TWiV 1274 Clinical Update

Host: Vincent Racaniello

Guest: Daniel Griffin

Aired 28 November 2025

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

[music]

VR: From *MicrobeTV*, this is *TWiV, This Week in Virology*, Episode 1274, recorded on November 27, 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. To you, Vincent, since we're recording this on Thanksgiving for the sixth time in a row, happy Thanksgiving.

VR: [chuckles] Thank you. Same to you. Yes, we don't let holidays stop us disseminating important information.

DG: Yes. That confused Christina Naula. She's like, "No, no, I celebrate Christmas." We're like, "What about Christmas Eve?" She's like, "Yes, no." "What about Christmas Day? It's just an hour. What about Boxing Day?"

VR: Yes. Right.

DG: [laughs] All right. Let's jump in with the quotation because we got a lot to talk about. I got a hot cup of coffee here because it's been a long day and it's still not over yet. I'm working today. I don't know. I'm seeing patients in the hospital, as well as this, and everything else that I'm doing, but one of the favorite things I like to do with the family is to watch the *Charlie Brown Thanksgiving*.

[laughter]

DG: Of course, I was looking for a Charles Schulz quotation. I thought this is very appropriate for our show. "Try not to have a good time. This is supposed to be educational."

[laughter]

VR: We make education a fun time, don't we, Daniel?

DG: It's this edutainment, right? I don't know who coined that, but that's what we try to make it. It's educational. It's fun.

VR: Daniel, last night on the stream, we're talking about viruses, and I decided to read a poem to everyone, and they loved it.

[laughter]

DG: Now, which poem did you read? I'm very curious.

VR I read *The Raven* by Edgar Allan Poe.

DG: That's fantastic.

VR: It's a fantastic poem. I gave it a lot of inspiration in reading, and they said, "We should have a poem every office hours." I said, "OK, no problem. I can do that."

[laughter]

DG: What is it Mike Osterholm does? He reads a song or something-ish.

VR: Really?

DG: Yes, I like the poem. I got my quotation, you can jump in with your poem.

[laughter]

DG: All right. It'll set the mood. Set the mood. OK, so let's start off with this first one. I think every so often, I put in the anti-science movement. What is going on? What's happening to destroy the health in America? Because there's this whole idea that there's this Make America Healthy Again, and it's really not. Right? It's like, "Oh, I would eat at McDonald's every day as long as they would deep-fry it in lard instead of something else." Just the shocking concepts of what is supposed to make us healthy.

One of the not making us healthy is this real targeted attack on infectious disease, on public health, on vaccines. Just so people are aware, because I don't want this stuff to go on unnoticed. Ralph Abraham, MD, the former Louisiana surgeon general, has been quietly named the deputy director of the Centers for Disease Control and Prevention, a controversial pick to help lead the nation's top infectious disease organization. I think we're going to have to think about whether or not we get to call it that anymore, as the second highest-ranking CDC official.

Now, Abraham is a longtime critic of COVID-19 vaccines. He advocated for the use of ivermectin during the pandemic. Also, a big hydroxychloroquine advocate, despite the lack of evidence, and then the evidence about the harms involved. He has also stated that the U.S. should stop those birth doses of hepatitis B vaccines. We've discussed it. It's going to really result in thousands, tens of thousands of little kids getting infected, having lifelong infection.

As the state surgeon general, he told the health department to stop promoting mass vaccination. Did not publicly respond to the pertussis, the whooping or whooping cough outbreak in Louisiana for two months, even after two infants had died.

VR: One of the jobs of the deputy CDC director, Daniel, is to respond to outbreaks, so I don't think this is a good choice on top of everything else you've told us.

DG It's really tragic. I know my wife at one point was commenting about, at some point, we're going to have children dying. Then the people are going to say, "This is just too much."

Yes, we want low taxes and apparently want to kick out a lot of the immigrants who are taking our jobs, but the children are already dying, as we're going to talk about in a moment, and we still haven't apparently had enough.

Let's go right into that. Let's talk about pertussis or whooping or whooping cough. Just this week, we heard that an infant in Kentucky who was unvaccinated against pertussis died. This is the third death in Kentucky this year. They hadn't had an infant die in Kentucky since 2018. It's been eight years since tragedies like this. Kentucky is seeing the most pertussis activity since 2012. We're expecting more in coming weeks. So far this year, Kentucky has had 566 cases of pertussis, of whooping cough. Nationally, there are more than 25,000 cases of whooping cough.

Texas is where we're seeing the most activity with at least 3,500 cases so far this year. They had two deaths already in Texas. There were two deaths in Louisiana, three in Kentucky. I'm up to seven children have already died this year. Now, before the vaccine, just to point out just how tremendous this vaccine is, there were an estimated 200,000 cases each year. We used to see 9,000 children die each year. Apparently, this is where these folks want to bring us back in the attempt to make America healthy again.

VR: Doesn't make a lot of sense, Daniel. I don't get it.

DG: I hope our production people will post this, but you can actually see where we're headed. I'm going to post this cdc.gov/schoolvaxview/data/index. The link will be in our notes. You can just see, we used to have, up until pre-pandemic, above 94% national vaccination coverage among kindergartners, but we've really had this precipitous drop. You may have heard, even in West Virginia, where they really have done a great job, now they're going to make it harder for the vaccine mandates to go forward.

