

TWiV 1266 Clinical Update

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Guest: Daniel Griffin

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Vincent Racaniello: *This Week in Virology*, the podcast about viruses, the kind that make you sick.

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VR: From *MicrobeTV*, this is *TWiV, This Week in Virology*, Episode 1266, recorded on October 30, 2025. I'm Vincent Racaniello, and you're listening to the podcast all about viruses. Joining me today from New York, Daniel Griffin.

Daniel Griffin: Hello, everyone.

VR: Back to the bow tie, and the suit jacket today.

DG: I am. It's going to be an experiment. We'll see if it impacts ratings, right?

VR: I can't tell. It looks like chains of bacteria, maybe. Is that possible?

DG: As people who are probably listening to this when it drops Saturday morning, right after Halloween, because I realized this Friday I'm not going to get to wear a sexually transmitted infection, I shift my syphilis bow tie to tonight because then on Halloween, part of my costume, I'm going to wear my orange bat bow tie.

VR: Wow. This is syphilis?

DG: This is syphilis, the purple spirochete there.

VR: *Treponema pallidum*, right?

DG: Yes. Excellent.

VR: Wow. Good for you. You threw me because it's Thursday, and I didn't guess.

DG: A rainy Thursday, Vincent, as I was checking with you, maybe our listeners, if they listen really closely, they can hear the drip of the water coming through the light fixture into the bucket in this room where I'm recording.

VR: Yes, I do hear it now, yes.

DG: You hear it now? OK. Look at that.

VR: I think it adds a little atmosphere. It's good.

DG: It is raining, and the rain is coming right through the roof. This house was built in the

1800s. On days like this, you remember that. All right, let's jump right into this. We've got a lot to cover. We've got some good science here. The first one is maybe, we've got some elections coming up here in a couple of days. I voted early. "When someone shows you who they are, believe them the first time," Maya Angelou. [chuckles]

VR: I have a question for you, Daniel, before we start. There's a nominee for Surgeon General, a Dr. Casey Means. She got her MD at Stanford, which is a pretty good medical school, right?

DG: I would agree, actually. I know some excellent graduates that have come out of Stanford.

VR: Went into a residency and left because she realized she was training to treat the complications of illness rather than the root causes. I want to know from you, is that what all doctors do?

DG: It's really not. There's this movement where people talk about holistic. That's actually, at least, how I was trained. As you move forward, you certainly start off with a lot of basic science, understanding biochemistry, but ultimately, when you have all those tools under the belt, you're sitting there with an individual and you're asking them, "What happened? How did you end up here? How did you end up in the hospital? How did you end up not feeling well?"

Even at the yearly physical, you're trying to prevent the person from ending up sick in the hospital. I always remember saying that once a patient is sick, we've already failed. So much of public health is preventing illness. So much of science that is under attack is all about preventing illness. Maybe she just didn't stay long enough. She was getting all the tools and then went off in a different direction.

I was just thinking about a couple examples today of some folks where you may talk to them about their symptoms, what's going on. Then one individual asked, "Tell me a little bit. What do you do when you're not in the hospital? How did you end up here?" He owns his own business, but now his daughters are coming in to help him. He just didn't realize how stressful that would be trying to teach them the business.

Another woman has been back and forth from Guatemala because her husband is having some issues with his paperwork and all the stresses of her trying to run his business while he is not available because of some reason. That's what a real doctor does, is they understand the person, they understand the root causes of what gets people sick.

VR: Certainly infectious diseases, you identify the organism. We do that on *TWiP* all the time.

DG: All the time like, "Where were you born? Where did you grow up? What do you eat? What have you been doing?"

VR: Even orthopedics, they replace your hip, they replace your knee. That's the root cause of you can't walk or whatever.

DG: Then there's usually a whole exercise program around that. Were you carrying extra weight? A lot of people are doing exercise before and after. It isn't just about, "Oh, here's

the pill. Good luck with that."

VR: OK. Thank you, Daniel.

DG: All right. Thank you. [chuckles] I want to start with what really is a great article. I'm going to leave a link into the deep dive from *TWiV*. You guys did a great job of covering this, Vincent. I'm not going to cover this in the same detail, so I'm going to recommend people follow the link. Let's talk about this really exciting article, "SARS-CoV-2 mRNA Vaccines Sensitize Tumors to Immune Checkpoint Blockade," published in *Nature*. Are you excited to talk about this again, Vincent?

VR: I think this is a wonderful paper. The title of the *TWiV* was "mRNA Vaccines Make Cancer Treatment Great Again."

