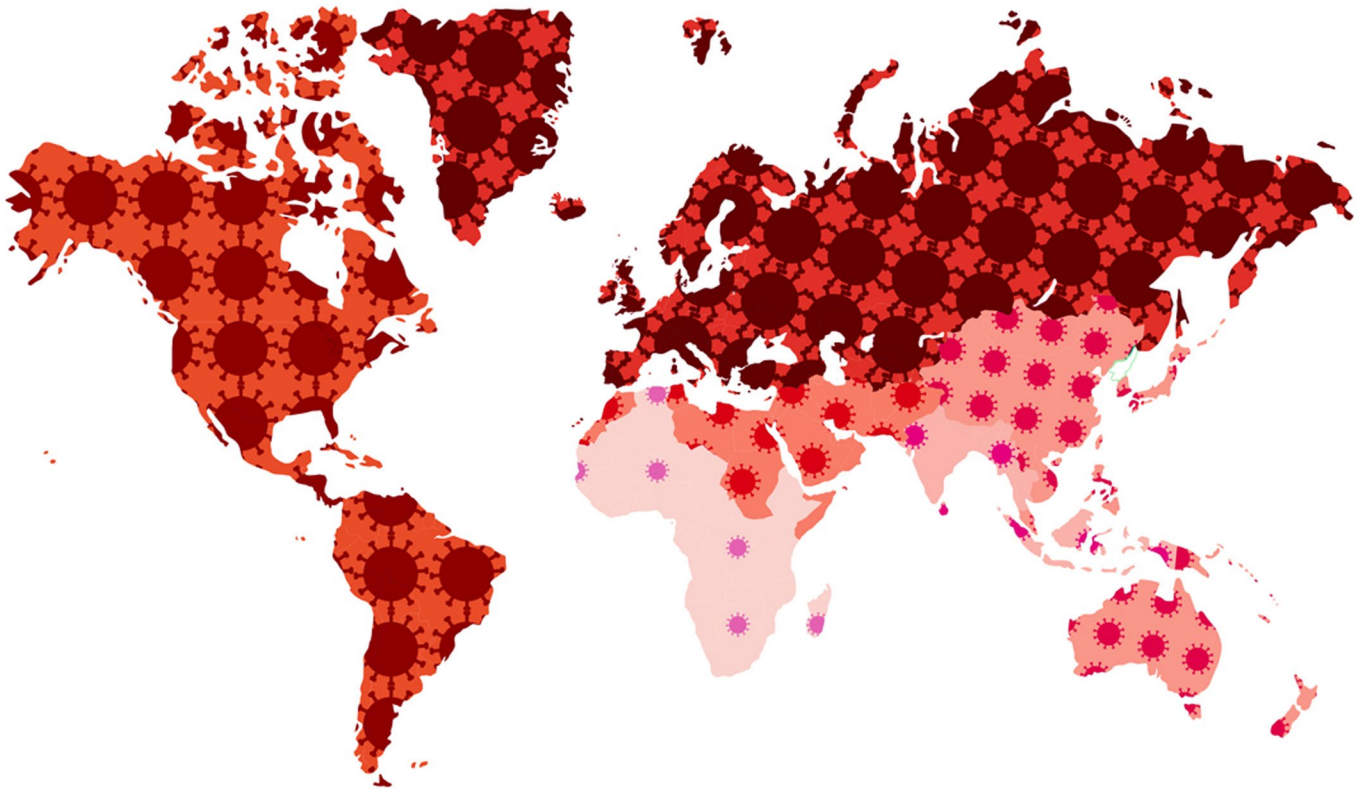

World COVID

Low- and middle-income countries face up to COVID-19

As cases of COVID-19 are being declared the Global South, low- and middle-income countries brace themselves for the pandemic.

Miriam Shuchman

The future of Zambia's health in the COVID-19 pandemic is keeping Duncan Chanda awake at night. The 'big three' diseases worrying him are polio, which has been nearly eradicated in Zambia, measles and AIDS. The human immunodeficiency virus (HIV) clinic he runs at the University Teaching Hospital in Lusaka is closed, and his hospital has suspended the program that ensures every patient who passes through gets screened and tested for HIV. "About 15% of contacts are positive," he says. Over 100 million children will miss their measles shots this year, according to UNICEF. He cannot see how to stop the train wreck from happening.

