PANDEMIC Qs

Fauci's straight talk

To many watching the White House press briefings on the coronavirus pandemic, veteran public health expert Anthony Fauci has become the voice of science and reason on how the country should respond. He made national news this week for his careful but candid assessment to *Science*'s Jon Cohen of the challenges of working for President Donald Trump during the crisis. "When you're dealing with the White House, sometimes you have to say things one, two, three, four times, and then it happens. So, I'm going to keep pushing," says Fauci, longtime director of the National Institute of Allergy and Infectious Diseases. His full interview is at https://scim.ag/QAFauci.

Q: The first question everyone has is how are you?
A: Well, I'm sort of exhausted. But other than that, I'm good. I mean, I'm not, to my knowledge, coronavirus infected. To my knowledge, I haven't been fired [laughs].

Q: How are you managing to not get fired?
A: To [Trump's] credit, even though we disagree on some things, he listens. He goes his own way. He has his own style. But on substantive issues, he does listen to what I say.

Q: You've been in press conferences where things are happening that you disagree with, is that fair to say?
A: Well, I don't disagree in the substance. It is expressed in a way that I would not express it, because it could lead to some misunderstanding about what the facts are about a given subject.

Q: You're standing there saying nobody should gather with more than 10 people and there are almost 10 people on the stage [and] more than 10 journalists.
A: I know that. I'm trying my best. I cannot do the impossible.

Q: We've had all this pandemic preparedness. What went wrong?
A: I think we'll have to wait until it is over and we look back before we can answer that. It's almost like the fog of war. After the war is over, you then look back and say, "Wow, this plan, as great as it was, didn't quite work once they started throwing hand grenades at us." Obviously, testing [for the new coronavirus] is one clear issue that needs to be relooked at. Why were we not able to mobilize on a broader scale? But I don't think we can do that right now. I think it's premature. We really need to look forward. ■

Dutch models of COVID-19 are designed to help prevent overloading of hospitals and the need to transfer patients.

CORONAVIRUS

With COVID-19, modeling takes on life and death importance

Epidemic simulations shape national responses

By **Martin Enserink** and **Kai Kupferschmidt**

Jacco Wallinga's computer simulations are about to face a high-stakes reality check. Wallinga is a mathematician and the chief epidemic modeler at the National Institute for Public Health and the Environment (RIVM), which is advising the Dutch government on what actions, such as closing schools and businesses, will help control the spread of the novel coronavirus in the country.

The Netherlands has so far chosen a softer set of measures than most Western European countries; it was late to close its schools and restaurants and hasn't ordered a full lockdown. In a 17 March speech, Prime Minister Mark Rutte rejected "working endlessly to contain the virus" and "shutting down the country completely." Instead, he opted for "controlled spread" of the virus while making sure the health system isn't swamped with COVID-19 patients. He called on the public to respect RIVM's expertise on how to thread that needle. Wallinga's models predict that the number of infected people needing hospitalization, his most important metric, will taper off next week. But if the models are wrong, the demand for intensive care beds could outstrip supply, as it has, tragically, in Italy and Spain.

COVID-19 isn't the first infectious disease scientists have modeled—Ebola and Zika are recent examples—but never has so much depended on their work. Entire cities and countries have been locked down based on hastily done forecasts that often haven't been peer reviewed. "It's a huge responsibility," says epidemiologist Caitlin Rivers of the Johns Hopkins University Center for Health Security, who co-authored a report about the future of outbreak modeling in the United States that her center released this week.

Just how influential those models are became apparent over the past 2 weeks in the United Kingdom. Based partly on modeling work by a group at Imperial College London, the U.K. government at first implemented fewer measures than many other countries—not unlike the strategy the Netherlands is pursuing. Citywide lockdowns and school closures, as China initially mandated, "would result in a large second epidemic once measures were lifted," a group of modelers that advises the government concluded in a statement. Less severe controls would still reduce the epidemic's peak and make any rebound less severe, they predicted.

But on 16 March, the Imperial College group published a dramatically revised model that concluded—based on fresh data from the United Kingdom and Italy—that even a reduced peak would fill twice as many intensive care beds as estimated previously, overwhelming capacity. The only choice, they concluded, was to go all out on control measures. At best, strict measures might be periodically eased for short periods, the group said (see graphic, below). The U.K. government shifted course within days and announced a strict lockdown.

It's not that the science behind epidemic modeling is controversial. Wallinga uses a well-established model that divides the Dutch population into four groups, or compartments in the field's lingo: healthy, sick, recovered, or dead. Equations determine how many people move between compartments as weeks and months pass. "The mathematical side is pretty textbook," he says. But model outcomes vary widely depending on the characteristics of a pathogen and the affected population.

Because the virus that causes COVID-19 is new, modelers need estimates for key model parameters. Wallinga is now confident that the number of new infections caused by each infected person when no control measures are taken—which epidemiologists call R_0—is just over two. And he trusts data showing that 3 to 6 days elapse between the moment someone is infected and the time they start to infect others.

