

This Week in Virology

TWiV 1234 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. [music]

VR: *From MicrobeTV*, this is *TWiV. This Week in Virology*, episode 1234. Yes, 1234, recorded on July 10, 2025. I'm Vincent Racaniello, and you're listening to the podcast all about viruses. Joining me today from New York, Daniel Griffin.

Daniel Griffin: Hello, everyone.

VR: Our episode number is like passwords of 90% of the people, 1-2-3-4.

DG: [laughs] Yes, that is the password to my iWatch, Apple Watch.

VR: What's on your tie, black and white?

DG: It's like the video quality is lower for you, but those watching on YouTube will see these little ectoparasites, supposedly bedbugs.

VR: No, I wouldn't have guessed. I just see squares, rectangles. You got the summer - what is it called? Seersucker.

DG: Yes. It is plenty hot. We still haven't gotten the air conditioning fixed.

VR: My God.

DG: I think I told like - I was like, "Oh, don't worry. My wife, kids are out of town," but then they come back and then they call my wife. She's like, "Oh, I'm sure there's like elderly people. Don't you have to rush." Then they get on schedule. Then they call me like, "Oh, we have all these other people, and can we push it off a little?" I say, "Sure," and now, I'm in trouble.

VR: The most famous infectious disease physician in the world can't get his air conditioning fixed.

DG: [chuckles] They're going to fix it eventually. It's OK. I'm building character.

VR: By the time they fix it, it'll be cool again.

DG: [chuckles]

VR: Oh my gosh. You spend most of the day in the hospital. That's why.

DG: Yes, that's why I like to work so hard, right? I'm like, "I'll stay for a few extra consults. You sure there's anyone you're missing?" All right. I'm going to start off with a quotation. It's really funny. This is from the book *The Anthropocene Reviewed: Essays on a Human-Centered Planet* by John Green. Actually, he attributes - this is what his brother said, what Hank Green said. John Green, people may know about him from his recent *Everything is Tuberculosis* book. He calls his brother Hank, who he describes as being a little more level headed, a little more evidence science based.

John has a bit of an anxiety issue that he has shared with the world. He asked about the beginning, the early days of COVID-19. He's hoping his brother will reassure him - he's told his brother he's stocked up for 30 - He's got enough food and water for 30 days. After Hank pointing out that John may not really understand how pandemics work with only 30 days set aside, he says, "John, the species will survive this."

VR: Which species? Cockroaches?

DG: [chuckles] Who knows? It's certainly not going to reassure your anxious brother. All right. Well, let's get into it, because I feel recently like this may be, when people ask me questions, that might be my response, the species will survive. I like your question, which species? I mentioned last week that I would spend some time on the science around myocarditis with COVID and with the vaccines. Part of what prompted this is we heard that FDA to look again at myocarditis risk from mRNA based COVID-19 jabs in young men.

I'm going to leave in a link to this, but in a presentation late on Tuesday, last week, entitled "mRNA COVID Shots Cause Myocarditis," Vinay Prasad, director of the FDA Center for Biologics Evaluation and Research or CBER, said the review is warranted given that rates of COVID-19 severe outcomes are declining due to widespread vaccination and natural immunity, and the evolving nature of the virus. I will sort of comment, kind of interesting, as he also noticed that once we increase the time between the first doses, and move to the yearly booster approach, the incidence of vaccine associated myocarditis has been greatly reduced. Really not seeing anymore.

Actually, this may not work out the way they want if their goal is to malign vaccines, because the point would be it's become really, less and less of an issue now that we've sort of figured this out. I'm on the wards, Vincent, with the medical students, the interns, the residents, and an epidemiologist, cardiovascular epidemiologist, who - I don't know if you know but Stephen Shea.

VR: Yes, I know.

DG: You know Stephen. He's one of those lifers, came for medical school 45 years ago, and never left. Bright guy, epidemiologist, so I really, really enjoyed spending time with him in the group. He's good, because he always reminds me like - I sort of think everyone knows everything. I mentioned like Operation Cat Drop, as if everyone knows about that. It gives me a hard time. One of the things, I brought up miasma, I brought up the Great Barrington Declaration. I was actually surprised. Other than Stephen Shea, nobody there knew about the Great Barrington Declaration.

VR: Wow.

DG: I thought I would just give a little background before I jump into what I'm going to talk

about next. Just a little background, because I don't want to, have people jump in now and be like, "Well, what are you talking about? What is this language?" I'm going to take a little time to talk about CFR, Case Fatality Rate; IFR, Infection Fatality Rate; COVID contrarians; COVID minimizers; and this Great Barrington Declaration. I think people need to understand what's the background, what's going on here.

Great Barrington, Massachusetts, not far from where I went to high school in Sheffield, Massachusetts, is the home of the American Institute for Economic Research, a libertarian think tank, and AIER sponsored a gathering of public health academics at the institute that met in October 2020. I think people need to remember this date, October 2020, and sort of think back to what was going on then. Trump's in the White House. We're six to eight weeks away from getting vaccines. I will mention - Do you know Great Barrington had the first traffic light in the United States?

