3 Takeaways Podcast Transcript
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Ep 59: Uncontrolled Spread: Why COVID-19 Crushed Us and How We Can Defeat the Next Pandemic with Former FDA Commissioner Scott Gottlieb

INTRO male voice: Welcome to the 3 Takeaways podcast, which features short memorable conversations with the world's best thinkers, business leaders, writers, politicians, scientists, and other news makers. Each episode ends with the three key takeaways that person has learned over their lives and their careers, and now your host and board member of schools at Harvard, Princeton, and Columbia Lynn Thoman.

Lynn Thoman: Hi, everyone. It's Lynn Thoman. Welcome to another episode. Today, I'm excited to be with Dr. Scott Gottlieb. He's a former Commissioner of the FDA and the author of Uncontrolled Spread: Why COVID-19 Crushed Us and How We Can Defeat the Next Pandemic. It is a great read. I highly recommend it. Scott was in regular contact throughout the pandemic with all the key players in the government and the drug and diagnostic companies. I'm looking forward to getting an inside account of how essentially a system-wide failure across the US Government left the country blind. And also, I'm looking forward to finding out how we can prepare for the next health crisis, whether it's a deadlier coronavirus variant, a flu pandemic, or even a man-made biological threat. Welcome, Scott, and thanks so much for our conversation today.

Scott Gottlieb: Thanks for having me.

LT: Scott, the US put together its first Health Emergency Preparedness Plan decades ago under the second President Bush. Why wasn't the US better prepared for COVID?

SG: Well, first of all, a lot of our planning was for influenza. When we thought about pandemic preparedness in the past, we always took a pathogen by pathogen approach to it, and we tried to anticipate what the pathogens were that we're going to threaten us and, invariably, we always focused on influenza as a naturally occurring risk, and then we also focused on what we refer to as special pathogens, things that could be used by would-be terrorists like anthrax or smallpox. We never anticipated coronaviruses, certainly, but we also never anticipated something that would occur naturally, but spread very differently than influenza. And so the capacities that we had built were really very flu-focused. We built what we call the influenza-like illness surveillance system, where we collected information inside hospitals to try to serve as an early tripwire to when a novel strain of influenza might be spreading, and we thought that that would also be sufficient for alerting us to the spread of any kind of novel respiratory pathogen, including coronavirus. We thought that that would be applicable here.

SG: And we stockpiled drugs like Tamiflu and other therapeutics that would be operable in the setting of a pandemic flu, never anticipating that the pandemic that would ultimately threaten us would be a novel coronavirus. What we really should have been doing was building broad capacities to try to thwart entire categories of diseases that had pandemic potential. And really the category of diseases that we needed to be worried about were diseases that replicated through RNA and spread through aerosols or respiratory droplets. Viruses that spread through droplets or aerosols have the capacity to spread very quickly. So those are the characteristics that create pandemic

potential, and if you're looking at threats through that prism, the universe of viruses that can potentially threaten us is much broader than just influenza.

LT: Interesting. Operation Warp Speed, the Trump administration's program of creating a portfolio approach to vaccines, of funding several different companies for each different type of vaccine was really innovative. The US government provided over a billion dollars each to Moderna for its MRNA vaccine, and to Johnson & Johnson and AstraZeneca for their more traditional vaccines, and these three companies created three of the world's most successful vaccines. Before Operation Warp Speed, the shortest time to develop a new vaccine, I think was about four years, but these three companies all developed vaccines in a few months, as did Pfizer. The US government also provided funding as part of Operation Warp Speed to companies to develop COVID treatments. Regeneron, one of the companies funded by the government, developed an antibody treatment which was one of the most successful COVID treatments. What do you think about Operation Warp Speed and its portfolio approach, and do you think the US should take a similar portfolio funding approach for developing vaccines and treatments for other major diseases?

