

Pandemic and Seasonal Influenza Vaccine Preparedness and Response: Harnessing Lessons from the Efforts to Mitigate the COVID-19 Pandemic – Report Release Webinar Perfected Transcript

WELCOMING REMARKS

DANA KORSEN

Good morning, everyone, I'm Dana Korsen, the director of media relations at the National Academies of Sciences, Engineering and Medicine. Thank you for joining us this morning for part one of today's public briefing on four reports that were released yesterday as part of the National Academy of Medicine's Advancing Pandemic and Seasonal Influenza Vaccine Preparedness and Response Initiative. If you haven't already, you may download copies of these reports and other supporting materials on the same page that you are viewing this webcast right now. Next slide, please. Those are the links as well now on your screen. For those of you not familiar with the National Academies study process, for each requested study, committee members are chosen for their expertise and experience and serve pro-bono to carry out the studies statement of task. The reports that result from the study represent the consensus view of the committee and must undergo external peer review before they are released, as did these four reports.

I'll now turn it over to Victor Dzau, president of the National Academy of Medicine, to kick us off this morning.

VICTOR DZAU

Thank you, Dana. I'm so pleased to open the public record briefings for this NAM initiative on pandemic and seasonal influenza vaccine preparedness and response. It's a monumental effort to deliver four timely and important concern studies at the same time, that's going to be discussed today. So, now I appreciate our close relationship with constructive partnership with the Office of Global Affairs at Health and Human Services on this very important critical work. I particularly like to thank Larry Kerr, director of the Office of Pandemic and Emerging Threats. Colin Weinberger, senior adviser and team lead for Influenza and Pandemic Preparedness. And Seth Ferrell and Adam Aasen, the senior global health officers. Of course, I'd like to acknowledge the star (UNKNOWN) and her team for outstanding work, they spend long hours tackling this topic, and we see that effort is reflected in these reports. So, by way of background, I can tell you that in July 2020, Larry Kerr contacted me and she said I have an important opportunity for NAM, to distill lessons learned from COVID 19 that can be critical advancing future influenza preparedness efforts.

Because she pointed out that we're not adequately prepared for a noble pandemic influenza strain. And also we must start implementing the lessons learned from COVID 19. And he's so right. So, because the initiative is timely because the world is focused on combating COVID 19 pandemic, seasonal and pandemic influenza remain an imminent global threat. We've seen how viruses such as SARS-CoV-2 have potential to disrupt the world and the importance of global preparedness response and the willingness to apply rapidly these capabilities to counter new measures. So, seasonal pandemic influenza remain an imminent global threat. Now, COVID 19 has enabled the emergence of new capabilities, technologies, collaboration, policy that can also be deployed before and during the next influenza pandemic. Lots of lessons learned. So, these four reports were developed with that purpose in mind. The underscore that preparedness has to be an ongoing commitment. It can be a year to year, a crisis to crisis.

As we learn from COVID 19 experience, surveillance, supply chain research infrastructure must be well resourced before and not in the midst of the next pandemic. So, given the global nature of this issue, we agree that this work should be international and complementary to the WHO influenza effort. With this background, we (INAUDIBLE) committee, range expertise and global public health from all sectors government, academia, industry, civil society and international public health organizations. Now, show the next slide, please. So, the committee. First, I'd like to thank the committee for their remarkable ability to assess fast changing landscape and identify advise on critical issues that require further study. That's capture the statement of task. The statement of task were useful for academy studies, we will review today. And the main recommendations, improve the global design, composition, clinical trials, production, scale up, regulatory approval, distribution of vaccines and post-approval surveillance, and we couldn't have done with those committee.

You see the names on it, and I want to thank them profusely. Next slide? So, this slide will show you the four concerns that are being released today. One is vaccine research, development to advanced pandemic and seasonal influenza preparedness response lessons learnt from COVID 19. Second, is the global resilient supply chains for seasonal and pandemic influenza vaccines. Third, is public health lessons for non-vaccine influenza interventions. Looking past COVID 19 and fourth is countering, the pandemic's threat through global coordination on vaccines. The influenza Imperative. I know the sequence of slides is different from what I'm reading, but you got all of them. I do want to thank the chairs of each concerned study for the Committee for incredible hard work to produce such impressive and comprehensive report, (INAUDIBLE) short timelines. They are Peter Sands and Devi Sridhar, Alexander Patron and Patricia Garcia, Ravi, Anupindi and Prashant Yadav and Enrequita Bond and Kanta Subbarao.