DG: [laughs] I like that. Well, that's exactly what's going on here. It takes a little background, but I think we have some pretty sophisticated listeners, people we've pulled you away from TikTok for the next 30, 40 minutes for a little bit more in-depth. Really, it takes a little bit, but I'm going to start off with what is the punchline. That's exactly what's really in the title here is, they're going to go through and describe the fact that getting a COVID mRNA vaccine can actually improve survival in patients who have cancer and get a certain type of cancer therapy.

They're going to show us that folks that got one of these COVID-19 mRNA vaccines, so it's the Moderna and the Pfizer is what we're going to look at, within 100 days of starting a certain type of cancer therapy, are going to have really improved odds of survival. If they're going to survive, let's say, three years, at three years, they're about twice as likely to still be alive, so 30% versus almost 60% that got that COVID shot. Then as far as time, we don't always cure everyone with cancer, but with this, we're going to actually buy people almost twice as much time. With survival, 20.6 months, we're going to bump that up to 37.3 months.

A little background. What is going on here? What type of cancer therapy are we talking about? It's a type of cancer therapy that people might know of as immune cancer therapy, or more specifically, immune checkpoint inhibitor therapy. They've got a wonderful acronym, ICI. We'll try to avoid using that three-letter acronym.

Here's the whole story, is, we had this idea for many years, and I think now it's been confirmed that people get cancer throughout their life. There's a number of stages that a cell goes through to go from being normal, healthy, good, part of the collective cell. First, you have this sustained proliferative signaling, and then you have the evasion of growth suppression. Then you have this resisting of cell death, so the cell just keeps multiplying without undergoing a programmed cell death, that apoptosis or apoptosis, however we're going to pronounce that. Think of the pterodactyls, I guess. [chuckles]

Then this really critical step, I'm going to leave a link into a paper that I published before, really pretty accessible, but immune evasion. Here you have these replicating cells that are not dying, and usually the immune system can step in, can clear these up, but somehow the cancer evades the immune system. How does that happen? Well, the cancer cells will actually put on their surface certain proteins that signal to the immune system, "Don't destroy me, nothing to see here."

I think some of these proteins people are familiar with, like PD-L1, programmed death ligand 1, sits on the surface, and there's a receptor that the T-cell has. When the T-cell comes along, it engages, and actually sends a signal to the T-cell, "Go kill yourself, don't bother me." That's exactly what it does. It sounds silly. It's exactly what it does.

The other is the cancer might have a protein called CTLA-4 on the surface, and when the T-cell comes along, again, has a receptor, engages, and the T-cell goes into this inactive state. I thought of this image. Instead of the T-cells killing the tumor like they're supposed to, they're all reading Sylvia Plath poems and committing suicide or sleeping next to the pool.

VR: What does the pool have to do with it, Dan?

DG: Sleeping next to the pool instead of doing their job.

VR: I see.

DG: Maybe they went to one of those legal cannabis shops, like one of our candidates for mayor, [laughs] just so we can get political here. What we've done over the years, we've realized that if you actually give medicines that cap off those signal proteins, then your body's immune system can actually go in there. Great stuff, but it doesn't really work for everybody when we give those medicines to try to block the cancer from stopping our immune attack. It doesn't always work. There are things called cold tumors. We find out here in this study that if you give these individuals an mRNA shot, they're going to tell us how this works, it's going to boost those drugs.

Actually, there's nice figures, we could really see this survival separation. I was really intrigued. It seems like it's separating more and more over time as far as your odds of survival. They look in and actually find out that there's a type 1 interferon signaling involved. They start back and forth looking at mice, going back into people to confirm this. I think basically, what we're seeing here is that mRNA vaccines are actually allowing your immune system to get in there and mop up the cancer.

Why did they even do this? I think it was the observation as opposed to the mythology out there, mythology about these turbo cancers. The observation was they actually had people saying, "I had this tumor, I got an mRNA shot, and the tumor melted away." This is actually the research explaining what exactly was happening there.

VR: It's also interesting that getting a vaccine increases PD-L1 levels on the tumor, which is a metric for whether you get this kind of therapy or not. If you have a certain percentage of tumor cells that produce PD-L1, then you're a candidate for surgery. This can increase that. If you weren't a candidate, then you could get to be a candidate after getting an mRNA vaccine.

