

"The idea that the pandemic is over... The virus hasn't gotten that memo."

An interview with Arijit Chakravarty on ending of the COVID-19 Public Health Emergency: Part 1

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This is the first part of a two-part interview. Part two can be read here.

Fractal Therapeutics is a science services company based in Cambridge, Massachusetts, that "offers model-based drug discovery and developmental services that help make drug R&D more efficient." When the COVID-19 pandemic emerged as a global threat in early 2020, the company decided to employ its modeling expertise in "building a clearer understanding of the public-health risks" associated with the policies being implemented by the Centers for Disease Control and Prevention (CDC) and the White House, as well as international health agencies like the World Health Organization (WHO).

The World Socialist Web Site spoke with CEO Arijit Chakravarty last year on the pandemic and their numerous reports whose results and accuracy in prediction have had far-reaching implications. One year later, we reached out to him to discuss the pandemic as the World Health Organization and every major government has opted to bring the public health emergency to an abrupt and premature end. The interview was conducted after President Joe Biden declared the public health emergency over on May 11, 2023.

Benjamin Mateus (BM): It's been exactly a year ago when we spoke. At the time when we discussed the COVID pandemic, you said that the emergence of the Omicron variant in November 2021 ushered in a dangerous phase in the pandemic.

Specifically, the variant was used to cause mass infection and rapidly push every country to return to pre-pandemic norms and accept a vaccine-only strategy to mitigate the impact of infections. You noted this would promote new variants of SARS-CoV-2 that could escape established immunity from both prior immunization and infections.

At the time you wrote, "In this modeling study we demonstrated that the return to pre-pandemic conditions following modestly high levels of vaccination will efficiently select for pre-existing vaccine-evading viral variants within the population, causing a high level of infection and potentially death."

Fast forwarding to May 2023, how do you think your predictions stood the test of time?

Arijit Chakravarty (AC): The only thing I would say that's a little different is that the timestamp on that statement about the return to pre-pandemic conditions is early May 2021. The preprint went out even before the Centers for Disease Control and Prevention (CDC) said, "If you're vaccinated, you can unmask."

I remember at that moment we experienced extreme frustration because

we had out in the public domain an explanation of what was gonna happen next, and it happened. And then, months later, Rochelle Walensky [CDC director at the time] said the virus threw a curve ball at us with the Delta variant. I suppose anything is a curve ball if you are poorly prepared.

Looking back, the only thing that we didn't fully anticipate in early 2021 was how much the observed infection fatality rate would drop. It has dropped quite a bit. And it's dropped because immunity is piling up due to hybrid immunity. That was a bit of a different nuance that we hadn't captured in the papers we produced on the fall of 2020 through the fall of 2021. But then starting from last year, in 2022, we started including that perspective.

We've had a slew of papers since then, both in preprints and published articles, and what we show is that this idea of using infection-derived immunity to blunt the mortality and morbidity burden of COVID is a dangerous construct.

BM: Are you referring to the "Gray Swan" paper your team wrote? [AC is principal investigator of the study: "The gray swan: model-based assessment of the risk of sudden failure of hybrid immunity to SARS-CoV-2."]

[The term gray swan was derived in the field of electrical engineering and applied to many others, including economics and epidemiology, by analogy. As opposed to a "black swan" event, one which is rare, transformational and unpredictable, a "gray swan" is rare and transformational, but predictable and even well understood. Both COVID and climate change fall in that category.]

AC: "Gray Swan" is one of them. There are quite a few ... maybe four or five preprints and peer-reviewed papers of ours that delve into this topic.

The WHO and Biden administration declare COVID "over"

BM: I'd like to discuss this preprint in the context of the World Health Organization (WHO) declaration on ending the Public Health Emergency of International Concern (PHEIC) and the CDC and Biden administration's efforts to end public health efforts directed at the pandemic.