VR: No. [chuckles]

DG: Apparently, no one else knew that. Yes, there are things that people don't know. My mind is full of this trivial uselessness. Anyway, the result of that conference was the issuance, and it's really just a one pager, this, you can read, I'm going to leave a link to it. It was the Great Barrington Declaration. A proposed plan for the management of the COVID-19 pandemic, advocating for discarding COVID-19 control measures such as lockdowns, school closing, masks, social distancing, the so-called non-pharmacological intervention.

Here it is, October 2020, they're critical about what's going on under President Trump during his first term. Instead, what they're going to advocate is allowing the development of herd immunity through natural infection with SARS-CoV-2. This document is signed by Sunetra Gupta from Oxford, Jay Bhattacharya from Stanford, Martin Kulldorff from Harvard, people may recognize a couple of those names. The declaration is short, and it doesn't have any detailed recommendations. It really is, as I said, just a one pager. They do, they give us certain assumptions. There were certain assumptions.

As history seems to be being rewritten before our eyes, I want to remind everyone of this background, as we're going to go into the actual science behind these different assumptions. A reminder that this declaration had number one, this is what they're these are assumptions we don't know yet. Their assumption is number one, infection by SARS-CoV-2 of non-elderly people without underlying medical conditions has a negligible risk of disease or of death or serious disease. Critical here, to moving forward is their first assumption, it's really important, moving forward that we minimize the seriousness of COVID-19 infections, especially in children.

You'll see going forward, these authors and people just get very bothered by any discussion of PASC, any discussion of Long COVID, or any discussion of the impact on children. Number two, this is the next assumption, October 2020. Infection by SARS-CoV-2 provides strong and long-lasting immunity from reinfection. You only get COVID once, you will never get it again. Now, this is October 2020, we already had a definition, we already were talking about the period of time between initial infection and reinfection, how do we document that it's reinfection.

It reminded me of - I actually listened to this episode of the Rogan show, I'll admit that, wash my hands afterwards. Malone, you know Malone, maybe our listeners know Malone. He's on the Rogan show. He's talking, he's explaining to Joe Rogan, Joe; once you get COVID,

that's it, you can't get reinfected. Joe's on there. He's like, "But I have a lot of friends, and they got COVID, and then they got it again." "No, Joe, you don't know what you're -" He's getting go back and forth. [chuckles] Joe's bewildered by this.

That's another one of the critical assumptions they make back in October 2020. Now, number three is elderly and vulnerable populations can be effectively isolated from the remainder of the population until this herd immunity, the one and done, is achieved through natural infection. This is actually an interesting discussion I had with Stephen Shea. Here we are at Columbia, in New York, we're in this epicenter. When we decide like, "Hey, this might not be great because kids are in the college dorms and this urban center, they're really at high risk of getting infected."

When we send them home, a lot of those kids were probably already infected. Then they go home. Probably talk to Rich and a few of our other a lot of our listeners, they probably never saw their grandkids as often as during the pandemic. They're home from college. How much of that sending college kids back home to hang out with their extended family impacted the dynamic of the spread? One thing I don't think that a lot of people are familiar with is there was actually a response. There was a John Snow Memorandum.

I'm curious how many of our listeners, raise your hands, not if you're driving, keep your hands on the wheel. There was a John Snow Memorandum. Very much in contrast, really got no press that I'm aware of, because the document was actually published in the peer-reviewed journal, *The Lancet*. It's got lots of references. There's like this humility that no one really likes to actually admit that there's certain things we don't know. There are a few things, October 2020, that they're already starting to point out.

One is they do, and this is the memorandum, I'm just going through it for everybody. They start talking about the fact that, OK, yes, SARS-CoV-2 spreads through - they say contact, we later turn to realize that maybe contacts, not such a big thing. They talk about larger droplets. Then they actually talk about issues with longer range transmission, when you're in areas with poor ventilation. They point out that this sort of dynamic can create a condition for rapid community spread. The next, and this is really in contrast to one of the assumptions of the Great Barrington, is they say, it is unclear how long protective immunity lasts.

Like other seasonal coronaviruses, SARS-CoV-2 is capable of reinfected people who have already had the disease, but the frequency of reinfection is unknown. We already knew this, we already had studies, they have nice references showing that by October, we already knew people got reinfected. We already knew this was not lifelong immunity for everybody. The next was they did point out that uncontrolled transmission in younger people risks significant morbidity and mortality, already pointing out that this is not completely benign in people under 65.

They do point out that this makes up much of the workforce and can really have an issue as far as overwhelming the ability of healthcare systems to provide care, and also becoming an issue for a sort of a crippled, sick workforce. Then their last conclusion is there's no evidence for lasting protective immunity of SARS-CoV-2 following natural infection, and the endemic transmission that would be the consequences of waning immunity would represent a risk to vulnerable populations for the indefinite future.

VR: Basically, these guys having no knowledge of infectious diseases or epidemiology made

these conclusions, just pulling them out of the air, because politically for them, it was convenient.

DG: Looking at this, it looks like they were convened to justify this ideology, this idea. We've really got to stop the lockdowns. We've really got to open things up. Can we justify it? The justification was, listen, it's a one and done. Once you get sick, you'd never get sick again. Turns out that wasn't right. If you're under 65, it's not a problem. Again, a very narrow focus, we're only talking about death. We don't care about thousands, hundreds of thousands of hospitalizations. We do not want to talk about children dying. We did not want to talk about Long COVID. Yes.