SG: Well, I think Operation Warp Speed was really a recognition that we didn't have a capacity in place that could both marry the scientific capabilities that we needed with the sort of operational and logistical capability that was required to do something on this kind of a scale to respond to a crisis of this magnitude. And we really lacked that early on in the crisis. And there was a recognition that if we wanted to be able to get a vaccine more quickly than what was traditional, we needed to get the regulators and the scientific agencies that would be involved in helping to develop that product, NIH, FDA, married to some kind of operational capability, someone with an operational mindset that could make the investments that we needed to do the rapid scale-up of manufacturing and distribution of a product, if we were going to launch a mass vaccination campaign. That was the DOD. So Operation Warp Speed was a marriage really between NIH and FDA and the Department of Defense to try to get this done more quickly.

SG: We were really at a technological inflection point and that's what, in my view, enabled us to come up with these vaccine constructs so quickly. And that inflection point was that we were right at the cusp of an age where we went from sort of a wet approach to developing vaccines, where the traditional approach was, you find a virus that you want to develop a vaccine against, you grow it in cell cultures, you inactivate the virus, you cleave off its surface proteins and then you use those proteins in the syringe effectively as the vaccine. That's how we make flu vaccine each season. And we moved towards an age where we were able to synthetically derive these vaccine constructs using the sequence information alone. In the case of the vaccines by Moderna and Pfizer, which I'm on the board of, the sequence was used to basically manufacture a strand of MRNA. And MRNA is a nucleic acid. It's like our DNA, but a coach for the production of proteins.

SG: And in this case, by giving an MRNA sequence, that coded for the production of a protein found on the surface of the coronavirus, the spike protein, they're able to basically use our bodies as a manufacturing plant for the spike protein to generate enough spike protein for our immune systems to recognize and then develop immunity against. So it really was the ability to use this fully synthetic technology that allowed us to pivot very quickly. If this was three or four years ago, we wouldn't have been able to do this. If this was three or four years from now, this probably would have been mainstream. The reason why Pfizer was able to pivot as quickly as it did was because they actually had a program where they were trying to develop a flu vaccine using this technology, so they were already starting to use this technology. The final point I'll make, though, just a sort of

an aside is there was nothing fast about the development process once we had the vaccine construct. These vaccines were put in some of the largest and perhaps the largest clinical trials ever undertaken against a single virus. People were motivated to get into the trials and they unfortunately read out quickly because we had a lot of COVID, so there were a lot of people in the placebo arms of these trials, getting infected and getting sick, so you reached the endpoint quickly.

SG: The endpoint was a certain number of people having symptomatic disease, and unfortunately there was so much infection around the country, that endpoint was reached much more quickly than what we anticipated.

LT: Scott, what will that new technology enable for the future?

SG: We're going to see other vaccines developed using the MRNA technology. Moderna recently had an R&D day. Pfizer has talked publicly about their portfolio, as well, and other companies are in this space also. These aren't the only two companies working on MRNA technology for vaccines. I think you're going to see a host of different vaccines that are going to be developed for different diseases using this platform. The observation with the MRNA technology is that the immune response that was generated in the clinical trials show a very consistent response across age groups. Typically, what you'll see is young people will derive a robust response to a vaccine, but it's harder to get older individuals to derive the same robust immune response. But when you look at the clinical data from the COVID trials, you see a very consistent response across all age groups. And that may be something unique to the MRNA platform, and that makes it particularly attractive. The technology is also being used to develop therapeutics. One of the places it's been put into development is developing cancer therapeutics to try to use MRNA in the proteins to elicit an immune response to epitopes found on cancer cells as a way to develop basically an immunotherapy that could potentially target different kinds of cancers. It also has a potential to be used in certain rare disease settings, but I think you're going to see it become a more common technology backbone for a broader array of therapeutics.

LT: Interesting. The US was extraordinarily successful at developing COVID vaccines. On the other hand, many other countries were much more successful at managing the public health side of COVID, that is everything except the vaccines. Can you tell us what the US failed at? And why you think that the US failed?