It succinctly captures, giving what has transpired as to ending all the policies directed at the pandemic, what we can anticipate moving forward

with regards to this coronavirus. For clarification, working with Boston University and Stanford researchers, you have attempted to contextualize the various possibilities that include the sudden failure of hybrid immunity to SARS-CoV-2 when all mitigation measures are lifted, and the virus has been allowed to become a permanent social fixture in day-to-day life across the globe.

Maybe you can begin by explaining what hybrid immunity is and what you mean by “gray swan.”

AC: Well, hybrid immunity essentially is a new term that has been coined (as have so many others during the pandemic) to explain, and—excuse the analogy—to “polish the turd” of repeated reinfection.

What we witnessed initially was all this talk about “flattening the curve.” Flattening the curve didn’t make much sense for this virus because it meant everybody would get infected, just not all at the same time, which was already a bad idea. There is a better way to “flatten the curve” and that is simply to suppress the disease.

But then “flatten the curve” gave way to hybrid immunity when it became clear that “herd immunity” through infection was no longer tenable due to the ability of the virus to cause repeat infections.

We predicted back in the fall of 2020 that the virus would rapidly evolve to evade immunity derived from the COVID vaccines and even monoclonal antibodies. However, at the time, we didn’t fully grasp that meant we would also be facing a huge problem with natural immunity. But now, as it turns out, this applies to natural immunity from infections as well. If you remember, everyone said that reinfection was not possible. Next, they said that reinfections were rare. Then they quickly pivoted to reinfections not being so rare, but not a bad thing as it would lead to hybrid immunity, which is immunity acquired through infection and vaccines.

[Hybrid “vigor” immunity is a concept derived from botany when different plant lines are bred together, and the hybrid is a much stronger plant. In the case of COVID, the theory stems from seeing a larger magnitude of antibody response in vaccination of previously infected people than uninfected. The implication is that reinfections will be milder and, therefore, acceptable as a public health policy, which is a policy unprecedented in the history of public health.]

So, it went from this thing that was impossible to being very rare to being “mild” and beneficial. And none of those things are true.

It’s [hybrid immunity in the US is at 48 percent of population] common now, but it’s not beneficial because there are other consequences of reinfection. There are thousands of papers on what happens when you get covid including long-term consequences of infection and reinfection. So, hybrid immunity is just a clever rebranding of the failure to control the virus. And it’s being promoted by the same people who were promoting the vaccine-only strategy, while we were saying out loud that the vaccine-only strategy was destined to fail.

There’s a paper called “Beyond the New Normal” that we posted in January 2021 and published in *PlosOne* in July 2021. In that paper we showed that if you rely on a vaccine-only strategy, you’ll end up with endless waves of disease.

[From the Abstract: As the COVID-19 pandemic drags into its second year, there is hope on the horizon, in the form of SARS-CoV-2 vaccines which promise disease suppression and a return to pre-pandemic normalcy. In this study we critically examine the basis for that hope, using an epidemiological modeling framework to establish the link between vaccine characteristics and effectiveness in bringing an end to this unprecedented public health crisis. Our findings suggest that a return to pre-pandemic social and economic conditions without fully suppressing SARS-CoV-2 will lead to extensive viral spread, resulting in a high disease burden even in the presence of vaccines that reduce risk of infection and mortality.]

“Hybrid immunity”: rebranding a public health disaster

Now, we aren’t management consultants, and we didn’t come up with the term hybrid immunity. But you can appreciate how they took a public health disaster, where they no longer had control over the spread of the disease and rebranded it as something desirable. That’s exactly what happened with the term hybrid immunity. As such, it only exists in the context of covid, as a public health concept which is being used to endorse repeated infections as *the strategy*. [Emphasis added by AC]

To put this in context, we have another set of papers and preprints that show that either by personalized dosing, using biomarker data, or by [vaccine] dosing more often, four times a year, you may be able to actually vastly reduce the rate at which people get reinfected. So repeated reinfections—and this is a really crucial point—are not inevitable. They’re a choice and we’ve chosen it because it is the easiest, laziest thing to do.

