The failed COVID-19 pandemic policies: An interview with Arijit Chakravarty of Fractal Therapeutics

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On May 6, 2022, the Washington Post *published a chilling report that the Biden administration was warning the United States could see 100 million coronavirus infections with a "potentially significant wave of deaths this fall and winter." The unmentioned by name senior administration official explained the predictions were based on "a range of outside models of the pandemic."*

Other public health experts agreed that with Omicron's dominance and waning immunity from vaccines and infections, in conjunction with complete loosening of all pandemic mitigation measures, such a prediction is in line with expectations. Justin Lessler, epidemiologist at University of North Carolina Gillings School of Global Public Health, told the Post, *"What they're saying seems reasonable—it's on the pessimistic side of what we projected in the COVID-19 scenario modeling run."*

In early April, Fortune *magazine interviewed Fractal Therapeutics CEO Arijit Chakravarty about a recent modeling study that was uploaded to the* Lancet-*affiliated preprint journal medrxiv: "Endemicity is not a victory—the unmitigated downside risks of widespread SARS-CoV-2 transmission." In the paper, their modeling analysis was in congruence with the White House's prediction for the fall/winter infection rates. They also warned that hundreds of thousands of deaths could result from these infections annually. Chakravarty told* Fortune, *"It's not a specific prediction about the future. We're not saying the world will end on Tuesday, April 7, 2024. But the goal is to make people say, 'Gee, some scenarios out there are really quite ugly.'"*

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 CDC and White House, and international health agencies in general.

The World Socialist Web Site *contacted CEO Arijit Chakravarty for an interview to discuss the pandemic and their numerous reports whose results and accuracy in prediction have far reaching implications.*

Benjamin Mateus [BM]: Good afternoon. Thank you for taking the call to discuss your work on COVID-19. Where are you now?

Arijit Chakravarty [AC]: Happy to speak. We are based out of Cambridge, Massachusetts, but I split my time between Cambridge, between Boston and D.C. I'm in D.C. right now.

BM: My first question for you begins with a caveat. I looked through some of the studies your team at Fractal Therapeutics have conducted. I was very surprised. They are quite innovative and thoughtful. How did a company working on modeling-based drug development move to working on modeling the COVID pandemic?

AC: So, we still are a model-based drug development company and what we do is sell mathematical modeling services to pharma and biotech companies who are looking to move their molecules forward.

But when the pandemic started, though, personally, I've been a biologist in the industry for many years—I have a mathematical modeling background—independent of that, the pandemic impacted everybody directly.

I had a serious conflict of interest! Nobody really wants to get COVID over and over again!

So, when we were watching from the sidelines initially and deep diving into this stuff and going, "Gee, this is interesting," because already very early on there were gaps in the literature and gaps in what people were saying. Some of it didn't make sense.

BM: For instance?

AC: For instance … People kept talking about the "six-foot rule." We are scientists. So, we dug into the question, "What's the science behind the six-foot rule?" And we were realized there was no science behind the "six-foot rule." [The CDC recommends that unvaccinated or high-risk individuals in indoor public spaces maintain a six-foot distance to mitigate against COVID-19 infection. However, the airborne nature of the disease makes the recommendation a moot point as there is no safe distance.]

And then later they said you don't need masks. We asked again, "What's the science behind that recommendation?" And, again, there is no science. And little by little, my team's and my anxiety needle kept ticking upward.

When it became clear that where we were headed … that we were going to give everyone the vaccine and then return to normal, that was when we started scratching our heads, because we knew at that time (this was in the spring of 2020) that it was a coronavirus, and we knew that you could get coronavirus diseases repeatedly. And here, you had people talking about herd immunity. And we knew the coronaviruses and vaccines are not a good fit.

We really started looking at all of this and said, "We should get involved in this." What we ended up doing initially was coming up with a bunch of different grant proposal ideas, putting them out there. We basically had three solutions in mind at the beginning. One was you need a widely distributed intranasal prophylactic that people can spray in their noses as often as they need. The second was a therapeutic for acute disease. And the third was a therapy for chronic disease. And we thought, "Let's get going on that because, pretty soon, the market will be flooded with these therapeutics because everybody will be doing that." We thought we would be awash in funding because this is a crisis and everybody, all the pharma companies, are going to be working on this. So, we though, "Let's get the jump on that!"