VR: This guy, Abraham, he says, "Oh, vaccines are important, but it has to be a decision between the family and the physician." What do you think about that, Daniel?

DG: That's the tough thing is that we're seeing here. If the kids are going to be, and these are infants, these are a lot of these kids, they're either unvaccinated or they're too young to be vaccinated. You're at risk. We live in this community, it's like, "Oh, if you want to fire your pistol in your backyard, go ahead."

You can't because that carries. That's the problem with whooping cough, and not being vaccinated, and measles, and all these other things. If you don't vaccinate yourself, you could kill someone else. That's why we have mandates. That's why you can't drive drunk. That's why you have to actually act in a way that looks out for the fact that we live in a community.

VR: Public health only works if everyone signs up. You can't have it everybody choosing.

DG: Yes. There's a certain point. If we can get ourselves all vaccinated against measles or whooping cough, we can protect ourselves, but what about early in life? What about before that first year? What about now if you're getting bad advice about which vaccines to get right at birth, and now your child, it's too late and they have a chronic infection? All right. Basically, we're at that dark period where when you mix politics with medicine, you get dead children and another child's dead.

All right, HPV. We've been talking a lot about the HPV vaccine. Really, a tremendous advance. It was actually a country recently then announced that they have had, I think it may be Australia, like zero cervical cancer cases this last year because they've really embraced the HPV vaccine. This is another target of the anti-science, anti-vaccine folks. We have the *Cochrane Review* - always reminds me of OJ Simpson for some reason. Maybe it's the lawyer's name. "Effects of Human Papillomavirus (HPV) Vaccination Programs on Community Rates of HPV-related Disease and Harms from Vaccination."

The review included 225 studies from 347 records evaluating over 132 million people. Robust data here. They included 86 cohort studies, four case control studies, 46 cross-sectional studies, 69 pre-post-vaccine introduction studies, 5 RCT extensions, and two self-controlled case series. Thirteen additional studies reported on more than one type of analysis. Tons and tons of data here.

Here are the results, just to sort of bullet point through them. For those vaccinated at or before 16 years of age, we're talking about 4.54 million person-years, there was an 80% reduced risk of cervical cancer. Moderate certainty from 23 studies that HPV vaccination reduces the incidence of cervical intraepithelial neoplasia grade 3 or higher, including 12 cohort studies.

For 1.5 million females vaccinated at or before the age of 16 in two cohort studies, there was a reduction of this CIN3+, 74% in the long-term. Moderate certainty evidence from 37 studies that HPV vaccination reduces the incidence of CIN2+. In cohort studies with females vaccinated at or before the age of 16, a reduction in risk was seen in the median term of about, well, relative risk, 0.59, so that's about a 41% reduction. Long-term, even better, relative risk 0.38, so about a 62% reduction.

Really, just going down the line, we're just seeing all these benefits, including not just cancer, but anogenital warts. Just horrible issue there. We're seeing a reduction of 47% in the short-term, 53% in the long-term. As far as safety, across a range of all these different study designs, HPV vaccination was not associated with an increased risk of, and then they go through all these different concerns. No incidence of an increased risk of Guillain-Barré, so incredibly effective, incredibly safe vaccine.

VR: You know, RFK has been advising law firms who sue Gardasil manufacturers saying it's dangerous, and it's all without merit. This is a wonderfully safe vaccine that prevents cancer, and that's the bottom line.

DG: Yes, yes. Really horrible. Yes, they're doing all they can to undermine. Wouldn't you love to have that result like they have in Australia? We don't have women getting cervical cancer anymore. It's amazing to me that these people's love of money is -

VR: That's it. It's all about money.

DG: It's all about money. Yes. All right, Marburg, Ethiopia's first outbreak of Marburg virus disease. We talked about this a little last week, so November 14, Ethiopia Ministry of Health reported the country's first Marburg outbreak. Most up-to-date data we have is that so far, five people have died. No reported Marburg illness outside of this outbreak, as far as getting outside of Ethiopia at this point. We'll keep an eye on that. All right, polio, Vincent. I'm expecting some commentary from you here because you have a bit of an interest, right, in polio, if I -?

VR: I would fail you. I have a lot of interest in polio, yes.

DG: [laughs] OK.. We've got the article, “Safety and Immunogenicity of Novel Live Attenuated Type 1 and Type 3 Oral Poliomyelitis Vaccines, Healthy Adults in the USA: A First-in-human, Observer-masked, Multicenter, Phase 1, Randomized Controlled Trial,” published in *The Lancet Infectious Diseases*. We've discussed before how the risks of vaccine-derived polioviruses and vaccine-associated paralytic poliomyelitis motivated the development of these novel oral polio vaccines.

Now these vaccines are designed to have similar immunogenicity, but improved genetic stability, with the idea being that this would potentially reduce the risk of neuroinvasion and paralytic disease relative to the Sabin strain oral polio virus vaccines. This study aimed to assess the safety and immunogenicity of the novel oral polio vaccine 1 and the novel oral polio vaccine 3, so NOPV1 and NOPV3 in healthy adults.

Here they did it. First-in-human, observer-masked, multicenter, phase 1, randomized controlled trial in healthy adults at four centers in the USA. Participants were block randomized. That's where you take a group and you say, "OK, this group gets X intervention, this other block or group gets this other." Because there might be some connection between one individual and another, so participants were block randomized, stratified by site, and according to polio vaccination history, or regimens that included IPV or OPV before. Then they were randomly assigned to receive either the novel OPV or the Sabin-strain monovalent OPV.

