Operation Warp Speed
What Happens Next – 08.13.2022

Paul Mango:

I wrote Warp Speed for two reasons. One is the whole effort occurred during a presidential election year. And I think the success of Operation Warp Speed got buried because the media was intently focused on the campaign. Anything that was going well maybe wasn't going to be talked about in the media, particularly if it was the incumbent president. The second reason was because there's a lot of lessons to be learned from what we did well and what we would do differently. It's important for government policy makers, for the American people, for private industry, to understand how this happened. The previous best time for bringing a vaccine to market was four and a half years. And the Operation Warp Speed did it in 10 months.

Why was it successful? Five reasons I talk about in the book. One is private industry had invested in technology called messenger RNA. It was a technology platform that had never been used to develop vaccines, but it was available to us and we took a shot at it. We invested a couple billion dollars in it and it worked. The second reason was that we had a principle that basically said, do not permit the federal government to do anything that the private sector can do better. That was a guiding principle for us. The third reason was we had secretary Alex Azar who was 10 years in the pharmaceutical industry before he was a secretary and he understood the risk thresholds and what the pharmaceutical industry would do and would not do.

And he understood that they wouldn't start manufacturing vaccines in a normal course if they didn't get FDA approval. So we did in parallel things that were typically done in series, and we started manufacturing vaccines long before the FDA approved anything.

The fourth reason was Moncef Slaoui, who was our chief scientific advisor had a venture capital mindset. He said, we're going to invest in six different vaccines across three different technology platforms. We only need one to win.

The very last reason was just a management philosophy that permitted experts rather than people with lofty titles, to do what was necessary to get the job done.

What would we have done differently if we could do it over again? I think we failed pretty miserably at communicating with the American people about how safe and effective these vaccines were.

And we were in a very difficult situation because if we started talking about safe and effective vaccines before the FDA adjudicated it, we would've been accused of trying to unduly influence the regulators. So, we didn't talk much about it, but what we could have talked about was the standards we raised for these clinical trials -- 50% more participants in these trials than in a typical vaccine clinical trial and a longer interval between the time people got their injections and the time we evaluated them for any type of adverse reaction. So, these were actually higher standards than was ever used before. So those were things we would do differently, lessons for why we were successful, and why I wrote the book in the first place.

Larry Bernstein:

Let’s go over the venture capital mindset. It's very rare that the government officials think like venture capitalists or apply portfolio diversification to solve public health problems. Tell us more about the venture capital mindset?

Paul Mango:

Steve Mnuchin, who was the Secretary of the Treasury at the time, came over and spoke to Secretary Azar and me and a number of individuals in HHS. And he said, every day the economy's running at half speed, I lose $6-7 billion of tax revenue. Whatever it takes to get these vaccines out as quickly as possible, my guess is it'll be worth it. We're also saving lives.

We brought in private sector leaders to become part of Operation Warp Speed. And Moncef Slaoui was the most successful vaccine developer of our generation. People never had heard of him, but he had put 14 successful vaccines into the market. And he understood our mission, which was to have at least one safe and effective vaccine manufactured at scale before the end of 2020. He was the one who thought through the need to really diversify our risks. There were some folks who wanted to stick with the tried-and-true technologies that we had used to develop vaccines in the past. But Moncef had come from Moderna, and he knew that they had mRNA technology that could be successful. He set it up in a way where we had three different technology platforms with two vaccine candidates in each one. He had to fight against the traditionalists. It worked. We had three successful vaccines across two platforms.

We took a little bit of a trust but verify approach to Moncef. After he chose the six vaccines, we went out and spoke to a number of experts, both on the Operation Warp Speed team and beyond, and asked them independently what they thought the probabilities were. And we conducted this pretty complicated cumulative probability analysis. And when it came back, the numbers were that we had a 75% chance of having at least one of those six safe and effective manufactured at scale, and a 32% chance of having two or more and less than 10% chance of having three or more.

