a full-blown epidemic.

Building such a model involved what Marathe calls “networked epidemiology.” First, Marathe and his team used census data to create synthetic populations that were statistically equivalent to the actual populations of the affected West African

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In a paper published in *Science* in October 2014, Ndeffo and Galvani compared the effectiveness of various intervention strategies used alone or in combination (graph), and calculated the daily number of new and cumulative cases after 6 months (bar chart) if the following interventions were to be implemented alone or in combination: sanitary burial of hospital deaths, sanitary burial of community deaths, case isolation of hospitalized patients, contact-tracing in the community, and quarantine of infected contacts.

countries. They then linked the individuals in those populations through virtual social networks, allowing them to interact through work, school, and household activities, and to mingle at home, in hospitals, and at funerals. And they used probabilistic methods to inject a realistic element of chance into nearly every aspect of their simulations, from how individuals moved about to how the disease itself progressed (incubation period, time to death, etc.).

The researchers used this stochastic agent-based model to create risk-profiles for other countries in West Africa that might be hit next; to determine which interventions (better contact tracing, new drug therapies) might have the greatest effect; and even to gauge what might happen if Ebola spread to the United States. Like the Yale group, the Virginia Tech team found that a combination of responses worked best. But they also found that even a successful drug intervention wouldn’t do much to curb the epidemic.

**Global Predictions**

Marathe’s friend Alessandro Vespignani, PhD, director of the Laboratory for the Modeling of Biological and Socio-Technical Systems (MOBS-Lab) at Northeastern University, also took a network-based approach to modeling the epidemic. But in his case, Vespignani used a multiscale modeling platform called GLEaM (Global Epidemic and Mobility Model) to predict how Ebola might spread across the globe.

Together with an international team of collaborators, Vespignani integrated an agent-based model of Ebola transmission with two other models: a global population model spanning 220 countries and thousands of subpopulations distributed around the world, and a so-called mobility model that allowed those populations to mix through short-range commuting patterns and long-range air travel. “We talk about individuals and geography,” Vespignani says. “But underlying all of that are large network models with people traveling from one point to another.”

By simulating the number of passengers traveling daily on each airline connection in the world, Vespignani and his colleagues were able to rank which countries were most at risk of importing Ebola. Their findings were eerily accurate: two of the top three at-risk countries—the United Kingdom and Nigeria—saw cases in 2014.

In addition to sharing data and methods amongst themselves, a number of modeling teams are now also working together to develop better tools for gathering such behavioral information—all in hopes of being ready for action when the next outbreak occurs. “As we learn from each other,” Marathe says, “the models will become even more useful.”