This Week in Virology

TWiV 1090 Clinical Update

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

[music]

From MicrobeTV, this is *TWiV. This Week in Virology*, Episode 1090, recorded on February 22, 2024. I'm Vincent Racaniello, and joining me today from someplace sunny, Daniel Griffin.

Daniel Griffin: St. Augustine, Florida. Hello, everyone.

VR: It's really nice there.

DG: It is. I'm on the water. A couple of dolphins just went by. There's a bunch of sailboats out there. It's a beautiful place.

VR: Have you gone to Florida to pass some advice to the health commissioner?

DG: [laughs] I don't think my science evidence-based advice would be necessarily welcomed by everyone down here.

VR: I'm sorry. You have no bow tie today, so -

DG: I know. They wouldn't even know who I was. Let's get right into it. I'm going to start off with a quotation. Maybe people know the history of St. Augustine, really fascinating history. It's just amazing how much of the history is Spanish, but also a lot of pirates. I'm picking a pirate quotation. It's a quotation from a pirate who actually, interesting enough, on the other side, not the Griffin-O'Connell side, but the other side of the marriage, there's descendancy from Sir Francis Drake.

“There must be a beginning of any great matter, but the continuing until the end, until it be thoroughly finished, yields the true glory.” A little bit of advice with sticking through. He starts off as a bit of a pirate. He starts off as a pirate. Then by the end, he's got a fleet of ships. He's got thousands of men. He actually becomes Sir Francis. Just see if you stick with piracy for a while, what can end up happening. Right into RSV, actually, I think good news here. We've really come off. We had that double peak. We've really dropped down.

RSV data for the United States is really going in the right direction. Oh, my gosh, good news on RSV vaccines, both active and passive, despite some shortages within nirsevimab, through January, 40.% of women with babies ages 8 months and younger said their infants received Beyfortus; 16.2% of women at 32 or more weeks of gestation received the RSV vaccine. That's Abrysvo. There was some sort of confusion there about which one you could get. Some people got the other. Not sure it's such a horrible foul. As of February 3, 2024, an estimated 22.4% of adults 60 years and older had already gotten their RSV vaccine. We've got another 13.2 that definitely plan to get it. Hopefully, that'll keep going in the right direction.

Influenza went down, went back up, and it's actually still pretty high in a lot of areas. Again, this is regional. Here in the New York-Long Island area, I say here, but I'll be back "here" to New York on Saturday. We've dropped down to a low minimal level, which is great. That's also true of a lot of the West. Down here in Florida, we are in the high zone. Texas, the whole Southeast, New Mexico, particularly seeing lots and lots of flu activity.

New York City itself is an outlier for the rest of New York. It's actually in the high, very high influenza level. It's actually interesting. Why can things be so different between New York City and, let's say, Nassau, Suffolk out here on Long Island?

VR: Population density is a big one.

DG: I think that's huge. There's population density, and there might be some other factors as well, but yes, that's a huge difference.

VR: People walking around on the sidewalk. There's not a big sidewalk traffic in Nassau.

DG: [laughs] There is not. A little bit in the evenings when people are out with the dogs, but no, otherwise quite different. Actually, never, ever reaching the levels it does just north of the incubator there in the city.

VR: Oh, yes. Sometimes you can't even walk on the sidewalk, Daniel. It's so crowded.

DG: It's crazy. It really gets crowded there. All right, COVID, right into it. Little bit of a tick in a positive direction. Still averaging about 200 deaths a day. This last week, we were a little bit lower. Maybe, but then let us look at the wastewater. We had a really high peak end of December, January. Things came down, going in the right direction. Now, actually, if you look at the national average, it's actually starting to rise a little. A lot of that is being driven by the Southeast and by the upper Midwest. We'll keep an eye on where we end up with that.

Moving back into testing. I think this is one of those times where you just keep reminding people. The article, “Self-Administered versus Clinician-Performed BinaxNOW COVID Rapid Test: A Comparison of Accuracy,” was published in *Clinical Microbiology*. As I started to say, I think it is worth reminding everyone that, yes, those rapid tests still work. These are results of a single-center study at a free community testing site in Baltimore City to assess the accuracy of self-performed rapid antigen tests for COVID-19, self-administered BinaxNOW rapid antigen tests were compared with clinician-performed rapid antigen tests.