DG: It was a 20%, 30% bump. If your doctor says, "Oh, I'm sorry, you're not a candidate, you get an mRNA shot," you're like, "Can you check again?" Now you might be a candidate. This is amazing stuff. We should talk about some real examples. People may remember many years ago before Jimmy Carter actually died, he ended up with a melanoma in the back of his eyeball. He got immunotherapy actually targeting these two immune evasion pathways. Within two weeks, his melanoma was gone. That was the same melanoma that killed Oliver Sachs not too many months before.

We talk about our buddy, Dickson Despommier, he got many extra years with one of his cancers from immune therapy. This is amazing stuff. Actually, here we're seeing this mRNA vaccine really boosting the ability of these, really, I'll say, less toxic and more effective therapies.

VR: This is good because people like to trash mRNA vaccines because they don't know anything. In fact, they've prevented a lot of COVID deaths and severe illness.

DG: Millions of people are alive today thanks to those vaccines.

VR: Now we see another benefit of these mRNA vaccines. What was interesting from the paper is that not all mRNA vaccines seem to do the same thing. The COVID vaccines work well, but in terms of their mechanism, another mRNA vaccine they tested didn't work as well. We're going to need to do more work here to see what's going on. Right now, you have off-the-shelf vaccines that you could get.

DG: The old-fashioned Moderna seemed to be better than the Pfizer, maybe because there was more mRNA, more reactogenicity. When they did some changes, the Kariko modification to the pseudouridine, change that back, get more reaction to the mRNA, you get a better anti-tumor response. We already have off-the-shelf. Go get a Moderna shot with your ICI, and you double your chance of survival, double your time with us. That's already amazing.

VR: The other thing that's very good about this paper is they had a mouse model for melanoma and non-small-cell lung cancer, which were the two cancers in people they looked at. They duplicated the effects in mice. In humans, this is an observational study, and we can't conclude anything, but in the mice, it's clear that giving the mRNA vaccine lets them live longer and clears metastases and so forth.

DG: Yes. All right. Amazing stuff. Another really interesting thing. Is this why the NIH is increasing the mRNA vaccine research support? Is that what's driving that? OK.

VR: Actually, they canned it.

DG: Yes, I know. I say that, but come on, stuff like this is amazing. Instead of it being about a cult or a mythology or misinformation, this is real science. You mentioned at the beginning of one of the deep-dive *TWIVs* that one of the great things about *TWIVs*, we discuss the actual papers, the actual science. Here it is, actual science.

VR: We don't have an ideology. We just believe in science. We don't blanket-say, "Vaccines don't work," for example. The science tells us that this is what it's doing. This could translate into lives for many, many people.

DG: An extra year and a half with someone you love, that's amazing stuff.

VR: Even with someone you don't love, at least you're living, right?

DG: Yes, you got an extra year with that aunt who drives you crazy or Uncle Jimmy coming down from Boston for Thanksgiving. [laughs] You'll miss him when he's gone or not.

All right. Another article. This is something we've talked about quite a bit, so I just really want to reinforce. "Viral Infections and Risk of Cardiovascular Disease: Systematic Review

and Meta-Analysis,” published in the *Journal of the American Heart Association*. We've talked a lot about this connection between viral infections and not necessarily getting sick and dying of the viral infection, but then in the subsequent period of time, a significant increase in your risk of having a heart attack, a stroke.

I've even shared, this is a lot of what drives some of the private insurance companies to really encourage vaccines because, boy, they can pay for a vaccine, and then they don't have to pay for you ending up in the hospital with your acute MI, and now you need to have a stent, or maybe you're not even going to survive.

Here they conduct a systematic review and meta-analysis of studies examining the association between viral diseases with the risk of cardiovascular disease, including coronary heart disease and stroke.

There's some nice figures that, hopefully, our YouTube viewers will be able to look at while I'm going through this. SARS-CoV-2, COVID-19, was associated with an increased risk of coronary heart disease, almost double, a relative risk of 1.74, and again, almost double your risk of stroke, relative risk of 1.69. If they looked at laboratory-confirmed influenza, even more striking, a fourfold increased pooled incidence rate ratio of ending up with acute MI after a laboratory-confirmed flu, and then stroke during that first month afterwards, fivefold increase.

I guess I've said that before. People say, "Oh, I got the flu shot, and I still got the flu," and I've always said, "but did you die?" Well, maybe we should add that, "but did you then have a heart attack? Did you then have a stroke afterwards?" Think about this. Get that flu shot, and potentially, you're going to reduce your risk of heart attack, strokes. They even saw, in association, herpes zoster. Not quite as impressive, but it elevated risk of coronary heart disease and stroke.

VR: Is this across all age groups, or does it tend to be in the elderly?