It didn't play out that way. Our grants got rejected. We put in many grants. They got rejected. We got feedback from reviewers saying that this is a problem in search of a solution because the vaccines will solve this.

And that's when it slowly started getting to the point where we realized that it wasn't a matter of doing our drug development thing and waiting for public health to sort this out. It came down to us as individuals. If you were personally invested in the idea of not drowning in your own *juices* [i.e., choking to death as your lungs overflow from the attack of SARS-CoV-2], then you had to roll up your sleeves and do something about it. So, then we got sucked into basically the public health piece of it because there's what we're thinking about or how we're viewing the science of the virus and the pandemic and then there is what is getting said or the policy of dealing with the pandemic and they're very different.

By the summer of 2020 we had developed three hypotheses. The first one was that evolution would be a big problem with the SARS-CoV-2 virus. Second one was that vaccines are not going to work to bring it under control. And the third one was what people were then referring to as the COVIDiots or people who were refusing to take precautions were going to cause a huge problem.

BM: If I may, I'd like to read from your webpage. On your COVID brief you wrote, "From very early on in the pandemic, we identified three major challenges. 1. That SARS-CoV-2 was likely to evolve quickly in response to spike-targeting antibodies, and the preprint posted to medrxiv was dated November 2020. 2. That rapidly waning natural and vaccinal immunity meant the vaccines alone could not control the disease, preprint in January 2021. 3. That individually rational choices, in other words, the refusal to mitigate SARS-CoV-2 spread, would lead to a high disease burden in society, posted on medrxiv in December 2020.

These were very far-reaching observations. And each one of these have come true.

AC: Unfortunately, I wish we had been wrong about all of the predictions.

We were working on these things in the summer of 2020, but it's not our day job. We were dragging our tails across the finish line with these manuscripts. It took many months to put the manuscripts together. If it was posted to medrxiv in December of 2020, we were working on it in the summer of 2020.

Our "Ah, ha!" moment came in the summer of 2020 when we looked at … there's some really nice work done by Jesse Bloom's lab and by Regeneron where they looked at the mutations on the SARS-CoV-2 spike protein that impact binding [to the host cell] and what are the mutations on the spike protein that impact antibody binding.

In other words, what mutations screw up the spike protein's ability to do its job and what mutations screw up the antibody's ability to block binding. And what we did was a very simple, silly thing. We just overlaid the two and when we looked at it, we realized that the virus could readily mutate to avoid antibodies while not being impacted in its ability to bind [to the ACE2 receptor]. And that was the moment when the penny dropped for us and we said, "We're in a rough ride here."

People I know socially outside of work were looking at me like I had two heads because I was saying the vaccine might not play out the way they were thinking it might.

Again, I wish I lived in a world where we as a service provider selling mathematical modeling to biotech companies weren't doing this with our time. But this is what we were doing because we were looking at what was getting said publicly and thinking, "That's not making sense."

BM: Were you able to bring any of these findings to public attention? Did anybody listen to you?

AC: I hate to put it this way, but it's the curse of Cassandra, right? When you say something that later is correct, it's only later that people will listen to you. [*In Greek mythology, Cassandra, Priam's daughter, was given the gift of prophecy by Apollo. As she refused his advances, he placed a curse ensuring that no one would believe her warnings.*]

When we had that "aha-moment" about the spike protein mutating quickly to evade vaccines, we drafted a manuscript and sent it to *Science*. A month later we received a form rejection from the editor saying, "Thank you but we only choose things that are of broad interest to our readers."

And I thought, "Geez, there must be something of a broader interest than the fact that this is all going to hit the fan in a few months."

BM: Since many of the predictions and stated implications of your modeling studies have come true, are they listening to you now?

