This Week in Virology

TWiV 1058 Clinical Update

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Guest: Daniel Griffin

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pdf of this transcript available (link)

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 1058, recorded on November 2, 2023. I'm Vincent Racaniello, and you're listening to the podcast all about viruses. Joining me today - How do I usually say this?

Daniel Griffin: From New York.

[laughter]

VR: Joining me today from New York, Daniel Griffin.

DG: Hello, everyone. We should start saying, "Live from New York." [chuckles]

VR: Let me repeat, "Live from New York. It's Saturday Night *TWiV*. That *TWiV* 1000"

DG: I guess it's Saturday morning is when this gets released, yes, Saturday morning.

VR: [crosstalk] It is, except if you are in another time zone, it could be early. It could be Friday night.

DG: That's true. All right?

VR: Yes.

DG: If you're in California, when it moves to California, you can start getting it dropped at like what, 9:01?

VR: 9:00 PM.

DG: Hello, everyone. First, Vincent, a shout out to - I'm going to be teaching a William & Mary class on Monday, and apparently required is listening to this *TWiV*.

VR: Excellent. That's a good idea. I love it.

DG: I'll start off with my quotation. "Human kindness has never weakened the stamina or softened the fiber of a free people." That's by FDR. I feel like in these difficult times, it's often, I think important to remind people to be nice to each other. I think I quoted Martin Luther King last time about how we do notice the voices of our friends when they're quiet. Let's be there for each other. I think we experience the difficulty a lot of folks are going through.

I will start off with an *MMWR*, "Routine Vaccination Coverage - Worldwide 2022." The expanded program on immunization was established by the WHO in 1974 to ensure that every infant in the world received vaccines against diphtheria, tetanus, pertussis, poliomyelitis, measles, and tuberculosis. Since then, immunization programs have broadened to include many additional vaccines.

Now, we read that a central target of the Immunization Agenda, the IA2030, is reducing the number of children who have not received the first dose of diphtheria-tetanus- and pertussis-containing vaccine, that's a DTPCV1 (zero-dose children) by 50% by 2030. Now, we read that the implementation was disrupted by the COVID-19 pandemic and global vaccination coverage declined to the lowest levels in more than a decade, resulting in a 40% increase in the number of zero-dose children. These are children that have gotten zero doses during the 2019 through 2021, with fewer vaccinations administered in 2021 compared with 2020.

Basically, what we're reading here is global immunization efforts were disrupted by COVID-19 and vaccination coverage declined to the lowest levels in more than a decade. We are now looking at millions of children at risk of vaccine-preventable disease.

VR: Daniel, what's on your bowtie?

DG: These are prions.

VR: Oh.

DG: These are prions.

(crosstalk)

DG: [crosstalk] Creutzfeldt-Jakob disease. That could be on the test. We'll find out if anyone listened, if they got that. RSV, lots of discussion around the new nirsevimab Beyfortus monoclonal for the prevention of RSV in children. I remember having a lot of discussions with providers about how do we communicate because even though this is on the vaccine schedule, it's a passive vaccination. It's a monoclonal. A lot of concerns. I don't know. Are people going to be excited about this?

Apparently, people are so excited about this, rightfully so, that we read the alert from the CDC. Demand is outstripping supply. In the context of limited supply during the 2023-2024 RSV season, CDC recommends prioritizing available nirsevimab 100 milligram doses for infants at the highest risk for severe RSV disease, young infants aged less than 6 months, and infants with underlying conditions that place them at highest risk for severe RSV disease.

Apparently, we're also seeing competition around the RSV vaccines with GSK getting two-thirds of the market versus Pfizer's vaccine only getting one-third. They had a discussion today

at our weekly urgent care provider meeting and actually was talking to one of our oncologists who's on our P&T committee locally. At this point, we have seen hundreds of thousands, millions of doses. I think Pfizer was saying they've released 2.3 million doses of vaccine already. We're not seeing issues. We're really moving a little bit away from the shared decision-making to just an all-out recommendation for our folks, older folks, getting the RSV vaccines.