VR: It's just unfortunate that it got so much press as if people thought, yes, we should have done this, but they're also not thinking. That Kulldorff is now on the ACIP and Bhattacharya is now heading NIH, completely inappropriate actions.

DG: I think a tough thing, right? This is why I give this backdrop is Now, they're asking these questions and trying to say, "OK. For instance, COVID is really not a problem anymore." This is what creates a problem for them. April 15, 2025, Dr. Fiona Havers, an epidemiologist at the CDC presents her findings to the CDC's Advisory Committee on Immunization Practices, ACIP. I'll leave a link into her presentation. I wanted to share a few highlights regarding COVID and children. I'm also going to leave a link into Paul Offit's substack where he talks a bit about how troubling this was.

Fiona Havers presents this data. They've collected the data. Here's the data for the last 12 months leading up till April. She points out that in that last year, over 7,000 children were hospitalized with COVID. About 20% of those ended up in the ICU. They were really sick, not just ending up in the hospital, but really sick enough to end up in the ICU. Here is what really bothers the people listening. Half of these children were previously healthy. Virtually, none had been vaccinated and 152 children died in the 12 months preceding. Most of those were less than 4 years of age.

How do you protect those less than 4 years of age? Less than 6 months, mom gets vaccinated. Less than 4 or 5, starting at 6 months, you can vaccinate the children. I wanted to compare this because we're starting to compare what's happening with influenza. We just had a really bad flu season. I'm going to give you updated numbers again. We are now up to a total of 256 influenza associated pediatric deaths occurred during the 2024-2025 season. Highest number of pediatric deaths reported in any non-pandemic influenza season since the condition became reportable.

There's sort of a parallel here: 152 kids, 256 kids. Again, the majority of the kids who ended up getting infected and died were completely healthy before this happened. This whole idea about only vaccinating the sick kids, you're going to basically not even protect the half of these kids. You're only going to reduce that one half of that. Any thoughts, Vincent?

VR: It's the same thing, Daniel. They ignore the data. This was presented to ACIP and still the recommendations are the same, right?

DG: Yes, it was a few days later that they came out unilaterally and said, "We have now decided to not vaccinate healthy children." They saw this data. They saw that you couldn't figure out who was going to die, that half of them were completely healthy. Their response was, "COVID is not, has never been a problem in children. We don't want to hear this. We're

not vaccinating."

VR: This is the problem when you have contrarians on the ACIP, all contrarians, not scientists who listen to both sides and have a discussion about it and come to an agreement. OK, so this is all one-sided, anti-vaccine, anti-science, and this is what we get.

DG: Yes. [crosstalk]

VR: They have an ideology and they're not scientists. That's the problem.

DG: Yes. They have an ideology. They're contrarians. The big thing is this contrarian issue. Now, you're there, you're the one in charge. You're going to be contrarian with yourself. All right. What are we doing in response? "Medical Groups Sue HHS, Kennedy over COVID Vaccine Policy Changes." Six medical groups have sued the Department of Health and Human Services and HHS Secretary Robert F. Kennedy Jr. in a U.S. District Court, Massachusetts for acting arbitrarily and capriciously in making recent changes to COVID-19 vaccine policy.

The plaintiffs include an unnamed pregnant doctor who has been barred from getting a COVID-19 booster based on the recommendations that Kennedy announced unilaterally in May. I just want to point out, they're taking away our choice when it comes to vaccines. The doctor contends that she is at high risk for exposure to infectious disease due to her job working as a hospital-based physician. The groups that signed on to the lawsuit are the AAP, the ACP, the APHA, the ISDA, the MPHA, and the SMFM.

Robert Hughes IV, partner at Epstein Becker Green and lead counsel for the plaintiffs, said in the statement, "This administration is an existential threat to vaccination in America, and those in charge are only just getting started. If left unchecked, Secretary Kennedy will accomplish his goal of ridding the United States of vaccines, which would unleash a wave of preventable harm on our nation's children." The lawsuit contends that coordinated actions by HHS and Kennedy were designed to mislead, confuse, and gradually desensitize the public to anti-vaccine and anti-science rhetoric.

It also contends that Kennedy has widely flouted federal procedural rules, including blocking CDC communications, cancelling federal vaccine advisory group meetings without explanation, and announcing studies to probe non-existent links between vaccines and autism.

VR: The thing that bothers me is that, during his confirmation hearings, he said he would not touch the childhood vaccine schedule and now he's - He just lied, and this is untenable just to lie. He's not even smart enough to make something up that makes sense. He just lies outright.

DG: Yes, he lied under oath. He was very clearly asked by Cassidy, "Will you will you go after? Will you take away the childhood vaccines?" "Definitely not." He's doing it. He's already done it. We've already seen him blocking access to vaccines.

VR: Daniel, you're a lawyer, right?

DG: Am I going to make believe I'm a lawyer? I'm not a lawyer. [chuckles]

VR: Yes, but you've probably hung out with enough lawyers.

DG: I have hung out with lawyers.

VR: This is a civil suit. What happens? Was it the judge makes a decision? Is that it? There's no jury, right?

