This Week in Virology

TWiV 1072 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.

[theme music]

VR: From MicrobeTV, this is *TWiV*, *This Week in Virology*, Episode 1072, recorded on December 21, 2023. I'm Vincent Racaniello, and you're listening to the podcast all about viruses. Joining me today from New York, Daniel Griffin.

Daniel Griffin: Yes, I'm back in New York. Hello, everyone.

VR: Are you happy to be back?

DG: It's mixed feelings. I loved the time in Uganda. I loved the time in Panama. Panama was a little special, right, because my daughter joined me again, so that was exciting. Yes, no, it was a great trip, right? Uganda was fantastic. It's great to see all my friends there and my cattle, and the Panama trip was really good this time. We went to one of the most remote islands, so, four-and-a-half hours by boat, living in the village with the locals, sleeping in a hammock, using the facilities that, same ones they use.

VR: Did you get a lot of bug bites, Daniel?

DG: I tend not to get bitten by bugs for some reason. [laughs]

VR: OK. What's on your tie this week?

DG: This is, it's almost Christmassy, right?

VR: Yes.

DG: It's a virus, right? It's got that nice symmetry, and the artist says they think it's HIV, but it could be, so many.

VR: OK.

DG: [chuckles] OK. Just a shout out to all the great folks that I had the opportunity to work with in Uganda, and then we had a bunch of medical students, Vincent, from University of

Buffalo were down there with us in Panama, and really an impressive bunch. I wasn't sure they were medical students because they were like, way too nice.

[laughter]

DG: All right, well, let's jump into it. “A sad soul can kill you quicker, far quicker than a germ.” That's by John Steinbeck. I'm not so sure how true that is but I think it's a good conversation starter. As people start making decisions about what to do with regard to the holidays, right? There's something incredibly sad about the holidays where people were alone and isolated. Hopefully, now with vaccines, with wise choices about air quality and ventilation, with jumping on treatment and testing, this can be, hopefully, a holiday season where people are not alone, and we can make some smart choices to allow people to be together and not have sad souls.

All right. RSV, we're going to jump right into it with the article, “The Annual Economic Burden of Respiratory Syncytial Virus in Adults in the United States,” recently published in *JID*. Now, I think as physicians, we don't often think about disease in these terms, but public health folks are aware that disease can have tremendous impacts on the economy. I like to say it's hard to make one's country great when we are spending billions of dollars on vaccine-preventable illnesses. Here is a cost-of-illness model where they develop an estimate of the annual societal burden of RSV in U.S. adults aged 60 and over.

Additional analyses were conducted to estimate the burden of hospitalized RSV in all adults aged 50 to 59, adults aged 18 to 49 with potential RSV risk factors. We read that U.S. adults aged 60 and over, the model estimated 4 million annual RSV cases, an annual economic burden of $6.6 billion. The RSV cases that were hospitalized contributed to 94% of direct medical costs. Additional analysis estimated $422 million in annual hospitalization costs among all adults aged 50 to 59. Among adults aged 18 to 49 with RSV risk factors, the annual per capita burden was highest among people with CHF, congestive heart failure, at $51,000, over $51,000 per 1,000 people. Of note, this is just adults. Add in the children and the numbers only get bigger.

VR: Daniel, can you get a rapid antigen test for RSV?

DG: We actually have those. They have these - Well, you can't do it yourself, Vincent, but we keep these guarded. Actually, a lot of our urgent cares have these quad testing kits where you can get a flu A, flu B, RSV, and COVID all at the same time.

VR: Nice.

DG: Yes, it's nice for a few things. People sort of wonder, why do we need all these answers? Well, COVID, we've got treatment. Flu, we've got treatment. RSV, it's a big infection control issue. You find out that somebody's got RSV and you can at least give them recommendations. That Christmas party you're about to go to tonight, maybe you shouldn't go.

VR: It has to be ordered by a physician to get those tests.

DG: Yes. Unfortunately, there was a brief period of time when those Lucira tests, you could actually do these at home. Right when they went bankrupt, I got a bunch for $8 each. Yes.