They’re going to use a reference molecular test as the gold standard. In this study of 953 participants, about 15% were positive for SARS-CoV-2 as determined by PCR. The sensitivity

and specificity were actually similar and quite outstanding for both self- and clinician-performed rapid antigen tests. Sensitivity, 83.9% versus 88%. Specificity, 99.8 versus 99.6. Great specificity. Subgroup comparisons based on age and race yield similar results. Now, an interesting issue was that 5.2% of the positive results were potentially missed due to participant misinterpretation of the self-card.

I want to remind clinicians when someone, "Oh, I did that. I did that test. It was positive. It was negative." I always ask them, "Can you take a photo? Can you send that to me? Can I take a look at it?" Because sometimes people miss the interpretation. Some of them have two, some of them have three lines. I do want to point out that the test did very well in symptomatic individuals with both self- and clinician-performed testing sensitivity at 88% and 90%.

VR: Daniel, when they say specificity, what are they comparing it to?

DG: This is great. Just a reminder, we throw these words out there. Sensitivity is someone actually has COVID. They have a positive RTP seromolecular test. How good are you at actually getting that? About 90% of the time in symptomatic, you're going to get a positive when you should be getting one. Specificity is this issue. If you get a positive test, is it really positive? You end up with a positive test and the person doesn't actually have it. Here we're seeing a fraction of a percent. We're seeing 0.2%, maybe 0.4% of the time, "We got a positive test," but they don't actually have a PCR that's positive.

VR: They have something else if they're symptomatic, right?

DG: Yes, so they're symptomatic. Maybe they've got parainfluenza. Maybe they've got, rhinovirus. Maybe they've got the flu, but you get a positive COVID test. As we saw, that's happening a couple per thousand tests.

VR: The PCR confirmation is the key there, right?

DR: Yes. That's how you know that this person - someone has a positive PCR or even better yet, someone has a negative PCR, but you get a positive RAT, you don't believe the RAT. Probably something wrong there.

VR: Got it.

DG: Ventilation transmission. I have to say, I found this interesting. I spent a lot of time on this article. The article, “Annual N95 Respirator Fit-Testing: An Unnecessary Burden on Healthcare.” [laughs] This article was published in *Infection Control and Hospital Epidemiology.* This is one of those journals that I always look through the table of contents, see if there's anything interesting. This article looks at whether we need that yearly N95 fit-testing. Part of what I liked was, I have to say, the intro was worth reading. I'm going to share a little bit of this.

Let me read. The control of airborne respiratory infection transmission in healthcare settings is achieved through a combination of administrative measures. For example, moving persons with the possibility of infection to single patient rooms; engineering measures, that's the negative pressure rooms, hospital ventilation, high-efficiency particulate air filters, those

HEPA filters, and respiratory protection devices. Those N95 respirators that we've all gotten familiar with. Now, the effectiveness of N95 respirators in the prevention of TB and other airborne infections has not been well-established but remains the standard of practice in most healthcare settings.

I'm reading the article here. A study that evaluated the hospital transmission of TB in the late 1980s and 1990s during implementation of control measures, administrative and engineering measures most likely led to the substantial decrease in transmission rather than the use of respiratory protection devices. In addition, comparisons between N95 respirators and surgical masks in the transmission of laboratory-confirmed respiratory infection, influenza-like illness, or workplace absenteeism have not demonstrated a significant difference.

Now everyone's all in a fuss here, but then we get in italics, it's OK. However, more recent work has indicated the utility of N95 respirators in the prevention of SARS-CoV-2 transmission in a combination of healthcare and non-healthcare settings. We've actually covered some of those studies. Now, after saying all that, they're going to restrict their investigation to an evaluation of the probability of failing respirator fit-test over time among a population of healthcare workers in Southern California.

We've got 15,757 persons with at least one fit-test result. After-fit testing for an N95 respirator, the probability of fit-test failure on the same respirator within three years is likely to be less than 0.5% based on this study. This is this whole idea, we're getting tested every single year, but what are you really picking up? Over those three years, you're picking up one in about every 200 people that is failing the-fit test. They go on to say, based upon this, "In addition to the hassle factor and the time commitment for getting this retesting yearly, they estimated that the total annual cost to healthcare in the United States for-fit testing is in the range of US $200-to-$400 million.

Now that more and more people are using N95s, this may even be an underestimation of the time and economic burden. I don't know if you know about this, Vincent, or our listeners do, but particularly for me, who practices at three different healthcare systems, the traditional thing is I had to go to the Catholics, I had to get my fit-testing, and they're doing the saccharin, I'm moving my head around and singing and reading something. Do I taste that sweetness? To me, it's bitter, but I know if I don't say sweet, I don't pass. Then I've got to go to Northwell, and then I've got to go to Columbia. You go right in the lobby of Milstein, it's over in the corner there on the right.