On and off the front lines, doctors are watching in alarm as COVID-19 hits areas with vulnerable populations and fragile healthcare systems. Peter Hotez, Dean of the National School of Tropical Medicine at Baylor College of Medicine in Houston, Texas, expects the pandemic to exact a bigger toll in the Global South than in North America or Europe, for several reasons. Exposure to the causative coronavirus SARS-CoV-2 will be higher in the densely packed slums of megacities such as Karachi, Dhaka, Mumbai and Lagos, where social distancing is impossible. Low- and middle-income countries' high rates of chronic health problems linked to COVID-19 complications, such as diabetes, are going to cause more severe cases, and on top of that, the countries' healthcare systems lack the critical-care resources to respond to the sort of surge in intensive-care patients seen in New York and Italy. "And mortality goes up in COVID when your health system gets overwhelmed," Hotez tells *Nature Medicine*. "So, what you're going to get is this perfect storm of forces."

Learning from the past

Computer scientist Achla Marathe of the University of Virginia's Biocomplexity Institute glimpsed "the worst" a few years ago, when she and her colleagues simulated the spread of influenza through the slums of Delhi, India, her first home town. Plugging in data on people's daily activities and social contacts in a neighborhood in which six people live in a single room and one hundred or more share a single

community toilet, they found that slums had a 'multiplier' effect on an epidemic throughout the entire city, increasing the size of the city's outbreak and spreading it faster. They modeled influenza, which is less contagious than COVID-19 and does not cause asymptomatic infections, "so you can just imagine everything would be a lot worse [with COVID-19]," Marathe says.

Today in Mumbai, more than half of those infected with SARS-CoV-2 live in informal settlements and slums, where nearly 25,000 people lack legal access to clean water, and instructions to wash hands have raised the price of water on the black market, says Amita Bhide, of Mumbai's Tata Institute of Social Sciences. She worries that others in the city believe slum dwellers "are responsible for bringing and spreading the disease in the city."

India's public-health surveillance includes extensive contact tracing by health officers experienced from tracking tuberculosis and other infectious diseases, who knock on doors and search out cases. But its healthcare system is very diverse, with only certain hospitals running intensive care units. "Hopefully, a lot of these people will be picked up and brought to facilities where they can be provided care," says Bharath Kumar Tirupakuzhi Vijayaraghavan, a physician looking after patients with COVID-19 in an intensive care unit at Apollo Hospital in Chennai. "How they will do depends upon which facility they go to and what resources are available there."

No clean water for washing hands is also a problem in Port au Prince, the capitol of Haiti. The small Caribbean nation lost over 100,000 people to an earthquake in 2010, then endured a cholera epidemic that has claimed the lives of nearly 10,000 over the past decade. Louise Ivers of Massachusetts General Hospital in Boston helped trace the epidemic to faulty sanitation at a camp for United Nations peacekeepers, and she has remained focused on the diarrheal disease. It was under control in January 2020, with the Pan American Health Organization (PAHO) confirming a full year of no new cases, but now, like Chanda, she is worried it could return, "while everyone's busy responding to COVID in Haiti."

Comorbidities abound

The COVID-19 outbreak in Europe and North America has shown that cardiovascular disease, diabetes and obesity raise the risk of complications for those afflicted; the special situation of Latin America and the Caribbean is the very high prevalence of such conditions. Mexico has the highest prevalence of obesity and diabetes in the world, says Enrique Acosta, a Colombian demographer at the Max Planck Institute for Demographic Research in Rostock, Germany; Brazil also has very high rates of cardiovascular disease and diabetes. These underlying diseases affect a younger population in Latin America, and reports are already showing what that means: a report on the first 30 days of COVID-19 in Brazil found the median age of detected cases was 39. By contrast, in New York City, the highest rates of the disease are found in those 75 years of age and older. A number of Latin American countries are also reporting that obesity in young people is a specific risk factor for the disease, according to Jarbas Barbosa, PAHO's deputy director.