The chairs of this concerned committee are here with me today and they'll discuss the finalized report recommendation, answer any questions that you have. Again, thank you all of you for joining us. And (INAUDIBLE) you know time to this very important work. Thank you. Now, it's my great pleasure to introduce Loyce Pace. She is the director of the Office of Global Affairs, OGA and Department of Health and Human Services, HHS. In her current role, Loyce is responsible for advancing the US international health agenda through multilateral and bilateral forums. She reports directly to secretary of HHS and she is the Office of Global Affairs lead on setting priorities and policies that promote American public health agencies interest worldwide. Loyce overseas HHS engagement with foreign governments and international institutions, as well as policy making bodies such as the G7, G20, the United Nations General Assembly and the World Health Assembly. Previously, she served as president and executive director of the Global Health Council and was a member of Biden-Harris Transition COVID 19 Advisory Board.

Part of her role, at global health council, Loyce spent a decade working with community based organizations in grassroots leaders in countries across Africa and Asia on campaigns calling for person centered asset to help. She's passionate about equity and inclusion. Loyce, thank you for your support. Thank you for joining us today. And thank you to OGA for supporting this work. Over to you.

LOYCE PACE

Well, good morning, everyone and thank you for having me join you. I want to thank Victor for your kind introduction and offer my congratulations to you and the staff at the National Academies for the incredible work put into these recommendations. Congrats on the release today. We realize it was a

very tight timeline. I also want to thank the many public health experts from around the world who contributed to the recommendations, recognizing that many of you were doing so in the midst of your own COVID-19 responses. So, the fact that you were able to dedicate considerable time given how overbooked you all truly are is something that shouldn't go unrecognized. So, I want to appreciate the time, expertise and thoughtful insight that you shared especially as we think of global preparedness for influenza and other respiratory disease pandemics. We know that influenza in particular remains a threat, and even though we saw a historic decrease in these cases during the COVID-19 pandemic. So far, this disease will likely be what we face in another pandemic.

And so we feel like we're at a pretty unique moment in our history right now, especially those of us who in public health. We want to really step back and understand everything that we've lost, but also everything that we've learned throughout this pandemic so far. And take a step back and understand, OK, well, what can we do with these And what what should we or how should we be doing these innovations at these innovations, interventions that clearly have something to teach us real time. And so even though we're still in the midst of our response to COVID-19, we recognize the importance of documenting and understanding the very real successes and challenges over the past couple of years that help us understand how to overcome those shortfalls. So, our Office of Global Affairs at the Department of Health and Human Services here in the US approached the National Academies to sponsor the pandemic and seasonal influenza vaccine preparedness and response. And specifically harnessing lessons from efforts to mitigate the COVID 19 pandemic.

And that's the formal title of this initiative, of recognizing that's been broken up into a few different parts. But we initially approach the academies to focus primarily on vaccines. However, we recognize that this can be applied across a spectrum of response areas, whether that's non-pharmaceutical interventions, supply chains or broader R and D. Again, I just wanna highlight the timeliness of all of this coming forth today, recognizing that we're still having conversations about persistent inequities across access to diagnostics, therapeutics, supplies as well as vaccines. And of course, in addition to everything that you all will be discussing today around these reports, we had OGA and the Department of Health and Human Services are also having some of these conversations in other forums and critically focused on how we close the equity gap in particular with regards to access to innovations. We're also having broader conversations about the global health security architecture and specifically how the world prepares not only response to a pandemic so that we do have a high degree of readiness and again incorporate these various lessons learned.

COUNTERING THE PANDEMIC THREAT THROUGH GLOBAL COORDINATION ON VACCINES: THE INFLUENZA IMPERATIVE

DEVI SRIDHAR

Hi, good morning, everyone. I'm going to be talking through the report on the coordination side of vaccines, and I'm fortunate today that we get to Q&A, several of the other commission members are available as well to take questions on the complexity of this issue and hopefully provide some clarity. So if we come to the next slide, our commission was made up of people from around the world with very extensive expertise, from economics to infectious disease control to legal expertise to actually operational as well as those, we've had very close ties with industry to understand the various dimensions and a big thank you to the National Academies staff. We had Janelle Winters, the study

director, as well as a very strong team supporting which helped us pull together this report in quite a short amount of time while we are living through the COVID-19 crisis and trying to look ahead and learn at the same time. So I'm going to talk through now what our remit was, of what we were going to cover, we thought, that we're going to ask for by (UNKNOWN) So if we come to the next slide, the statement of task was to look at the global coordination on vaccines for the next pandemic threat.