Larry Bernstein:

Why limit yourself at six vaccine choices? Why limit yourself to three platforms? Why not do 20 different strategies and get the likelihood of success up to 90%?

Paul Mango:

A lot of external experts asked us the same question. But the answer is very simple and very compelling. It was about the logistics, the logistics of manufacturing, the logistics of getting a minimum of 30,000 persons through each clinical trial, the logistics of acquiring syringes and needles to administer the vaccines and the complexity of the logistics goes up exponentially with every additional candidate. So I'll give you an example, even among the six that we had think about this logistically, they had different intervals between shot one and shot two. They took different size syringes. And remember we were in the midst of a global pandemic where everyone else in the world was looking for raw materials, was looking for syringes, was looking for needles. And by the way, every clinical trial site could only handle one vaccine type. And we made that decision because again, the complexity at the local level of trying to administer in a clinical trial, multiple vaccine types, we thought was going to compromise the data. So that's the reason we stuck with six, but we contemplated a seventh one. And when we ran through the numbers, the probability we'd have at least one good vaccine before year end was 75% adding a seventh one, took it up only to about 77.5%. Each additional vaccine candidate, if it only adds a couple hundred basis points, but it adds tremendous complexity, we thought that was not a good trade off.

The money wasn't the rate limiting factor at all. It was the logistical complexity. CVS hired 25,000 vaccinators in late 2020 and had to train them all. And they had to train them all in the different types of vaccine candidates that we had because we didn't know which one was going to be a winner. FedEx took every one of its ground drivers and retrained them on how to handle minus 80 degrees Celsius. It was a keen sense of how this would have to play out across tens of thousands of workers and eventually millions of Americans.

Larry Bernstein:

The first dose does a world of good in terms of reducing risk of hospitalization. And the second dose gives some incremental benefit. At the outset when there was limited vaccine supply, why not try to get as much single dose out to the public, and do the second doses when it was more widely available?

Paul Mango:

You're exactly right. But we didn't know what you just described when we were going through the clinical trials. The 95% effectiveness that came out of the phase three clinical trials were all based on two doses. I think where there could have been room for criticism, people have proven that three weeks was not long enough interval for the second dose to have as much impact as it should have. Maybe optimally, you give the first dose and then three months later, you give the second dose. I think there's a lot of legitimacy to that. We wanted to get through the clinical trials quickly. If you had a three-month interval between dose one and dose two, then it would've been much more difficult to get through the clinical trials in time.

Larry Bernstein:

Why did you decide that you had to live by the clinical trial results in the real world given the death rates and the efficacy of a single dose?

Paul Mango:

Because the FDA had laid out those standards by which they would conduct an accelerated evaluation. Peter Marks is the head of the what's called the center for biomedical evaluation and research, which is the center within the FDA that evaluates the clinical trials and eventually grants an emergency use authorization or full approval. Peter was absolutely committed to making sure not a single quality standard was compromised. The minimum effectiveness by which they would've granted an emergency use authorization was 50%. The vaccines wound up significantly higher than that. But my point is a typical timeframe to evaluate a vaccine could be easily three to six months at the FDA. So, the process of evaluation was transformed. The standards of evaluation weren't diminished.

Larry Bernstein:

Let's imagine I made you the President of a Central American country like Panama. Pfizer says I can give you a million doses. So, you're not constrained by the FDA. It's October 15, 2020, you got a million doses. What do you do?

Paul Mango:

I would not use them. This virus, despite its destructiveness, the case fatality rate is about 0.3%. Okay. 0.3%. If you're going to be vaccinating 280 million Americans, the vast majority of whom are very healthy, you better be sure that vaccine doesn't have anything wrong with it. So, if you think about the risk return ratio here, if there was something wrong with that vaccine that could have been revealed in the last couple of weeks of the trial, and you had gone ahead and given it to millions of healthy individuals, you would've done more harm than good.