How a virus interacts with diabetes or cardiovascular disease is a scientific puzzle that is not unique to COVID-19, says Hotez, who has written on the question. Infections with dengue virus, for example, are more severe and more likely to be fatal in those with diabetes or hypertension, and some of the research coming out of the COVID-19 pandemic may help determine how the diabetes–metabolic syndrome–obesity–hypertension axis increases the severity of a viral infection. But what is crucial for countries in Latin America is understanding that their working-age population is uniquely vulnerable, says Brazilian demographer Marília Nepomuceno, also of the Max Planck Institute.

Some think poor countries might see lower rates of the disease than elsewhere. "Maybe our demographics will help us because the majority are all below age 35," Joshua Kimani, who directs an HIV program for sex workers in Nairobi, tells *Nature Medicine*, and Paul Spiegel, of Johns Hopkins University's Bloomberg School of Public Health, also thinks death rates for COVID-19 might be lower in low- and middle-income countries. "It's purely mathematical because you have so few people over 60," he said.

There is also a theory that universal BCG vaccination for tuberculosis helped Japan and South Korea contain outbreaks of COVID-19 and could help countries such as South Africa and India, where BCG is also universal. Previous research suggests BCG could provide protection in a nonspecific way against severe respiratory tract infections, so in the case of COVID-19, "it might just drop the severity of the symptoms, which makes a big difference," says tuberculosis expert Andreas Diacon of Tygerberg Hospital in Cape Town, South Africa. He is leading one of several trials underway worldwide to test BCG in healthcare workers as pre-protection against COVID-19, but agrees with the World Health Organization that so far, evidence for its efficacy is lacking.

Like others, Hotez thinks the virus may move into the Southern hemisphere over the spring and summer months, following the pattern of influenza, although he says it is impossible to know and the seasonality of the virus is still a matter of debate among experts. Hotez worries that COVID-19 could become endemic in low- and middle-income countries, just as influenza is year-round in the tropics. "I think we've got to assume the worst and then prepare accordingly," he says.

Hunger and fear are exacerbating the crisis. With Nairobi's 7 PM curfew preventing sex work, Kimani is hearing of rising levels of food insecurity among his clients, many of whom are young women in their late teens or twenties with one or two children. It is a story being repeated across the Global South, where daily wage earners are out of work, schools that fed hundreds of millions of children are closed, and the United Nations is warning of a hunger catastrophe. And hunger itself is an engine for infectious disease: undernourished children have higher death rates from measles, malaria and pneumonia, and Ivers' team found that Haitians living with food insecurity have a greater chance of getting cholera and dying from it.

Stigma and fear

On Haiti's southern peninsula, Inobert Pierre of St. Boniface Hospital is facing off against fear. St. Boniface is over 3 hours from Port au Prince, but many patients travel long distances to get there because it is among the few high-functioning medical facilities in the country. In February, as Pierre and his staff were running simulations to prepare for the arrival of patients with symptoms of COVID-19, locals in the community were discussing on Facebook whether the hospital should turn such patients away. A friend forwarded Pierre a Facebook chat in which one person wrote they would burn down the hospital if it admitted a patient with COVID-19, and he knew it was not an idle threat.

He had seen videos of a bus that had arrived in Port au Prince from the Dominican Republic with 17 people, one of whom died on the journey. When the others were quarantined in a hotel, people in the nearby area placed burning tires near the hotel and tried to set fire to it. A college professor faced even worse when he informed college administrators that he was quarantining himself due to symptoms that could be due to COVID-19, after he had traveled in the USA. Word got out, and locals surrounded his car. "People were

trying to kill him," Pierre recalls. After he saw the Facebook messages, he and his staff began meeting with a group of about 30 local leaders, and a group of priests, pastors and vodou priests, in an effort to educate.

Caring for the stateless

Spiegel, an expert in the health issues of refugees and undocumented migrants, is concerned about the role of fear at higher levels, among government officials looking to wall off those groups. "Refugees have always been incorrectly seen as vectors of disease," he says. "We need to include them in [national] plans and to recognize it is not the refugees." But the *Guardian* and other news outlets reported that in Malaysia, police rounded up Rohingya refugees from Myanmar along with undocumented migrants, placing them in detention camps where social distancing and good hygiene may not be feasible. And Spiegel thinks things could get worse as the number of COVID-19 cases increases in areas with large numbers of refugees. He worries that in Lebanon, already facing protests about its economic crisis, Syrian refugees could be forced back into Syria. "If you want to do bad things as a country, now is the time because the world is not looking," he says.