The primary outcome was safety among vaccinated participants. Secondary outcomes included serum neutralizing antibody response measured before and 28 days after each dose in a per-protocol population. Also some fecal viral shedding, mainly in IPV participants assessed up to 56 days following each dose among vaccinated participants. 226 were randomly assigned, 205 received at least one dose, and then they break down into who gets which amount. About 70, somewhere between 36 and 70, get each of the different interventions.

What do they tell us? Both vaccine candidates appear safe, well-tolerated, able to elicit neutralizing antibody responses similar to those elicited by the monovalent, the originals. In addition, the profile of viral shedding was similar to that of the monovalent OPV, with shedding in most vaccine recipients limited to the first two weeks, with subsequent rapid decline to largely undetectable levels by four to six weeks after vaccination.

VR: OK, Daniel, this is a study that should never have been done because nobody should be using an OPV1 and 3. We're already using, not in the U.S., but in other countries, an OPV2. The idea there was to modify monovalent OPV2 to make it less paralytogenic. It is still paralytogenic. It's less, but it still paralyzes kids.

These viruses, NOPV1 and 3, are derived from NOPV2, just by popping out the capsid coating region and replacing it.

These will paralyze kids as well. There is no need to be using an oral polio vaccine that paralyzes kids because inactivated vaccine, IPV, used in the U.S. and many other countries, Europe, Scandinavia, does not paralyze kids. That's the vaccine you should be using. I don't see how it's ethical to use a vaccine that paralyzes kids. The WHO says, "Oh, it paralyzes them less. Sorry."

DG: I think it paralyzes maybe fewer kids is the idea because it's not like if you get paralyzed, you're less paralyzed.

VR: Yes, sorry. Yes, of course.

DG: [laughs]

VR: Fewer kids, yes.

DG: My wife's always good about fewer and less. [laughs]

VR: Yes, fewer kids-

DG: Fewer kids will get -

VR: -but still, kids are going to be paralyzed.

DG: Still, kids are getting paralyzed.

VR: It's not ethical. We don't allow these vaccines to be used in the U.S. for that reason. Why is it okay to use them elsewhere? The polio vaccine story shows you that the anti-vaxxers don't know what they're talking about because this is the one vaccine, the OPV, that they should object to and they don't because they don't read.

DG: Yes. We all should object to this. I do feel like it's this argument, "Oh, well, instead of 10 kids, only six." Only, there's no only-

VR: No.

DG: -in front of a paralyzed or a dead child.

VR: It's like Makary or whoever saying, "Oh, only 250 kids died of influenza." Right?

DG: Yes. No, and that's what they say, "Oh, it's only a couple hundred." Only a couple hundred, and yes. Yes.

VR: Unfortunately, this is being driven by Gates funding, and they like this idea, but they're misguided. I'm sorry. They're always saying it's improved, but it doesn't matter, unless it's zero. We know we can get zero paralysis from a polio vaccine. It's not acceptable.

DG: Yes. No, and I think it's important because we keep saying this. I do think people listen, and then they start asking this question and saying, "Oh, maybe that's not OK. Hopefully, if we keep saying this, people will realize that it's not OK.

All right, so now we're moving on to measles, and I just hot off the press, as of November 25th, a total of 1,798 confirmed measles cases here in the U.S. We're almost at, what was it, in the year 2000, declared eliminated? We're almost at 2,000 cases at this rate.

Canada, we're still seeing cases up there. This is, again, as we keep talking about, these are vaccine-preventable issues. Why are we seeing this take off so quickly? First, we have kind of a perfect storm setup, but the other is that we don't have the people responding the way they should. That's what the CDC usually does when there's an outbreak, they respond, they step in.

All right. Flu. Actually, we're starting to see a bit of flu here in the hospitals, Vincent. It was actually interesting, I had a guy I was seeing today, and he's got Flu A. He's got the H3, because usually, we get the H1 and the H3, right? He had the H3. I asked him, I said, "Did you get a flu shot this year?" He said, "I usually do, and this year, I didn't. Can I still get one?" I did mention, I said, "There's more than one type. You got H3. You still could get a vaccine here in a few weeks, and maybe that'll help you with the H1."

For those of you that have not gotten your vaccines, time to get out there. We're starting to see increasing activity. Again, this is what sets up the perfect storm, is you have flu activity, and then people are traveling all over the place for the holidays. If there's flu activity anywhere, now we end up with flu activity everywhere.

All right, so we've got our epidemic trend. We're basically in almost everywhere in the country, it's growing or likely growing. We're going to be seeing more of that. What do you do about it? I mentioned vaccines. We got a couple of vaccine studies, the actual science.

As people may know, I'm a bit of a fan of the cell-based versus the egg-attenuated flu vaccine technology. For a couple of reasons, but here's a nice article, “Superior Effectiveness and Estimated Public Health Impact of Cell versus Egg-Based Influenza Vaccines in Children and Adults During the US 2023-2024 Season,” published in the journal, *Infectious Diseases and Therapy*. These are results from a test-negative design study applied to a large linked real-world database to assess the relative vaccine efficacy of cell-based versus egg-based flu vaccines in preventing confirmed influenza during the 2023-2024 season.