To come to the next slide. So the first thing was to look at what do we have already in place for seasonal and pandemic influenza vaccine development, manufacturing and distribution? Much of this was developed in response to H1N1. We're trying to say what is already there so, we don't want to replicate what works already and what isn't working. What are the gaps? The second part was looking at COVID-19 and saying, Well, there are lots of new things that have been developed the act accelerator COVAX. Also, those in relation to outbreaks like Ebola, and so what has worked for these situations that we could perhaps learn for future influenza pandemics. And so looking ahead at some of the innovations and the business models, the distribution to say what has worked and not worked as we live through this COVID 19 pandemic. We come to the next slide. The third was actually to provide practical and feasible recommendations to say, OK, now how do we move forward in the months and years ahead to make sure that we can do better next time and on all areas, from looking at the coordination side to research manufacturing as well as equity distribution and access, which you know has been a problem through the COVID-19 pandemic.

The fourth part was looking at the business model. We know that it's very difficult to create incentives for this kind of work, that was with the thinking behind CEPI, behind COVAX. So how do we actually start to incentivize this kind of work in manufacturing and distribution when we don't know where and when the next pandemic will be? How do we actually get investment into an area where it's unpredictable, what the return will be for businesses. And if we come to the next slide, the final task was to provide recommendations on specific financing strategies and mechanisms, such as looking at risk pooling, trust funds, what kind of incentives there could be that could be sustainable in the months and the years to come. And hopefully this will encourage national investment as well, which is the flip side of just looking at the international picture. So huge remit. We looked at it over several meetings, a lot of discussion, and I'm going to now turn to kind of some of the context of where we got to.

So if we come to the next slide, some of our deliberations on the influenza imperative. So next slide. So the current pandemic influenza capacities we looked at. So the supply side, is that the 2019 global capacity producing pandemic influenza vaccine is approximately 6.4 billion doses in 2019 over 12 months. About 79% of that is based on egg based systems, and we have a PIP framework and others on the commission are quite expert in this, where industrial partners have committed to providing 400 million doses to low and middle income countries. Because, as we've learned through COVID-19, having the doses is one thing. Having them distributed to low and middle income countries is another question itself. On the demand side, we know that even though in U.K. and the U.S there's quite advanced seasonal influenza programs that most countries don't have these kind of vaccination plans and programs for adults and have not made seasonal influenza vaccination a priority, which means there's not really ongoing platforms that you can build off in these countries to then put on top pandemic flu distribution.

It's still needs to be built in the months in the years to come. So we come to the next slide. So, the partnerships for influenza vaccine platform technologies as you can see here, are distributed but what's

astonishing to see is there's very little being done across sub-Saharan Africa, across the entire African continent and Latin America. And so one of the things our committee deliberated upon was is it fine to have several hubs if they have comparative advantage and then hope they can distribute to the rest of the world? Or is it better to actually create these platform technologies and partnerships in a geographically distributed way? And I'll come to that when we get two recommendations, we come to the next slide. So we had four questions guiding the report's deliberations and recommendations. The report is now public, so hopefully you'll have a chance to look through it if you haven't already. And I'm going to go through each of the chapters and what we tried to look at each them. And really, this is going from, you know, the remit we were given and kind of looking forward.

So first Chapter two, we looked at the global governance landscape. So what existing structures are there? So this is useful to understand where we are today and what are the gaps that we have seen exposed? The second is we know that we need to get pathogen information, genetic sequencing shared incredibly quickly if we want to get to diagnostics, to therapeutics and to making vaccines. So we need to think about how do we make things faster? How do we get any part of the world willing to share samples and if they're going to share them, what are the benefits those countries will feel for sharing them with other partners in the world? The next is strengthening global partnerships for vaccine manufacturing and technology. So once we have those, how do we actually promote tech transfer, actually get the manufacturing and scale-up production? You can think of this as kind of a sequence from, a sequence, from cycle, from getting the sequencing to actually getting the manufacturing technology done to at the end of it.