Under-resourced public-health laboratories and hospitals are another part of the 'perfect storm'. PAHO virologists have provided training in the molecular diagnosis of COVID-19 to people in Haiti and 28 other countries in Latin America and the Caribbean, according to PAHO spokesperson Ashley Baldwin, and Barbosa says that the agency has delivered personal protective equipment and several million PCR tests to the region, with special support provided to Haiti and Venezuela, the region's most challenging countries. But in Haiti, Pierre waits a week for tests on patients hospitalized with symptoms of COVID-19. "I'm very positive that we have maybe ten times what's being reported right now, because we're not testing people and when we call [the Ministry of Public Health and Population], they take a lot of time to respond," he says. Ivers blames Haiti's unstable political situation: demonstrations against Haitian President Jovenel Moïse rocked Port au Prince last year, leaving sections of the city completely locked down, and he is essentially ruling without a parliament since canceling elections last fall. "Politics is just inherently part of outbreaks," Ivers says.

To prepare for a potential surge in cases, Mexico is hiring thousands of local doctors and nurses, while South Africa and other countries have brought doctors in from Cuba. Zambia has also hired doctors and paramedics. Richard Kojan, the Congolese critical-care physician who heads the Alliance for International Medical Action, has been working with a team at the teaching hospital in Ouagadougou, Burkina Faso, and has been urging national authorities in sub-Saharan Africa to open their borders so that specialist physicians can move between different African countries. He wants to ensure that a critical-care doctor in Senegal is able to work in the Central African Republic, which has no doctors with such training. Referencing the willingness of hospitals in Germany to accept French and Italian patients with COVID-19, he wrote to leaders at the World Health Organization, pleading "We need the same solidarity everywhere."

The solidarity that Kojan is hoping for has not arrived, but the pandemic has led to multiple such efforts by scientists. Hotez is part of a coalition supporting COVID-19 research in low- and middle-income countries, and his laboratories are working on two of the over ninety vaccine candidates currently in development.

The informal community Amita Bhide studies in Mumbai has applied repeatedly for years for a legal water connection. Mumbai authorities have now installed four pipes and connections, with a plan to install twenty-six more, and she is waiting to see if the pipes actually produce water.

Acosta, Nepomuceno and their Latin American colleagues, worried that the region's data are too scant to properly forecast its needs for the pandemic, wrote a petition appealing for increased testing. Scores of Latin American and Caribbean scientists signed it and sent it to leaders in their home countries. Then came the images of bodies piling up on the streets of Guayaquil, Ecuador. Barbosa says it was a crucial wake-up call for regional leaders about the need to test and to adopt social-distancing measures. "It's important that they can see it," he tells *Nature Medicine*. Brazil, which had been doing only one tenth as much testing as Chile, has since ramped up testing, he says.

Fond-des-Blancs, the community that surrounds St. Boniface, has responded to the hospital's diplomacy, opening schools to serve as isolation centers for people with mild symptoms of COVID-19, or those identified as contacts. "We can't say that we are successful, because there still is a lot of fear around it," says Pierre, but he thinks they have achieved a measure of security.

And Chanda attended a World Health Organization–run COVID-19 workshop in Brazzaville, Republic of the Congo, based on the agency's guidance for clinicians managing patients who are severely ill with COVID-19. Returning home, he trained his colleagues and, with them, developed a how-to guide for Zambia's doctors treating patients with COVID-19 who have severe respiratory infections. His group delivered it to nearly every hospital in the country, online or by e-mail. Today, when he is not caring for patients with COVID-19 or posting their X-rays to an infectious-disease WhatsApp group for advice, he is tracking his hospital's numbers of HIV clinic visits, childhood vaccination visits, cesarean sections and appendectomies so that afterward, he will be able to provide the details of what this pandemic did to health care in Zambia. ❐

Miriam Shuchman ✉
Freelance journalist, Toronto, Canada.
✉*e-mail: miriams215@gmail.com*

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