



## COVID-19: The Endgame

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Almost two years after the COVID-19 outbreak, much is still unknown. Why are heavily vaccinated countries such as Israel and the United States seeing record cases? Will children drive infections as we open up? And how will the economy stay on course? In this episode of *The Active Share*, Hugo Scott-Gall speaks with Global Research Analyst Camilla Oxhamre Cruse, who has a Ph.D. in infectious disease, and Global Strategist Olga Bitel about what's next in the COVID crisis.

Comments are edited excerpts from our podcast, which you can listen to in full below.

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**There are many things to discuss regarding to the next phase of the COVID pandemic, but I want to start with countries. Camilla, different things are occurring in Israel, the United Kingdom, and the United States in terms of infection rates, mortality rates, and vaccine efficacy. What can we learn from that?**

**Camilla:** Israel has been a guinea pig—a forerunner for the rest of the world—when it comes to vaccination. But in the past couple of months we've seen a sharp increase in case numbers. Since July, we've also seen an increase in hospitalizations.

But let's break down the numbers. The largest healthcare provider in Israel, Clalit, has vaccinated approximately 3 million people. Of those 3 million, 600 have suffered severe breakthrough cases since June. That's less than 1%. And of those 600 people, 75% are above 70 years old, and they were vaccinated five months prior or longer.

After five or six months, it seems like the protection we get from the vaccines starts to wind down. But real breakthrough cases are extremely rare, and it's primarily happening to the elderly (or people that have underlying diseases).

**So, what's happening now is not surprising to you?**

**Camilla:** It's actually quite expected to see some sort of winddown of protection. After a while, the body feels that the acute phase of whatever pathogen it has experienced has passed, and the neutralizing antibodies circulating in our body start to decline, because we cannot have circulating neutralizing antibodies for every pathogen we see through our lives. They would clog our circulation.

But that doesn't mean we don't have any protection at all. Our memory cells—B-cells, T-cells—are still active. And they still recognize the pathogen upon exposure and start a biological reaction. But it can take longer.

However, the elderly naturally have a lower immunological response to vaccines. The average protection provided for severe COVID hospitalization is approximately 92% to 96%, depending on the vaccine; for the elderly, it could be more like 70% or 80%. And if that starts to wind down you end up in more dangerous territory.

That's why we see severe breakthrough cases, primarily in the elderly. It makes sense that we're now talking about giving the elderly and those at higher risk a booster shot.

**Will boosters be normal going forward?**

**Camilla:** I think so, but it doesn't necessarily have to be every six months, because the booster trains the immune system to further recognize the antigen. I think it's fair to assume that maybe once a year we'll get a booster, much as we do for the influenza virus.

**Is Israel a leading indicator? Will what happened in Israel also happen in Europe, the United States, and the United Kingdom? If so, are we looking at a difficult autumn?**

**Camilla:** Yes, I think that Israel is a leading indicator. If we don't do anything, the pattern we're seeing there will manifest in the rest of the developed world (at least where there are large numbers of vaccinated people). But the number of severe breakthrough cases in Israel is still very low. The vaccine is very good. It will just become a little bit less good—in particular for those that are older and have weaker immune responses.

What we haven't talked about is children, who up to now have been relatively protected because they haven't been to school. They've been in a bubble. Now schools are opening up in-person, so we will likely see more cases among children. We know children are not reacting as severely as the elderly, but the question is how we will react. We don't have a lot of data yet on children.

That trend that will be very important to follow, particularly since we will not only battle COVID this fall; we will probably also battle other respiratory infections. We didn't see a lot of that last year because schools were pretty much closed in the developed world. But these other viruses will come back, and how will our immune system response to potential double infection of COVID and influenza or COVID and RSV?

