# News in focus

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**Peru has been one of the nations hit hardest by the COVID-19 pandemic. Here, patients are cared for in a hospital in Iquitos.**

## EMBRACE OF UNPROVEN COVID TREATMENT HINDERS DRUG TRIALS

Unchecked ivermectin use in Latin America is making it difficult to test how effective the anti-parasite drug is against the coronavirus.

**By Emiliano Rodríguez Mega**

As much of the world waits for an effective vaccine to curb the COVID-19 pandemic, some in Latin America are turning to an unproven treatment. There isn't enough evidence that the drug, called ivermectin, is safe or effective as a coronavirus therapy. So researchers are cautioning against using it outside clinical trials. Still, people in the region have rushed to take it, making it hard for researchers to properly test it.

Ivermectin, an inexpensive, over-the-counter medicine, has been used for decades to treat livestock and people infested with parasitic worms – and in the past few months, its popularity as a preventive against COVID-19 has surged in Peru, Bolivia, Guatemala and other Latin American countries.

The drug has been so in demand that in May, health-care workers passed out some 350,000 doses to residents in northern Bolivia. That same month, the Peruvian police seized around 20,000 bottles of animal-grade ivermectin that was sold on the black market as a treatment for human coronavirus infections.

But the evidence that ivermectin protects people from COVID-19 is scant. Some early studies in cells and humans hinted that the drug has antiviral properties[1], but since then, clinical trials in Latin America have struggled to recruit participants because so many people are already taking the compound.

"Of about ten people who come, I'd say eight have taken ivermectin and cannot participate in the study," says Patricia García, a global-health researcher at Cayetano Heredia University in Lima and a former health minister

for Peru who is running one of the 40 clinical trials worldwide that are currently testing the drug. "This has been an odyssey."

Ivermectin grabbed attention in April, when researchers in Australia noted that high doses of ivermectin could stop the virus from replicating in cells[1]. Shortly afterwards, a preprint appeared online suggesting the drug could reduce coronavirus-related deaths in people.

That report was later removed from the site by some of its authors because, they told *Nature*, the study was not ready for peer review. The preprint had included an analysis of electronic health records by the US company Surgisphere, which provided COVID-19 data sets that raised red flags for scientists in late May. By June, two other high-profile COVID-19 studies were retracted that contained data from the firm.

But as far as many physicians and patients in Latin America were concerned, ivermectin's reputation was already cemented. Physicians began justifying the drug's use against COVID-19, arguing that even if it didn't work, at least it had a proven safety profile for treating parasites, says César Ugarte Gil, an epidemiologist at Cayetano Heredia who is running the clinical trial with García.

## Rapid spread

The eagerness to use the treatment grew as the virus spread aggressively throughout Latin America. Brazil, Argentina, Colombia and Peru have all posted some of the largest case numbers worldwide. "I do not judge a doctor who has a dying patient before him and, desperate, tries anything [to save her]," says Carlos Chaccour, a Venezuelan researcher at the Barcelona Institute of Global Health in Spain. "The problem is when non-evidence-based public policies are made."

The implementation of such policies kicked off on 8 May, when the Peruvian Ministry of Health recommended using ivermectin to treat mild and severe cases of COVID-19. Days later, Bolivia's government added the drug to its guidelines for treating coronavirus infections. The Brazilian state of Natal also promoted it as a preventive — to be taken by people at increased risk of severe illness from the virus, because of "its safe pharmacological profile, clinical experience using it against other diseases, cost and dosage convenience".

Peru and Bolivia have been transparent about how slim the evidence is. "It is a product that does not have scientific validation in the treatment of the coronavirus," acknowledged Bolivian health minister Marcelo Navajas in a press conference on 12 May.

The situation troubles researchers who are trying to run clinical trials. Not only is the drug's popularity making it difficult to recruit people, but physicians are also not documenting possible side effects after they prescribe the drug, meaning valuable data on its safety are being lost, says Ugarte Gil.

Self-medication is on the rise because people can easily buy ivermectin, says pharmacologist Carlos Calderón Ospina at the University of El Rosario in Bogotá. Although most people tolerate ivermectin well, it has been linked to tremors, convulsions, lethargy and disorientation. A 2018 analysis found cases of brain damage and coma in people with a genetic mutation that allows ivermectin to pass from the bloodstream into the brain[2].

But that doesn't mean researchers have given up on collecting the necessary evidence. In late September, Alejandro Krolewiecki, an infectious-disease physician at the National University of Salta in Orán, Argentina, and his colleagues announced the results of a small clinical trial evaluating ivermectin's effectiveness against COVID-19. The researchers recruited 45 people with mild and moderate COVID-19 and gave ivermectin to 30 of them for 5 consecutive days at a daily dose about 3 times as high as that used to treat parasite infections; the rest of the participants received only standard COVID-19 care. Their findings suggest that in people who absorbed a higher concentration of ivermectin, "a clearer, faster and more intense viral elimination occurred", says Krolewiecki.

**"The problem is when non-evidence-based public policies are made."**

The news is encouraging, says Chaccour. But it's not enough to give ivermectin wonder-drug status, he adds, particularly because Krolewiecki's results have not yet been published, peer reviewed or replicated.

More data are on the way. In the next few weeks, Chaccour plans to submit results from a pilot study for publication. His team recruited 24 people with COVID-19 and administered ivermectin to some of them and a placebo to the others. Chaccour declined to tell *Nature* whether the results look promising, but he's encouraged that trials are yielding data, even if slowly.

"That's what we asked for from the beginning," he says. "There should be some guidance before making public-policy decisions."

Still, researchers might never have sufficient data to justify ivermectin's use if its widespread administration continues in Latin America. The drug's popularity "practically cancels" the possibility of carrying out phase III clinical trials, which require thousands of participants — some of whom would be part of a control group and therefore couldn't receive the drug — to firmly establish safety and efficacy, says Krolewiecki.

1. Caly, L. *et al. Antivir. Res.* **178**, 104787 (2020).
2. Chandler, R. E. *Am. J. Trop. Med. Hyg.* **98**, 382–388 (2018).

# HOW CHINA COULD BE CARBON NEUTRAL BY MID-CENTURY

Our special report examines the roles of renewables, nuclear power and carbon capture.

**By Smriti Mallapaty**

China, the world's largest emitter of carbon dioxide, has promised to become carbon neutral before 2060, and to begin cutting its emissions within the next ten years.

President Xi Jinping made the ambitious pledge to a virtual audience of world leaders at a meeting of the United Nations General Assembly last month. The news came as a surprise to many researchers, even in China, who weren't expecting such a bold target. It's the country's first long-term climate goal, and will require China to rein in $CO_2$ and probably other greenhouse-gas emissions to net zero, which means offsetting emissions, for example by planting trees or capturing carbon and storing it underground.

In the wake of the announcement, *Nature* explores several proposals from influential research groups that work closely with the government for how China could reach neutrality before 2060. The plans differ in their details, but agree that China must first begin to generate most of its electricity from zero-emission sources, and then expand the use of this clean power wherever possible — for example, switching from petrol-fuelled cars to electric ones. It will also need technologies that can capture $CO_2$ released from burning fossil fuels or biomass and store it underground, known as carbon capture and storage (CCS).

The news of China's carbon neutrality target