



A priest in Innsbruck, Austria, views photographs of his absent congregation. Austria eased social distancing on 14 April.

IN DEPTH

COVID-19

The lockdowns worked—but what comes next?

Easing the rules while keeping the virus at bay will be a process of trial and error

By Kai Kupferschmidt

The world is holding its breath.

After the novel coronavirus made its way around the world, one country after another adopted harsh measures to stop SARS-CoV-2 from spreading and overwhelming hospitals. They have hit the pause button on their economies and their citizens' lives, stopping sports events, religious services, and other social gatherings. School closures in 188 countries affect more than 1.5 billion students. Borders are closed and businesses shuttered. While some countries are still seeing daily case numbers increase, others—first in Asia but increasingly in Europe—have managed to bend the curve, slowing transmission of COVID-19.

But what is the exit strategy? “We’ve managed to get to the life raft,” says epidemiologist Marc Lipsitch of the Harvard T.H. Chan School of Public Health (HSPH). “But I’m really unclear how we will get to the shore.”

As they seek a path forward, governments around the world must triangulate the health of their citizens, the freedoms of their population, and economic constraints. Could schools be reopened? Restaurants? Bars? Can people go back to their offices? “How to relax the lockdown is not something around which there is a scientific consensus,” says Caroline Buckee, an epidemiologist at HSPH. Most researchers agree that reopening society will be a long haul, marked by trial and

error. “It’s going to have to be something that we’re going to have to take baby steps with,” says Megan Coffee, an infectious disease researcher at New York University.

The number to watch in the next phase may no longer be the actual number of cases per day, but what epidemiologists call the effective reproduction number, or R , which denotes how many people the average infected person infects in turn. If R is above 1, the outbreak grows; below 1 it shrinks. The goal of the current lockdowns is to push R well below 1. Once the pandemic is tamed, countries can try to loosen restrictions while keeping R hovering around 1, when each infected person on average infects one other person, keeping the number of new cases steady.

To regulate R , “Governments will have to realize that there are basically three control knobs on the dashboard,” says Gabriel Leung, a modeler at the University of Hong Kong: isolating patients and tracing their contacts, border restrictions, and social distancing.

TURNING THE KNOBS

Singapore, Hong Kong, and South Korea have all managed to keep their epidemics in check through aggressive use of the first control. They identify and isolate cases early and trace and quarantine their contacts, while often imposing only light restrictions on the rest of society. But this strategy depends

on massively scaling up testing, which has been hampered by a scarcity of reagents and other materials everywhere. Contact tracing is also labor-intensive. Massachusetts is hiring 500 contact tracers, but a recent report by researchers at Johns Hopkins University estimated the United States as a whole needs to train about 100,000 people.

Mobile phone apps could help by automatically identifying or alerting people who recently had contact with an infected person. But Western countries have yet to implement these systems. Google and Apple have teamed up to incorporate a contact tracing app in their operating systems. Germany, France, and other countries are developing apps based on a protocol called Pan-European Privacy Preserving Proximity Tracing. It relies on short-range Bluetooth signals to gauge the proximity between two devices without logging their exact locations, which helps sidestep some privacy concerns.

But short of making these technologies compulsory, as China has done, how can a country ensure that enough people download an app for it to provide reliable information and influence the spread of disease? And what exactly counts as a contact? “If I live in a big apartment block, am I going to be getting dozens of notifications a day?” asks epidemiologist Nicholas Davies of the London School of Hygiene & Tropical Medicine (LSHTM).

Science’s COVID-19 coverage is supported by the Pulitzer Center.

Davies adds that widespread use of the apps will further drive up the demand for testing.

As to the second control knob, border restrictions, most countries have already banned entry to almost all noncitizens. Quarantining returning citizens, as New Zealand and Australia began to do in the past few weeks, further minimizes the risk of new introductions of the virus. Such measures are likely to remain in place for a while; the more a country reduces transmission domestically, the greater the risk that any new outbreaks will originate with travelers. And foreign visitors are generally harder to trace than citizens and more likely to stay at hotels and visit potential transmission hot spots, says Alessandro Vespignani, a disease modeler at Northeastern University. "As soon as you reopen to travelers, that could be something that the contact tracing system is not able to cope with," he says.

The third dashboard dial, social distancing, is the backbone of the current strategy, which has slowed the spread of the virus. But it also comes at the greatest economic and social cost, and many countries hope the constraints can be relaxed as case isolation and contact tracing help keep the virus in check. In Europe, Austria took the lead by opening small shops on 14 April. Other stores and malls are scheduled to follow on 1 May, and restaurants maybe a few weeks later. A 13 April report from the German National Academy of Sciences argued for slowly reopening schools, starting with the youngest children, while staggering break times and making masks mandatory. But French President Emmanuel Macron has said France's lockdown will remain in place until 11 May.

