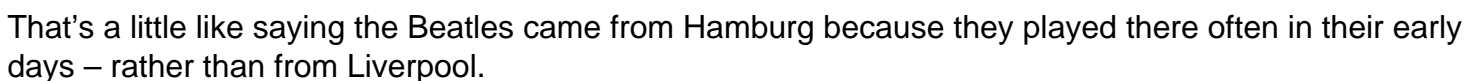


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On the origin of COVID

In that initial report, China claims that the origin of the novel coronavirus *“is still being investigated ... all current evidence points to wild animals sold illegally in the Huanan Seafood Wholesale Market.”*



An alternate hypothesis of the possible origin, based on genome sequence evidence, unfolds in a report on bats from Cambodian caves collected in 2010, published recently in [Nature](#). Predecessors of SARS-

CoV-2 might have arisen in many places, such as southeast Asia, where investigators weren't looking. (I covered the bats in [April](#) when the study appeared in preprint form – the pandemic has instilled a never-ending sense of déjà vu to science journalists.)

The Cambodian bats are the closest known relatives to the enemy, yet they are curiously missing the precise part of the genome that encodes the region of the spike protein that the virus uses to grab onto and slip into our cells. *Coincidence?* Perhaps. Genetic material is well known to flit from genome to genome, crossing what we humans call species boundaries. But there are other hypotheses.

As Fox Mulder said often in The X Files era, *the truth is out there*. But we may never know it.

Anyway, by January 3, the Chinese had sequenced the first genome of the novel virus. They submitted the short report on January 19, 2020 and the 2-pager appeared in the China CDC Weekly a day later – the same day that the US CDC reported the first lab-confirmed case of the new infectious disease, in Washington state, tracked back to January 18th.

Jump ahead nearly two years. More than 6 million SARS-CoV-2 [genomes](#) have been sequenced, as the death rate in the US exceeds 800,000.

Over the past unforgettable two years, the novel pathogen remains novel as we have weathered the undulations of viral reinvention. We are now on the precipice of an onslaught of a viral variant, packed with changes, that will swiftly overcome others that can't hold onto their shared niche – our bodies – with stunning speed.

On December 14, I listened in as the Massachusetts Consortium on Pathogen Readiness – [MassCPR](#) – held one of a series of zooms to keep journalists up to speed. I tuned in two weeks ago too, as the first reports of Omicron were trickling in. This time, the speakers appeared and sounded rather rattled, their concern ratcheted up, holiday plans altered, and for good reason. Here are highlights.

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South Africa isn't a crystal ball for the situation in the US

Now that Omicron is here – I had to laugh at the idea of keeping it out by limiting air travel – virus trackers in the US can look to the situation in the UK and Europe for a more apples-to-apples comparison than watching what's happening in South Africa. Several distinctions are converging to muddy that crystal ball.

“The difference between South Africa and the UK and US is that the Delta surge in South Africa was over by the time their Omicron surge began. Our Delta surge is ongoing and accelerating, and on top of that, add the Omicron surge. The combination of the two surges is going to put a lot of stress on an already stressed hospital system,” said Jacob Lemieux, infectious disease specialist at Massachusetts General Hospital.



Jacob Lemieux is a post-doctoral researcher in the Sabeti Lab and an infectious diseases staff physician at Massachusetts General Hospital. Credit: Sabeti Lab

Seasonal differences matter too, because viruses have their preferences, those of the respiratory variety

revving up in colder climes. “We’re entering into the heart of winter, whereas South Africa is in the southern hemisphere. There are other viruses here we’re concerned about, like flu, which has been rising in the US,” said Jeremy Luban, professor of molecular medicine, biochemistry and molecular pharmacology at the University of Massachusetts Medical School.

Additionally, more people in South Africa have had COVID and are now being re-infected, and fewer have been vaccinated, compared to in the US. Still, any predictions researchers can make are unsettling, at best.

Omicron is on track to be firmly entrenched in the US in January

“The numbers are growing quickly. In London today (December 15), Omicron is the most common variant, over 50%, and over 30% in Ontario. The US CDC currently projects 3% nationally, but I think that’s an underestimate and will change as more data come in in real time. Doubling time is 2 to 5 days. R naught (the average number of people an infected person infects) is 3 to 5, and maybe higher,” said Bronwyn MacInnis, director of pathogen genomic surveillance at the Broad Institute of MIT and Harvard. Some locations in the US are already reporting levels of 15%, added Lemieux.