BM: These have economic imperatives. Correct? Meaning, if you’re telling everyone that you must be vaccinated four times a year, you are already telling everyone that the disease is out of control, when what you really want is everyone to accept that the pandemic is relegated to the past tense.

AC: Look, economic “imperative” is a strong word, because I think the strategy we’re using is incredibly damaging for the economy. We’re knocking people out of the workforce in large numbers. We are subjecting ourselves to continuous supply chain shocks. So, nothing will get fixed with the economy. You can’t “interest rate hike” your way out of this because it’s being driven by the virus. So, from an economic standpoint, the strategy is a disaster.

I think it has political imperatives in the sense of the political imperatives of people working at these public health agencies whose priority it is to go home at five o’clock. Their life would be a lot more difficult if they had to say, “Look, you need to vaccinate a lot more often.” So, I think if you were phoning it in at your public health job, then yes, you would take that approach of saying, “Hybrid immunity!” But nobody who is serious about public health at this point should be advocating for repeated reinfections.

BM: With regards to the “Gray Swan” paper, I thought it was a very critical paper, but maybe you can speak to the findings of the study. What are the essential points you’d like people to consider?

AC: That paper sits in the context of several other papers and preprints that built up to it. And one of them is the “Shielding Under Endemic Sars-CoV-2 Conditions,” where we showed that shielding as a strategy for individuals is very difficult to accomplish.

[From the Abstract: As the COVID-19 pandemic continues unabated, many governments and public-health bodies worldwide have ceased to implement concerted measures for limiting viral spread, placing the onus instead on the individual ... Our results suggest that individuals seeking to opt out of adverse outcomes upon SARS-CoV-2 infection will find it challenging to do so, as large reductions in contact rate are required to reduce the risk of infection. Our findings suggest the importance of a multilayered strategy for those seeking to reduce the risk of infection. This work also suggests the importance of public health interventions such as universal masking in essential venues and air quality standards to ensure individual freedom of choice regarding COVID-19.]

We showed that to reduce the risk of being infected you must cut your contact rate by about tenfold. Now that is doable, but most people won’t be able to do it without a significant effort.

[From AC’s social media account: We have all “volunteered” for a mass infection experiment that is difficult if not impossible to opt out of. And for most people, this will come with very real costs—at an individual level, people who are vaccinated and not taking measures to reduce their contact rate can expect to spend an average of six days per year acutely

sick with COVID-19 and incur a 12 percent risk of Long COVID. In the US, the average number of paid sick days is eight. Twenty-seven percent lack health insurance. Sixty percent lack short-term or long-term disability insurance and average saving is \$3,240 to \$6,400. Many working individuals may find living with COVID to be beyond their means within a short period of time.]

In a different set of papers, we've advocated for looking carefully at vaccine scheduling because that's another way to have people avoid getting reinfected repeatedly. When we were examining the hybrid immunity scenario in the "Gray Swan" paper, we were starting from the premise that this is a choice that is being made by governmental public health agencies.

It was not an inevitable choice, and repeated disease wasn't an inevitable consequence. Somebody somewhere sat down and said, "This is a good idea." And we were asking, "What could go wrong with this strategy?" We were simply exploring it from the standpoint that if a particular course of action is taken, then what are the risks implicit in moving the world's population in that direction, because those risks are not being discussed with the public.

The key finding in the "Gray Swan" paper is quite intuitive if you think about it for a minute. When you look at new variants, they crop up based on immune evasion. The ability of a new variant to take root is determined by how much it can evade the existing neutralizing antibody response. Much has been said about how T-cells will save us and how T-cells are important for COVID immunity. We have a separate preprint that dissects that idea, and it really isn't true. Protection against COVID infections mainly comes down to the neutralizing antibody response.

If anything, COVID eats T-cells for breakfast. What we really need is to protect our T-cells from COVID. They're not part of the protective response. We and others have demonstrated that when you see a variant coming along with enough ability to evade the antibody response, that's when you get a new wave.