And this is Chapter five. What are the financial incentives to promote scale-up and equitable global access, and how much do we need to be customized for influenza? And how much can these be generically for pandemic preparedness? So we kind of try to take you through from start to finish and how you would have to move quickly to get vaccines made from the pathogens being shared to distributed and financed for all parts of the world. So we come to the next. Yes. So what do you actually need in terms of requirements for a pandemic preparedness and response system? And so again, you need from the start surveillance to detect something has occurred, then that pathogen has to be shared, you need the technology is ready to go, whether it's mRNA or egg based, ready to make the vaccines, and you have to manufacture them, you have to look at IP if you're looking at, is this going to be or we can have emergency IP transfers, is it better actually to work with existing companies, if they can manufacture enough regulatory issues and finally delivery onto the ground.

And one of the things we also debated was how much we want to integrate influenza into the broader pandemic preparedness agenda. But also how much is influenza unique or exceptional? And so this was something we debated and you can see here that with influenza, we have well-established existing networks and legal arrangements. We know there's unpredictability of where the next spillover event will happen and when, we know that this is going to probably come from animals through zoonosis, and so we need to kind of continually monitor those, that we have limited global use of antiviral therapeutics and diagnostics, which means vaccines become incredibly important tools. And we know there's a long historical pattern of pandemics and so the next one is likely around the corner and not a if, but a when. So if we come to the next slide. And so the key arguments were therefore, the first is that scale-up is required to overcome vaccine hesitancy during a future pandemic, and we know that we need a strong access and benefit sharing system.

But in acute scarcity, as we've seen with COVID-19, it's not going to really address equity. Rich countries will take the vaccines that they think they're needed even now taking boosters. And so it's good to have a system, we have to understand how it starts to break down in crisis. The second is that innovations are coming in terms of influenza vaccines. Platform recombinant technologies offer the potential for increased efficiency, efficacy and faster production. Universal flu vaccine, which we thought would be a game changer having that ready to go, but here, discussing egg based technologies versus mRNA, how much do we move and mix different kinds of innovations? The third is a business case for influenza has been heavily focused on seasonal vaccine vaccines because of their seasonal demand. But we need to look that at, that actually pandemic flu will require a surge and so the market for seasonal influenza is not going to meet that demand. So how do we think about the business case for a much larger market and seasonal flu one?

And finally, getting back to the graph, the figure that was showed, the regional manufacturing does not offer a full solution for vaccine equity issues because we don't want this just to come and end up with vaccine nationalism. So yes, we need to have geographically distributed hubs, but it shouldn't be that every country just takes care of its own because we've seen that that's not the full solution and we shouldn't be more isolationist and we should actually be more cooperative. So we have to find a balance between those two ends of the spectrum. Let's come to the next slide. So coming to the recommendations of where our group got to. So next slide. So, in terms of who are we trying to recommend this to? Obviously, we need an audience. And the idea here is that there will be appetite from the G20, the G7 to do more in pandemic preparedness and readiness, either through a new governance mechanism or new instrument. We've heard about new treaties being proposed or not proposing exactly how this should look.

We're not saying this is exactly what the agency or treaty or body, whatever it is to look like. We're just offering recommendations on how, the gaps and how they could be filled. And other parties, industry civil society organizations are just as vital as actual governments and trying to move this forward. So if we come to the next slide, so, recommendation, first, the WHO. This one is targeted at member states who can work with WHO to develop an integrated agenda to strengthen preparedness and response for all respiratory pathogens or pandemic potential. And this needs to move from surveillance, from the start, to the information sharing about the sequencing being shared quickly, to development, manufacturing and deployment of vaccines. Instead of each of these being seen in a silo, meaning that we're only talking about surveillance here and we're only talking about pathogen sharing here, and then manufacturing over there needs to actually be an integrated agenda where we see that as a full system of how we prepare from start to finish.