**Let's bring in Olga, because all of these uncertainties may have psychological implications. We thought once we were vaccinated we would put this behind us. That hopeful scenario seems a bit less likely now than it did**

**four, five, or six months ago. This could mean that economic activity is reduced, maybe even permanently. What say you to that, Olga?**

**Olga:** Well, that is definitely a tall question, so let me take it one step at a time. You're onto something when we compare where we are to the euphoria of the vaccine introduction. I vividly remember Camilla saying that a vaccine that is 30% to 50% effective is quite good, and we got vaccines that had efficacy rates in the mid to high 90 percent range, so nothing short of stellar.

The economic rebound we saw subsequent to the rollout of the vaccine has also been nothing short of stellar. In the second quarter of this year, both U.S. and European economies recorded double-digit growth rates. For those that are interested in comparisons, there aren't any. We probably haven't grown this fast since after World War II. But it's too far to go back into the reliable records to really compare.

That initial euphoria is definitely behind us. In terms of the permanent shift in behavior and attitude, that is more difficult to call, and I say that being a perennial optimist.

Perhaps I'm biased in what I'm looking at—prior pandemics, of which we've unfortunately had several. The most comparable one happened in the mid- to late 1950s. These pandemics usually last several years, and we have not seen any permanent shifts of behavior as a consequence.

Yes, there is a non-negligible cohort of people that is more cautious. Maybe it is as high as 20% to 25% of the population. These people will remain less mobile, less willing to interact, than before COVID.

But once a pandemic is truly behind us, with a passage of time (between 6 to 12 months), most people fully resume their economic and social activities. The reason is that biologically we're social animals. We're hardwired to interact. It's okay to exchange ideas on Teams, but it's hard to reach over and touch someone on the shoulder on Teams. And people crave that.

So, once the pandemic subsides, my optimist sense, which is backed by experience with prior pandemics, is that within 6 to 12 months people will return to their pre-COVID living patterns.

**Camilla, you're not quite as much of an optimist as Olga is. Do you agree with Olga that we eventually just decide as a species that there's no other way to carry on but as before?**

**Camilla:** I think Olga has a very strong point that we're social animals. To her point, when the United Kingdom opened nightclubs and restaurants, people went out in masses.

But how that physical interaction takes places can vary. We find new ways of doing things—new ways of interacting, new ways of socializing. Will it be exactly as before? Probably not.

We've been living with this for one and a half years. It's probably going to last for at least 6 months, maybe 12 months more. I think there will be a new normal. Exactly how that will look, I cannot predict.

**Can we talk about herd immunity? Back when this all started, people were saying herd immunity could come at 70%, 75%, or 80%. But now something like 94% of adults in the United Kingdom have some antibodies, yet the U.K. infection rate is quite high. Is herd immunity a red herring?**

**Camilla:** To some extent yes, because it's hard to define exactly what herd immunity is. We're dealing with a moving target. COVID-19 is changing, so what we need to reach herd immunity is also changing.

We've now seen a couple of new variants, and it's safe to say they are more virulent. And with more virulent variants we need a higher herd immunity to fully protect ourselves.

Then there's the changing immunological response. We have seen that even if we get fully vaccinated, six months from your second dose you might not be fully protected anymore.

That makes it quite difficult to have herd immunity as our main goal, as we've seen in other epidemics. Take measles, for example, the most virulent virus we know; we need to achieve over 96% or 98% immunity in order to achieve herd immunity. But we see pop-up local outbreaks when that herd immunity declines to just below 90%. The virus reemerges very quickly.

So, I don't think we should say, "Now we have reached herd immunity, so we are done." It doesn't work like that.

#### **Talk to me about variants.**

**Camilla:** So far, the new variants have been more virulent, but there haven't really been any changes regarding the immunological protection the vaccine provides. I think that we've now seen enough evidence in a real-world setting that vaccines are protecting us as well from the virulent variant as from the other variants.

But we're now changing the environment for the virus, right? We have a high level of spread and an increasing number of vaccinated people. That means the virus has a lot of shots at trying to evade the immunological protection that a vaccine provides. Evolution is the force of trial and error. The virus is constantly trying to become better, trying to evade obstacles.

