What is the omicron variant of COVID-19? What do we know about it?

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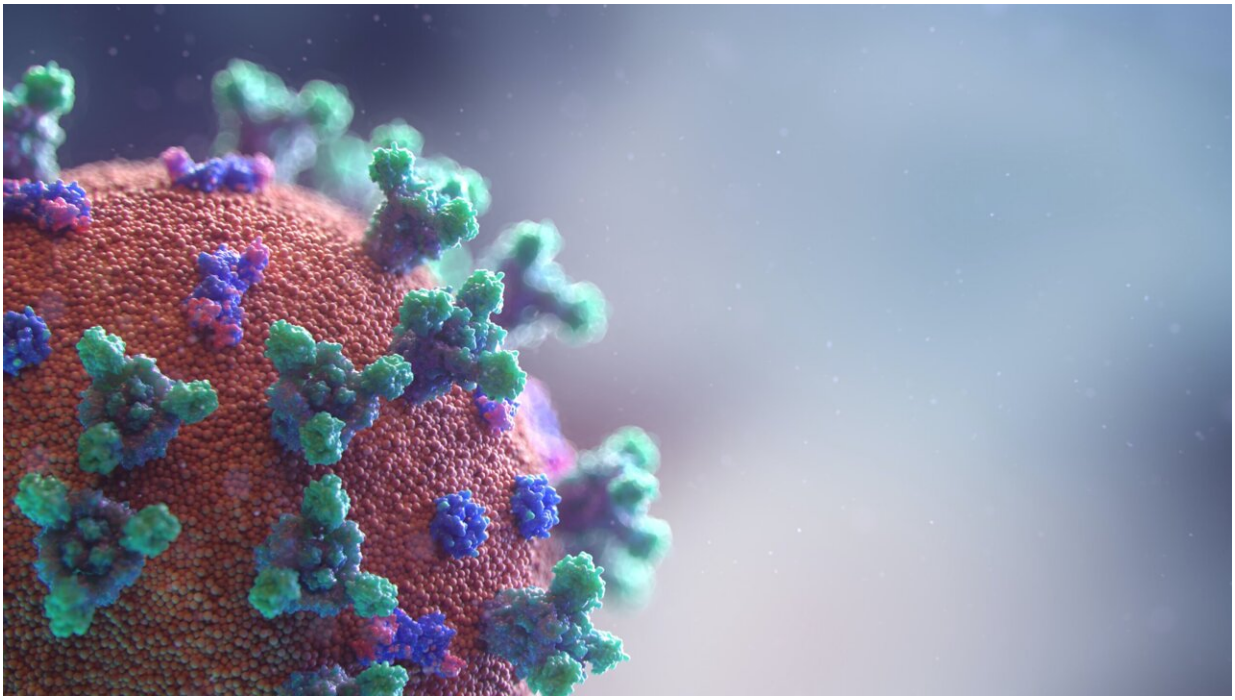

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You may have seen headlines recently about the omicron variant of COVID-19, or read about it on social media. There's still a great deal of uncertainty about this new variant, and some of the information people are sharing can be misleading. So we want to talk about the omicron variant, what we know about it, and what we still don't know.

To learn more, we talked with two NC State researchers who have relevant expertise.

Julie Swann is a systems engineer with expertise in public health and issues related to contagious disease. In 2009, she served at the Centers for Disease Control and Prevention as a science advisor for the H1N1 pandemic response. Swann is the department head and A. Doug Allison Distinguished Professor of the Fitts Department of Industrial and Systems Engineering at NC State. Matt Koci is a virologist and immunologist whose work focuses on host-microbe interactions in birds; he is a professor in NC State's Prestage Department of Poultry Science.

The Abstract: There's been a lot of discussion in the news recently about the omicron variant of SARS-CoV-2, and what it might mean for the COVID-19 pandemic. First off, when people talk about variants of the virus that causes COVID-19, what do they mean? What is a "variant"?

Matt Koci: I know. Keeping up with all the variants has been confusing.