So an overarching agenda and there should be one that of course, encompasses pandemic influenza, but should be focused on all respiratory pathogens. So, for example, COVID-19 would have been included in this, given again, many of the characteristics of pandemic influenza would be shared across other respiratory pathogens. To come to the next. Recommendation, two, we know that surveillance systems are quite weak in several countries regions, which means it can be quite a while before a new pathogen would be picked up and we'd be able to actually get the sequencing out and be able to start working towards a vaccine. So the weakest part of the system is probably where to start the surveillance systems to actually pick this up, and we need to increase the investments there to understand how to have sustainable financing for modern, timely surveillance, specifically for respiratory pathogens, which could quickly become and spread across the world into a pandemic. So we come to the next recommendation.

So the World Health Assembly should explicitly clarify that the PIP framework does cover genetic sequence data. We can discuss this in the Q&A, but there was some discussion over how much is genetic sequence data actually covered in terms of sharing and this means the PIP framework has been developed to balance the need to share data, share sequencing with actual, getting access to the products, the vaccines and make sure countries don't feel like they're left behind if they share and then don't feel like they get the benefit of sharing. And so you have to build off this framework to cover a broader range of pathogens and their genetic sequence data. So we have something that seems to work reasonably well, how do we take that further? We come to the next recommendation. Four is about, this is about how to support R&D for influenza platform technologies that we need to extend the mandates of, you know, bodies that have been created, CEPI and others to actually look at influenza and other respiratory viruses and looking at their industry partners platforms and saying, how can we structure these to look at whatever new respiratory pathogen might be on the horizon?

So if we come to the next one. Recommendation five is about what we might call a moon-shot program, which we're saying would be ultimate, would be to have a universal influenza vaccine, which, but we need to incentivize the development of this, the licensing, the procurement, and this requires push elements as well as pull elements to make sure that this could actually happen, and it could be coupled with a parallel effort for coronaviruses. We know there's efforts for a pan-coronavirus vaccine, but basically to get ahead of it, to already start developing these technologies that could cover a wider range of pathogens. Rather than thinking that for every single pathogen that comes along, we have to develop a specific vaccine for it. And so starting to think about the kind of new technologies and how are we actually kind of trying to get a moonshot. Take a jump to where we are right now. Next slide. And here comes back to the distribution of this, that we need to think carefully about hubs we've seen parts of Africa are asking, saying they want to have factories on the continent, they don't want to be reliant on other parts of the world.

And so how can we start to have a multilateral partnership to track emerging technologies that could be where we focus on tech transfer for influenza, promote partnerships with geographically distributed hubs and provide technical training ahead of time because we know one of the issues with COVID-19 is that there's also the issue actually not just the factories, but the technical training and the human capacity elements of having people who can run the factories and get them to scale to be able to produce at quality. Next slide. And recommendation seven is looking at giving funding explicitly for introducing and deploying next generation seasonal influenza vaccines, so not to forget the ongoing challenge each year of, the thousands of people who die from flu, and that the WHO regional offices could work with countries to do more extensive assessments of the readiness of how they could actually start to develop seasonal influenza programs for adults in high risk groups in the next one to two years.

Q&A

DANA KORSEN

We will now begin our Q&A session. Simply type your question into the chat box below the video frame to submit a question. And I want to acknowledge the other committee members who are here with us this morning to help answer questions. We are joined by Phyllis Arthur, vice president of infectious diseases and emerging science policy at the Biotechnology Innovation Organization. Amanda Glassman,

executive vice president and senior fellow at the Center for Global Development. And Alexandra Phelan, an assistant professor at the Center for Global Health Science and Security at Georgetown University Medical Center and adjunct professor at Georgetown University Law Center. So to get us started with the pandemic financing be targeted to have the most value are there particular aspects related to influenza that need to be accounted for? Where did you see gaps in pandemic financing at the country level? Who wants to take that one?

PHYLLIS ARTHUR

As we were moving, Dana, I think I missed the beginning of your question, can you repeat it?

DANA KORSEN

Sure, no problem. Where's your pandemic financing be targeted to have the most value? Are there particular aspects related to influenza that need to be accounted for? And where did you see gaps in pandemic financing at the country level?

AMANDA L GLASSMAN

I'm happy to... Shall I respond to that? So, well, thanks. This has been a great panel, and thanks to Devi and Peter for their leadership of our group. There are, of course, routine public health programs that spend on research and development and surveillance. And the case of influenza is actually, more developed in some respects than some other kinds of pathogens that organizations like CEPI work on. But that said, it's still totally inadequate to the scale of the threat and indeed the scale of the disease burden every year, especially as climate change changes the populations that are exposed to these diseases. And, the report goes over sort of the share of global health aid that is dedicated to preparedness. There are various kinds of estimates, but it's between two and 21%, depending on what you count to preparedness in general. And then surveillance in particular is really very, very underfunded and very patchwork. And our as our chair put it, it's kept together with string and sellotape.