Bronwyn MacInnis is associate director of the malaria and viral genomics focus areas of the Infectious Disease Program at the Broad Institute of MIT and Harvard, and a visiting scientist at the Harvard T.H. Chan School of Public Health. Credit: Sabeti Lab

Researchers calculate the proportion of sequenced SARS-CoV-2 genomes that are Omicron, while mathematical models track the rate of rise relative to other variants. “It’s difficult to know what the absolute number of infections will be. Omicron is moving extraordinarily fast, faster even than the most pessimistic among us thought it was going to move,” said Lemieux.

Our tools for genomic surveillance simply can’t catch up. Sequencing lags now by a week or two.

“In many ways we are seeing Omicron moving faster than the rate of detection. In contrast to previous waves, when we had a sense of what would happen by looking at the UK because we lagged by a few

weeks, we don't lag by that amount of time anymore; we may lag by a few days. Omicron is unfolding all around the world, in parallel, faster than most of us anticipated," said Lemieux.

Omicron as a riptide, blindsiding us

The conversation kept returning to the image of overlapping waves. This big picture is a little like wading into the ocean as waves roll in and being knocked down by a riptide coming in at an unexpected angle.

"Looking back we're in the midst of a surge in the US driven by delta. We may be at the cusp of the Omicron surge. The surge over the holidays is likely going to be a mixed Delta-Omicron surge," Lemieux predicted. He and MacInnis agreed that we are already *in* the Omicron surge, which will be confirmed in retrospect when the genome sequencing catches up.

"There isn't a surveillance system on the planet that could keep up with the pace of this doubling time," MacInnis said, her face a map of anxiety. She explained the challenge of fighting the lag:

Omicron cases were reported as 3% as of December 11, and in dog years time, that's a million years ago. Estimates are based on forecasting from the data in hand and modeling using known knowns at the time the model is generated. Data are coming in quickly, almost in real time as fast as we can generate them, from large-scale population sequencing. The data come in within 7 to 14 days from the point of collection of samples. That's what the CDC estimate is based on, a moment-in-time project. Then we fill in the picture with what we see from anecdotal data from smaller scale operations and in other parts of the world. It's safe to say that predictions are an underestimate of reality today and will be as we go forward.

What kept me up at night

The MassCPR team said it's too soon to tell the severity of Omicron. As of now vaccines provide [about 70%](#) protection against being hospitalized with COVID, and small molecule drugs are inching in, even as some [monoclonal-antibody-based](#) therapeutics are proving too narrow in their targeting to handle the mutational landscape of Omicron.

But the speed and numbers surrounding transmission rate do not bode well. With millions breathing the virus in and out, many unaware despite testing, which after all is only valid in the moment, the vulnerable are still at risk – and there will be more of them, us, for I'm older, than in the past.

MacInnis laid out three primary fears:

#1 It is spreading so fast and extensively that the concerns from the beginning about the virus are still true. Even in the early days, disease severity was not the biggest threat, but the threat to our hospital systems. With this level of transmission there will be enough severe cases to

overtax an already overstretched system.

#2 Even if people are fully vaxxed with boosters, it will hit the most vulnerable among us the hardest, especially at this scale of transmission.

#3 Even if it doesn't cause as severe disease, at this level of transmission the threat of continued evolution and the emergence of new variants that will potentially cause severe disease remains high. We absolutely need to take Omicron seriously.

So for most of us, assuming Omicron comes to reside in our noses and throats despite vaccines, the virus might indeed trigger only a bad cold with some weird side symptoms. But that's for the lucky.

I watched Jacob Lemieux's face and demeanor as he spoke passionately and eloquently near the end of the session, and it still resonates. I'll leave you with that.

We are all so tired. COVID has completely changed our lives. We all want this to go away, we all want to take our masks off and have our holiday parties. But we need to take a step back and forget about how tired we are, and look at objective data.

We have a highly pathogenic virus, SARS-COV-2, that has already killed millions of people. A new variant has emerged that we don't have complete information on, but what we do know is that it is the most transmissible variant we've ever seen and it is the most immune-resistant variant we've ever seen. It has spread around the globe in under 2 weeks, it has already resonated throughout the US, and there is a high likelihood it will come to your holiday gathering.

This highly pathogenic virus has already stretched our health care system to the brink on a number of occasions and in part of the US continues to do so, even before we see the effect of Omicron. And all of this is happening at a speed so fast that we can't collect information to measure it with day-to-day relevance or predict what will come.

I hope the severity is markedly lower. South African deaths are rising, although not as fast as the case counts. We don't know if that's due to immunity or a property of the pathogen.

We must invoke the precautionary principle: it is time to protect NOW. It is time to do all the things we know to do and do them in spades. I don't recommend going to gigantic, unmasked indoor gatherings. If you are on the fence about getting vaccinated, do it now. Wear masks indoors and avoid unmasked gatherings and avoid dense indoor gatherings. Several features of this variant are alarming.

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