DG: Most of what we were seeing when we were looking at this in the private health was people in their 50s and 60s, but you see this all the way across. You see the most absolute incidence when you have the highest absolute risk.

VR: It would be interesting to do a study seeing the effect of vaccination on this.

DG: That's really key, because I am extrapolating and saying, "Boy, if you get that shot, you're less likely -" and we're going to talk about this in a moment, "-I less likely to get the flu, less likely to get COVID." If you don't get it, you can't have this, but then even if you do get it, I would suspect that the lack of severity of disease, which really what we're preventing, is also going to translate. That's the great next study to do.

All right. Actually, I'm going to do it out of order because you asked that question, because that's a good one. What about how well are those vaccines working? If people have been following CIDRAP, they had this whole project, they're going to really give us timely, good information. The headline in CIDRAP this week, "Meta-analysis of COVID, RSV, Flu Vaccines for Fall Provides Sea of Data Showing Efficacy, Safety."

This comes from a publication, "Updated Evidence for COVID-19, RSV, and Influenza Vaccines for 2025, 2026," that was published in *New England Journal of Medicine*. Here they

go and they search through the database, identify 17,263 references; 511 studies meet the inclusion criteria. What do we find in this pooled analysis? COVID-19 mRNA vaccines against the XBB.1.5 subvariant had pooled vaccine effectiveness against hospitalization of 46%, half as likely to end up in the hospital. That's in cohort studies; 50% from the case control studies, 37% among immunocompromised adults.

In case control study, vaccines against the KP2 showed an effectiveness of 68%. Then as far as safety, we always talk about this, I look at the YouTube comments, maybe they're coming from a bot because they're like, "You never talk about the risks of vaccines." Well, here we go, bots, if you're listening. I don't know if bots listen. The diagnosis of myocarditis associated with COVID-19 vaccines occurred at rates of 1.3 to 3.1 per 100,000 doses in male adolescents. That's the high-risk group. Lower risk associated with those longer dosing intervals, we've talked about it, if you push that out to three months between those first couple doses.

VR: What is the risk of myocarditis in the actual COVID infection?

DG: It's much higher. It's probably a log higher and much more severe. That's probably the most important. Not only is it more common, but the severity is much more significant. Most of these few cases, one to three per 100,000, resolves within 24 hours. You really have to look for it, where on the other side, we're actually seeing people hospitalized with fulminant myocarditis from the COVID infection itself.

Maternal RSV vaccination to protect the infants, nirsevimab for the infants and RSV vaccines in adults who are 60 years of – or older, vaccine effectiveness of 68% or more against hospitalization. Vaccine safety again, the RSV pre-F vaccine was associated with 18.2 excess cases of Guillain-Barré per million doses. A significant association with preterm birth was not observed when the vaccine was given at 32 to 36 weeks gestation in the pregnant moms. Flu vaccination pooled vaccine effectiveness of 48% in adults between the ages of 18 and 64, and 67% in children against ending up in the hospital. Safety profiles consistent with previous evaluations.

Some really nice figures where you can look at all the different studies that were pooled for COVID-19, for RSV, for influenza.

VR: Is the Guillain-Barré rate after RSV a concern?

DG: It's a concern. It's why we're talking about not just giving it to everyone and thinking about targeting it. Eighteen per million, that's 18 people per million doses. You start rolling this out, more and more individuals, you're going to see more Guillain-Barré.

VR: What is the current recommendation? 75 and up?

DG: 75 and up, but then one of the vaccines, 50 to 74 are people with risk factors. All right. Bird flu update. We'll bounce back to bird flu. Over the last weekend, the U.S. Department of Agriculture's Animal and Plant Health Inspection Service, APHIS, I'm pronouncing it that way, reported more detections of highly pathogenic avian influenza in commercial and backyard poultry flocks. I tried to go to the link today, but it seems like they're having some issue. Imagine that. Our government is not as functional as we would like.

A couple highlights. Two large commercial turkey farms were hit in Minnesota. I think we

talked about before, Minnesota is the nation's top turkey producer.

VR: Washington, DC is.

DG: Washington, DC? You were saying that. [chuckles] We're talking about the real turkeys that we're going to eat at the end of next month. A commercial turkey farm was affected in Meeker County with 132,500 birds reported avian flu. Another 36,900 birds in Otter Tail County. This is the epicenter. The largest commercial turkey farm area in the U.S. is actually this epicenter of highly pathogenic avian influenza activity.

VR: I'm going to have sushi this Thanksgiving.

DG: Do you eat turkey on Thanksgiving there, Vincent?