AC: So, *Fortune* has been taking up a lot of our work. We've been very vocal about the implication of our findings. But we aren't a public policy shop, right? We're individuals who have a strong vested interest in not ending up with Long COVID or having friends and families die because the country is in a disastrous spot.

At the end of the day, we still have a day job to do. We're putting stuff out there, but we aren't a public policy shop. Hopefully people who are shaping public policy are reading what we're saying and thinking about it. If we can make people who are working in public policy think for a minute and if we can break through the groupthink, then great, right?

Mutation, selection and the evolution of viruses

For instance, when the question of evolution came up there were a lot of experts who said evolution shouldn't be a problem because this thing has a proofreading mechanism. Well, dogs, for example, are not very mutation prone, but if you look at dog breeds, they don't look like each other at all. And you know why that is? It's not because they are mutation prone but that they do very well with selection.

Evolution works that way in that you don't always need a high mutation rate as long as the genome can tolerate selection.

BM: And from what I understand, the SARS-CoV-2 genome is quite adept at tolerating selection.

AC: Precisely. So, you had to put those two pieces together.

The minute people came and said it has a low mutation rate and evolution shouldn't be an issue then that was it, it was settled. We had some experts say *that* and everybody washed their hands of it. They said, "That was the news we wanted to hear." It was reassuring. It was a salve to our concern. And everyone said, "Okay, we're done with that."

[Given the environment] when we were putting papers out there, we knew we were going to be ignored. But we were okay with doing that because we just wanted to call it as we saw it. And we are still publishing papers. And we're still taking the position saying, "Guys, if you're in public policy, if you're responsible for public health outcomes, take a look at our papers and think about it."

But we're not actively marketing it. We have no commercial stake in this.

At this point we have a collaborative team—a bunch of academics—writing because of interest and concern. But not because we want to make a career out of COVID. We really don't and it'd be awesome to not have to keep doing this. But because somebody needs to say these things.

BM: I asked you this in the email, but maybe you can explain it again. The White House had recently announced that they were expecting a hundred million infections this fall and winter. And when I looked at your paper stating that endemicity is a bad idea, the modeling of your study came up with a similar range of infections—50 to 100 million—and in the best estimate scenario possibly even 300 million COVID infections per year, almost the equivalent of the US population. Were you the source of the *Washington Post* story?

AC: We weren't. We were interviewed by *Fortune.* I don't know if there was any back and forth with the *Washington Post* and *Fortune* meaning the *Post* read the *Fortune* article and then looked at the White House numbers, but nobody contacted us. [In his email AC also thought that the numbers quoted by the *Post* came internally from the CDC.]

One of the other side points, if you look through our papers and read through the introduction and discussion, what we were doing each time was to pick a critical issue to do the mathematical modeling on and then put an essay together on the subject. If you read all our papers from the beginning, including the one about individual rational choices, we were going into political theory. We were doing this quite deliberately because [we wanted to show] what the math said [about these policies] and what that meant in practical terms.

And as much as possible, we were trying to leave a paper trail of "this is why we think this or that is going to happen" with the expectation on the hope that we weren't just shouting into the void; that there was somebody at the other end reading what we were writing. It hasn't always panned out, but time to time …

BM: Having been looking at the research quite extensively for some time, I happened to find your papers only recently and by chance. And I was glad to have taken the time to read them because their implication is quite stunning and in context of the third year of the pandemic, quite accurate predictions.

Long COVID and "endemicity"

The other important aspect of the *Fortune* article was the discussion on Long COVID. Can you speak about the number of people expected to develop Long COVID? Can you put it into context?

AC: Absolutely. I got asked by *Fortune* to justify the numbers. We dug into a bunch of references to understand the incidence of Long COVID from these studies. And then we justified it citing chapter and verse in terms of the references; I can back each of those numbers.

But here's the bottom line. I think when people talk about Long COVID they miss one point and that is under an endemicity strategy everybody is going to get COVID every year or two repeatedly. That means under an endemicity strategy, even if Long COVID has a low risk at any given time, we're going to be doing it again and again, which means with repeated COVID infections Long COVID will eventually catch up with you.