We had a totally different perspective for therapeutics. If you have COVID and you can't breathe and you're lying in a hospital bed, and there's something, maybe it's not perfect, maybe there's the safety profile isn't great, but the benefits could be there. Let's do it. That person has a higher probability of

dying if you don't than if you do. That's not the same with vaccines where you're giving it to literally hundreds of millions of healthy individuals.

Larry Bernstein:

Next hypothetical, let's take a healthy person, we give them the vaccine and then we inject COVID into their body to see if the vaccine works. This would clearly speed up the efficacy evaluation, because we don't have to worry about whether the patient was exposed to the virus. We know he did. So the sample size can be much smaller. We've guaranteed it.

We really are putting them at risk, but there are great scientific and public health benefits associated with it. And if we were able to the find volunteers who would be willing to do this for society and for potentially themselves, why not on an expected value basis potentially save millions of lives?

Paul Mango:

You still don't create a safety profile. You would maybe answer the question about effectiveness, but you would not have answered the question about safety. I'll give you an example. The FDA normally requires 20,000 persons going through these clinical trials. Because of the accelerated timeframe, the FDA wanted to be absolutely sure we were creating a safety profile and they said a minimum of 30,000 in each trial. And that wasn't for effectiveness that was for principally for safety.

Larry Bernstein:

We have two questions. One is, does the vaccine prevent serious COVID and number two, does the vaccine hurt you?

Paul Mango:

That's effectiveness and safety.

Larry Bernstein:

Why not first focus on effectiveness with human trials and then safety? Why not that order.

Paul Mango:

There were two other considerations as to why we didn't do that. There weren't that many doses available on October 1st or October 15th. Okay. So even if we had proven it, maybe there were a million or 2 million doses available, but not 20 million as we eventually had. The second reason is right up until the last couple of days, we were racing to develop an information technology system that could even track the distribution of these doses. So, we didn't even have a system to track distribution, equitable distribution, which you can imagine would be a big topic politically until about four days before we released the vaccines.

Larry Bernstein:

Was it a mistake to prioritize certain individuals for vaccination? Should we have just done first come first serve?

Paul Mango:

What we did was we eventually came down on a very simple principle. We'll allocate to the public health jurisdictions -- there's actually 64 public health jurisdictions -- on the basis of per capita. Why was

that decision made? I use a term in the book about the federal government. Never let your reach exceed your grasp. We didn't want to assume what the highest priority would be in California versus Oregon versus Florida versus Texas. We wanted the local leaders to determine what their priorities were based on vulnerability -- how many people were in nursing homes in that state, maybe based on wanting to get the kids back to school. We weren't going to impose our will on their prioritization of distribution. And therefore, we said the best way to do this is on a per capita basis.

Now to your point about first come first serve. On January 12th, 2021, eight days before we left, when we were looking at the data, and this was only a couple weeks into distribution, some jurisdictions had used 80% of every dose we distributed. Some had only used 30%. So, Alex Azar and Bob Redfield head of the CDC had a press conference and said, hence fourth, if have not used the equivalent of your previous week's distribution allocation, we're going to take your subsequent weeks' allocation and we're going to give the rest to those who are consuming more. Boy, did those numbers go up after that. The states started reporting their data much more quickly and much more accurately.

Larry Bernstein:

I want to discuss the terminology for the success of the vaccines. You mention that the Moderna vaccine was 95% efficacious. Which means in this context that patients who use that vaccine have a 95% chance of not being hospitalized with COVID. This has nothing to do whether the vaccine can prevent you from getting sick from COVID.

I think that definition is different and created confusion. When we look at a typical flu vaccine, what we notice is it's 55% efficacious.

We had Ofer Levy on a previous episode of this podcast. Ofer told us that the typical flu vaccine is like 75% efficacious for kids and only 35% for 65 and older. You shoot that vaccine into a kid; the immune system response is incredible. And you stick it to an old guy and nothing happens.