We're not talking about hospitalization, we're not talking about ER visits, we're not talking about deaths. This is just confirmed flu illness. The analysis included 2,119 cases. Then we're going to go through and break this down, and put on my glasses for all these numbers we've got here. The cell-based, and that's the QIV with a little c, as opposed to the QIV with the little e for egg, in preventing test-confirmed influenza, relative vaccine efficacy of 19.8% in the full population, 19.6% in the pediatric population, 18.5% in adults 18 to 64. Really consistent results were observed for all the different subgroups.

Now, interesting. You think, "Well, this is only 20% or so." Remember, this is relative, so this is the efficacy of egg, plus getting 20% better. Is that really going to add up to much? They estimate that this would prevent 2,379,395 additional symptomatic illnesses. Pretty amazing. Over 2 million.

VR: It's interesting that they looked at just test-confirmed influenza. That's a very high bar. I think it would look even better if they said moderate to severe influenza.

[background conversation]

VR: Oh, you're having a party there, Daniel.

DG: Yes, I am. Hold on a second. I'll have them quiet down. One second. One second, everyone.

(background conversation)

You guys, quiet down for the recording.

DG: We are. It's that holiday, right? It's that Thanksgiving.

VR: Yes. Daniel is putting a damper on everybody's fun.

DG: I know. I know. Yes.

[laughter]

DG: All right. See, I'm like Scrooge, but for the wrong holiday. All right, so can we do even better, right? Now we're all excited about - The other, why am I so excited about cell versus egg? Part of it is the ability to respond more rapidly, right? Because we've talked a little bit about years when we don't quite hit it right. We start to realize it's going to be more of an H3, and maybe the H3 is going to be a different strain or variant than what we're expecting. With cell or maybe mRNA, for instance, maybe we could switch around and be ready for it, get a little closer.

Here's the article looking at, "Efficacy, Immunogenicity, and Safety of Modified mRNA Influenza Vaccine," published in the *NEJM, New England Journal of Medicine*. These are results of a phase 3 trial where they randomly assigned healthy adults between the ages of 18 and 64 to receive either a quadrivalent modified RNA influenza vaccine or a licensed inactivated quadrivalent influenza vaccine. This is modified. This is not just mRNA, but the modified RNAs. We'll maybe talk a little about what are they talking about there. Special, new, modified RNA group.

They're looking in the 2022, 2023 influenza season in the U.S., South Africa, the Philippines. Primary endpoint was relative efficacy defined by the reduction in the percent of participants with lab-confirmed influenza associated with influenza-like illness. Really similar to that last one. Being sick and turning out that you're sick with the flu. They looked at 18,476, split them 50/50. The modified RNA compared with control vaccine, 34.5%. Not bad, actually.

Interesting, they say that it's non-inferior, but there was the issue, right? I don't think anyone was surprised about this. I've got some nice charts here. We do see a reduction in the number of cases. We've got about 9,000 in each group. In the modified RNA, you end up with 57 lab-confirmed flu cases. You end up with 87 in the control vaccine. That gives us a relative efficacy of this 34.5%. It's 34.5% reduced over your standard vaccine. You also get a lot of reactogenicity with the modified RNA vaccine.

VR: Again, Daniel, they're looking at PCR-confirmed influenza, which a couple of months after you get the vaccine, that's going to be going away. It would be really more informative to look at moderate to severe disease and see what you get. Same -

DG: It is interesting, right? I think that's what we care about, I'd say as doctors, as people thinking about public health. One of the things we like to see with flu vaccine is really good uptake. You protect yourself, you protect everyone, but most people are not altruists. If you say, "Hey, the vaccines, people who are potentially going to end up in the hospital, and that's going to be the little kids, those 65 and over, those with illnesses, great. Look at this great benefit here," but most people are going to be like, "I'm not going to end up in the hospital, so reducing my risk from a low percent is not -"

If I'm less likely to get the flu, like this guy who's in the hospital, he's like, "I'm miserable. Everything hurts. I feel terrible." I feel like, "Hey, we can reduce your risk of being in this situation in the future." I think that's where you get the big chunk of the population. It's like

you're just not going to be laying there in bed, moaning, feeling crummy, unable to work.

VR: The other issue here is this study was done in 2022, '23 season, before the current administration took in. As you know, they are not too positive on mRNA vaccines. I just wonder if this will ever see the light of day.

DG Yes, it's worrisome, right?

VR: Yes, for sure.

DG: They even let us have access, the option of a better flu vaccine. I would love a better flu vaccine. I don't like getting the flu. I don't like being sick. I don't understand this Make America Healthy Again, where you got to get sick instead of getting a vaccine. I'd rather get vaccinated than get sick.

VR: Oh, is that what Make America Healthy is Again, just getting sick?

DG: Yes, I think you get sick, and then survivor immunity and all this other craziness. That seems to be the argument. Natural immunity. I don't like acquiring natural immunity. I'll deal with like, "Oh, my shoulder's a little sore," but laying there with a high fever and feeling crummy, yes, I'm not up for that.

All right, RSV. Yes, so RSV, we have clearly entered the RSV season. The epidemic trend is going in the wrong direction everywhere. It's really growing all the way up and moving into this. We're going to basically be getting hit with RSV, the flu, and as we're going to see in a moment, also COVID at the same time. What about RSV? I thought this was entertaining. I didn't look to see if we got any emails. I don't know if you remember last time I was asking people to email in and help me with the math.