The danger of a higher infection fatality rate

What we found was that the variants that are the most immune-evasive will do the best in terms of proliferation. But also, there's a certain point at which if a variant is sufficiently immune-evasive, it will knock the infection fatality rate back to the baseline, meaning it will return to where it had been when there wasn't hybrid immunity among the population. In other words, sufficiently immune-evasive variants on the scale of around a 40-fold reduction in neutralizing antibody potency (which is not that far away from what we've seen already) would start making a real dent in hybrid immunity; a loss of hybrid immunity; a loss of protection against severe disease.

BM: Moving forward, the number of COVID vaccines being administered globally has already flat-lined. Their costs will skyrocket and I'm almost certain the CDC will only *recommend* annual vaccination, which means compliance will be poor. Protection offered by vaccines will be nonexistent in the coming months and with the pace of new subvariants evolving, I expect a massive wave of infections perhaps this fall. I can't help thinking we will see a considerable rise in the fatality rate from COVID again, given this layer of protection that was the prevailing official strategy will no longer be available.

AC: Yes. I would put it like this—if you tell me, "I've decided to take up drunk driving as a hobby," I can't tell you, "Don't take it up as a hobby because you'll die tomorrow if you drive drunk." Research shows that drunk drivers need to go out there on average 200 times before they wrap themselves around a tree. If you take up drunk driving as a hobby, I can't

convince you that it's a bad idea by making the case that you will die tomorrow if you do it. But you and I both know that your life expectancy will be radically different with drunk driving as a hobby.

Where I'm going with this is that I can't predict the outcome of the next wave. I can't predict the outcome of the next five waves. But, at the rate that we are going, a prediction can be made with a high degree of certainty that something bad will happen sooner than later along these lines.

If we think about it in statistical terms, the virus is drawing randomly from an underlying distribution of infection fatality rates. It's reaching into a bag and pulling out an infection fatality rate. Each time. We've shown in a separate paper [November 2022] that endemicity is not a victory and the infection fatality rate is not under selection [pressure].

[From the Abstract: The strategy of relying solely on current SARS-CoV-2 vaccines to halt SARS-CoV-2 transmission has proven infeasible. In response, many public-health authorities have advocated for using vaccines to limit mortality while permitting unchecked SARS-CoV-2 spread ("learning to live with the disease"). The feasibility of this strategy critically depends on the infection fatality rate (IFR) of SARS-CoV-2. An expectation exists that the IFR will decrease due to selection against virulence ... Our findings suggest large increases in virulence for SARS-CoV-2 would result in minimal loss of transmissibility, implying that the IFR may vary freely under neutral evolutionary drift ... Our modeling suggests that endemic SARS-CoV-2 implies vast transmission resulting in yearly US COVID-19 death tolls numbering in the hundreds of thousands under many plausible scenarios, with even modest increases in the IFR leading to unsustainable mortality burdens.]

The virus could kill everybody it infects and still not face any negative consequences in terms of how well it spreads. We know that the fatality rate is under genetic drift or randomness. If you think about it, if you keep drawing randomly from a bag and think about the maximum number you can hit, the longer you draw from a bag, the more closely you are going to reach that maximum number of whatever's in the bag.

So, what I'm saying is not only will you lose the protection from hybrid immunity knocking you back to the baseline infection fatality rate that you would've had if you didn't have immunity, but there's a second factor to keep in mind as well, which is that the infection fatality rate you get may be different.

I'm not saying that along comes a wave that's highly contagious because it's immune evasive and you've lost hybrid immunity. I'm not saying therefore, by definition, you go back to the fatality rate of the original Wuhan strain. I'm saying we don't know what that upper limit to the fatality rate is.

Must COVID variants become milder?

In a separate preprint, we've laid out the different evolutionary pathways by which the virus can start accessing much higher infection fatality rates. And we've shown—and that's not a mathematical modeling paper but a biology review—that many of the mechanisms that the virus has in place to suppress the immune system can be used to access a higher infection fatality rate and have been used by other viruses to do that. There's no reason to assume that what we've seen so far is all we're going to see.