VR: Not for years. I've got so tired of it.

DG: [chuckles] We have a lot of vegetarians in my family. Usually there is some turkey involved, but a lot of tofu and so many other things to eat. A broiler farm in Georgia also affected. A commercial broiler chicken facility in Georgia's Gordon County also reported avian flu affecting 139,000 birds, infected backyard flocks in Montana, Michigan. Three farms had confirmed HPAI in Lancaster County, Pennsylvania. That's where our Amish communities are. Avian flu activity is increasing across the country.

In the past 30 days, confirmations have been made in 64 flocks, 30 commercial flocks, 34 backyard flocks, 3.57 million birds affected in the outbreaks. As mentioned, Minnesota has seen the highest jump in activity with 665,720 birds affected.

VR: These were all culled, I presume, right?

DG: We cull them, and then I guess, we've been importing chickens from Turkey and some other countries. All right. Measles. We're getting updates, actually, which is nice. The CDC has been updating their measles tracking data. As of October 28, a total of 1,648 confirmed measles cases. That's an extra 30 cases seen just in the last week. It's worse than that, because these are confirmed cases. It sounds like there's a case in Utah, but the family's refusing testing. That doesn't count when we have these outbreaks.

Canada, another 19 new measles cases. We're up to 5,109. I wanted to mention, we're going to lose this status of measles elimination in Canada probably this next month. Then we're, in January, probably going to lose the status of measles elimination in the United States.

VR: Daniel, if a family refuses to be tested, I would say they need to be confined to their home until the potential of being infectious is gone.

DG: It's really tough. If you've got someone, "Hey, I think you're a risk to others, I think you -" There's the story of that famous actress where someone left quarantine because they really wanted to see her, and then her child was born with all kinds of issues. I think it's an Agatha Christie story based on that. This is not just your decision. Having measles, having these vaccine-preventable illnesses, you put other people at risk.

On that wonderful note, let's move on to flu. Still time for those flu shots. What did I talk about last time, that we were starting to see increasing flu activity in the UK? We'll try to

keep an eye on what's going on here in the US, but the CDC flu surveillance has not been updated since September. We'll talk a little bit about some other ways to track that. Let's talk about RSV next.

Now, RSV is tricky. This is a thought experiment. I want everyone to think about why is wastewater not a great way to track RSV? Think about who it affects. Its biggest target right here is the under-2. What do a lot of kids under two wear?

VR: They wear diapers.

DG: The urine and the feces end up in the trash. People really don't scrape that off and get all that into the wastewater. The urine, you're not going to get it scraped off there.

VR: You're not supposed to flush your diapers down the toilet.

DG: [laughs] Don't do that. Oh, my gosh. One of the better ways to track RSV than wastewater is really tracking ER visits by state. We usually start to see the earliest activity end of October, early November, down in Florida, Alabama, Georgia, that region, maybe some Mississippi activity. We're already starting to see a little bit of activity starting in Florida. I think we're on track for the RSV season to start rolling out.

We have a little more data on those RSV vaccines. This is on the mRNA-1345, so the mRNA option by Moderna. This is the article, "Safety, Tolerability, and Immunogenicity of Revaccination with mRNA-1345, an mRNA Vaccine Against RSV, Administered 12 Months Following a Primary Dose in Adults Aged 50 Years or *Older*, published in *CID*, open label, phase 3 trial. They're looking at revaccination with 15-microgram mRNA-1345 given 12 months after that first shot, that primary vaccination. Primary objectives were immunogenicity, so neutralizing antibody responses, tolerability, safety. This is not efficacy of preventing disease. We're following antibody levels, 543 folks revaccinated. Most adverse reactions were mild or moderate, no new safety concerns.

As far as the immunogenicity endpoints, they did meet their pre-specified non-inferiority criteria based upon day 29 geometric mean titer ratios. I think our listeners might remember hearing about those. I really like the figures actually, because they show primary vaccination, you get that nice rise, and then you get the contraction, and then you get nice rise with the repeat vaccination, really up to - a little higher level with RSV-A antibody levels, about the same with RSV-B. Greater than two-fold rise in titers in 91.6% of folks and 69.8% for the RSV-B.

VR: Wouldn't it be interesting if RSV mRNA vaccine also extended your life if you have certain cancer therapies?

DG: Yes. It's another one to look at, right?

VR: Yes.