DG: I don't know actually. We got to get a lawyer on and tell us like how this works.

VR: I'd like to know. What if he is found guilty or whatever you call it, right? What happens?

DG: Yes. We got to get someone.

VR: They say stop. Trump says, "Don't listen to them. You've got protection."

DG: But it's Massachusetts, so it's a state. The federal government can't pardon you from a state conviction. That's what I understand as a doctor.

VR: I think it's great. Look, I think this is great. I think every state should do this, but I just doubt the outcome or maybe I don't understand the outcome.

DG: Yes. Maybe some lawyers will write. Maybe we got some lawyers that listen.

VR: If you're a lawyer and you understand this and you understand how it's going to go, how a decision is going to be made and the consequences, please let us know.

DG: All right. Now, on to some good science. More good news with regard to vaccination preventing dementia. I'm excited about this, Vincent. "Lower risk of Dementia with AS01-adjuvanted Vaccination against Shingles and Respiratory Syncytial Virus Infections," published as a brief communication in *npj Vaccines*. This is brief. People, I'll leave a link. People can go and take a look at it. We have talked before about multiple studies suggesting that shingles vaccination can reduce the risk of dementia. Here, we have the results from a propensity score-matched cohort study with 436,788 individuals.

They found that both the AS01-adjuvanted shingles and respiratory syncytial virus vaccines, individually or combined, were associated with a reduced 18-month risk of dementia. No difference was observed between the two AS01-adjuvanted vaccines, suggesting as they say that the actual adjuvant itself was playing a direct role in lowering the dementia risk. For background, they referenced their prior publication in *The NEJM*, where they looked at over 100,000 people in this EHR database that the adjuvant system AS01-shingles vaccine also referred to as Shingrix was associated with a lower risk of dementia than the live vaccine Zostavax.

We actually talked about this before. We know that the attenuated vaccine lowered the risk. We know that the modern Shingrix is even better. If the shingles vaccines both reduce dementia, but the new one is better, they're going to suggest two possible mechanisms for the difference. One, they're going to say shingles or VZV reactivation increases the risk of dementia. The adjuvant vaccine better protects against dementia through better efficacy. That's one. Two, the adjuvant might itself provide some protection against dementia as suggested by some mouse models.

To try to get the answer, they analyzed EHR data to test the possibility that the adjuvant contributes to the reduction in the risk of dementia. They're looking at Shingrix, but they're also looking at Arexvy. This is this AS01, so the adjuvant, same adjuvant containing RSV

vaccine. The two vaccines were compared against each other and against the flu vaccine in terms of the risk of dementia diagnosis in the following 18 months.

For comparison, they've got 35,938 who get the RSV adjuvanted vaccine only; 103,798 who received adjuvanted shingles vaccine only; 78,658 who get both, all matched to an equal number of people who get the flu vaccine and don't get the shingles or the RSV vaccine. What do we get? If you get RSV only, adjuvanted RSV only, 0.71, so a 29% reduction. If you get shingles shots by itself, about an 18% reduction. If you get both, a 37% reduction in the additional time spent diagnosis-free. They've got some great figures. I love the figures.

VR: Daniel.

DG: Yes.

VR: How can aluminum adjuvant do this? Does it persist? I thought it's gone after a few months. How is it going to reduce dementia if it's gone?

DG: Yes, I don't know. There's the idea from the mouse model is this may do something with the immune system somehow. Recharging, waving, hand-waving. You've got to get the people on immune to come up with something that.

VR: If you make a memory immune response, that makes sense because you're preventing disease, viral disease, and that could prevent dementia. I don't understand how aluminum - RfK Jr. is going to go after aluminum adjuvant. Even though it works, we're not going to be able to use it.

DG: [chuckles] It is interesting. If you look at the curves, the curves seem to separate. Maybe it's starting. Maybe you need to get another shot after so many months. Maybe we need a yearly adjuvanted vaccine just to keep our immune system boosted.

VR: Maybe you don't need a vaccine. Maybe you just need adjuvant.

DG: Yes. I just put in for people to think about really are flu-vaccinated people the best control? Does flu vaccination reduce the risk of dementia? Is the highest rate of dementia in people that do not get vaccinated at all? I'm going to leave in a link to a review article, "Influenza Vaccination Reduces Dementia Risk: A Systematic Review and Meta-analysis," published in *Ageing*. It actually looks like, influenza vaccine is reducing your risk of dementia by about 30%. This is reducing risk of dementia even on top of that. I'm making more and more pro-vaccine, Vincent.

VR: [chuckles] It was an improvement over influenza vaccine, for sure, but that may have an effect on its own, which is also puzzling because the influenza vaccine is not adjuvanted.

DG: Yes.

VR: At least the one we use here, right?

DG: Yes.

VR: I don't get this. Also, one of the issues with the very first study, the Zostavax and dementia - was it the dementia? Yes. They had a study design, an observational study design that could rule out confounding factors. Did they do the same thing here, or could there be

confounding factors that they don't know about?