[laughter]

VR: Oh, you're a sale shopper, are you?

[laughter]

DG: I saw that. I was like, I jumped in. Now, unfortunately, I've lent them to other people. They're all gone, but yes, some of the data we get is actually based upon not just PCR for RSV, but also some antigen detection results. It looks like we might be peaking here with the RSV. We'll see but we're certainly way up there with RSV detections currently, so this is certainly RSV season. Remember, we've got vaccines, both active and passive, so we really want to use those tools.

Influenza. I was joking with a patient today. I don't know how funny my patients think I am, but about, he had flu A. I say, what happened? You opened the window and influenza? OK. I thought that was funny. Anyway, he didn't laugh. The article, "Recombinant or Standard-Dose Influenza Vaccine in Adults under 65 Years of Age," was recently published in *The New England Journal of Medicine*. Now, just a little background for folks. We now actually have specific recommendations for one type of flu vaccine over another in adults 65 and over, right?

We have a bunch of choices when it comes to flu shots. We've got the live attenuated, the stuff you spray up your nose, right? We've got the cell-based, the egg-based, the adjuvanted, the normal versus the high-dose flu vaccines. Quadrivalent recombinant influenza vaccines, for instance, contain three times the amount of hemagglutinin protein as our standard dose egg-based vaccines. The recombinant formulation is not susceptible to antigenic drift during manufacturing. Here we have results from a cluster-randomized observational study.

Kaiser Permanente Northern California facilities routinely administered either a high-dose recombinant influenza vaccine, so Flublok Quadrivalent, or one of two standard-dose influenza vaccines during the 2018-2019, 2019-2020 influenza seasons to adults 50 to 64, a little younger than that 65, that's the primary age group, and also 18 to 49 years of age. Each facility alternated weekly. That's how you got this clustering between the two vaccine formulations. The primary outcome was influenza A or B confirmed by PCR. Secondary outcomes included influenza A, B, and influenza-related hospitalizations.

The study population included, you ready for this, 1,630,328 vaccinees between the ages of 18 and 64, 632,962 in the recombinant-vaccine group, almost a million in the standard-dose group. During this study period, 1,386 cases of PCR-confirmed influenza were diagnosed in the recombinant-vaccine group, and 2,435 in the standard-dose group. Among the participants who were 50 to 64, 559 participants, so two cases per 1,000 tested positive for influenza in the recombinant-vaccine group as compared with 2.34 cases per 1,000 in the standard-dose group. Remember, we got more people getting that standard dose gross group, so that's where we're going to make that adjustment there.

They're giving us a relative vaccine effectiveness of 15.3%, not knocking your socks off. In the same age group, the relative vaccine effectiveness against influenza A was 15.7%. The recombinant vaccine was not significantly more protective against influenza-related hospitalization than the standard dose vaccines. We're seeing a subtle little bit of difference

here favoring recombinant over standard dose, at least with regard to PCR-confirmed influenza, not necessarily seeing that effectiveness translated into less hospitalizations.

VR: It's not clear to me what the outcome was here. They say PCR-confirmed. Is that all or was it symptomatic?

DG: You had two here, right? These are folks that are actually triggered. They weren't just screening, right? These are folks that were going to go with symptoms, so it's PCR-confirmed influenza disease.

VR: OK.

DG: Yes. Then they're looking at the hospitalization rate, which was not different. We're seeing subtle stuff. I sort of wonder when such subtle differences, how much, how far you want to go to the bank with this. I will say, that gentleman that I saw today, he got his flu shot. Though he didn't like my first joke, he did resonate with my comment about, well, since you did get a flu vaccine this year, I expect this to be mild rather than wild. He did say, you know, I'm an older guy and I got COVID after being vaccinated, and it was mild, so sort of buying into this vaccine decreased ferocity of the infections.

VR: As you said last week, Daniel, we need better flu vaccines.