I've got to do that at all three healthcare systems every single year, and I never fail. I've been doing this, I don't know, for 30 years. Anyway, it's amazing how many hundreds of millions of dollars is devoted to this annual testing.

VR: Where are the data that says it matters?

[laughter]

DG: That's what I think is interesting about their whole introduction. They're like, "Come on, we're dealing with this level of data, but yet we're spending hundreds of millions of dollars." They're basically saying, "Maybe we need to think about that allocation of funds." [laughs]

Moving on to COVID active vaccination. Another article actually demonstrating protection against Long COVID. The article, “The Impact of COVID-19 Vaccination Prior to SARS-CoV-2 Infection on Prevalence of Long COVID Among a Population-based Probability Sample of Michiganders*,”* I like that word, ”2020 through 2022,” published in *Annals of Epidemiology*.

They use data from the Michigan COVID-19 Recovery Surveillance Study, a population-based probability sample of adults with COVID. They've got 4,695. They considered 90-day Long COVID, considered other stuff, but I'm focused on this. Illness duration of greater than or equal to 90 days. They compared vaccinated who completed initial series greater than or equal to 14 days before the COVID-19 onset to unvaccinated individuals. Accounting for differences in age, sex, race, ethnicity, education, employment, health insurance, and rurality and urbanicity.

The full unvaccinated comparison group was further divided into historic and concurrent comparison groups based on timing of COVID-19 onset relative to vaccine availability. We end up getting prevalence ratios. We're going to look at the prevalence and we're going to do a ratio. Compared to the full unvaccinated comparison group, the adjusted prevalence of 90-day Long COVID was lower among vaccinated individuals. We've got a prevalence ratio here of 0.42. Then we've got a confidence interval. Giving us a 47% to 66% lower prevalence of Long COVID at 90 days in the vaccinated. These estimates were consistent across the comparison groups, the full, the historic, and the concurrent.

Moving into COVID early phase, really just keep hammering on this. You test positive, you're at risk of progression. Number one, Paxlovid. Best efficacy data there. Number two, remdesivir. Proved down to 28 days of age. Molnupiravir, inferior, but still another effective option. Convalescent plasma in a particular select subgroup, and isolation for the infected. We may get to that in our questions. Has that changed? COVID, the cytokine storm. That's that second week, remember?

We did not include steroids in that first week because it's associated with an increased risk of bad outcomes. During that second week, in patients with oxygen saturations less than 94%, dexamethasone, 6 milligrams a day times six days. Growing data that dexamethasone may actually be the best steroid, the steroid of choice. We have anticoagulation guidelines from American Society of Hematology. Pulmonary support, remdesivir still in the first 10 days. Immune modulation, consider things like tocilizumab. Remember, avoid the unnecessary antibiotics and unproven therapies.

There will be certain times when you want to use an antibiotic, when it may be appropriate and beneficial. We don't just throw these at 90% of folks as historically has been done.

All right. We're going to spend a lot of time again on COVID, the late phase PASC, Long COVID. I'm going to start with the *MMWR, “*Notes from the Field: Long COVID Prevalence Among Adults-United States, 2022.” As we've discussed, getting an exact number in terms of Long COVID incidence is challenging. Here, Long COVID was defined as the self-report of any symptoms lasting for greater than or equal to three months that were not present before having COVID-19.

Respondents were sampled using random digit dialing of both landline and cellular telephones. That had to be fun. Self-reported age, sex, previous COVID-19 diagnosis, and ever having experienced Long COVID were ascertained via telephone interview. I'm trying to decide what's more fun, like the cold calling to see if someone's going to vote for your candidate or cold calling to ask about this stuff. Who gets hung up on more often? Remember, it's a telephone interview. Now, nationally, 6.4% of non-institutionalized U.S. adults reported ever having experienced Long COVID.

There were notable regional differences, and we really have a nice figure with the maps. That's really what I thought would be worth discussing. There's really quite a bit of variation. We have areas with an 8.9% to 10.6% report based on this telephone interview. Areas like, what is that? Mississippi or Alabama? I can never tell those two apart. Can you tell, Vincent?

VR: Alabama.