DG: Yes. That was the great thing about those studies that, like in the UK and Australia, where basically they're really strict with the NHS in the UK. If you were born after this day, like it's like midnight, if you're born two seconds later, sorry, you're too old to never get vaccinated, we're writing you off. They looked at those people, like the two weeks and then the two weeks before, right? Then they said, "Hey, it was great. What a wonderful study design." They try to do adjustments. They try to like-match them. As we talk about - there's a difference between people who choose to get vaccinated and people who don't.

VR: Yes. People who get two vaccines, they're probably very concerned about their health and they do other things too that may impact their - [crosstalk]

DG: We talk about a healthy vaccinee bias. There's also the unhealthy vaccinee bias, where if you're not seeing the doctor or whatever, you're fine. People who are seeing the doctor, it might be the ones that, "You really should get that vaccine." You end up with either a healthy or an unhealthy. That's why we try to adjust. It's hard to do those studies. Measles, Vincent. We're finally there. The CDC data released Wednesday, yesterday, revealed that there have been now more measles cases this year than in any other year since we declared elimination in the U.S.

VR: Yes, making America healthy again.

DG: Yes. RFK Jr., he's barely been in there and he's already - it's a banner year. This is horrible. 1,288 confirmed measles cases reported by - we're up to 39 jurisdictions. There's only 11, 12 places without measles cases. Things are not great in Canada. They're up to 3,703. An extra 178 new measles cases. Measles is raging on, and there were a bunch of articles about - I'll leave in all these links, AP, *New York Times*, *Wall Street Journal*. Really, everyone had a piece basically about what is going on.

I'm hoping that, as we talked about, there's a large segment of our population that's not aware that we're in the middle of this huge measles outbreak.

VR: Yes, they don't talk about it on Fox.

DG: Yes, you got to talk about -- Guys, do an article on Fox. I'll come on again. We could talk about measles. Get your viewership back up.

VR: Were you on Fox once?

DG: I was on Fox a few times. It's really interesting. They let me talk more on Fox than any other show. I get on CNN, and little quick blurbs. Fox News, they just let me talk and talk.

VR: You said vaccines are good, and they didn't say anything?

DG: They seemed OK with that. [chuckles] I think I said it in a nice way.

VR: Why don't they talk about the measles outbreak?

DG: They really should. It's worth talking about, right? All right. Well, influenza, a couple of things here. One, sort of the sobering number, 256 influenza-associated pediatric deaths. I just want to make this clear. This is a high bar. You really got to say, that's what killed this

child. This child got flu. That was the immediate. That's why they died. It's not like, "Oh, by the way, they had flu, and then they drowned in a pool or got in a car accident." This is what happened. Sometimes, it's really tough.

There's these minimizers out there. They're like, "Oh, but was the child overweight? That's what they died from. They died from obesity." I'm like, "I don't think obesity kills you." Half of these kids didn't have anything else. This is all they had. By the way, if you're a little bit overweight or something else, I understand. People are saying, "I don't agree with that." That's not your fault. You don't deserve to die of flu just because you have issues with carrying extra weight or other things. Remember, these are children, 256.

As we talked about before, over 90%, not vaccinated. These are 90% of these little children could be alive. Go around to those Thanksgiving tables, to Christmas gatherings, holiday gatherings in December, and there's going to be all these families that lost a child. This is preventable. We do not need to have this happening.

Now, some good news. We're bouncing back and forth here. A new flu drug? "Cidara Therapeutics Announces Positive Topline Results from its Phase 2b NAVIGATE Trial Evaluating CD388, a Non-Vaccine Preventative of Seasonal Influenza." I don't think a lot of our listeners are probably familiar with this.

CD388, we need a catchy name, by the way, it's this investigational drug FC conjugate, developed by Cidara Therapeutics for prevention, not treatment, prevention of influenza. CD388 has multiple copies of a small molecule neuraminidase inhibitor, linked to a fragment of a human antibody. The FC fragment. Remember those antibodies you've got, like think of them as a slingshot, this is that part you hold in your hand. You got the Ys up above. This FC fragment, attaching this, this extends the drug's half-life.

Because what you really want to do is you want to do one shot in the fall, and then have it last through. CD388 is actually designed to provide protection against all known strains of influenza A and B. Broad spectrum, one shot, top-line results from this double-blind placebo-controlled phase 2b trial, NAVIGATE, looking at the prevention of seasonal influenza in healthy, unvaccinated adults aged 18 to 64. We'll come back to that.

The study met its primary endpoint, demonstrated a statistically significant prevention efficacy for each of three dose groups in individuals who received a single dose of CD388 at the beginning of the flu season, and were evaluated for laboratory and clinically confirmed influenza over 24 weeks. The study also met all secondary endpoints, safety and tolerability data, similar in all arms with no safety signals observed, no drug-related serious adverse events were observed, and treatment emergent adverse events showed no dose-dependent pattern.

The injection site reactions were similar across all the CD388 dose groups and placebo. What do we get? We end up with the difference. They're going to give us 150 milligrams, prevention efficacy, 57.7%; 300 milligrams, 61.3% prevention; and the 450 milligrams, 76.1% prevention efficacy. As I pointed out, you don't actually end up paying for the higher dose. There's no trend towards any side effects with the higher dose. A few comments. The trial involved 5,071 healthy unvaccinated adults, 18 to 64 years old, 57 U.S. sites, one UK site. They end up getting a single shot in the beginning of the flu season.

