

## *Why Didn't the U.S. Detect Omicron Cases Sooner?*

Genomic surveillance has improved enormously in recent months, but the system has built-in delays, and blind spots remain.

**By Emily Anthes**

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Last Friday, just a day after South African scientists first announced the discovery of the Omicron variant, Europe reported its first case: The new coronavirus variant was in Belgium. Before the weekend was out, Australia, Britain, Canada, Denmark, Germany, Israel, Italy and other countries had all found cases.

But in the United States, scientists kept searching.

“If we start seeing a variant popping up in multiple countries across the world, usually my intuition is that it’s already here,” said Taj Azarian, a genomic epidemiologist at the University of Central Florida.

On Wednesday, American officials announced that scientists had found it — in a California patient who had recently returned from South Africa. By then, Canada had already identified six cases; Britain had found more than a dozen.

On Thursday, additional cases were identified in Minnesota, Colorado, New York and Hawaii, and a second case was found in California, indicating that more are almost certainly lurking, scientists said. Why wasn’t the variant detected sooner?

There are various potential explanations, including travel patterns and stringent entrance requirements that may have delayed the variant’s introduction to the United States. But there are also blind spots and delays in the country’s genomic surveillance system. With many labs now conducting a targeted search for the variant, the pace of detection could quickly pick up.

### **Scaling up**



The United States' first case of the Omicron variant was sequenced at the University of California, San Francisco. Mike Kai Chen for The New York Times

Since the beginning of the pandemic, scientists have been sequencing the genetic material from samples of the virus, a process that allows them to spot new mutations and identify specific variants. When done routinely and on a large scale, sequencing also allows researchers and officials to keep tabs on how the virus is evolving and spreading.

In the United States, this kind of broad genomic surveillance got off to a very slow start. While Britain quickly harnessed its national health care system to launch an intensive sequencing program, early sequencing efforts in the United States, based primarily out of university laboratories, were more limited and ad hoc.

Even after the C.D.C. launched a sequencing consortium in May 2020, sequencing efforts were stymied by a fragmented health care system, a lack of funding and other challenges.

In January, when cases were surging, the United States was sequencing fewer than 3,000 samples a week, according to the C.D.C.'s dashboard, far less than 1 percent of reported cases. (Experts recommend sequencing at least 5 percent of cases.)

But in recent months, the situation has improved dramatically, thanks to a combination of new federal leadership, an infusion of funding and an increasing concern about the emergence and spread of new variants, experts said.

“Genomic surveillance really has caught up in the U.S., and it is very good,” said Dana Crawford, a genetic epidemiologist at Case Western Reserve University.

The country is now sequencing approximately 80,000 virus samples a week and 14 percent of all positive P.C.R. tests, which are conducted in labs and considered the gold standard for detecting the virus, Dr. Rochelle P. Walensky, the director of the Centers for Disease Control and Prevention, said at a White House briefing on Tuesday.

The problem is that the process takes time, especially when done in volume. The C.D.C.'s own sequencing process typically takes about 10 days to complete after it receives a specimen.

“We have really good surveillance in terms of quantity,” said Trevor Bedford, an expert on viral evolution and surveillance at the Fred Hutchinson Cancer Research Center in Seattle. He added, “But by nature, it lags compared to your case reporting. And so we’ll have good eyes on things from two weeks ago.”

This kind of delay is not uncommon in countries that have a lot of samples to sequence, Dr. Bedford said.

In some states, the timeline is even longer. The Ohio Department of Health notes that, from start to finish, the process of “collecting the sample, testing it, sequencing it and reporting it can take a minimum of 3-4 weeks.”

Sorting coronavirus test samples for genomic sequencing at Duke University. Pete Kiehart for The New York Times

But now that scientists know what they are looking for, they should be able to expedite the process by prioritizing samples that seem most likely to be Omicron, scientists said.

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In one small bit of luck, Omicron generates a different genetic signal on P.C.R. tests than the Delta variant, which currently accounts for essentially all coronavirus cases in the United States. (In short, mutations in the new variant's spike gene mean that Omicron samples test negative for the gene, while testing positive for a different telltale gene.)