Now, when you say the flu vaccine is 55% efficacious for the flu, we normally say that means that there's a 55% chance that you do not get sick from the flu. We don't say it's a 55% chance of not being hospitalized from the flu.

You talk about 95% efficacious for, let's say the Pfizer vaccine, you didn't say there's not a 95% that you don't get COVID, but merely that it's 95% chance that you don't get hospitalized from COVID. And I think there was a lot of confusion when all of a sudden you take the vaccine and then you get COVID.

Why did you define it differently in the flu case versus COVID and why was there public confusion over that efficacious definition?

Paul Mango:

I'll answer the second part first. It was very poorly communicated. The formal scientific term is what is the primary endpoint of the clinical trial. For COVID vaccines, the primary endpoint was not infection. It was serious illness, hospitalization or death. The intent of the clinical trials was never to evaluate whether or not the vaccine would prevent infection. It was the latter which you described, which is principally, would it prevent hospitalization, certainly serious illness, hospitalization, or death. Why that wasn't communicated that way? I'm not really sure, but from a public health perspective, it makes a big difference because people thought that, if I'm vaccinated, I can't transmit this virus.

Well, that was never true. That was never evaluated to be true or not. I think part of the reason we didn't evaluate it that way, if I had to speculate just a bit is, the logistics of the clinical trials would've been very difficult. We knew this virus could transmit asymptomatically and we knew that you could be infected and have zero symptoms. So, it would've been almost a constant daily monitoring for six or

eight weeks of everyone in a clinical trial, which I think just would've been overwhelming. That's why it's much easier to monitor serious illness, hospitalization, and death.

Larry Bernstein:

In your book you describe the public/private relationship between the government and the vaccine manufacturers.

In particular, you describe Pfizer's unwillingness to play by the HHS rules. Why was Pfizer being difficult and were there negative ramifications from their intransigence?

Paul Mango:

The vast majority of the private sector mobilized in an extraordinarily patriotic and committed way. I'm sure many of those companies lost money on their participation. People ask me if I'm worried if any of them did make a profit. And I said, I hope they did. Their efforts were absolutely extraordinary. And I'll say the same thing about Pfizer, despite our challenges with Pfizer, what they delivered to the American people was spectacular. The difference is though between let's say a Pfizer and a Moderna or Johnson and Johnson were pretty profound in terms of how they collaborated with us.

The NIH, the National institute of Health, wanted a common data and safety monitoring board for every clinical trial. Why? Well, because there was an opportunity to exchange some practices and learnings across the trials. A data and safety monitoring board is an independent body that looks at the data before it goes to the FDA and says, we have enough data now in terms of positive cases or whatever, to take the information to the FDA. Pfizer is the only one who had its own DSMB. They didn't want to collaborate. "Oh, the government will slow us down."

The second and more serious issue was Carlo de Notaristefani, who was our manufacturing expert, 35 years in pharmaceutical manufacturing, developed this program called persons and plants.

And what Carlo did was form multidisciplinary government teams to go out into each of these facilities every day, such that if they encountered any problem whatsoever -- I need an electrician. I need raw materials. I need equipment flown in from Germany -- boom, they would communicate back to DC. We'd mobilize the resources. We'd used a Defense Production Act, whatever we needed to do, we'd get it done. Pfizer gave us the stiff arm. They didn't want us in their plant. They didn't want our help.

And we expected 40 million doses. What we got was 18 million doses. It hurt us two ways. One is every governor in the country and every public health jurisdiction was asking us in September and October, how many doses will we have? And we assumed right up until the last minute that we'd have 20 million from Pfizer in November and 20 million in December, because that's what they told us they would have. And we didn't have any line of sight into what was really happening in their plants. So, when they kind of pulled the rug out from underneath our feet in November and said, we don't have any in November. We hope to get you 20 in December. That really hurt the planning process.

And then second it hurt poor General Perna. He's out there telling the states, this is what we're going to give you. And then he had to say, we can't give you that because Pfizer didn't deliver what they said they were going to deliver.