[Excerpt from the Abstract: The question we have tried to address here is whether there should be concern about a potential for increased virulence in future variants. Based on what is currently known, there does not appear to be overwhelming evidence supporting the hypothesis that the virus will evolve to be less virulent over time. Indeed, the breadth of the literature at this time suggests that there are many mechanisms for

increased viral virulence that have a neutral to beneficial effect on transmissibility.]

BM: Could you speak in more detail to this issue. It is very relevant but never really discussed anymore.

AC: Well, we asked, “What are the various ways in which the virus could access a high infection fatality rate on a purely evolutionary basis, and we looked through the literature to get our answers. We were able to map out a variety of different mechanisms that this virus [in older variants] has previously demonstrated.

For example, suppression of the interferon response, suppression of the innate immune response, higher viral loads, change in tropism. All of these are perfectly capable of causing higher infection fatality rates. When the Delta variant came along, it had a different tropism. In India it burned through the country because it was escalating to lung failure much more quickly than previous variants.

The experience with a “mild” Omicron was not foreordained and it is not some consequence of Omicron being, as it were, less lethal because it is more contagious. Primarily, Omicron’s infection fatality rate went down because it was capable of infecting people who already had immunity. It wasn’t intrinsically milder. And so, the one place where we dodged a bullet, which was in terms of the lower airway tropism, this was not foreordained, and we can’t be guaranteed that the next time something comes along that is highly contagious and highly immune evasive will give us a pass on that one [lower airway tropism].

And that’s just one small example, but I’m saying enough has happened already with the virus that we know the virus has plenty of tricks up its sleeve. To continue playing chicken with the virus and to say, “Hey, what else can you deliver us,” or, “What new surprises do you have in store for us,” is guaranteed to give us new experiences that we’ve not had before in terms of public health. Keep this pandemic running for another five years and you’ll face a debacle on a scale that you haven’t yet seen. That’s a given. It can only get worse if you don’t want to do anything about it.

BM: I will have you state it bluntly. Do you think the pandemic is over, and what are your thoughts about the WHO, CDC and the US ending the public health emergency?

AC: A pandemic is not a feeling. I prefer this, because the term “pandemic,” before COVID-19 had a very specific meaning, that was entirely about what the pathogen was doing and not at all about what people were doing. The idea that the pandemic is over because we feel it’s over is Orwellian Newspeak in action.

That’s the most important thing to understand. We can all have the *feeling* that it’s over. We can all have the *feeling* that we’re not gonna take precautions anymore. And I know very few people who are. And that doesn’t change anything from the virus’s perspective.

The virus hasn’t gotten that memo. And it’s very much game on. In terms of continued spread, if you look at the wastewater data, transmission levels mostly are where they were with Delta a year and a half ago. We’ve just gotten used to that. The death toll is lower, but it’s still shockingly high. You’re still looking at hundreds of thousands of deaths a year. And this pretty much counts as what I would say is a lull in the action.

To reiterate, we still have shockingly high rates of transmission, shockingly high death totals, and we have NO plan. And if something worse happens, we will react to it. And this is the key point in the “Gray Swan” paper, which underscores a *reactive public health strategy*, which is the kind of strategy where first you see something go wrong and then you do something about it. If I was generous about defining our global public health “strategy,” that’s our strategy. And in that kind of reactive strategy what will happen is billions will be infected before we realize something is wrong. And that’s too late to do anything about it. So not only is the pandemic very much not over, but by creating the impression that the pandemic is over in the face of rampant viral spread and

continuing rapid viral evolution, we are essentially sticking our chin out and asking the virus to do its worst.

I think an important point here is that endemicity has a real meaning. And the meaning is not “repeated waves of emergence of new viral variants.” There’s no definition of endemicity that includes rapid viral evolution.

To be continued



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