As we mentioned, with the nirsevimab shortage, really trying to get pregnant women in that last trimester the protection that they can then transfer to their children for this upcoming season.

VR: Daniel, I just got a text from CDC V-safe. Remember that program where you'd -

DG: Yes, yes.

VR: Now they say it's open for 60-plus adults who get an RSV vaccine. They say, "Register and tell us how you feel after RSV vaccine." How do they know I got one?

DG: [chuckles]Did you get your RSV vaccine, Vincent?

VR: Yes, I did. I got RSV, COVID, and flu all at once.

DG: That's fantastic. Let's talk about that for a second. The way they know, and this is nice, a lot of states actually have a centralized place where, for instance, my patient comes and sees me, that gets uploaded to the state. There's a nice system where I see that a person has covered their recommended vaccinations, other health maintenance things. It's really a great resource. What you did is really what we recommend.

There was a little bit in the media that came out recently about, I don't know if people should RSV and flu at the same time. Because there was one study where we looked at a specific age group over 85, and there was a slight, minimal, statistically significant increase in strokes. That's getting to the point of data mining when you start looking for something like that because we have lots of other studies, you really decrease your risk.

Interesting enough, with the flu vaccine, you're decreasing your risk of having heart attacks, of strokes, of getting hospitalized for even non-flu related issues. The recommendation across the board is don't miss an opportunity to vaccinate. Just like, yes, Vincent, you're a role model there, probably because you're wearing the cape and the spike t-shirt. Yes, let's get everyone protected so that this becomes the year when we say. “what happened with RSV?”

VR: I got mine at a CVS. Would they report?

DG: You got GSK.

VR: I got GSK.

DG: How I know that is that's actually why GSK is winning over Pfizer. They got the CVS contract on -

VR: Oh.

DG: - RSV vaccines.

VR: Would they report it to CDC?

DG: They report to the state.

VR: I see.

DG: That's a state thing.

VR: I got COVID in one arm because she said, "Oh, you get a lot of inflammation."

[laughter]

VR: I put the other two in the other, and I had nothing anywhere.

DG: That's great. That's good to hear. Strep throat, we're talking about strep throat this time, Vincent.

VR: Wow, we haven't talked about that in a while.

DG: This is something our local providers were asking about. It was actually Scott, one of our urgent care providers. "What's going on? Why are we seeing so much?" I said, "It's not just you." We have the article*, "Outbreak of Invasive Group A Streptococcus* in Children—Colorado, October 2022–April 2023," published in *PIDS*. That's the *Pediatric Infectious Diseases Society* journal. Just for background, in the fall of 2022, this is last year, they observed a really sharp rise in pediatric invasive group A *Streptococcal* hospitalizations in Colorado.

These are folks that get strep throat, and then it progresses. They decided that they were going to look at this. They compared the epidemiology, clinical features, and patient outcomes in this outbreak compared to prior years. They identified almost 100 cases of invasive group A strep. We read that these are kids, so median age of 5.7. And this is, I think, one of the things I want our listeners to really hear. 70% were previously healthy. Everyone's, "Oh, these are those kids, they had problems, they were going to end up in the hospital anyway." No, no 70%, almost all these kids, no obvious risk factor, progressed, end up in the hospital.

They end up, I'm going to say, ''Really in the hospital." Forty percent of them required critical care, four died, 60% had respiratory symptoms, 10% toxic shock syndrome, 4% necrotizing fasciitis.

There were significantly more cases, about triple the number that we normally see during this outbreak, including more cases of pneumonia, multifocal disease, and all this is statistically significant. Why do I bring this to attention? One is we are seeing enough of this that our providers are asking, "What's going on here?" I want to be honest. This is not an easy problem. We see lots of sore throats. About 20% of the population will have a positive strep test just because of high rates of colonization. Do we just treat everyone? Who do we treat? With what do we treat them?

This is something I've actually done a number of talks for our school nurses about. One of the things that I'll share is we use a modified Centor criteria. You probably remember, or maybe you remember your children being asked these questions. "Is there a fever?" They look in the back of the throat. "Is there an exudate?" Basically, pus on the tonsils. "Are there tender lymph nodes in the front of the neck? Is your child in the right age group," which is that 3 to 14 years when we see a peak incidence?