And what happened is in the late fall of 2020, Moderna had received a Defense Production Act title three priority contract, which meant the following: any supplies they needed from any supplier in the country would have to put Moderna first, before they delivered anything to anyone else, or the government could literally confiscate that factory and operate it itself.

So, what happened in the late fall was, Pfizer was running into trouble getting raw materials because guess who was getting them all: Moderna, because they had the title three priority. Why didn't Pfizer

have a title three priority? Because when you grant a title three defense production act authority, it is intervening in a supply chain. It is basically disrupting commercial contracts that already exist. And in return for that, the government expects you as a manufacturer. Who's asking for that priority to provide information precisely what do you need from whom, and what quantity, and how are you going to use it? And by the way, all of what you produce with this DPA defense production act title three priority has to be used in the United States unless you get a presidential waiver. Pfizer did not want to comply with the requirements necessary to get a priority rating.

As the raw material started to dry up for them because Moderna did get the priority in the late fall of 2020, they said, we cry uncle. We want our DPA title three authority and we'll let you see all of what we're doing with it and we'll report all this data. Remember we had already given them a $2 billion advanced purchase contract. We acquired all of the needles and all of the syringes for them. We set up 70,000 distribution sites for them. We even acquired the dry ice necessary to ship their doses. Pfizer likes to say, we didn't participate in warp speed. Well, you participated in almost every other aspect other than having us manufacture the doses or having people in your plants.

It just left a bad taste in our mouth about what were their motives and why were they doing this. And remember they were in a race with Moderna. The first company to have a vaccine, the brand elevation associated with that was fantastic. Right. The whole world knew it. Every other company with whom we dealt was so cooperative, so patriotic and Pfizer stood out as an exception to that.

Larry Bernstein:

Incredibly, the Federal Government funded the manufacturing of vaccines before they knew it worked. You didn't wait for the clinical trial results. It was all about speed of execution. By manufacturing in advance, you could save lives by coming to market faster. What happened?

Paul Mango:

Yeah, that's a hundred percent attributed to Secretary Alex Azar who spent 10 years at Eli Lilly before he became the Secretary, understood what risks the pharmaceutical industry would take independently and which ones the federal government needed to assume. And the benefits that we talked about $6 to $7 billion, a day of federal tax revenue, of saving American lives, the vast majority of those benefits accrue to the government, to society, to us, not to the manufacturer. So, it made a lot of economic sense for us to assume that risk. But if we're ever going to get millions of vaccines into American arms before year end, we have to start manufacturing right away. The other benefit it produced a sense of urgency to get the syringes and needles before the rest of the world was even thinking about that.

Larry Bernstein:

In your book, you mention the anti-trust concerns related to pharmaceutical firms collaborating and sharing information, techniques, methods, et cetera, and you made an exception because of the public health crisis. You weighed two different public interests: competition benefits versus saving lives now.

Paul Mango:

The Department of Justice would not permit sharing pricing information. The primary concern is higher prices. The DOJ appropriately said, even during this public health, there was no need to transmit prices or contractual arrangements. The primary reason we wanted it is because there were some pharmaceutical companies that could liberate capacity to manufacture vaccines, but weren't manufacturing them themselves. Merck tried to develop a vaccine. It failed, they pulled out, but they had manufacturing capacity available. We wanted Merck to manufacture vaccines for Johnson and

Johnson, but in order to do so, JNJ had to hand over all of its recipes to Merck. In a normal course of action someone could have accused them of an antitrust violation, but the DOJ addressed that.

Larry Bernstein:

What policies did the rest of the world adopt for vaccine research, development, and manufacturing that differed from the US approach. What worked and what failed?