DG: That's Alabama? It's the one state I've never been to. We've got Alabama, we've got Tennessee, we've got West Virginia, we've got Oklahoma, Montana, North Dakota, Wyoming, all with these really high incidences. Then some of the lowest incidences, U.S. Virgin Islands, DC, 3.7% to 5.3% in the Great Pacific Northwest, up in the Northeast as well. Really interesting, gives you a chance to ponder what might be the factors associated with the different incidences of Long COVID or the different incidences of not slamming down that phone when you get called.

VR: Yes, that's right. I also think that states are artificial boundaries. There's probably a blurring that we don't see in these data, but it's self-reported. That's always a concern, right?

DG: Yes, it definitely is. Interesting that we're seeing some kind of a pattern here. The article, "Estimates of Incidence and Predictors of Fatiguing Illness after SARS-CoV-2 Infection," was published in *EIS, Emerging Infectious, EIS*. What does that stand for?

VR: Emerging infection. Actually, it should be *EID, Emerging Infectious Diseases*.

DG: OK. This is a retrospective cohort analysis. Here, the investigators analyzed electronic health record data of 4,589 patients with confirmed COVID-19 during February 2020 through February 2021 who were followed for a median of 11.4 months and compared this data to data from 9,022 propensity score-matched non-COVID-19 controls. This data was collected from the University of Washington. That included three hospitals. We've got Harborview Medical Center, UW Medical Center Northwest, and UW Medical Center Montlake, and greater than 300 primary care and specialty clinics providing healthcare services across the state of Washington.

Just a moment to look at the methods. I thought this was interesting. Fatigue was defined by them basically finding that a physician had coded an ICD-10 diagnostic code or ICD-9 code. Diagnostic codes recorded in the electronic health care system, the electronic health record during the post-acute period. These are the ones they're looking for. They're looking for G93.3, post-viral fatigue syndrome; R53.82, chronic fatigue unspecified, code I use a fair amount; R53.83, other fatigue, 780.71, chronic fatigue syndrome, post-viral fatigue syndrome; or 780.79, malaise and fatigue.

They defined incident fatigue as a patient who had greater than one diagnostic code for fatigue during the post-acute period. As we talked about last week, this is dependent on the treating provider, not just recognizing incident fatigue, but actually adding this coding to the visit. I made a note to self here, we did not see the G93.32 code in there, a subset of the G93.3. That's the myalgic encephalitis chronic fatigue syndrome, so the ME/CFS code, but it is a subset of the G93.3. Now among COVID-19 patients, about 15% were hospitalized for acute COVID-19, 85% weathered the storm outpatient.

The incident rate of COVID was 10.2 per 100 person-years, and the rate of chronic fatigue was 1.8 per 100 person-years. Compared with non-COVID-19 controls, the hazard ratios were 1.68, so about two times as likely for fatigue, and 4.3, more than four times for chronic fatigue. The observed association between COVID-19 and the significant increase in the incidence of fatigue and chronic fatigue reinforces the need for public health actions to prevent SARS-CoV-2 infections. What I thought was really interesting here. Forget about definitions, forget about the people that don't believe.

We're actually seeing people going, people having a recognized chronic fatigue diagnosis four times higher after they had COVID-19.

VR: Daniel, it says here, to prevent SARS-CoV-2 infections, that's not correct. It's to prevent symptomatic infections because we just saw that vaccination, which doesn't prevent infection, decreases the incidence of Long COVID. You don't need to prevent an infection, you just need to prevent having some sort of symptom.

DG: Yes, whatever it is that triggers this Long COVID is what we really need to prevent. Because yes, I think it's probably great that you point this out, because the whole idea if you set this idea that you're never going to end up with a positive PCR, that's just probably an unattainable goal.

VR: No, can't happen, no.

DG: I was left with lots of questions after reading the following article, "Long-Term Risks of Respiratory Diseases in Patients Infected with SARS-CoV-2: A Longitudinal Population-Based Cohort Study," published in *eClinicalMedicine*. Let's go through this and see if I can't tease out a little bit about what this study is telling us. This is a longitudinal population-based cohort study, where they built three distinct cohorts, aged 37 through 73 years, using the UK Biobank database.

We've got a COVID-19 group diagnosed in medical records between January 30, 2020, and October 30, 2022, and two control groups. We've got a contemporary control group and a historical control group. They have these different cutoff dates. October 30, 2022, contemporary, October 30, 2019, respectively, so pre. The follow-up period of all three groups was 2.7 years. They included 112,311 individuals in the COVID-19 group, with a mean age of about 56.2; 359,671 in the contemporary control; 370,979 in the historical control. They found elevated hazard ratios for a number of different respiratory disorders in the COVID-19 group.

