Modelers Struggle to Predict the Future of the COVID-19 Pandemic

Disease experts have largely focused on how we got to where we are now with coronavirus infections. Improved data collection and sharing can enhance projections of what's to come.

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While politicians and the public obsess about how and when the coronavirus pandemic will peak, the scientists able to make such projections are struggling to get a grip on what's happening right now. "Sorry, not doing any interviews at the moment so that we can fully focus on our local and regional response," one leading US epidemiologist wrote in an email when contacted by *The Scientist*.

Like any other models, the projections of how the outbreak will unfold, how many people will become infected, and how many will die, are only as reliable as the scientific information they rest on. And most modelers' efforts so far have focused on improving these data, rather than making premature predictions.

"Most of the work that modelers have done recently or in the first part of the epidemic hasn't really been coming up with models and predictions, which is I think how most people think of it," says John Edmunds, who works in the Centre for the Mathematical Modelling of Infectious Diseases at the London School of Hygiene & Tropical Medicine. "Most of the work has really been around characterizing the epidemiology, trying to estimate key parameters. I don't really class that as modeling but it tends to be the modelers that do it."

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> —Maciej Boni, Penn State University

These variables include key numbers such as the disease incubation period {between 5.2 and 5.5 days}, how quickly the virus spreads through the population {latent period: perhaps 10-33 days}, and, perhaps most contentiously, the case-fatality ratio {about 1.6%}. This sounds simple: it's the proportion of infected people who die. But working it out is much trickier than it looks. "The non-specialists do this all the time and they always get it wrong," Edmunds says. "If you just divide the total numbers of deaths by the total numbers of cases, you're going to get the wrong answer."

Earlier this month, Tedros Adhanom Ghebreyesus, the head of the World Health Organization, dismayed disease modelers when he said COVID-19 (the disease caused by the SARS-CoV-2 coronavirus) had killed 3.4 percent of reported cases, and that this was more severe than seasonal flu, which has a death rate of around 0.1 percent. Such a simple calculation does not account for the two to three weeks it usually takes someone who catches the virus to die, for example {the difference between incidence and prevalence}. And it assumes that reported cases are an accurate reflection of how many people are infected, when the true number will be much higher and the true mortality rate much lower. {The inflated numerator vs suppressed denominator problem.}

Edmunds calls this kind of work "outbreak analytics" rather than true modeling, and he says the results of various specialist groups around the world are starting to converge on COVID-19's true case-fatality ratio, which seems to be about 1 percent. {But this has a large variance based on population groups: young, middle aged, old, more than 3 comorbidities, viral load at time of exposure, etc.}

Once such numbers are pinned down, then modelers can move onto what's called "situational awareness," Edmunds explains. Much of that work looks backward, asking how many cases there might have been in a specific location a few weeks ago and using that information to work out how it could have spread since.

Deaths are the most useful data points for these analyses. For example, if modelers assume a case-fatality ratio of 1 percent, and that it usually takes 15 days for an infected person to die, then they know a death reported today in a specific region means that 100 people were likely infected there 15 days ago. Add in the time it takes cases to double—Edmunds says it seems to take five days—then modelers can estimate that over those 15 days the number of cases swelled to 800. So, for every death in a region, that means about 800 others are already infected, {Take equation $N(t) = 0.87 \exp(0.14t)$ and if No=100 cases, on day N16 you have 800 cases;

therefore 1 death in 800 cases.} most of whom will not have been identified. This pattern was verified in Italy, Edmunds says, which as of today has reported 12,462 cases and 827 deaths. When officials tested people living near where someone had died from the disease, in many cases they found hundreds of others were already carrying the virus.

Maciej Boni, a biologist at Penn State University who has studied the spread of influenza in the tropics, says this high number of undetected cases means the spread of the virus can't be tracked from the numbers of confirmed infections. "At this point, the spread is a moot point," says Boni. "We can slow it down by canceling all these events, which we completely should do. But it's still going to spread to most places."

Left unchecked, infectious outbreaks typically plateau and then start to decline when the disease runs out of available hosts. But it's almost impossible to make any sensible projection right now about when that will be, Boni says, or about how many people will ultimately be affected. Modelers can try, but to do so they need much better information, such as how many people infected show natural immunity.

Most of these forward-looking "scenario planning" models currently assume everyone on the planet is susceptible, Edmunds says. Only better surveillance and data, in particular, from serum tests that would indicate whether people have been exposed to the virus whether or not they developed symptoms, will make those calculations more realistic. "At the moment, we've got no data to tie that model down. But as the epidemic proceeds and every time more data comes out, like every day or every week, we refit the model and then we redo our projections."

To build better models, some disease experts argue that the world needs to improve the way such data are handled and made available. In an editorial published this week in Science Translational Medicine, Scott Layne, an epidemiologist at the University of California, Los Angeles, School of Public Health, and his colleagues propose a new data bank be created in which researchers can share results on, for example, how much virus is shed by infected people and when that starts.

"We're all in the process of collecting that information. What this effort would do is, as that data comes in, it would point to it and help to organize it," Layne tells The Scientist.

Backed by better information, models could help determine policies to control spread, he adds. "If those models do have any validity, then you can perturb them or pressure test them against various sorts of interventions, whether it's making people move less or cutting down contact by a certain percentage."

According to Reuters, Chinese officials say the restrictions on travel they put in place have pushed the epidemic to peak in China. {The Chinese data is suspect based on recent news that their initial mortality rates were 100 times deflated. It is better to look at data from South Korea, an open society that has taken draconian measures to stem the spread of the virus.} Zhong Nanshan, the Chinese government's senior medical adviser, claimed at a press conference this week that if other nations follow China's lead, then the pandemic could be tamed within months. "My advice is calling for all countries to follow WHO instructions and intervene on a national scale," he says. "If all countries could get mobilized, it could be over by June."

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