Viruses, for better or worse, are the best real-time example of Darwinian evolution, and unfortunately right now we all have front-row seats. In every infected person around the world, in each infected cell, the virus makes hundreds of copies of itself. As it makes copies of its genome, sometimes it makes small mistakes. Each of these copying errors leads to a genome that's a little bit different from the original. This is probably happening dozens of times in each infected person, if not more.

The SARS-CoV-2 genome is around 30,000 nucleotides long. Written as letters on a page, that fills up about eight pages. Just think if you had to

make hundreds of copies of an eight-page story, by hand. You'd probably make a few copying errors too.

Every new virus that has a copy error in its genome that's different from the original virus is considered a variant. Then as these copied viruses leave one person to infect someone else, they take their changes with them. This new variant then becomes the template for all the new copies that get made. Some of the new copies will have their own mistakes, which get added to the mistakes in the first copy. And so on and so on. That's how we end up with some variants with just a few changes and others, like omicron, that have a lot.

Scientists around the world have been taking some of the nasal swabs and spit tubes from all the testing going on and analyzing the SARS-CoV-2 genomes to get a sense of how many variants are out there and how many changes each variant has. When these variants are first identified, we don't know what they mean. Just because the virus has a change in its genome doesn't mean it's going to spread faster or be more deadly.

That's why as new variants are detected around the world they are added to a database. If a new variant sequence has changes that we think could be associated with how the immune system recognizes it, or how well vaccines and other therapies would work against it, it is classified as "variant of interest." This means people start paying more attention to it.

If we see that a given variant of interest starts to show up as a larger and larger percentage of genomes found in a particular area, or it starts to spread outside of the area it was first discovered, it becomes a "variant of concern." That's what happened with omicron. The increasing number of cases in South Africa, and its detection in several other countries, on multiple continents, led to it getting promoted from a variant of interest to a variant of concern.

Now just to be clear, and I hate that I even have to say this, but: no, this variant wasn't planned. I've seen several people on social media, including some politicians and others who should (or do) know better, suggesting that this variant was intentional. Some conspiratorial nonsense is circulating to this effect. Please, if you see anyone trying to spread this nonsense saying that because "they" knew the name of the variant before the variant arrived means this was all planned, don't let that go unchallenged. It's like saying that hurricanes are intentional because we know what the next hurricane is going to be named.

Julie Swann: Wow, I have been away from social media. I am glad that you pointed that out. Your description of the variants made me think of monks copying books with dark lighting. If monk number three made a change when copying, it gets repeated down the line. The more copies that you make, the more changes that accumulate.

TA: My understanding is that there are a lot of things we still don't know about the omicron variant. What are the things we do know at this point?

Koci: We know that there's a new variant of concern that has a lot more changes in its genome than we've seen in the previous variants. A lot of these changes are in places that look like they would affect how well the vaccine and monoclonal antibody therapies might work. We also know that it has popped up in countries around the world, but this is still early, and most places are just now starting to really look for this variant. So, I expect the list of countries with this variant to grow. [Editor's Note: Hours after this Q&A was posted, the first confirmed case of omicron variant was reported in the U.S.]

Swann: I will add to that. As Matt noted, we do know that this variant has a large number of mutations relative to other strains. Initial data is

that omicron has about 50 mutations, with 26 mutations that were not in the other named variants, and 32 changes to the spike protein. An image has been released comparing it to delta, and it seems to have at least twice as many mutations. We also know several of the mutations of omicron were seen in other variants that were highly infectious or had the ability to escape previous immunity. Several of us have been expecting another variant to arise, and there could be evolutionary benefit to a strain that could break-through previous immunity, at least partially, which would enable it to spread more widely. It is possible that omicron is such a variant.

TA: What are the big questions that we still don't know about the omicron variant? Do we know if it's more contagious or if the COVID-19 vaccines offer protection against it?

Koci: We don't know either of these right now, with any high degree of certainty. In late November, there were a handful of reports from different countries suggesting that the omicron variant is more contagious than delta. Those reports are not proof that it is, but they were enough to get epidemiologists and virologists around the world to say, "We need to know a lot more about this one." I think at the end of the day we'll find out omicron is more contagious than delta, but to know how much more we need more information.