It is literally financed by paying per diems to experts to participate in the network of surveillance. And of course, that's been strengthened with COVID 19 as another respiratory pathogen. There's still so much to be done to get surveillance working more intentionally at high scale. Likewise, on R&D, there's of course, lots of investment in high-income countries, but less that's directed to the specific needs of low and middle-income countries. If there were indeed a need to access pandemic influenza vaccine given a spreading a pandemic potential pathogen. And then ever more manufacturing of course, we've had this huge vaccine scale up with COVID 19, but it's all a question of the platforms. How flexible are those platforms to produce different kinds of technologies? So just to say, I think overall financing low debt is the scale of the threat and much more to do in this space.

PHYLLIS ARTHUR

I'll add one other thing to Amanda's list of things that have not been well funded. I think it's important to note what we're learning from COVID and what we probably all knew in the back of our minds as people who think about pandemic preparedness all the time is that the ground game and the health systems were never really funded to do mass immunization like this, particularly adults. I think that he mentioned this, but we're used to worldwide US everywhere really have great systems in place to vaccinate children. And if you look at H1N1, where it was predominantly children, the elderly, pregnant women, the childhood part of vaccination in many countries went relatively more smoothly. The

systems are built around that. They are not built around trying to vaccinate every person over 18. And that was hard in the United States, where the health systems are relatively rigorous and robust. So I think one of the other places is really health systems where financing of public health has not been, where it needs to be to do a massive response.

DANA KORSEN

Thank you both for that. Moving to the next question. His comments, thank you for these reports. There is an issue around the quote pandemic preparedness paradox, whereby pandemic investment slash governance reduces threats, which makes it more difficult to justify further or continued investments. How come this? Chime in, whoever wants to go ahead.

DEVI SRIDHAR

Yeah, I can jump in on this one. Which is I think that we have a very good window right now that people understand, particularly business, the losses that can be incurred if we don't prepare and get ahead for the next pandemic. And I think there is a lot of thought going into which countries have done better in terms of their domestic economies and how they prepared to do that better. And so there is definitely a paradox that generally in public health, which is if you say something's going to go really badly and then interventions are put in place to prevent that from happening and people say, well, you overreacted. We saw this early on in COVID with Norway and Australia and other countries that preemptively responded didn't get hit that badly and were said, told you overreacted rather than saying, we've averted a crisis. But I think right now we do have a moment of time when there is the world is still suffering from COVID 19. We're still not through the pandemic. And so there is a chance now to have the attention of governments to say, well, let's make sure that next time this happens, we're better prepared and it's we don't suffer as much lives, but also in terms of livelihoods.

PHYLLIS ARTHUR

I think the key is to try to get everyone to think of this as national defense. And there's a place where we never take our eye off the ball. We are always thinking about innovations that protect the nation, that protect the warfighter. And we should think of this as something that requires the vigilance that we apply to our homeland and defense strategies. It is part of our health defense and the trillions of dollars that the economy in the US and worldwide have lost from this pandemic should be the impetus for that continued investment.

DANA KORSEN

Thank you for that. Next question is from Erin Dutton from MDHHS, Michigan disability (UNKNOWN). Do you see additional funding to ensure those marginalized in the US have representation at the table to ensure equity and equality?

PHYLLIS ARTHUR

So actually, yes, and I hope that's another thing that is sustained, certainly the administration is very committed to health equity. They have health equity officer, Dr. Marcella Nunez-Smith and her team are really making this a top priority for the administration. I'll say, in addition, the private sector is as well and continued investments in how to get more balance in clinical trials, how to have more data, how to have community leaders really close to their communities educating on these issues of why they're important. I think you're going to see a lot of focus more on health equity, and that includes thinking about not just access financially, but access physically. There were a lot of innovations in this pandemic in terms of getting vaccines and therapeutics closer to people in underserved areas, and that's a broad

term. And I hope and I think we're seeing that as well applied worldwide. Hopefully, that leads to better health care delivery in different ways as well.

