

## 'Kraken' variant & vaccine stroke risk: Everything you need to know with Sandra Fryhofer, MD

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AMA Update covers a range of health care topics affecting the lives of physicians, residents, medical students and patients. From private practice and health system leaders to scientists and public health officials, hear from the experts in medicine on COVID-19, monkeypox, medical education, advocacy issues, burnout, vaccines and more.

### Featured topic and speakers

In today's AMA Update, the latest on Pfizer's COVID vaccine and stroke risk. Sandra Fryhofer, MD, breaks down vaccine safety statistics following new FDA and CDC announcements about possible increased risk of stroke after getting Pfizer's bivalent booster shot. Also covering VSD, other vaccine databases and what's expected at the Vaccines and Related Biological Products Advisory Committee (VBRPAC) meeting this January. Plus everything you need to know about the 'Kraken'—a.k.a, the XBB.1.5 Omicron variant. AMA Chief Experience Officer Todd Unger hosts.

### Speaker

- Sandra Fryhofer, MD, chair, AMA Board of Trustees and AMA Liaison to ACIP

### Transcript

**Unger:** Hello and welcome to the AMA Update video and podcast. Today, we're discussing new announcements from the FDA and CDC about a possible increased risk of stroke following the Pfizer bivalent COVID booster and what we know about the new XBB Omicron variant.

I'm joined today by AMA Board Chair Dr. Sandra Fryhofer who's also the AMA's liaison to ACIP, the CDC's Advisory Committee on Immunization Practices and a member of ACIP's COVID-19 vaccine workgroup. I'm Todd Unger, AMA's chief experience officer in Chicago. Dr. Fryhofer, thanks for joining us today.

**Dr. Fryhofer:** Todd, thanks for having me.

**Unger:** Well, let's get right into it. What do we know about this possible link between the updated Pfizer booster and increased risk of stroke?

**Dr. Fryhofer:** A new preliminary safety concern and increase in stroke risk has been identified for those 65 and older after receiving a dose of Pfizer's bivalent booster. Now, I want to be clear. There is no established link. This is just an early safety signal and one of many vaccine safety monitoring platforms. And on Friday the 13th of January, CDC and FDA made this joint announcement that an increased risk of stroke had been identified for those 65 and older who had received Pfizer's Omicron bivalent booster.

The preliminary signal found an increased risk of ischemic stroke and the 21 days following the Pfizer bivalent vaccine dose as compared with days 22 to 42 following vaccination. As I said, this is just a signal. The signal has only been seen for Pfizer's bivalent vaccine, not for Moderna's bivalent version. And the signal is only from one vaccine safety platform, VSD. That CDC's vaccine safety data link. And there are multiple different platforms which look at vaccine safety in different ways.

This signal has not been seen in the other vaccine safety platforms. Again, no other safety systems have shown this signal. So this may be a false alarm, or it could turn out to be real. Only time and further study and more data will tell.

**Unger:** Dr. Fryhofer, this announcement demonstrates a lot of transparency on behalf of the CDC and FDA. And it's especially important since the mRNA vaccine platform is somewhat new. And safety is being closely monitored and scrutinized. Tell us more about that.

**Dr. Fryhofer:** Well, I agree. Transparency is so important to encourage trust in the system and trust in vaccines. And that's why CDC and FDA made the joint decision to alert the public so early about this preliminary safety concern. But again, it's still unclear if this is a real signal or just an aberration.

We need more data. This preliminary signal has only been seen in just that one platform, VSD, CDC's Vaccine Safety Datalink. And the signal only applies to Pfizer bivalent updated vaccine. This signal has not been observed for Moderna.

**Unger:** So you said the possible stroke concern has been identified in one safety platform. Can you just for the perspective of folks out there, how many different safety platforms look at COVID vaccines?

**Dr. Fryhofer:** Well, there are several of them. And there's been no signal so far in the BA database. It has not been observed in the CMS database. It has not been observed in VAERS, which is CDC and FDA's Vaccine Adverse Event Reporting System. In addition, Pfizer's global safety database has not

indicated the safety concern is real, which seems to be a step ahead of us.

And vaccination administration has also not reported this finding. There have been no red flags from any of the other vaccine safety platforms indicating an increased risk of ischemic stroke. This preliminary signal has only been seen in just this one platform, CDC's Vaccine Safety Datalink.

**Unger:** So at this point, has the CDC made any changes to its COVID vaccine recommendations?

**Dr. Fryhofer:** No. There is no change in current recommendations. CDC continues to recommend everyone six months and older stay up to date on COVID vaccinations. And that includes getting a dose of the updated bivalent vaccine when eligible.

**Unger:** So what's the current evidence supporting COVID vaccination with the updated bivalent booster doses?

**Dr. Fryhofer:** Well, here's what we do know. Getting a dose of the updated vaccine, which is the bivalent vaccine, cuts the risk of hospitalization by nearly three-fold as compared to those previously vaccinated but not bivalently boosted. The updated COVID vaccine also reduces risk of death by COVID by nearly 19-fold as compared to those who are unvaccinated. To repeat, at least for now, there is no change in CDC recommendations for COVID vaccination. But for transparency, CDC and FDA wanted the public to be aware.