SG: Well, I think there were different failures at different time points along this crisis, but I think at the outset, other countries were able to use testing and tracing and quarantine to try to control the introduction of the infection and blunt the peaks of their early epidemics. This was going to become a global pandemic. Every nation was going to be impacted by this. I don't think getting to "zero COVID" here in the US and having an experience like what Australia is having or New Zealand, where they're willing to implement and really sustain shutdowns in order to keep the infection out entirely. In China, as well. I don't think that that was sustainable here. Our early shutdowns were to try to preserve the capacity of the healthcare system and blunt the impact of that first wave of infection until we could get to some effective therapeutics and have better capacities in place to deal with this. It wasn't to keep the virus out of the country. We were never going to be able to do that, but we could have mitigated the impact that COVID had on us. And early on, I think the key missing ingredient was the lack of a diagnostic test that could be used to diagnose patients and do effective tracking and tracing of the virus. And also, not only tell us where the virus was, but tell us where it wasn't, so that we could target our mitigation more effectively.

SG: CDC failed to roll out the diagnostic on time. Everyone knows that part of the story. But even if CDC had been successful, we still wouldn't have had enough diagnostic testing. We had taken an approach where we had a very sequential process where CDC was going to design this diagnostic, make it available to the public health labs. They were going to start doing testing. That highly sequential process was going to take far too long to unfold in the setting of a fast-moving pandemic and was never going to provide the kind of capacity that we needed up front. We needed a completely different mindset. We needed a novel test, we needed to get it out on novel platforms. In many cases, we needed to build the capacity to collect respiratory swabs. And in order to get that, we couldn't rely on CDC to roll that out. We needed to turn very quickly to commercial manufacturers. Sometime in January, someone needed to call up the large commercial manufacturers who made diagnostic test kits and said, We need your help. But that call was never made and the commercial manufacturers were never spun up. We were overly dependent upon the CDC process. And so that prevented us from being able to use testing and tracing of infection and getting people into quarantine as a way to control the early spread. But what it also did is it prevented us from knowing where the virus wasn't. And so in the beginning, back in March, we shut down New York, San Francisco, Boston, New Orleans.

SG: We knew that those cities had epidemic spread, but the virus wasn't really spreading at any appreciable level in Austin or Jacksonville or in Wyoming. So there were parts of the country that didn't need to shut down. You could have still used testing and tracing and quarantine as a way to control the spread and then you would have preserved the political capital to implement the population-wide mitigation later on when the virus eventually became epidemic in those parts of the country, as it did later in the summer. But as it turned out, when it eventually became epidemic in Arizona and Florida and Texas and other parts of the Deep South, people down there and said, Look, we've already shut down. You told us to shut down in the spring. We did. We didn't have to. We're not shutting down again. And so you lost the political capital that you needed to implement the mitigation later when the virus eventually became epidemic because you did it too early. And so the lack of a diagnostic test was the root of a lot of our subsequent problems. That's why South Korea did so well. It's because they turned to their private industry immediately and started mass-producing diagnostic tests and scaled a level of testing that we would never achieve in the first six months of the crisis.

LT: Your example of South Korea, I found extraordinary that within one week they had approved tests, they had drive-through testing. The US still does not have massive community testing. Why is that?

SG: Well, I think right now we're in a much better place with respect to testing, but the nature of the testing has shifted. More of the testing is point of care. More of the testing is moving into the home. So you're seeing community-based testing sites, these mass testing sites, be reduced. You don't want a platform where people have to go to these mass testing sites in order to get a diagnostic test. You want it to be much more accessible to consumers. So right now, I think we have enough testing to keep up with the pandemic. It's just that we're not really measuring a lot of the testing that's getting done because more of it's not getting reported. A lot of the negative results are getting lost. So it's actually overstating probably the positivity because we're not capturing a lot of negative tests that are happening.

LT: Why isn't there testing, though, every time, for example, someone enters a building or enters a

subway system, just massive community testing in order to track and identify where cases are and how people are getting infected?

SG: Yeah, I think we could be doing much more community-based testing than we are. And the best example of that is the schools. If you look at the literature on what can be done to prevent outbreaks of COVID in schools, the two most impactful measures that people can take are to keep students in geographically contained social pods and also implement routine testing at school, ideally, twice a week, at least once a week. There is plenty of resources available to do testing in schools, yet you're still seeing most schools not implement routine testing as a way to identify cases and prevent outbreaks in the school setting. And also testing to keep students in the classroom. So the question is, Why aren't schools doing it? And the only answer I can arrive at is they don't want to deal with the complexity of turning over to positive cases. That if you end up putting a testing protocol in place, you're going to identify a symptomatic infection. Parents are going to get upset.