The results have not yet been published in a peer-reviewed journal, so we'll look forward to

seeing that. It is a shot, and also, they're doing it in what we would think of as a lower-risk group. The other caveat is now we've got to look at people 65 and over. We've got to start looking at people under 65 with comorbidities, things that might affect their immune response. And, as we've talked about, children. We haven't looked at under 18, so that's another group to be thinking about.

VR: Pregnant women.

DG: Pregnant women, Vincent.

VR: This is lasting, looks like six months, right?

DG: Yes.

VR: You get one shot to last the flu season. This is basically an antiviral. It's a fancy antiviral.

DG: Fancy antiviral with six-month efficacy that covers all the different strains.

VR: Interesting.

DG: Yes.

VR: Daniel, what could go wrong?

DG: You could get resistance, right?

VR: Yes. Maybe that's why they have multiple copies of this inhibitor. Maybe that makes it harder. For Relenza and Tamiflu, you get resistance to Tamiflu, but less so with Relenza, which looks more like sialic acid than does Tamiflu. I don't know how this looks like if it looks closer to a sialic acid, which is the ligand for neuraminidase.

DG: Yes. That would be, yes.

VR: Cidara. Where is Cidara? Is this a U.S. company?

DG: Oh, I don't know, actually. I hope so. Otherwise, they'll make it overseas and then we'll have to -

VR: The trial was in the U.S., so 57 U.S. sites.

DG: Yes.

VR: Interesting. You'd be ready for H5N1.

DG: Yes. All right, moving on to RSV. I think articles like this are really important. Here's RSV, and we're going to read the article. "Readmission Following Respiratory Syncytial Virus Hospitalization among Children <5 Years of Age, published in JPIDS. We've always talked about this. People sort of focus on, you get admitted, what happens, and then they stop looking. Here, hospitalization with lower respiratory tract infection by RSV and other respiratory viruses is common in young children, but what about the issues getting readmitted?

You make it through the hospitalization, you get discharged. We talked a lot about people

getting clapped out with COVID. Do you just end up back a few days later? These results come from a prospective study that included children less than 5, hospitalized with laboratory confirmed RSV, lower respiratory infection at two hospitals in Salt Lake City, Utah, Primary Children's and Riverton Hospital. Actually, my wife, Jessica, used to do translations at Primary Children's in Salt Lake. That's what she was doing when I met her, for Spanish. She's fluent in Spanish.

For comparison, they retrospectively identified children less than 5, hospitalized during the same period with influenza or human metapneumovirus, lower respiratory tract infections. They're going to track readmissions for 1.5 years post-discharge. What do we find? For children hospitalized with RSV, influenza, human metapneumovirus, lower respiratory tract infections, all-cause hospitalization readmissions were actually common, with 30-day readmission proportions ranging between 5% and 9% and increasing to between 19% and 30% 1.5 years post-discharge.

Respiratory-related readmission varied by virus, with RSV having higher proportions, increasing to 16.8% 1.5 years post-discharge, compared to only 6 to 7 for flu and human metapneumovirus. The hazard ratio of ending up back in the hospital with RSV, compared to flu, 3.6, compared to human metapneumovirus, 3.6. You're more than three times as likely of ending up back in the hospital if you ended up there initially with RSV. Vincent, it's your favorite part, the COVID update, looking at the multicolored curves.

VR: Looking good, Daniel.

DG: It really is, actually. It's good to be wrong. I did get a little bit of message, some of our urgent cares, "Hey, Dr. Griffin, we're seeing an uptick in the number of COVID." All right, we'll see. I like wastewater. Everyone's using their facilities. This is data that you see or you don't. Still, it's pretty flat, and it's been flatter for a longer time than ever.

VR: Yes, we're at the end of June. Last summer, at the end of June - I don't know, that's the beginning of July last summer. It just started to go up. If it's going to go up, it's going to go up in the next week or two.

DG: Maybe it won't, right? I zoomed in, so people watching on YouTube can maybe see, what's been going on in the last 45 days. You might see a little inflection in the South, but that could just wobble. Fingers crossed, Vincent. Nimbus is still increasing when you look at the variants, so keep an eye on that. What was the other? What was it you told me? XFG? What was that called last time? Stratus?

VR: Stratus.

DG: All right. A little bit of Stratus, but Nimbus is going strong.

VR: That's another thing these Great Barrington authors didn't consider, variants. There were no variants yet because they didn't emerge until December 2020, right? Alpha. They had no idea that this was going to happen and confound this idea of herd immunity. It's just that you cannot take a virus that nobody knows anything about and make these proclamations. This is what burned me about the Great Barrington Declaration to begin with. They don't know what they're talking about. Nobody knew at the time.

DG: I think that's the issue is a lack of humility. Basically, this is new. We don't know. We

don't know what the long-term consequences. As we learn, you've got to be willing to let the science drive what you do, not start with ideology and then just close your eye to when something is presented that doesn't go with your ideology. All right. COVID early viral phase. Not a lot of big changes here. Early antivirals during that first week in folks that are at risk of progression. Paxlovid, remdesivir, molnupiravir, some cases convalescent plasma.