VR: Yes.

DG: Because we talked about this article, and it was, “Estimating Risk of Guillain-Barré Syndrome in U.S. Medicare-enrolled Older Adults Following Medically Attended Respiratory Syncytial Virus Disease: A Self-controlled Case Series.” This is where they were saying, "OK, there's this maybe 1-to-2 million people, so you vaccinate a million people, you might see one case of Guillain-Barre associated with the vaccine."

Then they saw that you get RSV, and there's going to be this two-to-fourfold increase. You're trying to sort of do this calculation of like, so is it safer to get the vaccine, even with that one in a million chance, versus to not be protected, get RSV, and then end up with the paralysis, the Guillain-Barré paralysis?

I looked at this a little. The math is actually complicated. The CDC estimates that about 3,000 to 6,000 people get Guillain-Barré each year in the U.S. Then divide that by 348 million people. We sort of get somewhere in the one case per 116,000 at the low end. Divide it by 6,000, it's one case for 58,000. This works out to about 10 to 20 per million people. If you bump that up two to fourfold, that gets us to 20 to 40 per million, versus that 1-to-2 million with the vaccine.

Then again, there's even a higher incidence of Guillain-Barré in people over 50. That would even stack it even more worrisome with getting RSV, being over the age of 50, versus what we're seeing with the vaccine. I tried to do all this math, and I realized it's pretty

complicated. Then I realized I'm not the only one that has problems with math.

I don't know if you heard this quotation. I was very entertained. Mehmet Oz is talking about the reduction of prescription drug prices. He says, he's talking President Trump, "You'll notice, President Trump, these," and he's talking about drug prices, "are discounted from $242 to $10. I don't know what the math is on that. We can't even calculate it. It's too high to calculate." [laughs]

Now, I feel like I could handle this one, so I'm going to do the math here. $242 minus $10, that leaves us $232. Now, the question is, what is $232 of $242? What percent? $232, you divide it by $242, you get 0.96, multiply it by 100. That's a 96% reduction. That's good news for consumers, but I just wanted to offer up my math skills for, I'm going to say, easy stuff like that.

VR: I think you need to call Dr. Oz and offer your services, Daniel, because he's, like everybody else in this administration, is unqualified for his job.

DG: I think I can do that, right? Let's say it went from $242 to like $121. That's a 50% reduction. No, no, that's 100% reduction. I'm like, "No, no." [laughs]

VR: Does he think he's fooling people when he says it's too high to calculate?

DG: I don't think it's too high to calculate. That's a 96% discount. That's a great discount. It's doable. It's doable math.

VR: It's the guy who's heading Medicare services, right?

DG: Oh, my gosh. OK.

VR: Daniel, I'm very excited for this next chart.

DG: I know, it's been a long time coming. We got our multicolored lines back. They sort of came down. We'll see, but we got them back, right? They're a little bit outdated. I'm, unfortunately, going to expect in the future, based upon the ER visits, the epidemic trend, that most of the country looks like we're going to be on the rise here with COVID cases.

VR: Look at this. We see our nice little peak from August to October, right?

DG: Yes.

VR: Then it got down into the very low. Now, it's only November 15t so we're a bit behind here. We expect it to go up, because last year, it started to rise in December as well. Very interesting, this double peak, right?

DG: It is, right? Then, the interesting thing is, Europe, they get a summer peak, but not much of a winter peak. It is a very odd behavior.

VR: It's just in line with everything else going on in the U.S., Daniel.

DG: Everything is just odd. All right, speaking of odd, let's talk about them COVID vaccines. Do they still work, right? I always want to keep asking this question. Here, they looked again. The article, “Effectiveness of BNT162b2 and mRNA-1273,” basically, they're looking at the

Pfizer BioNTech, and they're looking at the Moderna, “JN.1 Adapted Vaccines against COVID-19 Associated Hospitalization and Death: “A Danish, Nationwide, Register-based Cohort Study,” published in *The Lancet Infectious Diseases*.

These results come from this nationwide, registry-based cohort study that include ed all Danish residents, which is great when you've got a system like this, older than 65 on October 1, 2024. We're looking at 1,247,315; 894,560 met the inclusion criteria. Among those without JN.1 vaccination, there were 278 COVID-19 hospitalizations and 84 deaths were observed. Now, what if you got a vaccine? The vaccine effectiveness for the Pfizer BioNTech was 70.2% against ending up in the hospital and 76.2% against death. The mRNA vaccine effectiveness was 84.9% against hospitalization, 95.8% against death.

VR: What's going on here, Daniel? These are mismatched, right? Because there's significant antigenic variation escaping neutralizing antibodies, yet you're still protected against hospitalization and death. Who's protecting you?

DG: I thought that was interesting. They look at this. They've got really nice figure. We can actually see over time. This was a JN.1 vaccine that we're talking about. Very quickly, the JN.1 goes from being like 50% of the variants in like June and so when they're talking about it. By the time you get into September, it's like 10% or less. You're really getting into the KP.3.1.1. Later on, you're getting the XEC.

They went ahead and they said that. Let's look at the KP.3.3.3 and the XC, and what did they find? When they looked at infection with those variants, not the JN.1, the Pfizer-BioNTech J.1 vaccine effectiveness against hospitalization was 71.4%, with KP.3, and 76.8 with XEC. The vaccine effectiveness against death from these variants was 90.9% for the KP.3 and 76.3 for the XEC. Really, no discernible issue with the variants when you're looking at protection with the JN.1. What do you think, Vincent?