An interesting thing is you subtract a point, if they're over 44, they don't get any points, 15 to 44, and actually you subtract a point if they have a cough, but I just wanted to point out in this series, we actually were seeing quite a bit of lung involvement, so just a little caution there. It does actually take an evaluation to determine not just a strep test. A strep test without any of these may just be colonization. We don't want to overtreat. The big thing here also, as we discussed with our providers, is there is a growing problem with drug-resistant group A strep.

Number one, group A strep cannot become resistant to our penicillins or beta-lactams. We always have those as a go-to, but so many people walk around with this, "I'm allergic to penicillin," and that's a problem because if we move from penicillin, we say, "Oh, we'll just treat you with one of those Z-Paks that everyone seems to love." Already by 2017, a quarter of the times, that was useless. The group A strep was resistant. Clindamycin, that's another go-to. Also, about a quarter of the time by 2017, that was resistant. A lot of parts of our country, it's even more so.

Part of what is creating a problem for us here is this soft, "Oh, I'm allergic to penicillin." The child gets an alternative agent, and that alternative agent does not actually do any good, so you're sending out a child untreated with group A strep infection in their throat.

Moving into COVID, what's going on there? The average number of cases is down a little bit. The number in the hospital is down a little bit. The number in the ICU is still holding pretty steady, and we are still at over 200 deaths a day in the country. That's not just New York. About 1,478, we're actually averaging about 1,500 a week.

Number of folks in the hospital, as I mentioned, is down a little. If we look at wastewater, look, we're all doing reasonably well. We've come down off that hump, and we'll keep you posted. The wastewater is a nice way for us to follow this going forward. All right. This is one that came up just today, children, COVID, and other vulnerable populations. We have the article, “Nirmatrelvir/ritonavir Use in Pregnant Women with SARS-CoV-2 Omicron Infection: A Target Trial Emulation,” published in *Nature Medicine*. Vincent, I sometimes like to say, "Pregnant people," because it certainly generates a comment every time. If I say, "Pregnant women," also generates a comment every time, so I can't go wrong. I can only go wrong.

This trial was conducted in Hong Kong, where women with confirmed COVID-19 were treated with Paxlovid within five days of symptoms onset and matched in a one to 10 ratio with pregnant women who were not given antiviral treatment. Oh my gosh. The outpatient study took place from March 16, 2022 to February 5, 2023, when Omicron variants were circulating. They looked at any maternal morbidity and mortality. They use this maternal morbidity and mortality index.

This index includes vaginal bleeding, high blood pressure, eclampsia or preeclampsia, preterm birth, other adverse outcomes, including HELLP syndrome. That's where you get hemolysis, destruction of red blood cells, elevated liver enzymes, low platelets. Paxlovid treatment was associated with a significant reduction in this MMMI. In this maternal and morbidity index, they reported a 72% reduction, so a relative risk of 0.28. Not only did Paxlovid protect mom, but it was associated with a significant 90% reduction in risk of preterm birth and rates of cesarean section, 81% reduction there.

VR: Daniel, would being pregnant be an indicator for getting Paxlovid?

DG: It certainly is an indication for getting Paxlovid. I think here, like the question came up today, I had a young lady, her third trimester. Are you ready for this, Vincent?

VR: Yes.

DG: Third time with COVID during her pregnancy. She just was at wit's end.

VR: No.

DG: We have the ability with Paxlovid to protect mom and to protect the baby. There was a nice little CDC COVID flu and RSV facts thing that came out. They send these out, just sort of giving people a context and this little info cartoon, I'm not sure how to put a link in. We get from the CDC, in the U.S., more than 15 million children have tested positive for COVID-19 since the start of the pandemic. We hear that COVID-19 caused 22,000 hospitalizations in children, 800 deaths in children.

They also give us comparatives for flu. Flu, about 20,000 hospitalizations, about 100 deaths in children just last year; RSV, 58 to 80,000 hospitalizations, 100 to 300 deaths in children every year. We're trying to turn these things around. More about Paxlovid, I guess.