Choosing a prudent path is difficult, Buckee says, in part because no controlled experiments have compared the effectiveness of different social distancing measures. "Because we don't have really strong evidence," she says, "it's quite hard to make evidence-based policy decisions about how to go back." But Lipsitch says that as authorities around the world choose different paths forward, comparisons could be revealing. "I think there's going to be a lot of experimentation, not on purpose, but because of politics and local situations," he says. "Hopefully the world will learn from that."

Finding out how any particular measure affects R is not straightforward, because infections that occur today can take weeks to show up in disease reports. In 2004, mathematician Jacco Wallinga of the Dutch National

Institute for Public Health and the Environment and colleagues published a statistical method to estimate R in real time, which is now used around the world. Researchers are also incorporating data on mobility patterns and people's behavior to make the estimates more accurate. Having real-time estimates of R is important, says Adam Kucharski, a modeler at LSHTM: "If governments put a measure in or lift it, they can get a sense of what the immediate implications are, rather than having to wait," he says.

There's one other, unknown factor that will determine how safe it is to loosen the reins: immunity. Every single person who becomes infected and develops immunity makes it harder for the virus to spread. "If we get 30% or 40% of the population immune, that really starts to change that whole picture, it helps us a lot," because it would

bring R down by the same percentage, says Michael Osterholm, director of the Center for Infectious Disease Research and Policy at the University of Minnesota, Twin Cities.

Immunity will inevitably build up as more people become infected, but some researchers argue for ramping up immunity more quickly, by letting the virus spread in younger people, who are less susceptible to severe illness, while "cocooning" more at-risk patients, such as the elderly. The United Kingdom floated this "herd immunity" idea in February but backed away from it, as did the Netherlands. Some scientists say other countries should consider it once the strain that the first wave of cases has put on their health care systems eases. "Is it better to have a controlled burn in younger populations right now than it is to prevent it? I think that's a very important conversation to have," Osterholm says.

Skeptics doubt that vulnerable populations could really be protected. In many countries, multiple generations live under one roof, and young people work at nursing homes. Nor are scientists certain that COVID-19 produces robust, long-lasting immunity. Several studies seek to address these questions.

EXIT STRATEGY

For now, the most likely scenario is one of easing social distancing measures when it's possible, then clamping down again when infections climb back up, a "suppress and lift" strategy that both Singapore and Hong Kong are pursuing. Whether that approach can strike the right balance between keeping the virus at bay and easing discontent and economic damage remains to be seen.

Even Singapore and Hong Kong have had to toughen some social distancing measures in recent weeks after a surge of cases, Lipsitch notes; Singapore's social distancing regime is no longer very different from that in New York City or London. And both cities' strategies are much harder to implement across a big country like the United States. "We have to have every single town and city and county be as good as Singapore for this to work," he says.

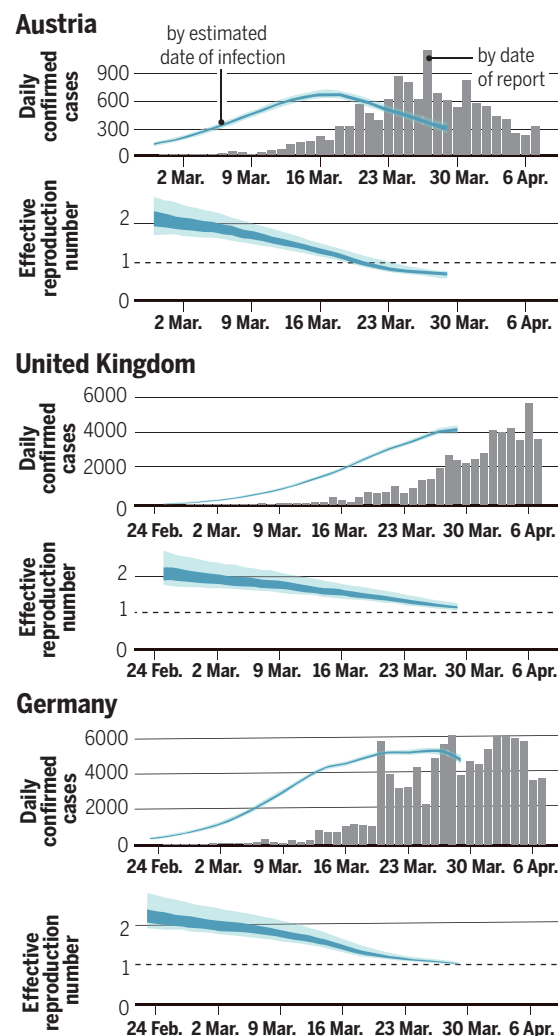
Ultimately, says Jeremy Farrar, head of the Wellcome Trust, a path out of the dilemma now facing the world will come from research. It might take the form of an effective treatment for severely ill patients, or a drug that can prevent infections in health care workers, or—ultimately—a vaccine. "Science is the exit strategy," Farrar says. ■

With reporting by Kelly Servick.

The number to watch

Lockdowns lower the number of new cases as well as R, the effective reproduction number. If R drops below 1, the epidemic shrinks.

● 50% confidence interval ● 90% confidence interval



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