VR: Does that mean you don't need to get a booster every year?

DG: I think you still may need to get a booster, because they're seeing effectiveness of basically people that got boosted versus not. I'm not sure that we need to keep chasing the variants, right? That's the big issue.

VR: That really should have been my question, right?

DG: Yes. This brought me back to this whole discussion we've had, B-cell versus T-cell, or really, antibody versus cellular protection. We've got this article, “Immunogenicity of JN.1- and KP.2-Encoding mRNA COVID-19 Vaccinations Against JN.1 Subvariants in Adult Participants,” published in *Open Forum Infectious Diseases*. Now, here they looked at neutralizing antibodies against a bunch of these variants after vaccination. Some really nice figures. A little bit of a difference here. Not a lot, right?

VR: Yes. This is the thing, studies come out right away when there's a new variant. They say, "Oh, it's escaping previous immunity," but it's just the neutralization assay in the lab. The real issue is the clinical relevance. I think this study shows that it's not clinically relevant.

DG: Yes. I do wonder. I do wonder if we need to keep chasing every variant, right?

VR: Yes.

DG: All right. Safety, right? We're talking about efficacy. Those were some great numbers, right? Somewhere between 70% and 95% reduction ending up in the hospital, ending up dying. You get your shot once a year. We're still seeing, as we saw, people ending up in the hospital, people dying. One of the big things that people have been concerned about since the early days is vaccine-associated events, particularly myositis, right?

Despite the bots and the trolls seeming to have missed the fact that we always make a point of discussing these issues, we're going to discuss vaccine-adverse events again. This is the article, "SARS-CoV-2 Vaccination and Myositis in Norway and Sweden, published in the journal *Rheumatology*. Here they're looking specifically at the risk of myositis after SARS-CoV-2 vaccination with mRNA or adenoviral vector vaccines. They conduct this population-based cohort study in Norway and Sweden of 13 million persons who turned 12 or older in 2021 and were residents at the start of follow-up on December 27, 2020.

Persons were followed until incident diagnosis of myositis, censoring, or end of study. They observed 101 myositis events in over 7 million unvaccinated person years and 99 myositis events within 180 days of any combination of mRNA vaccines, and 13 with the adenovirus vaccines. Interesting enough, I just want to point out, 7 million unvaccinated, 6.2 million vaccinated with mRNA, 13 and about half a million that got adenoviral vector vaccines.

The adjusted incident rate ratio for the 180-day risk periods following any combination of the mRNA vaccines was 0.84. It's actually 16% lower. There's wide confidence intervals, so you can't say. They really conclude that in this nationwide study of greater than 13.6 million persons, actually, they're not really seeing an increased risk of myositis compared to this background. Kind of amazing, right?

VR: Yes, it's very clear. The data are clear. Yes.

DG: All right, so we're going to move on to the late phase, the Long COVID section. The article, "Digitally Assessed Long COVID Symptomatology is Associated with Lymphocyte Mitochondrial Dysfunction and Altered Immune Potential," published in *Open Form Infectious Diseases*. Here, a detailed clinical immunologic and mitochondrial analysis on 27 patients with Long COVID and 27 who recovered from COVID and were healthy. Symptom burden and severity were assessed and qualified via a digital platform with the modified COVID-19 Yorkshire. People apparently don't like that I pronounce it Yorkshire, so the Yorkshire Rehabilitation Scale.

Mitochondrial function of circulating immune cell populations, so lymphocytes, monocytes, were assessed by measuring mitochondrial mass, mitochondrial membrane potential. Really assessing the mitochondria. It looked at 11 cytokines, so 11 cytokine production after whole blood stimulation.

Really going through this whole thing, and particularly patients with - Patients with long COVID had decreased mitochondrial membrane potential of CD56 natural killer cells, particularly in patients that experienced, what symptoms? Dizziness. Where reduced mitochondrial membrane potential in CD4 positive lymphocytes was found in patients with worsening breathlessness.

Now they do LPS stimulation. Patients with Long COVID demonstrated significantly lower interferon gamma production. In response to viral ligand R848, they saw impaired interferon beta and IL-10 responses, and this was associated with worsening cough and

executive functions. I don't know, did you do much of this R848 resiquimod, the toll-like receptor stimulation in your lab? You are more kind of a hardcore virologist, I think.

VR We did a little innate, but we didn't use resiquimod, no. [chuckles]

DG: Okay. Yes, this is basically just testing the innate immune system. Really, like a pattern associated microbial pattern. Really seeing those toll-like receptors.

VR: Sounds like something out of *Moby-Dick*, Daniel.

DG: [laughs] It does, right?

VR: All these tests they did for mitochondrial membrane potential, they should have just got RFK Jr. He can look at kids and tell if they have a mitochondrial dysfunction. Did you know?

DG: Oh, my gosh. Yes. Yes, I do. [laughs] OK. All right, the other one, I didn't know what to make much about this, but I will mention, it seems to be getting a lot of press. It's the article, "Long COVID Trajectories and the Prospectively Followed RECOVER-Adult U.S. Cohort," published in *Nature Communications*. Really, what they're doing is identifying these, as they say, eight distinct longitudinal profiles based upon this Long COVID research index.