We are moving into COVID, the early viral phase, not just for pregnant women. Recently, a dear friend and colleague of ours in their 80s with several comorbidities came down with COVID and asked if he should bother starting on treatment or just wait to see how he did. After a little talk about whether or not he had been a good Catholic and was ready to move on to the next level, or if he planned on as much time in purgatory as I have ahead of me, we agreed to start Paxlovid.

This seemed like a good place to share an article that is very similar to a recent one that we discussed. The article is, “Outcomes of SARS-CoV-2 Omicron Variant Infections Compared with Seasonal Influenza and Respiratory Syncytial Virus Infections in Adults Attending the Emergency Department: A Multicentre Cohort Study,” published in *CID*. These are results from Sweden, a retrospective multi-center cohort study looking at adults attending the emergency department in six acute care hospitals in Stockholm County, Sweden, with an Omicron influenza or RSV infection during 2021-22. Then we've got some historical 2015-19 comparison.

During the 2021-2022, patients were tested for all three viruses by a multiplex PCR. The primary outcome was 30-day all-cause mortality. Secondary outcomes were 90-day all-cause mortality, hospitalization, ICU admission. A total of 6,385 patients were included in the

analysis, 4,833 with Omicron, 1,099 with influenza, and 453 with RSV. For starters, COVID, about five times more likely to end up requiring hospitalization compared to flu, 10 times compared to RSV. The 30-day mortality, 7.9% for Omicron, so about 8%, about one in 12 chance of dying if they showed up in the ED with Omicron, 2.5% for influenza, 6% for RSV.

Interesting that they had these, but among unvaccinated Omicron patients, stronger associations were observed compared with both influenza. Here we had a 5.51-fold increase, RSV, it's ratio 3.29, and these were consistent when they looked to RSV and flu outcomes pre-pandemic. Just to swing it together, in patients attending the ED, infections with Omicron were both more common and associated with more severe outcomes compared with influenza and RSV, and particular among, not surprisingly, unvaccinated patients. What do we do? Number one, Paxlovid; number two, remdesivir; three, Thor's hammer, molnupiravir; four, convalescent plasma in certain contexts. Let's not do those harmful and useless things.

Next, is the second week, the cytokine storm week. Certain percent of people are going to have issues during that second week. We can reduce that, as we mentioned, with those tools. Some folks during the second week, if their oxygen saturation has dropped to less than 94%, we can jump in with steroids. If they end up in the hospital, we have anticoagulation guidelines, a number of recommendations for pulmonary support.

What about remdesivir? I'm confident our listeners have all learned the importance of timing with regard to antiviral medications. The science certainly supports the sooner-is-better message, but when is it too late for remdesivir? The article, “Remdesivir Is Associated with Reduced Mortality in COVID-19 Patients Requiring Supplemental Oxygen Including Invasive Mechanical Ventilation Across SARS-CoV-2 Variants,” was just published in *Open Forum Infectious Diseases*.

Here, the authors examined the comparative effectiveness study of remdesivir on in-hospital mortality among patients hospitalized for COVID-19 requiring different levels of oxygen. We're going to look at folks that require low-flow oxygen, high-flow oxygen, and non-invasive ventilation, or folks that require invasive mechanical ventilation, or ECMO, and we're going to look at different variant-of-concern periods. We're really asking this question, which is a challenge of, are we still able to provide some benefit for these folks?

Remdesivir treatment was associated with a statistically significant reduction in in-hospital mortality at 14 days, and we'll go through. If they came in and it was just low-flow oxygen, adjusted hazard ratio of 0.72, so about a 38% reduction, that's not bad. If we move to the high-flow non-invasive, hazard ratio 0.83, so only about a 17% reduction. If we don't get there until invasive mechanical ventilation or ECMO, we actually still saw a 27% reduction, and then we follow this out. We also have some outcomes at 28 days, as well as that 14-day mortality, basically lower risk of mortality among remdesivir-treated patients observed across all levels of oxygen and observed across all variants-of-concern periods.