DG: Yes, I think we do. I think we do. All right. Got another article. We're working on this theme, "Maternal Vaccine Effectiveness Against Influenza Associated Hospitalizations and Emergency Department Visits in Infants," published in *JAMA Pediatrics*. These are the results of a prospective test-negative case-control study using data from the new vaccine surveillance network from the 2016-2017 through 2019-2020 influenza seasons. Infants younger than 6 months with an ED visit or hospitalization for acute respiratory illness were included from seven pediatric medical institutions in U.S. cities.

Control infants with an influenza-negative molecular test were included for comparison. Sorry, test-negative design. Data were analyzed of 3,764 infants, 223 with the flu, 3,541 control. Fifty-three percent were born to mothers who were vaccinated during pregnancy. Overall vaccine effectiveness in infants was 34%, 39% against influenza-associated hospitalizations, and 19% against ED visits. We see the best, so among infants younger than three months, effectiveness was 53%. Effectiveness was 52% among infants with mothers who were vaccinated during the third trimester and only 17% when mothers were vaccinated during the first or second trimesters.

All right, so just we should sort of start building a list of when mom's in that last trimester. We've got the RSV shot, the flu shot, the COVID shot, all these things we can do to protect that child for the first three, six months of life. Yes, we are full-on in influenza season. We have lots of flu out there, so keep that in mind as we gather for the holidays.

All right, COVID. New cases, 274,398. That is up. The average is going up. The number in hospitals is going up. The number in ICU is going up. New deaths, 1,693, so the average is up over 100. We are still sitting there over 200 deaths a day. If we look at our wastewater, I feel like they changed the scale. Remember it used to top out at 1,200? Well, now you can top out

at 1,500 and just still rise in there, particularly in the Northeast. Sort of see what happens in the Midwest. They've hit that nice high level.

I'm hoping we get maps for COVID, the way we do for flu, where we get to look and see where the flu is, and then when people travel, compare them. Because right now, right, the flu activity is just going gangbusters in the South, in the West. We'll look at that in a couple of weeks and anticipating that anywhere that's in the minimal low, we'll see the Christmas travel spread.

VR: You know, Daniel, you can always use a positive test as an excuse not to have to go to some event.

DG: Not that I would ever do that, Vincent. [laughs]

VR: No, I'm sure you wouldn't do that, no.

DG: All right. The article, "Risk of Severe Maternal Morbidity Associated with SARS-CoV-2 Infection During Pregnancy," right? We talk a lot about what moms can do to protect their babies. What about moms protecting themselves? This is an article recently published in *Open Forum Infectious Diseases*. We have talked repeatedly about the fact that SARS-CoV-2 infection during pregnancy is not great for mom, definitely not great for the neonates. Here are the results from a national cohort study of 93,624 deliveries that occurred between 11 March 2020 and 1 July 2021 using medical claims information from Optum Labs Data Warehouse. A little plug for Optum there. Do I have that little thing? Oh, it's on this side of the shirt. OK. They now signed my check so I've got to be nice to them if I want that to continue.

SARS-CoV-2 infection was identified from diagnostic and laboratory testing claims records; 4.8% of deliveries had a record of SARS-CoV-2 infection, 27% less than seven days before delivery, 13.5% within seven to 30 days delivery, and then about 60%, so 59.5% earlier in the pregnancy. Compared to uninfected pregnancies, the adjusted risk of severe maternal morbidity was 2.2 times higher among those infected less than seven days before delivery, 1.66 times higher for those in that seven to 30. The highest risks were observed for acute respiratory distress syndrome, and that was an adjusted relative risk of 13.24. Interestingly, acute renal failure was almost 4 adjusted relative risk, so. All the limitations inherent in the study design were looking at, labs, were looking at medical claims data, et cetera. Just not great to get SARS-CoV-2 when you're pregnant.

OK, moving on to testing. I'm hoping people are thinking about doing this. I think poor Barnaby got something stuck up his nose this morning because the in-laws were coming, and we definitely don't want to make my in-laws sick. Just a reminder, right, that article we talked about last time, "COVID-19 Rapid Antigen Tests with Self-Collected vs Health Care Worker–Collected Nasal and Throat Swab Specimens." Use the tests in the way that they were designed, in the way that they were validated. Yes, you don't - Well, I guess unless you're trying to get out of that Christmas party and then drink yourself a soda and rub it on your tongue. All right.