[AC sent me the following email explaining the numbers, incorporated here in the discussion.]

If everyone goes back to living their pre-pandemic life and doesn't take precautions to limit their risk of getting COVID, our modeling suggests that you can expect to get COVID about 1–2 times a year.

The risk of getting Long COVID (post-acute sequelae of COVID, or PASC) each time has been reported as being anywhere between 10 and 80 percent (1,2,3,4). Let's say your risk of getting Long COVID each time you get COVID is 10 percent, to be conservative.

If you're fully vaccinated, that reduces your risk of getting Long COVID by about 50 percent (6,7). (Estimates for reduction of risk from vaccines range from 13 to 78 percent, with one outlier study, so we could say 50 percent as a median estimate).

So now, that means you have a 5 percent risk of getting Long COVID each year, to be conservative. The average American is 38 years old. Say you can expect to live to be 78. So, after 40 years of "learning to live with COVID," you have an 87 percent chance of "learning to live with Long COVID."

Put differently, if the whole world was vaccinated tomorrow, and we spent just three years now "learning to live with COVID" under the current strategy, we could well have over a billion people living with Long COVID.

Of course, it's possible that this might not come to pass. There are things we don't know yet about the virus. But failing to plan for a scenario because you might get lucky doesn't seem like a very good strategy.

By analogy, research on drunk driving shows that most drunk drivers drive around 200 times before they get into a fatal collision. You could always use the argument that my odds of dying in a drunk driving accident is one in 200. You might say, "I'm just gonna down four shots of tequila and get behind the wheel."

It's a valid argument because on any given day your odds of dying in the crash on that day are low. What we realized was that the risk of Long COVID is low on any given go-around of COVID. But if you've committed to a strategy where everybody is getting COVID every couple of years or every year then it's going to catch up with you.

We are working on a paper on Long COVID right now, which is looking at it a more holistic way, including looking at the natural immunity numbers.

BM: Have you looked at the potential financial burden of this kind of disease in your model?

AC: We haven't looked at it. Again, just to explain, the numbers I went over with you are not the results of any modeling. They are results of basic calculations using the data provided in these studies and I justify them. We are building a model that is looking at Long COVID risk over time under different strategies. There is a preprint coming out on that in a little while.

The point I'm stressing here is that leaving Long COVID as an unmitigated risk on the table and then choosing to "let her rip" could be orders of magnitude worse than people are thinking it will be. And now just to justify that the GAO [Government Accountability Office] already has numbers for Long COVID. If I remember correctly around 23 million people [7 percent] in the US are living with it.

There is a chunk of the Great Resignation that's not necessarily people being lazy, but people simply having Long COVID. The Office for National Statistics (ONS) in the UK released a study and I think they're looking at 3 percent of their population have Long COVID already. [As of April 2022, approximately 1.8 million people in the UK are suffering from Long COVID, accounting for 2.7 percent of the population. Source ONS.]

And here's the important part. Whatever's happened with Long COVID until now doesn't tell you what's going to happen with Long COVID going forward. Why? First, because the virus is a lot more contagious than it used to be two years ago. Second, because the vaccines don't work as well at preventing infection as they used to a year ago. Third, because we are consciously taking the decision not to mitigate the risk of infection.

So, if you have everybody running around like COVID is over and the vaccines don't work to prevent infection and the virus is super contagious, everybody's going to get COVID. In other words, the Long COVID we have seen so far, the rate of production of Long COVID we have seen up to this point in the pandemic, could be a lot lower than the rate of Long COVID we will see based on the current strategy [moving forward].

BM: Those are great points. Not to preempt a study you said you were publishing soon on "let it rip" policy, if I understood correctly? Would you speak on it?

AC: We've kind of already done that with the endemicity preprint, which is really "let it rip." We've looked at "let it rip" in many ways.

There was a paper that we wrote that came out in preprint in January 2021 called "Beyond the new normal." And in that paper, we looked at what would happen if we "let it rip" using the old numbers for the virus, which was a lot less contagious then. We asked what would happen if we

let it rip and we estimated we'd have about 400,000 dead. And in 2021, that was where we ended up.