We often get this confusing history about patients, "Oh, I've only been sick for a few days," but here they are already on high-flow nasal cannula. Maybe they're on high-flow nasal cannula because this is really the second week, and that history is not accurate, or maybe something else is going on. Maybe they have CHF, congestive heart failure. Maybe they have some underlying pulmonary disease. Maybe there is a secondary bacterial pneumonia

complicating the case, which we sometimes see. Basically, this just really enforces low risk with starting the remdesivir and potential benefit. I guess the only harm I can see is maybe the impact on the hospital's pharmacy budget.

Number five, immunomodulation, sometimes tocilizumab or baricitinib, and again, only jumping in with the antibiotics and other therapies if the person actually has a proper indication.

All right. This is the one I've been getting a lot of questions about, Vincent. I actually feel like either you or Amy maybe sent this my way, in addition to about six other people. The article, “Effectiveness of Nirmatrelvir-Ritonavir Against the Development of Post-COVID-19 Conditions Among U.S. Veterans: A Target Trial Emulation,” published in *Annals of Internal Medicine*.

These are the results from a retrospective target trial emulation study comparing matched cohorts receiving nirmatrelvir/ritonavir, so Paxlovid, versus no treatment. The participants were nonhospitalized veterans in veterans care, Veterans Health Administration, VHA care, who are at risk for severe COVID-19 and tested positive for SARS-CoV-2 during January through July 2022. It's an interesting design. They tell us that they executed these five nested sequential trials. They really broke people down into, were you treated on Day zero or 1, or 2, 3, or 3, 4, sort of grouping people. I thought this was really interesting. Potentially you can pull out whether or not, earlier treatment versus later treatment had some impact.

They go ahead and they look for 31 potential incidence post-COVID conditions as captured by IC-10 codes. We'll get into this, but this is going to require the patient not only reporting an issue, but the doctor actually adding that code to the medical record, et cetera. They report that they observed no differences between participants treated with nirmatrelvir/ritonavir. We have an N of 9,593, and they're matched untreated comparators in the risk or the incidence of most post-COVID conditions examined individually or grouped by organ system, except for a lower combined risk for venous thromboembolism and pulmonary embolism. There we have a 0.65 hazard ratio.

What's the story here? Because a lot of people are basically saying, "Boy, we've seen several other studies," and they actually reference those in this article. "How come we're not seeing differences here?" The way they're actually reporting it is not that they failed to show differences, but that they did not show differences and suggesting that we, I don't know, shouldn't be using this to prevent Long COVID.

There's a number of limitations that the authors discuss. The biggest is that they were just looking at diagnoses that were coded. They really didn't do any survey or individual assessment. They're really expecting the doctors working in the VA clinic to see a patient. I have to admit my first real job, Vincent, when I was out there in the world, was I was the VA doc up in Montana at the Helena, Montana, VA, and you'd see your classic VA patient, which had like the big five.

They've all got COPD because they all smoked. I think they were given like, with their meal rations, a pack of cigarettes or something. [chuckles] They all have high blood pressure. They all have high cholesterol. They all have diabetes. You had already this list of things. I guess

now they're going to come in and say, "Since COVID, I'm just not feeling so great. My energy is low. Am I going to actually add a couple extra diagnoses when I've already got five on the sheet?" Because you can only send in four. Anyway, so that's one of the big things I want to point out.

They also excluded some of the people who ended up getting hospitalized. Lots of trends in the right direction, but not reaching statistical significance. Maybe wording things a little bit different. They fail to show a statistically significant difference. Even though we seem to have a large number, when you start chopping that up into 31 variables, you actually start getting into smaller numbers. Actually it's going to become a little bit more challenging to reach that statistical significance. Also, to point out the older male population of veterans, is that really generalizable?

As I mentioned right up front, they also referenced a number of studies so far that actually have showed a reduction in post-COVID conditions in folks that get early antiviral treatment.

VR: Very small differences, right?