DG: All right. We also have the article, "Vaccine Effectiveness of a Bivalent Respiratory Syncytial Virus (RSV) Pre-F Vaccine Against RSV-associated Hospital Admission Among Adults Aged 75-79 Years in England: A Multicenter, Test-negative, Case-control Study," published in *The Lancet Infectious Diseases*. This is the protein-based, guys. September 1, 2024, an RSV immunization program for older adults was introduced in England.

The program offers a single dose of bivalent RSV pre-F fusion, this is Abrysvo, the Pfizer, to all adults turning 75 alongside a one-off catch-up campaign for those aged 75 to 79. Remember with the shingles one, it was like, "Too bad, you're over the hill, you don't get it,"?

VR: Yes.

DG: This is, "Too bad, we're not going to be able to do that wonderful analysis." [chuckles] Anyway, we did learn a little bit about vaccine effectiveness. 82.3% against hospitalization for any RSV-associated acute respiratory illness, 86.7% severe disease including oxygen supplementation, 88.6% among individuals admitted due to lower respiratory tract infection including pneumonia, 77.4% due to exacerbation of chronic lung disease, 78.8% due to exacerbation of chronic heart disease, lung, and or frailty, 72.8% in folks with immunosuppression. Really impressive.

VR: Good numbers, yes.

DG: These are great numbers across the board. All right. COVID, no cool multicolored graph.

VR: I miss that.

DG: It's going to be back. By "it's," do I mean the multicolored graph or COVID? We'll see. What should we be doing now during this lull? We still get questions about the benefit of yearly COVID jabs. My youngest brother just got married, so this was one of those gatherings where people, "By the way, what do you think about getting a COVID shot? As a doctor, what's your opinion?"

Nice for me to be able to refer to the literature. Here we have the article, "Association of 2024–2025 Covid-19 Vaccine with Covid-19 Outcomes in U.S. Veterans," published in *The New England Journal of Medicine*. Observational study that used the electronic health records of the Department of Veterans Affairs to evaluate the effectiveness of 2024-2025 COVID-19 vaccine among veterans who got COVID-19 and flu vaccines on the same day, 164,132 participants.

They've got an active comparator group who received flu vaccine only, 131,839 participants. I have to clarify, flu vaccine versus receiving the flu, because this is the military. There are some settings where they give you the flu and you volunteered for that. No, this is vaccination you're volunteering for here. These are veterans, so I don't think they have to volunteer for those flu challenge studies.

Here are the results. At six months, estimated vaccine effectiveness was 29.3% against COVID-19 associated emergency department visits, 39.2% against COVID hospitalization, 64% against COVID-19 associated deaths. Nice figure with all the different outcomes.

VR: Could be better, right?

DG: It needs to be better. We want better outcomes here. We just talked about those RSV outcomes that were all pretty much in the 80s. That's what we want.

VR: The deaths is really the best one, 64%, because in an older population, it doesn't take much to get them to the ED, right?

DG: Yes, you feel crummy, you end up in the ED, maybe even end up in the hospital, you're not doing well at home.

VR The deaths, it's 64%, that's pretty good.

DG: This is in this particular population. Let's talk about another article, "Durability of 2024-2025 COVID-19 Vaccines Against JN.1 Subvariants," published in *JAMA Internal Medicine*. August 22, 2024, a year ago, the U.S. FDA authorized, for emergency use, the updated 2024, 2025 messenger RNA COVID-19 vaccines targeting the KP.2 strain variant of the JN.1 variant for a person 6 months or older. August 30, the FDA also granted emergency use authorization for Novavax.

Here they collect individual level data on the uptake of this updated COVID vaccine. They're going to look at approximately 1.8 million persons using this Nebraska Electronic Disease Surveillance System, Hospital Discharge Data System, Office of Vital Records, and State Immunization Information System. They're going to look at three outcomes. We're going to look similar to above, SARS-CoV-2 infection, COVID-19-related emergency visits, COVID-19-related hospitalization or death.

Then who gets what? We've got 237,203 individuals, 86,594 got Moderna, 148,429 got Pfizer-BioNTech, and only 2,180 got Novavax. Let's walk through the data. The vaccine effectiveness against infection reached a level of 44.7% at four weeks and then declined to 35.5% at 10 weeks, and then down to 16.7% at 20 weeks. You can really see the drop-off there.

For emergency department visits, we peak at 45.1% at four weeks out, 42.9% at 10 weeks, and then 39.1% at 20 weeks. Not terrible. As far as hospitalization or death, 57.3% at four weeks, 49.7% at 10 weeks, and 34% at 20 weeks.

VR: The drop of protection against infection is not surprising. That's fine. These results are broad, right?