SG: So the complexity of the politics around testing is what's, I think, causing a lot of schools to be reluctant to do it. And I think the same thing is transferable to the workplaces. As it's become something a little bit more akin to the flu where it's an expectation of life that we are going to be at risk of this coronavirus in perpetuity, I think the idea of turning over cases in a workplace setting will lose some of the stigma, and maybe you'll see more businesses start to implement routine testing. The problem with doing it in something like a subway or a public venue is just the queueing up. It's hard often to operationalize that, but in an office setting or a school, those operational challenges go away, and I think it's more the policy challenges.

LT: The data and analytics in the United States seem to be lacking, in many cases. The US does not do much genomic sequencing, and there seems to be little, if any, data on hospitalized patients in terms of which vaccine they got, the length of time since vaccination, their age, their co-morbidities. Why does the US seem to have such little data and analytics around COVID?

SG: Yeah, we do a poor job of systematically collecting the kind of public health information that you need in a setting of a crisis. And I think this is another challenge associated with CDC. CDC is not in the business of producing real-time actionable information that informs current decision making. CDC is an agency, it's a high science organization with a very retrospective mindset. They do very exquisite analyses of outbreaks that have occurred and are in the business of providing the definitive answer. They're not in the business of providing a partial answer in a real-time basis. We don't have an agency like that. In the case of breakthrough infections, the data that the CDC's been relying on, are these so-called cohort studies where they have prospectively followed certain cohorts of people. These are groups of tens of thousands of people, not hundreds of thousands of people. So there's a cohort of nursing home patients, there's a cohort of essential workers, there's a cohort of health care workers. They've followed groups who are perceived to be at high risk of getting COVID or having a bad COVID outcome to see what their experience is over time, so it's very likely that there's a higher rate of prior COVID infection among these groups even before they got vaccinated.

SG: So this isn't a representative sample of the US population. This shouldn't be the data set that we're using to derive conclusions about the risk of breakthrough infections, yet that's what we're forced to rely on because that's what the CDC is collecting. We need a capacity to collect and disseminate much more real-time information, because the reality is policy makers are forced to make decisions in the moment. They need as much information as possible to inform those

decisions.

LT: And it seems like the other issue is that nobody reports to the CDC or the FDA, or the federal government. It's not as if any kind of state or city health officers report up on a federal level. What would effective leadership from the US government need to look like for a pandemic?

SG: That's right. States aren't forced to report information. There's arrangements that the CDC has with state public health authorities for gathering certain information, but a lot of this information, you shouldn't have to be dependent upon states to report it. The CDC should have had the ability to consolidate existing healthcare information to try to answer some of the questions like, How many people are being hospitalized every day for COVID? But instead they've relied on states to report these bespoke feeds separately from what states normally report to other kinds of databases. And so, they became dependent on the states. Well, this became a problem when the drug Remdesivir became available and suddenly you had a therapeutic that was in short supply that the government wanted to make available to hospitals that had hospitalized COVID patients. And what the people in the White House said, Deborah Birx said is, we can't ship a scarce drug to hypothetical patients derived off model. We need to know how many patients are in each hospital, and that's when they took away the function from CDC. They basically said, we can't rely on your data anymore. We're going to create a new system and we're actually going to get hospitals to report the number of hospitalizations they have every day.

SG: And the system got started. It had some kinks early on, but it ended up being the most reliable data set in the whole crisis. The people who did the COVID tracking project at the Atlantic, which was a great aggregation of data that was used by public health officials all across the world to gauge the epidemic in the US, when they concluded that project, they basically said that the data set that they came to rely on most was the hospital reporting data. It was the most reliable data. The CDC just didn't do it and then didn't want to move away from the system that they had. And so this is where the system needs to change. Just a whole orientation to how we collect and disseminate information needs to be handled differently.