They're hoping by establishing these groups, they can figure out, are there certain things that might benefit one group? When you find a particular intervention, it seems to help some people. Maybe now you can know ahead of time, like, "Oh, you fall into this particular profile, and you're the profile that might benefit from a particular therapeutic." At least that's the hope there.

The last is negative data, but it's important to get it. This was the article, "Evaluation of Interventions for Cognitive Symptoms in Long COVID: A Randomized Clinical Trial," published in *JAMA Neurology.* Results of a five-arm, multicenter randomized clinical trial of three remotely delivered interventions, conducted between August 17, 2023 and June 10, 2024. Study took place at 22 trial sites. Participants end up in one of these five arms.

They're doing a bunch of different things. They've got this adaptive computerized cognitive training, this cognitive behavioral rehabilitation involving both groups and individual counseling sessions. PASCt cognitive recovery paired with BrainHQ, transcranial direct current stimulation paired with BrainHQ. They have these two comparator arms. Basically, the whole gist is they did this primary outcome, and they have a total of 378 individuals, 328 ultimately participate. No benefit for any intervention, for any of the primary or secondary benefits.

VR: None of this cognitive training is of any use?

DG: Yes, none of it appeared to show any demonstrable benefit, so a little disappointing. All right, as we've been saying for years now, no one is safe until everyone is safe. I'm hoping everyone will pause the recording right here. This is the clinical update, right? That the families get together, and Uncle Joe from Boston, and the relatives from all around the country are getting together with all their mixed views on science and politics.

You can listen to this and then yell, or not yell, or applaud, and food for discussion over the coming weekend. If people like what we do, or they just want us to keep doing it, as I say,

on *ID Puscast*, then go to parasiteswithoutborders.com, click on Donate. Now's a great time to do it because we are in the middle of our *MicrobeTV* fundraiser, so November, December, and January.

VR: It's time for your questions for Daniel. You can send yours to daniel@microbe.tv. Anonymous writes, "I'm a 64-year-old female with chronic migraine at the disability level, which means I don't spend a lot of time out and about having social fun of the intimate kind. This is important because in 2024, during a stressful period that was also affecting heart rate, but in a non-worrying way for the two cardiologists that I saw, they attributed the variances in heart rate to anxiety, probably about the state of HHS, et al. LOL. I also, for the first time ever, had a positive HPV test from my regular pelvic exam. Again, no chance I picked this up recently.

In 2025, after increasing fluoxetine to deal with the anxiety, the HPV was absent after Pap, and my gynecologist said, it can flare with stress, and then go back into remission when stress decreases. That my immune system, which tends to be very good, never had COVID, cannot remember the last time I had a cold or flu, but I don't let that stop me from getting my vaccines. Might have been suppressing this since my 20s.

Naturally, I'm concerned now about the cancer risk, and so is Kaiser because due to this test result in 2024, I am now on once-a-year pelvic exam schedule rather than once every three years. Am I a good candidate for getting the HPV vaccine? If so, what is the best study article to refer my gynecologist to so she'll approve me getting it at this later age? Kaiser doctors tend to be very proactive and open to preventative methods, so I would like to send her a link that as an OB-GYN she will be able to read with confidence and approve me. Thank you as always for your help, and keep spreading medical truth."

DG: Thank you. Now, I think the deep dive that you guys did, Vincent, do you have a link to that? Do you know which study that was?

VR: Yes. That's a meta-analysis, and I think the OB-GYN will be able to take the conclusion from that very clearly. I'll put that in the show notes.

DG: OK. Yes, and it's very compelling. It's really this compelling evidence that you don't necessarily need to get vaccinated before because that's what it says on the CDC site. I think I discussed it in my clinical update the week after, sort of a condensed easier to digest. Yes, it looks like the vaccine is therapeutic and can help you clear HPV infection.

VR: Daniel, is that correct that you could have an HPV infection from 20 years old to this person is 64, for 44 years? I've never seen that.

DG: I think so. I think that the issue with HPV, right, so often people will get exposed and infected in their teens, early 20s, and then they won't develop the cancer until years later.

VR: All right, another HPV question from Zane. "I very much appreciate the work that TWiV does on making good science accessible. Thank you so much. Your recent discussions of HPV cancer and vaccines are particularly timely. My partner is scheduled for a LEEP procedure in a matter of weeks. This is her second occurrence of precancerous lesions, and she had the procedure previously 20 years ago without receiving the vaccine.

Happily, her current doctor has suggested she receive the vaccine this time, and I have

encouraged her to get it as soon as possible. That is before the LEEP. I'm almost 60, have had a vasectomy, and so we have been engaged in unprotected sex for several years now. My question is, should I get the vaccine also? Unfortunately, it's not covered after the age of 45, and it runs about $600 in Canada. I'm already saving up to get the shingles vaccine in the spring, also not covered by our medical plan here, and wondering about my own risks and priorities."

DG: Yes. Zane, it makes sense, right? We've got this science showing that if a woman, and this is perfect, and I love what the doctor's doing here, going to go ahead and do the procedure, going to go ahead and give the vaccine. If your wife, if your sexual partner has HPV, you probably have HPV as well. Initially, we weren't vaccinating men, it was just women, but now we realize, where do the women get it most of the time? They're mostly getting it from the men. There's this back and forth.