That second week, early inflammatory. We're looking at the oxygen saturations, trying to figure out if they're developing secondary infections, steroids at the right time in the right patient, anticoagulation, pulmonary support. Looking at, are we still in the window where remdesivir or immune modulation makes a difference? I will close with an area that really bothers the contrarians. This is this unfortunate situation where a lot of folks get COVID and then they live those two weeks and now they have long-term issues. We have a couple articles this time.

One is the article, "Association of SARS-CoV-2 With Health-related Quality of Life 1 Year After Illness Using Latent Transition Analysis," published in *OFID*. What a title. These results come from a prospective multicenter longitudinal registry study where patients were enrolled from December 2020 through August 2022, completed three-month follow-up assessments until 12 months after enrollment. Participants were adults 18 or older with acute symptoms suggestive of COVID-19 who got an FDA-approved SARS-CoV test.

Participants received questions from PROMIS-29, a whole bunch of scores there, physical function, anxiety, depression, fatigue, social participation, sleep disturbance, pain and interference, and PROMIS-SF-8a, cognitive function. Latent transition analysis was used to identify meaningful patterns in HRQoL scores over time. Four HRQoL categories were compared descriptively using multivariable regression. There were 1,096 COVID-positive, 371 COVID-negative. Four distinct well-being classes emerged, the optimal overall poor mental, poor physical, and poor overall.

COVID-positive participants were more likely to return to the optimal HRQoL class compared to COVID-negative participants. The most substantial transition from poor physical to optimal occurred by three months, whereas movement from poor mental to optimal occurred by nine months. Just giving us this transition where, and I think we see this in practice, is you see a certain transition right at about three months. That's right about when we're saying, is this medium going into Long COVID? Are you going to recover? Then there's another sort of inflection point about nine months in when we see these changes.

In adults with COVID-19-like illness, the COVID-positive participants demonstrated meaningful recovery in their physical score by three months after infection, but the mental actually took longer to improve. Unfortunately, we were seeing about 20% of folks that were still having trouble at the different time points. We've been trying to prevent that. One of the ways is, could we just jump in early with different therapies? Just as a recap. Not showing that we did much to prevent Long COVID with the monoclonal antibodies, mixed results with Paxlovid as we've talked about.

What about remdesivir? The article, "Remdesivir and Risk of Multi-systemic Long-term Sequelae Following COVID-19 Hospitalization," published at *CMI*. It's really a good study looking at our ability to prevent PASC with early treatment with remdesivir, 30,175 COVID-19 hospitalizations included in the cohort. Looking at long risk of long-term sequelae, 37.6% received remdesivir, 88.9% fully vaccinated, 60% had gotten a booster dose, 77% infected during Omicron. Risk of long-term, new onset diagnoses across cardiovascular, neurologic,

respiratory, autoimmune system up to 300 days, not significantly different in the folks that got remdesivir versus the untreated.

VR: Remind me, Paxlovid have any effect on PASC?

DG: Depending on how you look at it. It's not clear that it prevents the Long COVID ME/CFS type syndrome, but it does tend to be associated with reduction in major cardiovascular and some of the other post-acute sequelae.

VR: Then vaccination does have an effect on -?

DG: Vaccination is huge. Vaccination, 80%, 90% reduction in people ending up with post-acute sequelae of COVID. I think that's one of those issues to think about with the Great Barrington. We talked about last week that adolescents that get COVID are somewhere between two- to seven-fold increase in their likelihood of getting a new diagnosis of type 1 diabetes if they get infected, if they got infected pre-vaccination, without vaccination. That's huge. Let it rip in people under 65. I think if a child ends up with diabetes type 1 for the rest of their life, that's not an insignificant issue.

All right. As we've been saying for quite a while, no one is safe until everyone is safe. We can't do this without your support. Pause the recording right here. Go to parasiteswithoutborders.com. Click on that Donate button. Every small amount helps. May, June, and July is our last month. We're doing our FIMRC fundraiser. Again, doubling your donations, hoping to send our maximum donation of \$20,000 to FIMRC. I got an update from Brian Park, who just got back from being on the ground there in Uganda. Yes, thanks to your support.

The clinic, it's up and running. It's doing great. Seeing more patients than ever, really making a difference. Everyone who's contributing, who's part of that, I want you to feel good. You're making a difference.

VR: It's time for your questions for Daniel. You can send yours to daniel@microbe.tv. Gail writes, "If someone over 65 gets Pemgarda every three months, is it still recommended that they get the COVID vaccine every six months? I read several months ago that it was still worthwhile to get the vaccine, even if someone may not mount much of an antibody response. Is that still true, assuming it was accurate then?"

DG: Yes, we still recommend that. I think this goes to our theme. The vaccine isn't just about antibodies. Have we been talking about T-cells now for five-plus years, Vincent? [chuckles]

VR: Yes.

DG: We still think there's an advantage. Yes, particularly these high-risk folks that you're going through all the hoops to get Pemgarda, we do recommend every six months getting those vaccines.

VR: EJ writes, "I love your show. I've been following since the first year of the pandemic. Thanks for your selfless service in this endeavor to keep us informed and know that I pass your knowledge on to so many patients. As a family physician in the Chicago suburbs, I love to continue my education by listening to your podcast. Just a little correction that you probably already know regarding U.S. citizens traveling to Honduras."