Again, we never made these predictions (and we don't make these predictions now) as specific indications of what the numbers are. All our modeling studies are just thought exercises asking if [a particular policy] is a good or bad idea. What are the risks? We're not in the business of giving hard numbers, but we are very much in the business of saying, think about it for a minute what the downside risk could be.

One of the things we've repeatedly seen that's been very concerning to us as private citizens is that for some reason downside risk is not considered and people are very worried about fearmongering or creating panic. I'd love to see a little more concern given that we're at a million dead already. This is the single largest mass casualty event in the history of the Republic. I think some concern may be warranted.

What strategy for fighting COVID?

BM: I 100 percent agree with you. President Joe Biden acknowledged today that 1 million Americans have died from COVID. He prerecorded a very brief statement to the fact. During his tenure more than 560,000 people have died. The Democratic Party has attempted to blame former President Trump, the anti-vaxxers, the Republican Party for the lack of funding, even the virus. But they don't take any responsibility for their policies, which have mirrored the Republicans' and led to the wholesale dismantling of all public health measures against the pandemic. For two weeks, the District of Columbia hasn't reported a single COVID statistic, essentially achieving Zero-COVID because no one is tracking it. Can you comment?

AC: Unfortunately, I would not like to comment on that. Here is the deal. We're scientists and what we're doing is we're putting on the table the things that people can do if they choose to be rational.

I agree with you about the Democrats. I agree with you about the Republicans, but why stop there? It's the World Health Organization, it's every other country in the world. Nobody has got this figured out. And the main reason nobody's gotten this figured out, in my opinion, is because we keep framing it as a false dual choice—Should we lock down? Or should we deal with COVID?

It's not like that.

The tools that worked in the beginning—lockdowns, masks, social distancing—were there to buy us time. We bought that time. We got to a vaccine. The vaccine too bought us time. The vaccine gave us six to nine months of a decent amount of disease control. But then we needed to have transitioned from the vaccine to other biomedical interventions and we missed that bus. Where we should have had effective biomedical interventions in place today that went beyond the vaccine, instead, the whole world indulged in magical thinking. And this is everybody's fault. This is beyond a partisan issue.

It's a complete failure of the imagination in the political process, in the scientific classes. The unthinkable and the impossible, these are not the same thing.

BM: You noted back in September 2020 that if schools were to reopen it would lead to widespread disease propagation, which it did. You also wrote that the CDC metrics for assessing disease spread in schools are deeply flawed. You had even written that when the CDC announced that the pandemic was over for the vaccinated, the relaxing of restrictions prematurely would lead to variant-driven rebound in cases. Then Delta appeared. Now we are even seeing more vaccinated people dying. The observations you made were quite far-reaching at the time.

But there were many principled scientists during the same time saying that if schools were reopened it would fuel the pandemic. Data from multiple countries proved that schools were accelerators of infection waves. One of the largest studies came from India that looked at transmission amongst children as a leading factor for community spread.

Yet, people like Emily Oster of Brown University, Rochelle Walensky of the CDC, even Biden when he was elected, said that children wouldn't get infected, and children wouldn't transmit COVID. Can you comment on this issue?

AC: Yes. In the summer of 2020, we started modeling from first principles the behavior of COVID in schools. All of this was driven by our day-to-day conflict of interest. I have two kids and I really didn't want them to go into in-person learning unless it was safe for them. I didn't believe at that time that getting COVID was just a cold. So, we asked, "Is this a good idea?"

The first question was narrowly selfish: "Is this safe for my kids?" But as we started modeling it, we realized two disturbing things. And one is that schools … Let's put it this way. Children are mostly asymptomatic. If you don't do contact tracing, you won't be able to spot spread in schools. And second, it dawned on us that like roughly half the country, I don't know the exact number off the top of my head, but roughly half the country is either in school as a student or in school as a teacher or staff or has a relative who's in school for one of those reasons.