Paul Mango:

The Department of Health and Human Services is linked in globally to a lot of public health agencies. So, we had some insight into what was going on for China and for Russia. They wanted to win the race so that they could exercise what we call vaccine diplomacy. China had a Sinovac vaccine. The Russian one was called Sputnik V, the V is for vaccine. They wanted to get theirs done and then distribute to the world in a way that they could generate friends and potentially allies. interestingly, the Sinovac vaccine when it was approved by the World Health Organization had a minimum standard for effectiveness globally was 50%. The Sinovac vaccine came at 50.4%. So that raised a lot of suspicion and other countries wound up saying, that's probably not for us, same with the Russian vaccine. They never had any transparency about the quality of it. So those two fell apart when manufacturing started ramping up for Pfizer, Moderna.

Larry Bernstein:

Let's focus on the EU. This is a region that has a population, wealth, and scientific literacy similar to the US. The EU used a different regulatory regime and incentives to discover and manufacture vaccines. How did the EU approach compare with the American Operation Warp Speed and what were their results?

Paul Mango:

The UK was probably the most successful with AstraZeneca, and early on we made a big investment in AstraZeneca. That was our first investment in the early summer of 2020. The UK approved the AstraZeneca vaccine and they're still using it. And that became the primary export vaccine into continental Europe as well. AstraZeneca's a British firm. The AstraZeneca vaccine in the course of their clinical trial, which is a big no-no, they changed the dose rate in the middle of the trial without asking the FDA.

The FDA denied emergency use authorization to AstraZeneca. But maybe their trial submission data was better in the UK. AstraZeneca in the UK and Oxford is a real success story. India wound up doing a lot of contract manufacturing, so that expanded the capacity of vaccines available.

But there was nothing like warp speed in terms of government, public-private partnership, multiple vaccine candidates. European governments were pretty severely criticized by their own populations for not having done something faster.

Larry Bernstein:

The American government has a responsibility to save American lives. But we also have a desire to help mankind. Could we have done more to manufacture vaccines in India as an example? When we started production of the Moderna vaccine in March 2020, could we have done the same in India, maybe at our expense, as a gift to the world?

Paul Mango:

The Defense production act and the ability to acquire the raw materials with the exception of a few reciprocal agreements with Canada does not extend beyond our shores. Pfizer, Moderna, Johnson and Johnson, AstraZeneca had contracts for like 3 billion doses of vaccines were going to be manufactured outside the United States, under licensing agreements from those manufacturers. We encouraged that the pandemic readiness and emergency preparedness act and what it does is in the time of a national emergency, indemnifies them against any future lawsuits. So, if there were a safety issue after the FDA granted an emergency use authorization and someone died because of the vaccine injection, not because of COVID, but because of the vaccine, they cannot sue Pfizer or Moderna under this PREP Act. What they really wanted was the liability protection and that's what the PREP Act gives them. However, we cannot extend that to a foreign country that may also have made some of the manufacturers reluctant to engage India if they didn't have that type of protection.

Larry Bernstein:

Vaccine hesitancy is the next topic. I was hospitalized with COVID for 10 days in December 2020 in Miami Beach. At that time the vaccine had just become available to hospital workers but not to the public. I asked the nursing staff who worked in the COVID ward if they were getting vaccinated and they said, no. I asked the physicians and they said, yes.

What do you make of the nurse's vaccine hesitancy?

Paul Mango:

This was one of the more perplexing things that public health leaders encountered when we started distributing vaccines because most of those jurisdiction leaders prioritized their frontline healthcare workers. In the first three weeks, 30% of those workers did not want the vaccine, which created a real problem for us because once you opened the box that was stored at minus 80 degrees Celsius of vaccine doses, you only had 10 days to use them. So, if some big hospital found out four days into it, oh my gosh, we ordered 5,000, but only 3,500 of our employees want this, it was very difficult to get rid of those other 1500.

Some hospitals began calling the community come on in and get vaccinated, even though you're not a frontline healthcare worker. Let me give you maybe a speculative reason. 20 million healthcare workers in the country, fewer than 200,000 of them actually had contracted COVID. They were the ones who had the most exposure, but they had less than 1% infection rate.