It makes a lot of sense. Have we done the specific study to screen men and then do the vaccine afterwards, so the similar therapy? We haven't, but it still, it makes a lot of sense. It's tough. We're talking about hundreds of dollars of you spending here, but you hate to have this situation where your partner goes through this. Maybe they're able to clear it, but then you keep re-exposing them because you haven't cleared it from your system.

VR: I think it's just unfortunate that these vaccines aren't covered, right?

DG: Vaccines are the most cost-effective intervention, but it's a question of who's paying for what, right? Do you want to pay for the cervical cancer, or do you want to pay for the interventions associated with that? Do we want to be losing people to these horrible diseases, or do you just want to jump in with a really penny on the dollar intervention?

VR: Russell writes, "If my purpose of getting a flu vaccine or a COVID vaccine is to reduce the chance of acquiring or transmitting infection during the time that antibodies are circulating, then should I avoid donating blood during that period, three months, so as not to lose a clinically-meaningful number of antibodies I gained from vaccination?

DG: That's great, Russell. No, I do not think you're going to lose a clinically-meaningful number of antibodies. Basically, you're producing those antibodies. No, I think you should go ahead. If you're donating blood, kudos to you.

VR: It's just a pint, right, that you typically donate?

DG: Just a pint.

VR: How many do we have in us, like nine?

DG: They always said five to six. I don't know how accurate that really is.

VR: Jean writes, "First, I want to express my gratitude for all you both do. I found my way to this podcast in 2020 when absolutely nothing I was reading in the mainstream media or on social platforms felt satisfying. People seemed to quote illogical things as facts, and it was maddening, and during a pandemic, that's really saying something.

I first heard Dr. Griffin on Brian Lehrer's politics podcast, so at that moment, I wasn't even seeking out science, but his explanations were clear and well-evidenced. I should add here that I have no science-based training, but I've always had a natural curiosity. I listen weekly.

I've learned so much from you both.

The reason I'm writing today is that my husband recently went to the GP with a respiratory virus. During the appointment, he told the doctor that he had done three COVID tests on three consecutive days in the early phase of illness, but all three were negative. The GP replied that the COVID tests don't work on the current strain of virus and that he probably did have COVID.

I'm certain you spoke about this on the podcast in the last few months and said something along the lines of, although there are variants, the antigen being tested has remained stable, and therefore, the tests will work. In spite of searching and reading through the archives on the *TWiV* site, I haven't been able to find when this was mentioned. If possible, could you put this urban myth to rest again?"

DG: Yes, let's put this to rest again. The COVID tests still work, and as we've talked about, the recommended way you do it is first thing in the morning, you do a test. If it's positive, it's positive. It's negative, you wait 48 hours, repeat it again. Again, first thing in the morning is going to be your most sensitive time to test.

VR: Ian writes, "I'm an emergency medicine doctor. I see a lot of very young kids with RSV in the ED. Are you aware of any ongoing studies that are looking at clesrovimab and nirsevimab or similar monoclonals for treatment of RSV in the under 2 population to prevent ICU admissions, need for respiratory support, hospitalization, et cetera? I think this would be an interesting and important study. If these monoclonals are found effective, I would love to be able to give them to these kids with early RSV who have not had them previously to help prevent severe disease."

DG: This is great, Ian. Let's think about it. If the kids are showing up and they haven't had their nirsevimab or the clesrovimab, so these are the monoclonals that are supposed to prevent them getting RSV. Is there any harm doing it right then? Forget about the studies saying, "Oh my gosh, you haven't had this. This might not be the episode of RSV that gets you in the hospital, but here you are. It's RSV season. Let's get those in."

Now, the other which you bring up makes a lot of sense. Is it too late to get that in? Is there a therapeutic for giving it right away? Most of our monoclonals, if you get them within the first 48, 72 hours, tend to make a difference. We even saw with COVID, you could probably do that out to eight, 10 days, even longer. It seems to me like if they show up and they didn't get their RSV, now's a great time to say, "Let's go ahead and do it." Yes, it would be nice to do these studies as well, look at it therapeutically.

VR: Will writes, "I thought this quote is worthy of your attention, particularly the first part. I've heard modern historians say similar things. Everything in life is political. The quote is, 'In our age, there is no such thing as keeping out of politics. All issues are political issues, and politics itself is a mass of lies, evasions, folly, hatred, and schizophrenia.' That's by George Orwell, who is not around these days. It was around a long time ago."

DG: What brilliant insights George Orwell had. I don't know how many people have studied the Spanish Civil War, but that conflict actually really inspired a lot of Hemingway. I think there was a Salinger connection. Actually, George Orwell fought on the side of the republic with the communists. That's where he became disillusioned and realized like, whether you're fighting on the side of the fascists or you're fighting on the side of the communists,

everything about politics can just become so difficult and messy.

VR: For all of you celebrating Thanksgiving, I offer you this poem by William Carlos Williams, who was a physician who worked in the Patterson, New Jersey area. My dad, who was a physician, knew him as well. This one is called *The Red Wheelbarrow*. "So much depends upon a red wheelbarrow glazed with rainwater beside the white chickens." That's *TWiV* weekly clinical update with Dr. Daniel Griffin. Thank you, Daniel.

DG: Thank you. Everyone, have a happy Thanksgiving and be safe.

[music]

[00:58:40] [END OF AUDIO]