VR: Daniel, can I ask, if Barnaby tested positive, what would you do? Lock him in his room or tell your parents not to come?

DG: Well, first off, we would call the in-laws and say, turn around. [laughter] Then I would lock Barnaby in the room. [laughter] Actually, I'm working over this holiday weekend, so for me, the exposure would be low. All right. Ventilation, transmission. We'll be talking a little bit more about this next week, right before the New Year's parties. Leave those fans on, crack those windows. We'll talk a little bit about the relative risk in different situations. As we've talked, it's time, it's distance, it's poor air quality. This is something you breathe in. I still want people washing their hands, but – all right.

Now, unfortunately, you test positive. You're a high-risk individual. What do you do? Number one, Paxlovid. When do you start? Do you wait around, Vincent, see how people do, wait around, let that immune system kick in?

VR: No, no. you start right away.

DG: Exactly. All right. Let's talk about some science. We've got the article, "Optimal Timing of Nirmatrelvir/Ritonavir Treatment After COVID-19 Symptom Onset or Diagnosis: A Target Trial Emulation," recently published in the august journal *Nature Communications*. Here, these investigators performed a two-territory-wide retrospective cohort analysis using the target trial emulation approach to examine the effect of timing of Paxlovid initiation on the incidence of all-cause mortality, all-cause hospitalization, and viral burden rebound among all adults aged 18 and over. Looking at patients that had initiated Paxlovid in the Hong Kong Special Administrative Region, China, between the 16th of March 2022, and that's when Paxlovid first became available, and the 15th of January 2023.

During the study period, COVID-19 infections in Hong Kong were predominantly caused by Omicron and its subvariants. The authors are going to talk a little bit about VBR, viral burden rebound. The authors point out that a number of case reports and studies have reported symptom recurrence or viral burden rebound after initial recovery upon completing a standard five-day course of Paxlovid. I will mention that also happens if you don't take it, so I'm not sure how you call that Paxlovid rebound. Anyway, it has been hypothesized that initiating the Paxlovid too early after symptom onset may in some cases be associated with the VBR, thus prompting some folks to say, why don't you just sort of wait around for a while before you start that life-saving medication? [laughter]

Well, due to early viral suppression of viral replication by Paxlovid, the idea is the host adaptive immune system may not have sufficient stimuli and time to develop. OK, let's see what happens here. Early initiation was defined as a prescription of Paxlovid within one day from the date of COVID-19 diagnosis or first symptom onset. Late initiation was defined as prescription on or beyond days two, day two. Index date was defined as that of either the SARS-CoV-2 infection diagnosis or symptom onset, whichever occurred first. A total of 87,070 Paxlovid users who had confirmed diagnoses of SARS-CoV-2 infection were included in the analysis.

Early initiation of Paxlovid within one day was associated with a significantly lower risk of 28-day all-cause mortality or hospitalization, adjusted relative risk of 1.5, so about a 33% reduction versus late initiation. A significantly lower risk was also observed if you got the Paxlovid initiated within two days versus three or more days, and that's about a 30% reduction within three versus four. You just keep seeing this trend. The data suggests that

early initiation of Paxlovid may be associated with an elevated risk of that VBR, but they do comment, they say that without much certainty, there was a paucity of these VBR events, wide confidence intervals, but clearly early treatment was associated with better patient outcomes.