They reported for asthma, hazard ratio of 1.49, bronchiectasis 1.3, COPD 1.6, interstitial lung disease 1.8, pulmonary vascular disease 1.59. This is the one that caught me, lung cancer 1.39.

What is up with that? I spent a lot of time looking through and the discussion. As I mentioned, I was caught by this lung cancer connection, but the authors suggest that our study found a significant association between COVID-19 and lung cancer, but we fully recognize that this may be due to large-scale chest CT scans performed on a large proportion of suspected or confirmed patients with COVID-19, leading to more early tumor cases being detected.

Therefore, clinically, more caution is required when interpreting the association between them. I thought it was interesting. It makes sense. I'm always looking for a mechanism. Does this make sense? To see that someone may have had damage to their lungs. We may see the COPD, we may see the interstitial lung disease, but the association was with lung cancer in this 2.7-year cutoff suggests to me that probably not driven by the SARS-CoV-2, probably driven by the diagnostic testing. Some discussion about the mechanism for the other respiratory issues.

They conclude, "Our research suggests that patients with COVID-19 may have an increased risk of developing respiratory diseases, and the risk increases with the severity of infection and reinfection."

VR: Daniel, if you have influenza or respiratory syncytial virus disease or others, do an increase of other lung problems after those as well?

DG: There's some increase, but not as dramatic as we're seeing reported here.

VR: Is that just because there are so many cases of SARS-CoV-2 infection or are they comparable with the other viruses?

DG: I don't know. Is there something, is there more inflammation? Is there more damage? If you've got someone who ends up, let's say parainfluenza virus, really severe, ends up in the ICU, and I think we've looked at some studies where you end up with a really severe respiratory infection, you can have a lot of these sequelae afterwards. Yes, a lot of this, you'd probably want to do a study where you compare apples to apples on this.

VR: Also, remember that different influenza viruses have different virulence. H3N2 and H1N1 are different, so you have to be careful not to mix them all together.

DG: Exactly. I'm going to wrap it up here. I know last time we spent over an hour, so I'm going to keep it a little shorter this time. [laughter] No one is safe until everyone is safe. I do want everyone to pause the recording right here. Go to parasiteswithoutborders.com and click 'Donate,' because we are doing our American Society of Tropical Medicine and Hygiene fundraiser, where for February, March, and April, we will double your donations up to a potential maximum donation of $20,000.

I should point out, this money mainly goes to scholarships, bringing women from low-income and low-middle-income countries to the annual event, giving them a chance to make connections, network, and really open up the opportunities for them.

VR: Time for your questions for Daniel. You can send yours to daniel@microbe.tv. Peter writes, "Listening to your fine show, *TWiV* 1088 RE: Post-influenza sequelae. My wife picked up HPIV-2 and came down with overall feeling very weak, went to local clinic, displayed heart

rate of 160, ambulance took her to Cleveland Clinic here in Vero Beach, given adenosine along the way, VQ in the ER because she was allergic to iodine, displayed EF of 26%. Pam usually is fine, living with RA, methotrexate, SVT was also apparent, so angiogram was performed, clean and ablation for the SVT, along with Entresto, B-Metoprolol, and Eliquis.

Sent home in a life vest to have to uncomfortably wear for three months. Are you seeing this virus in adults, 70 years old, and having sequelae like this? January 16 entering ER, February 18, feeling great, just wears out early."

A lot of jargon in there for our listeners, but this is human parainfluenza type 2. We actually have seen a lot of severe cases of human parainfluenza type 3. Often they can be quite severe. There's a little bit of a hierarchy between severity at a population level but as an individual, we can see people end up in the ICU, we can see really severe cases, we can even see this as described here, this reduction in cardiac function. The RA, rheumatoid arthritis on methotrexate, so we have an immunosuppressed individual here. I think maybe this goes back to your point before, we've really learned a lot and we really have SARS-CoV-2 and COVID-19 sequelae under a microscope.

A lot of our other respiratory viruses can - we talked about RSV, 10,000 to 20,000 adults die each winter from that. Hundreds of children don't survive because of RSV. Human metapneumovirus coming in a little bit after the big three, but the parainfluenza viruses can cause a tremendous amount of morbidity as well.