It dawned on us that not only is this an issue of "is it safe for my kids," but it's a question of, "is it safe for the community?" So, the very first paper we wrote in the fall of 2020 said, "If you keep schools open, you will seed chains of transmission." And those chains of transmission will spread undetected through the community because children are mostly asymptomatic. So that was our first paper.

And then we went from there to an even more disturbing observation, which is a preprint which we did with Lauren Ancel Meyers [Director of the University of Texas COVID-19 Modeling Consortium] from the University of Texas, who is a well-recognized epidemiologist where we realized that even if schools were spreading very aggressively, the metrics that the CDC were using were not going to pick that up.

They were looking at this ratio of the rate of COVID in schools to the rate of COVID in communities. And they were saying it's correlated so schools cannot be driving spread in communities. They were using correlation to imply a lack of causality, which is a simple and straightforward logical fallacy. And I wrote to the CDC at the time to the MMWR [Morbidity and Mortality Weekly Report] and I said, "Guys, logical fallacy." And they wrote back saying, "We're not implying causation or lack of causation." And I followed up saying that that was how people were going to read it.

[*Correlation and causation can seem deceptively similar. While causation and correlation can exist at the same time, correlation does not imply causation. Causation explicitly applies to cases where action A causes outcome B. On the other hand, correlation is simply a relationship. We cannot simply assume causation even if we see two events happening, seemingly together, before our eyes. One, our observations are purely anecdotal. Two, there are so many other possibilities for an association. In the case of the CDC, they were implying that equivalent COVID rates at school and in communities meant schools could not be seeding the community. In other words, they did not prove this.*]

BM: Just for clarity on these statistical terms, when you say correlation is not causation, what you are trying to say is that because children are predominantly asymptomatic, when you're measuring COVID cases among them in the schools and compare it to the community, you're missing a massive number of infections that have been undetected?

AC: No. Actually, it's even worse. So, what happens is if a kid gets COVID, somebody at home is going to then get it. The kid will be recorded as "school transmission." The person at home will be recorded as "community transmission." Basically, the fact that it's correlated can

mean one of two things, either schools are not driving community transmission or schools are driving community transmission so well that the two rates are correlated.

BM: Meaning that the CDC is not tracking the community transmission as a by-product of a school transmission that led to community transmission?

AC: Yes, but it gets even worse. If you read the paper, we wrote you'll see it gets worse because the way the CDC was doing contact tracing was going to make it very difficult to spot transmission chains.

To put it to you simply, the way they were doing contact racing was essentially semi-voluntary. First, you had to have symptoms. Then if you had symptoms, you would contact them. Then they would contact everybody that you were in contact with, and they had a very narrow definition of that. And then you had to volunteer to be tested. What all this means is that the way that we're doing contact tracing was guaranteed to miss most of the transmission to begin with.

If you look at things like the Sturgis motorcycle rally, where a massive number of bikers showed up in South Dakota, Sturgis didn't create chains of contact-traced transmissions. And everybody said it was safe to have a million bikers hanging out together in bars. It won't spread that way. But the other inference, the other way you could have interpreted the data, was to say, "Is your contact tracing working?"

Another case—there were two hairdressers in Missouri cutting hair while with active COVID for a week and nobody got COVID. Either it's extremely safe to get your hair cut by someone who has COVID, or contact tracing is not working, especially in voluntary contact tracing, because if you think about it, who is more likely to get infected? Who is more likely to be part of the follow-on chain? It's going to be the people who are not taking precautions, but the people who are not taking precautions may also be not enthusiastic about talking to contact tracers.

BM: Before I go to my last question regarding your drug modeling, do you have a modeling for a spray vaccine and for secondary antivirals?

AC: Yes, we are working on those, and we're very interested in them. And again, the reason we put these things on the webpage is in the hope that somebody else picks up those ideas and works on them as well. It's not typical that you will do that to encourage competition, but frankly speaking, we all have a personal stake in this.