DG: They're really wide confidence intervals. We're getting a trend. In 57, 49, 34, it does look like there's some contraction of the protection.

VR: Right. The T-cells are what are protecting you against severe disease and deaths. They're not supposed to worry about the variant that you're infected with. I think the decrease is maybe a statistical issue and nothing else, because the intervals are broad, and you can look at the hospitalization or death, and the upper limit is maintaining protection there pretty much.

DG: It's actually true. If you look at ER visits, that's actually fairly level, right?

VR: Yes.

DG: That's going to wrap us up this week. Not a lot of changes with management of acute COVID. Not a lot of management changes with second week. As we've been saying for years now, no one is safe until everyone is safe. We are now in our *MicrobeTV* fundraiser. Vincent, this is exciting.

VR: All right. I've been waiting all year for this.

DG: Thank you for all your support for our American Society of Tropical Medicine and Hygiene fundraiser. I guess, you and I, Chuck and some other folks are going to be heading - Peter Hotez will be there. All of the Parasites Without Borders directors are going to be there in Toronto. Moving on to *MicrobeTV*, we're going to be doubling those donations. We want to get up to that maximum donation of \$20,000. Go to parasiteswithoutborders.com, click that donate button. Help us continue to do this great work.

VR: Time for your questions for Daniel. You can send yours to Daniel@microbe.tv. Eli writes, "How does giving a newborn hepatitis B vaccine produce protection when the child is not yet immune-competent?"

DG: Eli, that's a sophisticated question. I'm going to take your word "immune-competent" and be a little critical of that. When a newborn is born, they may not have a fully mature immune system, but they still do have an immune system, and that immune system still has the ability to respond to challenges, still has the ability to acquire memory. We've actually seen, with hepatitis B, with BCG, which we think is mainly working through T-cells, that newborn children can actually get protection. Why do we give hepatitis B right at birth? Because when we didn't, when we were waiting, we were seeing children actually about 25% breakthrough, we were missing cases. Maybe the child would get it through breastfeeding or other exposures, not sexual exposures in the early period of time. Newborns actually have a mature enough immune system, enough immune competence to respond to some of these vaccines right at birth.

VR: The fact is they work, right?

DG: They work. That's the proof of the pudding.

VR: Rita writes, "I've been then listening to *TWiV* early in the pandemic when Dr. Ginger Campbell recommended it on the *Brain Science* podcast. I have been an avid listener to the regular episodes in the clinical update ever since. It's been a shining light in these dark times. Thank you and the whole *TWiV* team for all you do to fight misinformation.

Now, on to my question. I'm a relatively healthy 58-year-old woman. On October 3, I crossed Lake Chilwa in Malawi to visit Chisi Island. I had limited contact with the lake water, no swimming or wading, but it definitely came into contact with my skin. Colleagues recommended that I see a doctor, which I did. She prescribed praziquantel for me to take eight weeks post-exposure, whether or not I develop symptoms. I got the pills and have them on-hand.

My primary care provider's initial response in consultation with an ID specialist is that I get a blood test at 12 weeks post-exposure. If it's positive, she will do urine and stool to confirm infection, then I would take praziquantel. I would likely have to pay for this out of pocket as I have not yet met my yearly deductible, and all this tending might extend into 2026. I saw my provider today and told her about the Malawian physician's advice. She said it was up to me.

My specific questions are, what are the risks of taking praziquantel if I never develop symptoms? I read the list of side effects and the medication seems safe except for the rare seizure. I've never had any adverse reaction to any medication. If I do take the medicine prophylactically, should I be tested at some point in the future? If I never develop symptoms, should I just ignore the whole thing?"

DG: [laughs] The most impressive is the leaving it up to you, because this is complicated. First, let's talk about your risk. Limited contact with lake water. You weren't swimming. You're not giving me a description. Were you in the shallows? Were you going to come in contact with the cercaria? We've got this snail lifecycle thing there. It sounds to me like your risk is very low. We'll start off with that. Very low risk here, but not zero. Low risk, but zero.

Now, the other side is what is the risk associated with praziquantel? Very low risk also. A lot of folks, let's say you were in the State Department, you lived in Malawi, you were swimming in Lake Malawi, and you had all these exposures, when you leave, what you were talking about here, eight weeks after your last exposure, you go ahead, you take your praziquantel. Very well tolerated. You ran through the side effects. Not something I would expect there to be a problem.

I don't really know if it makes sense to go through all the hoops and all the expense of doing serology testing, following that up with urine or other testing. It is very low risk to start off with. You would lower that risk even a little more with going and taking the praziquantel. I'm not sure if it makes sense to go down all these other roads.