From a 2017 survey of the Dutch population, the RIVM team also has good estimates of how many contacts people of different ages have at home, school, work, and during leisure. Wallinga says he's least confident about the susceptibility of each age group to infection and the rate at which people of various ages transmit the virus.

Compartment models assume the population is homogeneously mixed, a reasonable assumption for a small country like the Netherlands. Other modeling groups don't use compartments but simulate the day-to-day interactions of millions of individuals. Such models are better able to depict heterogeneous countries, such as the United States, or all of Europe. The World Health Organization organizes regular calls for COVID-19 modelers to compare strategies and outcomes, Wallinga says: "That's a huge help in reducing discrepancies between the models that policymakers find difficult to handle."

In their review of U.S. outbreak modeling, Rivers and her colleagues note that most of the key players are academics with little role in policy. They don't typically "participate in the decision-making processes … they sort of pivot into a new world when an emergency hits," she says. Rivers argues for the creation of a National Infectious Disease Forecasting Center, akin to the National Weather Service. It would be the primary source of models in a crisis and strengthen outbreak science in "peacetime."

Policymakers have relied too heavily on COVID-19 models, says Devi Sridhar, a global health expert at the University of Edinburgh. "I'm not really sure whether the theoretical models will play out in real life." And it's dangerous for politicians to trust models that claim to show how a little-studied virus can be kept in check, says Harvard University epidemiologist William Hanage. "It's like, you've decided you've got to ride a tiger," he says, "except you don't know where the tiger is, how big it is, or how many tigers there actually are."

Models are at their most useful when they identify something that is not obvious, says Adam Kucharski, a modeler at the London School of Hygiene & Tropical Medicine. One valuable function, he says, was to flag that temperature screening at airports will miss most coronavirus-infected people.

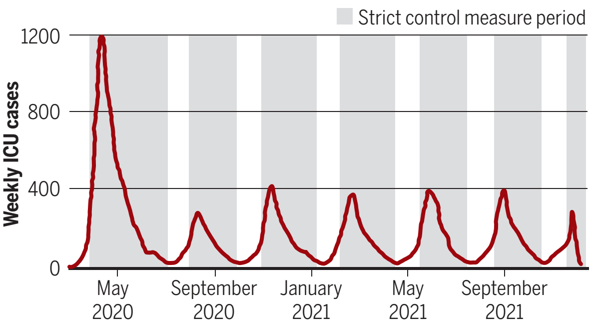
There's also a lot that models don't capture. They cannot anticipate, say, an effective antiviral that reduces the need for hospital beds. Nor do most models factor in the anguish of social distancing, or whether the public obeys orders to stay home. In Hong Kong and Singapore, "It's 2 months already [of such measures], and people are really getting very tired," says University of Hong Kong modeler Gabriel Leung. Recent data suggest the virus may be spreading faster again in both cities, putting them on the brink of a major outbreak, he adds.

Long lockdowns to slow a disease have catastrophic economic impacts and may devastate public health themselves. "It's a three-way tussle," Leung says, "between protecting health, protecting the economy, and protecting people's well-being and emotional health."

The economic fallout isn't something epidemic models address, says Ira Longini, a modeler at the University of Florida—but that may have to change. "We should probably hook up with some economic modelers and try to factor that in," he says. ■

Modeling a bleak future

U.K. control measures could be let up once in a while, a model suggests, until demand for intensive care unit (ICU) beds hits a threshold.



GRAPHIC: IMPERIAL COLLEGE COVID-19 RESPONSE TEAM, ADAPTED BY C. BICKEL/SCIENCE

TOXICOLOGY

New mercury compound spotted in mass poisoning

Chemical found in 60-year-old cat brain reopens debate over Minamata disaster

By **Joshua Sokol**

The city of Minamata, Japan, is dotted with monuments commemorating victims of an industrial mass poisoning decades ago. High in the hills, a small stone memorial honors other deaths—of cats sacrificed in secret to science. Now, after restudying the remains of one of those cats, a team of scientists is arguing, controversially, that the long-standing explanation for the tragedy is wrong.

No one questions the root cause of the disaster, which at minimum poisoned more than 2000 people: mercury in a chemical factory's wastewater that was dumped into Minamata Bay and taken up by seafood eaten by fishermen and their families. At first, the chemical form of the mercury, which ultimately killed many of its victims and left many babies with severe neurological disorders, was unknown. But in 1968, the Japanese government blamed methylmercury, a common byproduct of mercury pollution. Many studies supported that conclusion, finding methylmercury spikes in shellfish, bay sludge, and even hundreds of umbilical cords from babies delivered during the time. But methylmercury is not the culprit, says Ingrid Pickering, an x-ray spectroscopist at the University of Saskatchewan. "Our work is indicating that it's something else": an unusual mercury compound that may say little about the broader threat of mercury pollution.

Minamata has long been a vivid case study of mercury's dangers. The metal is toxic on its own, but it becomes far more dangerous when bacteria in natural environments convert it into methylmercury, an organic compound, readily absorbed by living tissues, that can be concentrated and passed up food chains. Since the 1990s, scientists have argued that the Chisso chemical factory in Minamata produced

Science

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