We have published some work like how to optimize nasal sprays and how to identify drugs that would make good repurposing candidates. We are working on a nasal spray vaccine and anti-viral. But it's still in the very early days. [*Later AC wrote that things look really bleak. "We are also working on solutions to the problems, but all of those need an acknowledgment that there is a problem before funding becomes available. At present the well is bone-dry when it comes to COVID research, particularly on the question of new drugs and vaccines."*]

Zero-COVID or "infinite" COVID

BM: Shifting topics, on the question of China. We have been tracking cases and they have done a remarkable job bringing down the number of infections through their comprehensive pandemic prevention measures. In your opinion, why has elimination been discarded?

AC: I'll put it to you this way. We'll never be able to get rid of pollution. That doesn't mean we should all build the biggest bonfire we can in our backyard and pollute as much as we want. We will never get rid of drunk-driving deaths, but that doesn't mean we should abandon seatbelts.

To say we will never get rid of COVID is not synonymous with encouraging rampant spread. Everybody talks about how Zero-COVID is a bad strategy. Maybe it is and maybe it isn't. But we are nowhere near that. The strategy, the path that we are on I like to call infinite COVID. And infinite COVID is going to be a more expensive strategy than Zero-COVID would be. The idea that we will all get COVID once a year and we will be fine is recklessly optimistic.

BM: What do you hope to gain from your work on COVID?

AC: I think in the larger picture we're hoping to be influential. We are hoping that policy makers and decision makers are reading them and thinking for a minute about the consequences of what they're doing. We've had a lot of talk about how Zero-COVID is a bad strategy. But there's been no balance in that discussion about why infinite COVID might not be a great idea.

BM: The perspective the Socialist Equality Party and the WSWS supports is a Zero-COVID policy on an international scale. Not in one country, but through a coordinated effort to end COVID in all the regions of the globe. This is feasible …

AC: There's a different way of thinking about it, right? Instead of framing it as Zero-COVID, the first step is to look for less COVID. Less COVID is going to be better than more COVID at any point along the way. A steppingstone to Zero-COVID (whether that is feasible in the end is another question). It is almost a philosophical question because it's an extremely contagious disease.

So, it may never be possible to get to Zero-COVID, which is my opinion if you ask me. But whether Zero-COVID is possible or not, we should treat COVID as a highly dangerous, highly communicable deadly disease, because that is what it is. First, we should come to terms with the reality that it is a highly contagious, highly communicable and deadly disease. And then ask the next question—If we are faced with such a highly communicable and deadly disease, does closing our eyes make the monster go away?

BM: Another question I wanted to ask you regarding the US dismantling all their COVID dashboards, cutting back on testing centers, no contact tracing, etc., all the while we are back to pre-pandemic social movement. What will the fall and winter look like?

AC: Well, it's going to make it much harder for us to see when the next wave is coming. And I think, again, this is the problem with the infinite COVID strategy. The virus is evolving very fast, and the virus is changing the terms of the deal on us from time to time.

If we don't have a good way of tracking variants, we won't have a good way of tracking infection and fatality rates. We won't have a good way of tracking how well the vaccine is working. If we only use hospitalization and death rates, those are lagging indicators. The problem is that there may come a point when you realize the vaccines aren't working so well. But by the time you get there you've lost all the levers at your disposal from a public health perspective to deal with that.

As a private individual, if we are not able to … we are told we must manage our risks … but one of the tools that I need as a private individual to manage my risk is *accurate daily case counts*. Without that I have no way of doing anything rational.

The stated public health strategy, which is individuals manage their risk, also means that the vaccines continue to work well to prevent disease and death and we will course correct when needed. The tools that are needed for us, both at an individual and at a public-health level, to enact that strategy are slowly fading, exiting stage left. So, from a rational perspective, that's not going to put us on a good footing to handle whatever curveball the virus throws at us next.

BM: An epidemiologist once said, and it stayed with me, that a pandemic/epidemic is a community disease. The pathogen needs a community to survive and only a community can fight it. But the way the CDC is treating it is like a boutique. You can choose to go in or not, I can wear a mask or not, I can test or not.

But for working people, they must work closely with each other. They must take public transportation.