So, we are putting ourselves at a risk. No one can really define exactly how big that risk is. But we have an increasing number of vaccinated people, and the virus gets a lot of chances to try to evade that immune protection. And sooner or later we will see new variants that can evade a vaccine.

It's not really anything strange. We see that every year with influenza. But the time aspect is very important. If we see new serotypes a couple of years from now, we will be prepared to change the vaccines and roll out new programs. Should we see that anytime soon, however, I think it would be detrimental to people and the economy.

#### **The speed and efficacy of these vaccines is pretty amazing. With your broader healthcare analyst hat on, will this optimism extend into a real period of innovation?**

**Camilla:** Absolutely. With the development of mRNA vaccines we've seen a completely new vaccine model that will be used not only for COVID but for a vast number of different diseases.

It would be a huge game changer for influenza, for example. A good influenza vaccine provides maybe 60% protection—not particularly good compared to these new COVID vaccines that generate 90% protection.

We're also seeing many positive developments that together could spill over to other developments in healthcare: the digitalization of the healthcare system; the use of artificial intelligence (AI). I think we will see huge changes not just in how we think about disease, but in how we think about patients, who will be consumers.

That enthusiasm has attracted a lot of capital. So, there are a lot of forces working together, with capital coming in, with research development, with clinical development. I think we're standing at a very interesting inflection point in healthcare that will drive massive growth over the next decade.

**Olga, based on what Camilla said about a more potent variant that can evade vaccines—a game of cat and mouse—are you still as optimistic around economic recovery?**

**Olga:** Economic recovery following the introduction of the vaccines and the reopening has been extremely strong—as strong, if not stronger than, we anticipated.

But that recovery would be fading even if the virus had died away and we were living in a post-COVID world. It is simply impossible for developed economies like the United States and Europe to maintain double-digit growth rates for anything like a multi-quarter time period. We're already starting to see that slowdown unfold.

The relevant question is what is the cruising altitude for our economies? In other words, what kind of growth rate do our economies settle at? Are we going to go back to the last decade's very mediocre growth rates of just around 2% (and in the case of Europe, below 2%)? Or are we going to reach a higher cruising altitude of perhaps somewhere between 2% and 3% growth?

Over a decade or even longer, that makes a tremendous difference in terms of the quantum of output we produce and our quality of life. We're talking about trillions of dollars in income, in consumption, in investments, etc. And that remains an open question. But for the next six months we're looking at decelerating growth almost irrespective of what the virus does.

Obviously, that would change if the worst materializes and the virus mutates in ways that are completely unpredictable at this point, such that we are forced to have some more forms of lockdowns because our hospital systems are inundated again. This is very much not our base case at this point. It's a bear case with a relatively low probability of materializing. But if something like that were to happen, the economic recovery would stall out more substantially.

**Camilla was extremely optimistic about an innovation surge. Do you share that optimism? Should we never let a good crisis go to waste? Do you see the potential for beneficial innovation coming out of this?**

**Olga:** "Never let a good crisis go to waste" usually refers to governments or other public policy vigilantes taking up the baton and doing something to promote development. But in this case, I'm actually more optimistic because no further government action is required. Crises—any kind of crises—usually produce a bout of innovation.

COVID was as close to an existential crisis as we've seen in recent history, and there's no doubt that it will spur the type of innovation that Camilla talked about. Whether we see the benefits of this on the investment landscape or as patients, and whether we see it within 5 years, or 10 years, or 20 years, remain open questions.

But there are many companies and researchers already very excited about the fact that mRNA research has been massively underfunded for decades, and the kind of funding that it's already getting will result in a step-change. That is nothing short of revolutionary.

Need is the mother of all invention. We definitely have the need, and increasingly we have the resources, the tools, and the personnel to bring those innovations closer to us as consumers and to us as investors—much faster than we've ever done before.

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