DG: Yes, I was looking at this. The 28th, we've got that initial and then they - I don't know if they so much clarified it or updated it. I'm going to open it up. I think I've got my tab here. We have on the June 28th, that was the one we said where they say, including the United States for any travel, you've got to show your proof. Then July 4th, that's a good date, July 4th. I think we were celebrating No Kings Day. This is an update to the step message, and they basically say the new requirement is that Honduran citizen minors age 12 months to 10 must provide evidence.

VR: Basically, you can go to Honduras without having any proof of measles and rubella. If you're younger and you want to come back, you need to have it.

DG: Yes, that's interesting. If their citizens come to the U.S., they say, "Oh, that's a risky place. You can't come back if you're in this age group unless you show us that you're vaccinated. You're not bringing it back into our country."

VR: John writes, "Thimerosal is the same as Merthiolate. I'm sure you knew that, but I didn't. I wonder if Junior Kennedy does. If thimerosal caused autism, all baby boomers should have become autistic, at least all the ones who played outside as kids. Of course, I'm exaggerating my case, but it would be interesting to know what the blood thimerosal levels were in kids with an average scraped knee an hour after being painted up with Merthiolate. I guess that they vastly exceeded the levels in vaccine vials before the dose is diluted into someone.

Relatedly, since you mentioned MRSA/MSSA at the start of 1232, I wonder how much the rise in MRSA can be attributed to the demise of Merthiolate replacement by other topical antimicrobials in the '90s. I'm a fan of Neosporin, but I wonder if people reach for topical antimicrobials less than they used to. By the way, since there's a sulfur atom in it, it's pronounced 'thimerosal,' not 'thimerosel.'

I could go on about MRSA/MSSA, the length of time it currently takes to discriminate the two, and the annual cost to the average hospital system to reverse kidney damage in the fair percentage of patients who were initially treated with vancomycin, out of an abundance of caution for what turned out to be MSSA and how this could all become moot with a test that delivered results in hours versus days, but for now, just remember that I slipped this in."

DG: Yes, John, that's - yes, I remember skinning my knee as a child and my mother putting like hydrogen peroxide. You didn't want to even tell her because that hurt worse than whatever happened. [chuckles]

VR: Hydrogen peroxide hurt, and then it would bubble.

DG: Yes, pour it on there - Actually, fortunately, a lot of our hospitals are now using this molecular or they're using MALDI-TOF within hours. Actually, a perfect case last night. I had a patient I was consulted on. The hospital is giving me a hard time because I'm like, "Oh, they meet criteria for sepsis." "They didn't say they had sepsis." I'm like, "Jeremy, they don't say they have sepsis." They had fever. They had tachycardia. They met criteria. I'm starting antibiotics. The blood culture comes back positive, gram-positive, cocci.

I say, "All right, not a problem, Jeremy. I'm going to set my alarm for three hours." Three hours later, it comes back the molecular, it's MSSA, *Staph aureus* bacteremia, and we're

able to optimize therapy. Yes, we're really moving forward. Otherwise, it could have taken days to see what grew, what it was, and so great stuff.

VR: Richard writes, "Kennedy will not be able to close HHS divisions or order additional layoffs as the lawsuit moves forward," and he sends a link to an Axios article, 'Judge Halts RFK Jr.'s Health Agency Restructuring.' This is a judge in Rhode Island, ordered him to halt reorganization. The executive branch does not have the authority to order, organize, or implement wholesale changes to the structure and function of the agencies created by Congress, Judge Melissa DuBose wrote in her decision."

He was going to restructure things and fire people and so can no longer do that. I don't know what they're going to do in the meantime. All this law stuff, Daniel, I don't understand.

DG: I know. [chuckles] We need a special podcast just for that.

VR: Philip writes, "I'm well vaccinated. I'm 67 with well-controlled type 2 diabetes and obese. I had my last COVID booster and flu in September 2024 prior to a trip to the UK, Ireland. I've also had RSV vaccine. I'm planning a trip to Chile in September 2025." Good for you. You get around. I like that. "August would be early for my flu vaccine for the USA, and I would assume the flu season would be waning in Chile. Thoughts?"

DG: Yes, that's probably the case. You're like, because we're sort of off cycle, but you can get a sense of what's the activity there. Hopefully, your provider can help you with that.

VR: You can.

DG: Yes, because it's the timing of when to get the flu shot.

VR: You can get it in August usually, right, Daniel?

DG: You can, but as we've talked about - and actually, I remember you talking about this like years ago before you and I were doing podcasts about the waning that we see, like you get your shot and then you lose 10% or 15% per month. Timing matters.

VR: It would protect them for Chile.

DG: It would protect them for Chile, but then what's he going to do when he gets back here and we have another bad flu season because no one's getting vaccinated anymore in the USA?

VR: It's good. It's an interesting problem. It's something that travelers encounter. That's why we have travel physicians, right, Daniel?

DG: We do. We have specialists in travel medicine, and it's worth the money to get some guidance on what to do to stay safe.

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

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

[music]

[00:55:19] [END OF AUDIO]