You go with. They live in multi-generational homes. They have children, grandparents, extended family all sharing the same space. They don't have the luxury of taking time off to go get a PCR test, let alone isolate or quarantine under the current conditions. There is this massive

disconnect between what the CDC is telling the population and what the population can do.

What should the CDC do? What do you want to tell the readers the CDC must be doing to keep them safe?

AC: The first thing that the CDC, and beyond even the CDC, the first thing that global public health needs to do is call it based on the facts. We have often seen that there is a disconnect between the facts and what public health says. Though I can name a half dozen off the top of my head, the best example was when the WHO didn't want to accept that COVID was aerosol spread for the longest time.

And on that note, accepting that this is an aerosol-spread disease is crucial because the minute you accept that, you must put your attention to mitigating spread. When you have an aerosol-spread disease, you can't opt in or opt out à la carte. Like you said, right? We don't tell people smoking causes lung cancer and that secondhand smoke is bad, but if you go into a building where somebody else is smoking, hold your breath because it is aerosol spread. Your choice impacts me. So, the first thing that the CDC and global public health needs to do is after acknowledging it is aerosol spread then go through your recommendations step-by-step and ask if they are rational considering the airborne nature of the disease. And again, the position that we may never be able to eliminate it completely absolves us of any responsibility to control the spread, simply doesn't compute.

BM: You said in the endemicity paper that SARS-CoV-2 isn't going to become less virulent. There's no evolutionary drive to make it less virulent. Push for it to become less violent. However, it has two mechanisms by which it can become worse. It can become more contagious, and it can evade immunity better. Can you comment?

AC: Our work suggests that the virulence is free to float up or down, drift upward or downward. That means any given viral variant will either be better or worse than the previous one, or the one that we are dealing with now.

And what that means is you keep rolling that dice long enough you're going to come up snake eyes. This is basically Russian roulette with evolution. And just in the same way with Russian roulette, I cannot predict with great certainty whether the next roll of the chambers is going to be the last one for you. But I can predict that if you keep playing it long enough, it's not going to be a happy ending story.

BM: Can we return to the issue of drug development. There is very early data coming out that once Paxlovid is used in large quantities, resistance could be selected against it by SARS-CoV-2. How is modeling drug development helping with these issues?

AC: It is still in the very early days. But what we are doing is we are looking at multiple different targets on the virus for antivirals, and we encourage people who are thinking about antivirals to think about it.

There are two key principles here if you're coming up with antivirals for this disease. One is you need antiviral prophylactics because antiviral prophylactics can help vaccines, any vaccines, because they provide a different evolutionary pressure on the virus. It would be good for us to be thinking about having antiviral prophylactics at the same time as vaccines. It's not either/or.

The second thing is when you're looking at antiviral treatments, consider having antiviral treatments that are hitting multiple targets on the virus because I think we're still underestimating the ability of the virus to escape from any kind of evolutionary pressure.

And that is also the problem with the variant-specific vaccine strategy. Chasing variants is not a good idea. What we are recommending is looking for vaccines that target parts of the viral protein that impose a cost on the virus to evade the mutation.

I'll explain what I mean.

This is what they did for HIV, they looked at the evolutionary barrier, that is, the disadvantage to the virus from creating mutations that evaded the therapies. We should be thinking about the evolutionary barrier each time we design vaccines, or monoclonal antibodies, or even therapeutics for this virus. And at the same time, we must be prepared for the fact that any set of biomedical tools (vaccines, therapeutics) we bring to bear against the virus at present will be defeated very quickly. So, we have to have other tools in development as well—it's an arms race right now, and we are losing so far. (By the way, slowing down transmission will slow the evolution of the virus—one more reason why less COVID is always better than more COVID).

Everything against this virus needs to be designed with evolution in mind. The public health strategy needs to be designed with evolution in mind. The biomedical interventions need to be designed with evolution in mind because evolution keeps changing the deal on us with this virus. It has become five times more contagious, different profile of side effects, different profiles of long-term effects. So, everything we do both from public health and from a drug discovery and development perspective should be designed with that in mind.

BM: Thank you so much for your comments and time. It has been my pleasure.

AC: Thank you.

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