The short answer to that is they were extremely well protected. They had N 95 masks, they had goggles, they had everything. They had a real sense of security. It wasn't like they were dropping like flies because they were getting infected. And they're the ones who were working with all the COVID patients. They represent the American people, which is still 25% are hesitant to get the vaccines. Hopefully we can figure out how to deal with this a little bit more effectively next time around.

Larry Bernstein:

Paul, you ran for a Governor of Pennsylvania a few years ago. Imagine that you had won that election and you were in charge of this decision in your state. You had data that healthcare workers were not getting sick, that the face masks were protecting them. Why not do first come, first serve. It is a logistical nightmare to get the vaccines to specific populations. I'll see you at Veterans Stadium in Philadelphia parking lots. We're going 24-7. Let's go.

Paul Mango:

I would not have done that even though that is appealing for many reasons. One is the impact of COVID on individuals was tremendously asymmetric. A Stanford varsity athlete has a 0.0001 chance of being hospitalized if they get COVID. But if you're a 75-year-old in a nursing home that might be a 70% chance of being hospitalized. I'd want to at least offer the limited vaccine supply to those who are most vulnerable first.

The second argument is one around accessibility. Not everyone has a car to get to the Veterans Stadium. And we were hypersensitive to underserved populations who may not have access driving down to the stadium. You can't get out of your nursing home bed to go to the stadium. There was 2 million Americans in nursing home beds. We engaged companies to offer vaccines to every one of those citizens lying in those beds and the follow up second dose. And that was a very, very successful program.

Scott Atlas was seriously criticized for this and the Great Barrington group, but if you look at it two and a half years into this, they were a hundred percent right. Which is why didn't we just put all our resources protecting the most vulnerable, because for the vast majority of Americans, this is not really much more serious than the flu. And for some Americans, it's deadly. If I were the Governor of Pennsylvania, I would've focused on the most vulnerable first, given them the option. And, I never would've forced them to take it if they chose not to take it.

Larry Bernstein:

You mentioned probabilistic chance of hospitalization for the Stanford athlete, but you didn't multiply it times the number of life years saved. How should public health officials think about that? The nursing home patient may only have a year of expected remaining life while the Stanford athlete has 60 years. Should we consider that in the calculus?

Paul Mango:

The UK and the National Institute for Clinical Effectiveness talk about exactly this quality-of-life years. I don't think it's the ethos of the United States. The ethos of American medicine is heroic intervention. Do what you absolutely have to do to save a life, whether that's an 85-year-old or a six-month-old. It’s not the culture of American medicine to sacrifice some who just don't have as many years left.

Larry Bernstein:

Let me push back with three examples: the ER, the battlefield and the legal system. The ER uses triage to decide where to employ resources. If they have the 96-year-old woman and the seven-year-old boy, they're going to choose the seven-year-old boy because they make that calculus. And the similar arguments will be made on the battlefield. This guy's not going to make it, let's focus on the guy who can make it, injured on that battlefield. In the legal situation, there's a car crash and someone is culpable for that. When calculating damages, we look at the number of expected years left. Damage claims incorporate that idea.

Paul Mango:

Certainly, for insurance claims, you're absolutely right. The emergency room ethos is similar to the battlefield one, which is we triage on the basis of the probability that this person's going to make it. I don't necessarily think they do it based on age. I think they do it on a clinical basis, what is the probability that if I intervene, it's going to help this person versus this other person. And I only have limited resources. I think the American people have an expectation that why should we ever have to make those trade-offs? Aren't we the wealthiest country in the world? Why can't we do this? So, I think that's the underlying piece that makes it difficult for us as opposed to the UK, which formed the national

health system on the basis of social equity, not heroic intervention, that that's why they formed the national health system.

Larry Bernstein:

The vaccine became a hot political issue from both parties. Biden, Harris and Cuomo attacked the Trump Administration and its vaccine efforts. And there was significant Republican voter vaccine hesitancy once Biden became president. How did politics play into vaccine hesitancy?