We know even less about how well the vaccine will protect against this variant. The number of mutations in the spike protein is not a good sign, and several of them are in places that previous variants showed make it more difficult for antibodies to neutralize the virus. But again, we need more data to know for sure. Additionally, while antibodies are great, they are only half of our adaptive immune system. We likely still have our T-cells working for us. That would likely mean more breakthrough

infections, but those infections would still be milder with fewer deaths than we'll see in the unvaccinated.

Swann: Here is a summary response from my perspective. There are a number of things we don't know yet. While we know there is confirmed or probable evidence of the variant in many countries worldwide, we do not know the full extent of the spread.

It is very likely in the United States already, but in how many locations and how widely distributed?

We believe this variant is more contagious than the original strain of COVID-19, although scientists are still trying to determine just how much.

We know that the virus has infected people who were vaccinated, although work is still being done to assess the extent to which it can break through existing immunity.

Lastly, we are still determining how likely the variant is to cause severe disease, either in the unvaccinated or vaccinated populations.

TA: Omicron was first detected in South Africa, but that doesn't mean that the variant actually developed there, right? Can you explain that for me?

Koci: Yes. The list of countries that are doing a better job than the U.S. looking for and alerting the rest of the world about new variants is embarrassingly long. This is also why the WHO, and the infectious disease community at large, pushed to stop naming viruses after where they were first reported. You end up with a virus variant that can be found on just about every continent, but travel restrictions are only

implemented against the place that told you about the threat.

Now that most people in the U.S., E.U. and U.K. have their vaccines and have decided we need to go back to work, global travel is up. That means viruses like SARS-CoV-2 can move around the globe as if it was December 2019. That's not an argument for going to back to a global shutdown, but we need to recognize the pandemic isn't over. As people move, we take our diseases with us. We can't keep the economy closed forever, but as we try and figure out how to live with the virus, people need to be smart about how they reclaim aspects of their lives without recreating ideal conditions for the virus to mutate and spread.

Swann: Bottom line—South Africa is doing significant testing and sequencing of virus samples, so it is no surprise that a new variant was identified there. An early case was found in Botswana, and we know that the strain has been confirmed in a number of other countries. A strain can travel from one location to another with people, and this is more likely in places with lower vaccination rates or higher levels of travel. We should be thoughtful and not penalize South Africa for bringing the variant to our attention, since it is likely in many places already and may have arisen elsewhere.

TA: When do you think we'll know more about the omicron variant, such as whether it's more contagious?

Koci: We should start to know more about how well the antibodies against the vaccine work against omicron by the end of this week. [Editor's Note: This Q&A was conducted Dec. 1.] Most of the labs that have been doing that work have already started to make the tools they need to be able to test things even before they have the actual virus.

As for how long until we know for sure if it's more contagious and by how much, that will take a bit longer. Really, the only way of knowing that is looking at how quickly the number of omicron cases increases, relative to delta cases. But every country around the world is a little different in terms of vaccine status, current number of COVID-19 cases, mix of young and old, and so on. It may take a few weeks to really know what's going on.

Swann: I believe there is enough data for me to think this variant is more contagious than the original strain. As my colleague states, the extent of it depends on local characteristics such as previous immunity, vaccination rate, social distancing, etc. For me, the bigger question is to what extent it can break through existing immunity, and another question is around how severe disease may be in vaccinated or unvaccinated populations.

If we wait for answers to everything before making decisions, it will be too late. We should take actions now. Of course, this includes prioritizing vaccinations for adults and children and boosters. Just this week the CDC recommended that everyone 18 and older receive a booster, which could help provide protection against omicron, even if that protection is not perfect. We should also increase our testing in the population, such as for anyone who has gathered socially with people not in their household without masks—and do more testing throughout the holiday seasons. Even though I am vaccinated, I will wear masks in all gatherings with non-household members (professional or personal). Our governmental agencies also need to be sequencing samples to understand the existing spread of this variant, and we should be tracking cases by vaccination status. Early action will save lives and reduce the chance our hospital systems will be overwhelmed. Long term, we need to continue investing in the infrastructure to respond to infectious diseases and other public health challenges.

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