Number two, remdesivir, if you can get it. Number three, molnupiravir. Number four, convalescent plasma in certain circumstances. Isolation for the infected. Barnaby also almost was isolated for days, and let's not do those harmful, unuseful things. I'm just always shocked at the amount of antibiotics that get thrown at people. I just had a patient today, yesterday got diagnosed with COVID. We had the whole discussion. We started with Paxlovid. I get a message from the office that my patient now has a sore throat and he would like you to send in a script for antibiotics. Bam. OK. [chuckles]

All right, week two, the cytokine storm week, steroids only at the right time in the right patient at the right dose. This is after that first week, oxygen saturation is less than 94%. We have anticoagulation guidelines, pulmonary support, remdesivir still in the first 10 days, immune modulation perhaps with tocilizumab. Now we will move into COVID, the late phase, PASC, Long COVID, really still seeing a significant number of folks suffering from this. I included this article, sort of prompted a comment that my wife made about maybe we just see a lot of Long COVID versus "long flu" because we're just looking. I said, no, actually, I think it's more actually, so let's throw some science at this.

The article, "Long-Term Outcomes Following Hospital Admission for COVID-19 Versus Seasonal Influenza: A Cohort Study," published in *The Lancet Infectious Diseases*. This is a cohort study where the authors use the healthcare databases of the U.S. Department of Veterans Affairs. This turned out to be a great resource. They analyzed data from 81,280 participants admitted to hospital for COVID-19 between March 1, 2020, June 30, 2022, and 10,985 participants admitted to hospital for seasonal influenza between October 1, 2015, and February 28, 2019.

Participants were followed for up to 18 months to comparatively evaluate risks and burdens of deaths, a pre-specified set of 94 individual health outcomes, 10 organ systems, overall burden across all organ systems, readmissions, admissions to ICU. There's a lot in here, so it's worth reading. Over 18 months of follow-up, compared to seasonal influenza, the COVID-19 group had an increased risk of death hazard ratio of 1.51. This is really, I think, what is shocking. An excess death rate of 8.62 per 100 persons in the COVID group versus the influenza group. Just really shocking, right?

People always ask, oh, what's the case fatality rate for COVID? They quote sort of in the 2%, 3%, 4%. This is an extra 8.6% of these folks dying versus folks that ended up in the hospital with flu over just 18 months. Compared to seasonal flu, COVID-19 also had increased risk of hospital readmission, excess rate of 20.5 per 100 persons, and admission to ICU excess rate of 9.23 per 100 persons.

VR: Daniel, this is not Long COVID, right? Dying is not Long COVID.

DG: [laughs] It's worse than Long COVID, perhaps, depending who you talk to.

VR: We have no information of whether they had Long COVID up until the time of death, right?

DG: Yes. Well, I say this, there's this push, and I sort of agree with this push, of talking about post-acute sequelae of COVID, right? Long COVID is really just a subset of the bad things that can happen to you. Yes, I'm glad you bring this up because you get COVID, and there was a lot of people who were just sort of, maybe it's dismissive, I'm not sure the right word, but they're like, oh, two weeks, you either live, you die, and then you move forward, but that's not true. Some people develop diabetes, they develop heart failure, they develop heart arrhythmias, they die, they end up readmitted, they end up unable to care for their family or return to the office. Post-acute sequelae of COVID is really more than just this chronic fatigue, ME/CFS type syndrome.

On that note, other things that can happen, this is post-acute sequelae of COVID that's not actually Long COVID. The article, "Risk of Arrhythmias Following COVID-19: A Nationwide Self-controlled Case Series and Matched Cohort Study," published in *European Heart Journal Open*. This study was based on national registered data on all individuals in Sweden who tested positive for SARS-CoV-2 between first of February 2020 and 25 May 2021. The outcome was incident cardiac arrhythmias, atrial arrhythmias, paroxysmal supraventricular tachycardias, bradyarrhythmias, and ventricular arrhythmias.

These results are from a self-controlled case series study and a matched cohort study performed to determine the risk for arrhythmia event following COVID-19. Large numbers here, a total of 1,057,174 exposed individuals were included in this study, as well as 4,074,844 matched unexposed individuals. The incidence rate of atrial tachycardias, paroxysmal supraventricular tachycardias, and bradyarrhythmias was significantly increased up to 60, 180, and 14 days after COVID, respectively. In the matched cohort, the risk ratio during the first 30 days was 12.28, 5.26, and then 3.36, respectively, for the three outcomes. The risk was generally higher in older individuals, unvaccinated individuals, and individuals with more severe COVID-19.