Paul Mango:

Governor Cuomo when he said he was going to set up his own equivalent of an FDA within the state, so that even after the Food and Drug Administration, granted an emergency use authorization, he wasn't going to permit New Yorkers to get that until they made their own determination. And we said, well, that's fine. We'll just reallocate your doses the first week until you guys' figure that out. And he dropped that. It had to be politically motivated. It was obviously a shot at the administration, when you had Biden and Harris saying they'd never trust a Trump vaccine. And then the following Spring, they're scratching their head and saying, why are Americans hesitant to get the vaccine, well, look in the mirror, that's part of it, right?

Larry Bernstein:

What is your view on transparency for clinical trial results in real-time? We could have shared all the information with the public so that they could make decisions about schooling, employment, or future income, and companies didn't know how to plan for supplies, hiring, or new business. The public was left in the dark. Why not open the kimono?

Paul Mango:

Publicly traded companies themselves have the full right to reveal that information. I talk in the book about the CEO of Pfizer coming out in late September and saying, our internal models tell us we're going to have really good data before the end of October as government officials, we were absolutely prohibited from revealing what they call market moving information. Now we had that data internally, but to reveal that would've been market moving information and ethically we can't.

Larry Bernstein:

Why not for public interest's sake demand that the information be released after the market closed under an executive order?

Paul Mango:

The data and safety monitoring board are the first one that knows. The company knows how many positive cases there are. The DSMB could not reveal any data until they got the 32 positive cases. The DSMB could say the 32 cases are ambiguous, keep on going. The DSMB could say, wow, all 32 cases are in the placebo group. This looks like a really good vaccine. Let's go to the FDA. Or they could say all 32 cases are in the vaccinated group. Let's shut this trial down. The company does not even know on a daily basis what the status is of their vaccine efficacy. It's only when the DSMB releases it and that's important because that's an independent body that the company can't manipulate anything in the midst of the trial until an independent body says it's time to release the data. Maybe we should have relooked at that in the context of the pandemic. But I think all of that is in the spirit of safety and effectiveness.

Larry Bernstein:

New topic: kids. Why were the kids' studies so delayed?

Paul Mango:

My understanding is that sequence, adults and children is precisely the sequence that is followed for virtually every vaccine. The second reason kids' mortality was relatively negligible.

Larry Bernstein:

So, if you think that if the kids had been at risk, they would've changed the process?

Paul Mango:

Absolutely. Absolutely.

Larry Bernstein:

In your book, you mention that you went to great lengths to have the clinical trials match the American population with minority representation. Why was this so important?

Paul Mango:

Two reasons why we were insistent. One is different races have different reactions, it could be safety, it could be effectiveness, but I think the larger reason was one around vaccine hesitancy. A lot of minority populations are hesitant to take vaccines in the first place. And if they found out that there, they weren't even represented in the clinical trials, we thought they would be even more hesitant.

Larry Bernstein:

It's a wonderful objective, but were there cost and consequences? Did it slow down the timing of the clinical trials? Did it add to the logistical complexity and cut down the number of trials that were done?

Paul Mango:

It might have slowed down the Moderna trial a couple weeks, but we felt the trade-off of the integrity of the study of representing American Indian, Asian, Hispanic, African American was very important. It was just one of those tradeoffs we made.

Larry Bernstein:

I end each episode on a note of optimism, Paul, what are you optimistic about lessons learned from Operation Warp Speed?

Paul Mango:

I'm very optimistic that the federal government and America's private sector have the ability and the innovative spirit to respond. No one else in the world could do what we did in such a short period of time. And despite all the political divisions, the result was spectacular. I'm extraordinarily optimistic about what the average American can do when challenged. The America I saw was very patriotic, committed, capable, innovative, entrepreneurial, and caring.

Listeners, if they get a chance to read the book will understand, this is an uplifting story about American exceptionalism.