LT: So if you were asked to design our health system to prepare for the next pandemic, from A to Z, what changes and what capabilities do you think that we need?

SG: It's a really big question. I'll touch on some of them. I think, first of all, COVID exposed how excessively vulnerable certain communities in our society are to disease and healthcare crises of any magnitude, but certainly of this magnitude. We saw that COVID hurt much worse certain communities than it hurt others. People from lower incomes who lived in crowded housing situations, who had multi-generational families, where if one person brought the virus home, the whole household was exposed to the virus. Older individuals who are excessively vulnerable. People who faced racial bias in the delivery of healthcare. And so we're going to need to address that. I think COVID has galvanized some level of public support and public recognition in a way that hopefully we will be addressing these issues going forward. The other thing we lacked is just the capacity to scale a response. We didn't have the resiliency we needed in the healthcare system. We didn't have the ability to mass produce diagnostic tests. We didn't think about building those capacities and creating that resiliency as a matter of our national security. That needs to change, as well.

LT: It seems like there need to be changes in leadership, that the CDC is not ideal to lead in a real-

life pandemic. It seems like there also need to be changes in infrastructure, hospital beds, you talked about equipment, maybe manufactured domestically, some of the biologics and other drugs.

SG: I think we had enough hospital capacity, or we have a lot of hospital capacity. It was clearly the healthcare system at points became a COVID-only healthcare system, and we could think differently about how we maintain certain residual capacities or require hospitals to maintain the capacity to surge their healthcare. But I think it's a question of having the planning in place to be able to quickly use the existing infrastructure in a surge capacity. New York did that very effectively. What New York achieved, I think, is going to be studied very closely. The fact that they were able to effectively turn their healthcare system into a COVID-only healthcare system and deliver crisis levels of care at the proportion that they did is phenomenal.

LT: How about global monitoring and cooperation? It seems like the world is not doing a very good job of that. What could we do differently or better to prepare for the next global health crisis?

SG: Well, I think we've relied for far too long on international conventions and the idea of building capacities in foreign nations that may be hot spots for emerging infections and just sort of coming together as a global community, holding hands and promising that we're going to share information in time of a crisis. And if you're a country that's host to an emerging infection, you're going to tell everyone and you're going to share the strains of the virus, so everyone can get a head start in developing therapeutics and vaccines. That doesn't work. We've seen time and again, and we saw in this case, that when other countries are host to emerging infections, they often times don't share that information in a very timely way. I think we're going to have to lean much more heavily on our foreign intelligence services to gather this information and make public health an explicit part of our national security preparedness and an explicit part of what the mission is of our foreign intelligence agencies. If anything, the behaviors in SARS-CoV-2 condition nations to be even less forthcoming, and that's going to make us even more dependent upon our foreign intelligence services.

LT: So interesting. I would not have thought that health would be a new area for our intelligence services. Scott, what are the three takeaways you'd like to leave the audience with?

SG: Well, I think we touched on a lot of them. The idea that we need to build better resiliency into our public health system. We can't just operate for maximal efficiency in terms of how we manufacture products, but also operate for some level of resiliency. The fact that we're going to need to look at public health preparedness through a lens of national security and get our foreign intelligence agencies more engaged in this public health mission. And then just the idea that CDC is a great organization, a high science organization, does exquisite analyses of outbreaks, but it's got a very retrospective mindset. We need an agency with a much more operational focus, with a fidelity towards real-time information gathering and information dissemination. And that can be CDC, but we're going to need to build it. We don't have it right now. I think that there was this perception that CDC had this, that they had the ball, they would be able to operationalize a national response to COVID. I think people had a misperception of what their capacities were, what their resources were, what their mission was. So we're going to need to build a much more operationally focused agency. And it's going to look something like the current CDC, married to a FEMA or married to something that looks more like the DOD, where you have an operational and national security aspect to the public health work.

LT: Thank you, Scott. This has been great. I really enjoyed your book, "Uncontrolled Spread."

SG: Thanks a lot. Thanks for having me.

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