All right, and I'm going to wrap it up there, Vincent. I'm going to keep this short for the holiday weekend. I already started working on the one that's going to fall after Christmas, so we've got a lot coming up, but I just want to remind everyone, no one is safe until everyone is safe. I do want everyone to pause the recording right here, go to parasiteswithoutborders.com, and click on that large 'Donate' button. Even a small amount helps. We're right in the middle of our MicrobeTV fundraiser, which for November, December, and January, we're almost done, only a month to go after this. We double your donations up to a potential maximum donation of $20,000 to support MicrobeTV.

VR: It's time for your questions for Daniel. You can send yours to daniel@microbe.tv. Len writes, "Hi, I'm a long-term listener and truly appreciate the objective knowledge you share with humanity. That said, this is a burning question of mine and likely many other curious minds out there. When using a nasal dilator like Afrin to decongest your nose, one usually only needs it for a few days at most, which is what the manufacturer recommends as well, so we are left with a nearly full container to throw away. Given we become immune to the virus that causes our common cold or COVID-specific variant or whatever, can we wipe the

applicator with alcohol and safely reuse it up to its expiration date? Really looking forward to your insight on this."

DG: [chuckles] That's actually what I do, because that is, right, you've got the containers of Afrin sitting around. You only want to use three days because if you go past five, you get this horrible rebound, which unfortunately I've seen. Yes, I usually just wipe them off with alcohol, let it air dry, put it back in the cabinet. Yes.

VR: OK. There you go. [chuckles] Volker writes, "I'm 49 years old, good health. I run 100 kilometers each month. I've been vaccinated three times and had COVID-19 at least once almost two years ago. Last Saturday, I started to notice some symptoms and performed a SARS-CoV-2 test on Monday morning, which returned positive result. Since you recently took Paxlovid, despite having no comorbidities or risk factors that I am aware of as a very long-term listener, I requested my general practitioner to prescribe it to me. He did so, albeit reluctantly stating that I would not benefit from it. Could you please explain how I might benefit from Paxlovid? Are we talking about a shorter recovery time, milder symptoms, lower viral load, reduced risk of Long COVID? Could you also provide links to relevant studies that I could forward to my GP? Generally, who should take Paxlovid in the absence of risk factors?"

DG: OK. Now, this is a great question because should everyone get Paxlovid? That's sort of the sort of thing out there. I am over the age of 50. Hopefully, I look younger than the stated age, that's what you like to see in your history. You never want to hear, “appears older than the stated age,’ but so yes, I am over the age of 50. Now, otherwise, actually, I'm healthy, like no blood pressure, no other issues. I keep my BMI right at 25 plus just, so I've got that as another risk factor to allow me access. I'm joking. The most compelling evidence for Paxlovid and really the evidence-based recommendation there is for folks that are high risk at progression to severe disease, ending up in the hospital, not surviving. That group, it's a no-brainer. It's really pretty clear.

There is some growing evidence that you may actually reduce your risk of Long COVID in adults. Actually, there's some recent data in children as well. Sort of a suggestion there, not just the acute, but as we keep talking about the post-acute sequelae. There's data that we've talked about where there may actually be a quicker symptom resolution. No, the real big push for Paxlovid is for the higher-risk individuals, who are going to progress, who are going to end up with severe disease.

VR: Lauren writes, "Is there any news regarding updating antigen tests with more accurate versions? I imagine the commercial value of developing better antigen tests is low as demand has probably dropped, but they're such an important tool for those of us who are still trying to avoid COVID. It would be incredible to be able to depend on them a bit more and be able to gather more safely via testing friends, family, caretakers, colleagues, et cetera."

DG: Yes, I think this is an excellent comment. Remember, much of what happens in the United States is driven by market pressures, the ability to make a profit when you invest into new technology. When I talked about that article last week, right, where people were somehow getting these Q-tips into the back of their throat and swabbing the palatine tonsils and the posterior pharynx, not the tongue, not the sides of the cheek. There was a discussion about

the fact that manufacturers could upgrade their kits and spend millions of dollars on validating these modified tests.