Many labs are now expediting these samples, as well as samples from people who recently returned from abroad, for sequencing.

"All of the agencies that are involved with genomic surveillance are prioritizing those recent travel-associated cases," Dr. Azarian said.

That may have been how the first California case was flagged so quickly. The patient returned from South Africa on Nov. 22 and began feeling sick on Nov. 25. The person tested positive for the virus on Monday and scientists then sequenced the virus, announcing that they had detected Omicron two days later.

"The quick turnaround by the U.S. genomic surveillance system is another example of how much better our system has become over the past few months," Dr. Crawford said.

## Blind spots

As much as surveillance has improved, there are still gaps that could slow the detection of more cases in the United States, including enormous geographic variation.

“Some states are lagging behind,” said Massimo Caputi, a molecular virologist at the Florida Atlantic University School of Medicine.

### The Coronavirus Pandemic: Key Things to Know

**The Omicron variant.** The latest Covid-19 variant was identified on Nov. 25 by scientists in South Africa and has since been detected in more than 20 countries, including the U.S., which reported its first case on Dec. 1. Should you be concerned? Here are answers to common questions about this variant.



Over the last 90 days, for instance, Vermont has sequenced and shared about 30 percent of its virus cases and Massachusetts has sequenced about 20 percent, according to GISAID, an international database of viral genomes. Six states, on the other hand — Kentucky, Pennsylvania, Ohio, South Carolina, Alabama and Oklahoma — have each sequenced and reported fewer than 3 percent of their cases, according to GISAID.

Moreover, scientists can only sequence samples from cases that are detected, and the United States has often struggled to perform enough testing.

“Testing is the weakest part of our pandemic response,” said Dr. Eric Topol, the founder and director of Scripps Research Translational Institute in La Jolla, Calif. “It has been from day one.”

Testing in Houston. Experts say that while testing has improved since the early days of the pandemic, the United States still struggles to perform enough tests. Brandon Bell/Getty Images

Although testing, like genomic surveillance, has vastly improved since the early days of the pandemic, it is still highly uneven. And while rapid, at-home tests have many advantages, the shift of some testing from the lab to the home may present new challenges for surveillance.

“With increasing at-home rapid diagnostic tests, if that isn’t followed up with, like, a P.C.R. test, those cases won’t get sequenced,” said Joseph Fauver, a genomic epidemiologist at the University of Nebraska Medical Center. The problem is not insurmountable, he added, but “maybe there’s a little blind spot there.”

There are other, more optimistic reasons that scientists have not detected more cases, although they remain theoretical.

“Perhaps infected patients have mild symptoms, and hence are not getting tested and are not subject to genomic surveillance,” said Janet Robishaw, the senior associate dean for research at the Florida Atlantic University College of Medicine.

(It is still far too early to know whether Omicron causes disease that is any more or less severe than other variants, scientists stress. Even if the cases are disproportionately mild, which is not yet clear, that could be because the variant has mostly infected young or vaccinated people so far, who are less likely to develop severe disease.)

It is also possible that there was not much community spread of the variant in the United States until recently. When the cases are mostly isolated, and tied to foreign travel, they can fly under the surveillance radar.

“We’re kind of looking for a needle in the haystack if we’re looking for just single cases that are unrelated,” Dr. Azarian said.

Although it is not yet clear where Omicron emerged, the first outbreaks were detected in South Africa, where the variant is now widespread.

There are fewer flights between southern Africa and the United States than between that region and Europe, where other early Omicron cases were detected, Dr. Caputi said.

And until early November, the United States had banned international travelers from the European Union and South Africa, he noted. Even when officials lifted the ban, travelers from those locations were still required to provide proof of both vaccination and a recent negative Covid test. These measures may have postponed Omicron's arrival.

"It is conceivable that Omicron spread is lagging behind in the U.S.," Dr. Caputi said in an email.

Either way, he added, he expected scientists to find more cases soon.