FDA described this finding to the media as listening to the radio and hearing static in the background. Now, static doesn't mean someone is really talking. This issue will be addressed at the upcoming VRBPAC meeting on January 26. VRBPAC is FDA's independent Vaccine and Related Biologicals Product Advisory Committee. So more to come.

**Unger:** So you outlined a lot of benefits, obviously, of getting the bivalent booster. In this case, there isn't—this transparency does engender confidence in the system. But I think it probably could be a little confusing to folks out there. So could you help us put this in context for everyone?

**Dr. Fryhofer:** Well, Todd, you are so right. And I respect and appreciate the transparency. But the announcement comes at a time when daily COVID deaths are rising and vaccine uptake remains low. CDC says only 16% of those age five and older have received the updated bivalent booster. This signal involves those age 65 and older. And this is group is one of the most vulnerable to complications from COVID. And only 39% of them have been bivalently boosted.

So this message is very confusing and a little scary if you only read the headline and not the fine print. And that's why we're talking today. And it may make some people afraid to get the updated shot. FDA told media outlets that if they continue to dig deeper, they hope the signal will disappear.

And, of course, that's my hope too. And I think everyone hopes that. But understand this preliminary safety signal is only for Pfizer, not for Moderna. Those who need a dose of updated vaccine and feel nervous about this announcement could go ahead now and get a Moderna dose of updated COVID vaccine. So there is another option.

**Unger:** Dr. Fryhofer, let's turn our attention now to XBB, which is the latest Omicron variant and perhaps one of the most transmissible that we've seen so far. What can you tell us about this new variant?

**Dr. Fryhofer:** Well, since Omicron became dominant, it's made many twists and turns. First, there was BA.1. And then we went on up to BA.5. Then the shift to BQ. But now, if you look at CDC's COVID tracker, the new Omicron variant, as you mentioned, XBB is taking over. All these variants are subvariants and part of the Omicron family. BQ is a descendant of BA.4 and BA.5. XBB is a variation of Omicron BA.2. And the 1.5 version of XBB is the one that's now spreading like wildfire.

CDC's COVID tracker, survey with ending January 14 says this variant's responsible overall for up to 43% of all U.S. COVID cases. Its proportion is even higher in the Northeast where it's already to blame for more than 80% of COVID infections. And it's probably also spreading faster because most people are no longer wearing masks. And this might be a good time to start wearing a mask again if you're not already. And I will say I've seen a lot more people wearing masks in the airport.

**Unger:** Do we have any evidence on how effective vaccines work against XBB or about the severity of the infection with this subvariant?

**Dr. Fryhofer:** Well, since this subvariant is new, there's not yet any real world data on vaccine effectiveness for it against severe disease or death. But published studies are showing neutralizing activity of a bivalent boost seems to be lower against XBB. WHO, the World Health Organization, says XBB.1.5 is the Omicron variant with the highest immune escape to date. But although XBB.1.5 is one of the most antibody-resistant variants, it doesn't seem to carry any mutation known to be associated with a potential change in severity. However, studies of disease severity are now ongoing.

**Unger:** Now, some people are calling XBB.1.5 the "Kraken" variant. It brings "Clash of the Titans" to mind. We've heard lots of different names for different variants and subvariants. How did this one happen?

**Dr. Fryhofer:** Well, it is definitely an unusual name. "Kraken" is the name of a mythological sea monster. And XBB was given this name by a Canadian biology professor who has been trying to demystify COVID variants by giving them mythological names. Now, it is a little easier to say the XBB.1.5. But the name sounds scary. But just because it's been given the nickname of a sea monster doesn't necessarily mean it's more dangerous. Of course, we need hard data to make that determination.

**Unger:** I hope to give Harry Hamlin a call and see what he can do about the "Kraken." Dr. Fryhofer, before we sign off, any final thoughts?

**Dr. Fryhofer:** A reminder. The stroke risk signal for Pfizer's bivalent booster for those 65 and older is just a preliminary signal at this point. This signal was not seen from Moderna's updated vaccine. The signal has been detected in just one of many vaccine safety platforms. CDC says the totality of the data currently suggest it's very unlikely this signal and only one vaccine safety platform represents a true clinical risk.

So at this point, there has been no change in COVID vaccination recommendations. Everyone six months and older should get a dose of updated COVID bivalent vaccine when eligible. Again, this signal is only for Pfizer and has not been seen in those who received Moderna's bivalent version.

**Unger:** Well, thank you so much, Dr. Fryhofer for being here today and providing us that information. We'll keep folks out there updated as there are developments. And that's it for today's episode. We'll be back soon with another AMA Update. You can find all our videos and podcasts at [ama-assn.org/podcasts](https://ama-assn.org/podcasts). Thanks for joining us today and please take care.

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