VR: Roberta writes, "I wanted to provide you with an update following our discussion during the recent *TWiV* 1088 regarding vaccine eligibility. First, I want to express my appreciation for the advice you provided. I took steps and inquired at three additional different chain pharmacies about the possibility of paying out of pocket for vaccine. Regrettably, I received the same response from each pharmacy. Despite my willingness to cover the cost, I did not qualify due to corporate protocols. Despite my request, they declined to show me the protocols. Undeterred, I continued my efforts to secure the vaccine and endeavored to educate the pharmacies on the need for additional vaccinations.

Unfortunately, it appeared that they were not up to date with the latest information. However, I am pleased to share that my persistence paid off at a fourth chain pharmacy. The pharmacist agreed to check corporate protocols and had an understanding of waning immunity and the need for additional vaccination. He checked corporate protocol and successfully ran the Novavax through my insurance. I received confirmation that it passed through both. As a result, I received my vaccine and no payment was necessary. I'm going to try and contact corporate and obtain these protocols. Once again, thanks for your help and encouragement."

DG: I think you followed, like in the words of Francis Drake, and you finally yielded that true glory at the end. Congratulations for the rewards of your perseverance on that.

VR: Anne writes, "Given that you happen to live on Long Island, I'm hoping that you have an opinion as to why Nassau County for months has been doing measurably worse than New York City or Suffolk or the rest of the country for that matter, at least according to the *New York Times*. What's going on?"

DG: I don't know, but let me speculate. Doing worse, are we doing worse as far as numbers of diagnoses? Maybe, but maybe that's a good thing. If you don't test for something, you don't see it. I know our Nassau County providers hear me, hopefully echoing in their ears every time they see something, think about COVID, treat the COVID. Hopefully, we're doing better when it comes to outcomes. No, it's amazing. Things really change when you move from that really population-dense New York City out to Nassau County. Your initial idea would be that we should be doing better. We've got a better environment, less population density. I can only speculate.

VR: Tamar writes, "My physician, who specializes in geriatric care, does not like to prescribe Paxlovid for her COVID-positive patients because of problematic drug interactions, rebound, and undesirable side effects. She says she prescribes molnupiravir as an alternative. I tried to convey your explanation of rebound and how this phenomenon had been seen even before Paxlovid was on the market, but I'm not sure she was convinced. I'm a 69-year-old female. I'm pre-diabetic, have high cholesterol, have GERD, and neuropathy in my feet. My husband has Barrett's esophagus for which he takes a PPI.

I say we're basically healthy. Can you comment on whether molnupiravir is as effective as Paxlovid? If not, would you recommend finding another doctor who would prescribe Paxlovid?"

DG: It's not as effective. We've looked at the studies. The initial study, we were very excited, but then when it finally came out, 30% reduction compared to 88%, 89%. About one-third as effective, so clearly not as effective. It's an easier lift, I'll give you that. You don't have to sit there, run the medicine through a drug-drug interaction, but come on, that's what we're paid to do. We get paid actually quite well, even though we grumble and gripe. If your provider is not willing to spend a few minutes to run the medicines through, look for those drug-drug interactions, understand how to prescribe the medicine -

This is sort of a telltale thing. If your provider believes COVID rebound, Paxlovid rebound is a thing, I think you got to ask how much other science are they getting wrong.

VR: Finally, Will writes, "What evidence, if any, does CDC have for abandoning five-day isolation guidance for COVID-19 patients?

DG: There's a nice *U.S. News & World Report* article where I discuss what might be going on here. I think my quotation is along the lines of, the science hasn't changed. The CDC is struggling to make public health recommendations that will improve our behavior, that will improve our health. It's a tough arena to be in. In the early days, when it was 14 days, we had a 2% compliance with the 14-day recommendation. When they shortened it, still was never great. Currently, the five-day recommendation, we've talked about studies where 75% of people, they'll lie, they won't even test. People don't want the repercussions.

The science has not changed as far as the transmission, but there are a number of things that have changed. Vaccination, pre-existing immunity, or unfortunately, the privileged access to medications. I think it's just a realization that no one's really doing the five days. The five days, if I'm thinking about being around older individuals, my parents, I'm not going to suddenly

say, "Oh, as soon as my fever goes away, I'm not contagious." That's not the science. The science hasn't changed, this public health guidance has.

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

DG: Oh, thank you. Everyone be safe.

[music]

[00:36:07] [END OF AUDIO]