DG: Yes, yes, not huge differences here. I am going to wrap it up there with, "No one is safe until everyone is safe." Vincent, this is your favorite time of year. We have just finished our Floating Doctors fundraiser. We reached our goal. I just sent off a check to support Floating Doctors, $20,000 for the great work they do. Now, we are doing our MicrobeTV fundraiser for November, December, and January. We'll double your donations up to a maximum donation of $20,000 for the great work that MicrobeTV does.

VR: This is your chance folks go to Parasites Without Borders and support MicrobeTV. All the other causes are very good too, but this is what makes this program and many others, so please do that.

DG: People are already doing it. I think we must have put out some information on social media, et cetera. Yes, already a few donations came in this morning. Thank you, everyone.

VR: It's time for your questions for Daniel. You can send them to daniel@microbe.tv. Ellen writes, "How soon after one has gotten over the flu, should one get a flu vaccine? Do the same rules apply as after a COVID vaccination? Why or why not?"

DG: It's really a good question actually. Let's think it through. With influenza, you'll notice it's a quadrivalent flu vaccine, but it probably is going to be trivalent going forward. It'd probably be one of the influenza Bs, a couple influenza As. There's a couple of things going on there. One is that probably whatever influenza you just got, you've probably had a nice boost. There's probably germinal center maturation going on. That's great for that one. What about the other two? That's where the science becomes a little bit challenging. Do you stick with the COVID type recommendation where you say, "Hey, wait three months," you say, "Let's see about that. It's November, December, January, season's going to be over by then."

The recommendation is not clear. Some of us say, "Wait three months," but we're going to be thinking about timing. Others say, "Wait about a month, and then you may not get as much of a boost from what you just got, but you're going to get that vaccine for the other." I'm usually thinking of an individual who didn't get their flu vaccine, got the flu. Maybe in general,

I'm going to say think about a month after that infection. If you did not get your flu for the season, get that in. You're going to protect yourself against the other couple and you're probably going to be OK with the one that you already had.

VR: Mark writes, "I'm an internist in primary care and hospital medicine for my patients. For several years, you have been saying we should not repeat COVID antigen testing after we have a positive test because it's not very predictive of how contagious one may be. I have been repeating that recommendation to my patients, but I see you have changed your recommendation. I missed the discussion of the science behind it. As you said this week, one tests negative twice over consecutive days, after day five, you can go without a mask. I know the CDC has been saying this but in the past, you have suggested that there was no data to support it. I'm confused. Can you please help straighten me out?"

DG: [chuckles] Now, this is excellent. I'm glad you sent this email in. Vincent and I had a bit of a discussion about this last week, actually. We were talking about a study where they were looking at children and they were doing viral cultures and they were saying really the median period of positive viral cultures was about three days, really making a comment about this recommendation of five days of isolating most of the transmission. I think we've talked about, over time, is during those first five days. We're also talking a little bit about the public health issue about how long are people willing to isolate more than five days, like what do we do with influenza, which is a contagious disease? What do you do with RSV, which is a contagious disease? What do we do with a lot of these other transmissible pathogens?

The science hasn't changed much. The science is still that most of the transmission, probably 80%, 90% is in the first five days. There probably is still some transmission past that may be impacted to some degree by early antiviral. In the study we talked about, vaccines didn't seem to have a big effect on the period of time that a person was culture-positive. That is the CDC's. I went through the updated CDC guidance where they have that in there. Science hasn't changed very much other than what we've shared. When I recently had COVID, I actually did a full, strict five-day isolation. Then despite having those two negative tests, I continued to wear a proper mask out past day 10.

VR: Janice writes, "I don't think I've heard this question asked before, but it applies to me. I tested positive for COVID the day after I got my flu vaccine. I had no idea prior to my flu vaccine. I normally get body aches, slight headache, low-grade fever, sore arm after my flu vaccine, and I didn't really think twice about it when I got those symptoms after my shot. I decided to do a rapid test and to my disappointment, I was positive. I took three different tests from two different boxes just to be sure. Thankfully, I was able to access Paxlovid the next day.

Will my flu shot be compromised by my COVID infection, any interactions with Paxlovid and flu shot? What are your recommendations for protection from flu going forward this season given my situation?"