VR: Jessica writes, "Sorry to bring up another potentially troublesome topic, but I hear our leadership wants to import lots of beef from Argentina. I also heard there's a lot of hoof and mouth disease, foot and mouth disease in the cattle there. Meanwhile, our food inspectors are fired or sidelined. What should consumers think about this? Is there cause for concern?"

DG: Jessica, this is an interesting topic. Hoof and mouth disease, personally, has been an issue because when I was first over there in Malawi and I was wanting to buy a cow because we were heading into the pandemic, I thought that would be a great thing for source of protein nutrition for some of the staff and some of the support staff at the clinic in Eastern Uganda, there was a hoof and mouth disease epidemic going on. That then got under control and later, I actually lost one of my cattle to hoof and mouth disease.

Now, Argentina is a totally different situation. Argentina is actually WHO-certified hoof and mouth disease-free as of May of this year. We think they may not have even had hoof and mouth disease since 2000. There's even about half of the country where they don't even require a vaccine because they really have done such a great job here. I've seen a little bit back and forth about this in the news, but I really don't think that's really an issue, hoof and mouth disease in Argentina.

I guess what is an issue, and talking to people that are ranchers that are involved in this, they're pretty upset about the whole idea, as you can imagine, about their tax dollars going to subsidize the competition and their tax dollars going to bring cheap beef into the country to undercut their ability to make a living. I don't think there's a medical. It's more of an economic issue here. This may be some kind of an excuse.

VR: Barbara writes, "I'm 70. I had chickenpox as a child, raised four children, all of whom had it as well. When I turned 60, I got shingles vaccine, which was one shot. I ended up with a strong reaction. I went to the pharmacist to see if I needed a doctor. She told me the reaction was evidence that my immune system was reacting, so OK, I got over it.

In the meantime, Shingrix vaccine became available, but I've been reluctant to get it because of the adverse reaction I experienced with the first one. My doctor did tell me I don't have to get Shingrix, but I want to know if you believe I should for the dementia angle.

To make this decision even harder, my older sister has Alzheimer's and is in decline after being diagnosed seven years ago when she was about my age.

As you can probably imagine, I'm fearful that I could be next. Our parents did not live long enough to know whether they would have had dementia. To my knowledge, my sister is the only person in my family who's had dementia. She's been afflicted. I only found *MicrobeTV* in January this year when the administration began its assault on public health, and I looked for alternate sources to stay up to date as possible. It galls me that I never found you during the COVID pandemic. I relied on MedCram throughout, and so far, I've never had it, but still, would have been so good. Y'all are a gift. Thank you so much."

DG: Wow. Thank you, Barbara. This is a challenging question because, as we've mentioned a few times during this episode, vaccines can have side effects. You can have issues with reactogenicity like you're describing here. We've, over the last year, talked about several studies where - the great study out of the UK that I alluded to showing the original vaccine for varicella zoster was associated with a reduced risk of dementia, some other studies that maybe the Shingrix is even better than the original. The Shingrix is a protein-based vaccine.

It is tough because you have Alzheimer's history in the family, so reasonable concern. In a context like this, getting the shot, getting the Shingrix is reasonable. You might end up with that sore shoulder again, that sore injection site.

VR: That's a good trade-off for preventing dementia, right?

DG: I would think so.

VR: Dan writes, "I'm a regular *TWiV* listener, and I appreciate your factual information and insights during these challenging times. I have a question. I'm a healthy 70-year-old, a noVID, and plan to receive another COVID booster in the next few weeks. Last fall, I had Novavax, all priors had been mRNA vaccines, hoping it might provide more durable protection. I believe there isn't hard data on that. My question, I'm thinking of having Novavax booster again, but I'm concerned that it still is only against the JN.1 lineage, so not updated. In view of the XFG variant being predominant, do you think updated Pfizer or Moderna targeting LP.8.1 might be more effective?"

DG: Dan, it is a great question. Proof of my belief is I went ahead, I got the Novavax booster this fall, as did my wife and everyone else. As Vince and I have talked several times, I think a lot of the protection against severe disease is T-cell-based. They, certainly, are contributions to antibodies, to prevention of infection, which is relevant concern. No, I'm not convinced that there's any compelling data that you need to do the mRNA if you had Novavax before, if you tolerated it well.

VR: That's *TWiV* weekly clinical update with Dr. Daniel Griffin. Thank you, Daniel.

DG: Oh, thank you. Everyone, be safe.

[music]

[[00:50:21] [END OF AUDIO]