Then I do remember like a bunch of years ago, there was somebody who was on our show who had a desk-full of these like saliva tests that he could make for a dollar a pop. Forget who that was at the moment. Those seem to have never come to the market. Don't laugh, Vincent. [laughter] No, I think that's what we're getting into. There's sort of a loss of reward here. I don't really know how much people are testing and how much of a market really is there for people coming up with newer tests. The current tests we have are still reasonable. Particularly if you do serial testing, they're still an effective tool.

VR: Alan writes, "With respect to rapid tests, is there any meaning to them after one is tested positive? I have patients and family who have COVID who monitor the redness of their positive test line. Does a lighter color mean anything? Does a negative test after five or six days mean that you don't have to mask till day 10? Is there magic in two negative days in a row? If that were days five and six, would it really mean you are not contagious?" Listen to what he says, Daniel. “By listening to *TWiV*, notwithstanding being a psychiatrist, people come to me for advice on COVID.”

[laughter]

DG: I like that. That's great. It is tough, right? Because there's even this like, I don't know if it's still up there on their website, but this whole test out protocol from the CDC about, if you get two negative tests and it's five days and your symptoms are gone - I'm not really sure I'm convinced that repeated testing does anything other than help you develop some sort of a neuroses and that probably drives your business. I want to stop that from - This is a test that tells you, do I have COVID or not? Then as we've talked about, it's a little bit suspect how good those tests really are at all for judging whether or not you're contagious.

Lots of little, catchy, enough to detect, enough to transmit or infect, or whatever people want to say. It's not really clear to me that after you get a positive test that you need to keep doing any of those tests. We've talked about the lack of correlation with culture positivity, nothing compelling really with regard to those ongoing positive antigen tests and transmission tracing. I usually tell people once you're done, save those tests for the future.

VR: Nicole writes, "Many doctors remain unsure how to answer this question, so I'm hoping to get your expertise. Are you universally recommending RSV vaccination for adults over 60, even those without cardiopulmonary or other comorbidities or immunocompromised strictly on the basis of age? The CDC website highlights the small neurologic signal seen in the trials, and therefore some have only been recommending this vaccine to the highest-risk patients defined by comorbidities or perhaps extreme of age, not solely based on age over 60. Would you recommend it for everyone over 60, despite the small neurologic signal, which may or may not be related to the vaccine? If not, would your answer change for even older adults, i.e. over 70, but without significant comorbidities or immunocompromised?"

DG: Yes, so this is a great question. I like this. I want to avoid eminence-based pronouncements. I'm going to basically share, what do we know and where are we. In the spring, right, May 2023, these vaccines became available. They got approved. In May, the

initial recommendation was shared decision-making. This sort of questionable signal was shared with the public and with everyone and that was supposed to be part of your decision-making. We have now seen millions of doses. We are not hearing of any concerns.

What I'm going to say is a lot of us, based upon the science, based upon what I will say is post-marketing surveillance of millions of doses being given out, we are not seeing concerning neurological signals here. Here we are, peak of the RSV season, lots of folks ending up in the hospital, thousands of people dying, right? We'll get a total at the end of this season, but it's usually going to be in that 10,000 to 20,000 range for adults. Also, you get it, you transmit it, et cetera. Most of us, based on the science, a lot of us based on the science are now sort of moving from that initial May shared decision-making to a universal recommendation of folks 60 and over, but based upon the science, not just based upon my eminence.

VR: That's *TWiV*, weekly clinical updates with Dr. - Let me start over again. [laughter] The eminence thing, I'm trying to work in with eminence, Dr. Daniel Griffin. That's *TWiV*, weekly clinical update with Dr. Daniel Griffin. Thank you, Daniel.

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

[theme music]

VR: His eminence.

[laughter]

[00:39:13] [END OF AUDIO]