DG: Now, this is a good question. We've talked a little bit about this, the interference that to some degree can occur as it's described. In this situation, we still think you're going to get the protection from the flu shot. We don't think there's going to be some huge amount that's going to mean that you have to go back and get another flu shot at this point.

I think jumping in with Paxlovid like you did, it was really the right thing to do. Boy, when we had more and more COVID early on and we were just starting to roll out the vaccines, and a lot of times the vaccine centers were peoples' super-spreader exposure event. This was always a challenge for us trying to sort out what was a vaccine reactogenicity versus what was actually you got something at that center. I think you're good with flu for now. I think you did the right thing with Paxlovid.

VR: Lani writes, "I recently tested positive for COVID and messaged my physician at the Orlando VA Hospital requesting a prescription for Paxlovid. I'm 63, hypertension, CAD. I was told that we don't prescribe that any longer. I asked for an explanation. I was only told to take general measures to ease symptoms. I am attempting to escalate this issue with the VA hospital, but I doubt anything will come of it before my five days are up. I only wish Paxlovid were available over the counter or that more physicians were in the know". I thought we should read this because this is really unacceptable, Daniel.

DG: It really is unacceptable. Who's the “we?” Is it the man? Is the man keeping you from getting the Paxlovid? Who's the “we?” Because really you got to ask like, "No, no, you as a physician, you who took an oath, you who really has an obligation." I have to say, some of my colleagues probably think I'm a bit of a jerk when I say this, but I think, it is quite a privilege to take care of fellow human beings when they call you, they expect you to be up to date. They're really relying on you to give them the best guidance.

We've talked about a couple hundred people still dying a day, and your VA population is really, as we've described where, you've got those high risk folks who may progress. I would instead of say, "Forget about the we, what about you? Why are you going to not offer me antiviral treatment when it's available? There's a lot of evidence out there that it can provide me with benefit.”

VR: John writes, "I'm male, 62, previously very healthy, but I have had Long COVID for about 16 months, have been off work for over a year with severe fatigue and brain fog. I was vaccinated three times before March, 2022. I've had follow-up vaccinations in November, and was vaccinated in May. Each time I've been vaccinated, I feel my Long COVID symptoms have gotten noticeably worse, more fatigue leading to brain fog and more rest periods and breaks required to live my daily life. I've read that some Long COVID patients get better with a new vaccination. Some get worse and some stay the same.

I'm due to get another shot probably in a month, but I'm leery about doing so given my past history of feeling worse after a vaccine. Can I skip the vaccine when offered and perhaps rely on Paxlovid if I get COVID again? I've had a total of five vaccinations and two COVID infections so far. My doc says, "Ask the Long COVID clinic," and the Long COVID clinic where I'm a patient says, "Ask your GP." What should I consider in making this call?"

DG: First off, I'm not going to pass the buck. I'm going to give you an answer here. The first off is you're describing the three potential outcomes that we saw. People get better, no effect, they get worse. Those are just really the three possibilities that you knew at a time and the question were what were the percentages? Early on, before people were vaccinated at all, we saw that most people got the improvement with the first shot. I think we're 40% with the first shot, another 20% with the next shot, and a few more percent with the third shot.

After that, we're talking about single digits. We're reporting improvement, getting further after the first three. Really the first three shots were the therapeutic vaccination for people with Long COVID. Each time we also saw a certain group of people that just really nothing happened. We did see, like you described, people that actually feel worse for a time after that vaccine. We do not have any blood test. There's really no way for us to know ahead of time going into this. I am going to say once you've gotten your three shots in, the chance that vaccine is going to really be therapeutic for your Long COVID is pretty low.

If you're describing a history of every time you get the shot feeling crummy for a while, that's probably what's going to happen for you. The other thing you bring up, and this is huge. If you get COVID, that's a big thing, is most people, who have Long COVID, who get COVID, they have a rough time. It's not something that is therapeutic, so you do want to jump in as early as possible with the Paxlovid.

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

DG: Thank you. Everyone, be safe.

[music]

[00:39:02] [END OF AUDIO]