ALEXANDRA L PHELAN

And if I can supplement Phyllis Arthur's comment is I think there's increasingly increasing awareness globally that many of the decisions we've seen through COVID 19 have been decisions of bad governance and reflection on what good governance means for decision-makers, both in preparedness and response. And that includes fundamentally equity and participation in those decision making processes. And, interestingly, for example, in the state of Maryland, they mentioned, there've been community consultations about how would we do the ethical rationing of ventilators and tools like that in response? And I think we might see well, hopefully, we may see we see more of those sorts of inclusive, community-based participation planning for pandemic preparedness.

AMANDA L GLASSMAN

And maybe I could address the issue of equity as it relates to the way that we finance R&D and then finance, manufacture and supply to low and middle-income countries because obviously, you know, the big lesson learned from COVAX is as one of the questions I think that's coming in now suggests, you know, of the six and a half billion doses that have made available to date, only 400 million have reached lower-middle-income countries. And that has to do with a couple of things. First is that every government, no matter at what level of income, really needs to think about preparedness as a policy and to be part of entities that are preparing to obtain medical countermeasures in case of some kind of threat like this. So I mean, I think about that, especially for middle-income countries or upper-middle-income countries where there is a sort of wait-and-see game. I think governments really can't afford to wait and see. That's one issue. And then second, in the multilateral global efforts to try and assure supply and drive the R&D investments necessary to get us to approved products.

The imbalance of financing provided for, just in the US versus the rest of the world is really incredible, right? I mean, Operation Warp Speed spent \$30 billion to developing and manufacture vaccines for the United States since about \$38 per capita while COVAX had 1.7 billion for the rest of the world. There's just no way to make the advanced procurement contracts that were in any way able to compete on the market and to reserve the supply that was necessary. So we just have to put a lot more money upfront at the ready sufficient to buy the supplies on behalf of low-income countries for middle-income countries, we have to figure out what to do, but I think every government really does have to say this is something I have to prepare for in the same way that I prepare for natural disasters. And it goes back to that first question that we were addressing, which is, is this part of national security or not? And it really is, as we've seen in this case and the other the key thing is that, a COVID pandemic was less probable in any given year than an influenza pandemic.

So we should prepare for that. And I hope that these reports help with it.

ALEXANDRA L PHELAN

If I can add to that as well, I think when we think about the frameworks at the international level, that might help address this, this is where the potential. We've obviously got the framework when it comes to the equitable distribution of vaccines, but you're will still subject to the potential risks that we've seen during COVID-19 in terms of vaccine nationalism advance purchase agreements, export controls. And so there's a real question and a lot of question whether that's going to form part, addressing those issues will form part of any negotiations for a new international instrument like a pandemic treaty. And I do

think fundamentally equity has to be at the center of any negotiations for pandemic treaties going forward. And that invariably includes looking at what role can international governance play in addressing those efforts, as well as building up capacity and financing more broadly.

DANA KORSEN

Thank you for that. Perhaps we've touched on this a bit, but next question is 6.4 billion doses available, but only 400 million committed to about 25% of the population in low and middle-income countries seems suboptimal. How can we better manufacture and distribute to reduce the threat for flu pandemics and COVID?

PHYLLIS ARTHUR

Amanda, you want to carry this forward yourself? And then I'll follow you.

AMANDA L GLASSMAN

Yeah. So I think, you know, part of the key is just to do the research and development on vaccines in periods when we are not in the midst of a global pandemic. So, that's why the committee encourages both push and pull financing to develop a universal flu vaccine or something that is useful or that would make it easy to produce vaccine quickly in a number of distributed sites as quickly as possible as soon as sequencing is completed, and that the scale of that at the moment is insufficient. So maybe Phyllis could remark a little bit on that sort of. We do have a mechanism in influenza preparedness, which works much better than what we've seen for COVID, so that's good. But the question is the scale that's available to move forward. I think this is a kind of global public good. And so the other piece is, is the global community prepared to really scale up financing for manufacturing in intra-pandemic periods that would enable quick deployment of vaccines once when pandemic may hit or an outbreak may hit?

And there you know, there are lots of different estimates of what is the requirement to sustain that ever war manufacturing and a lot of questions because, you know, we also know that vaccine manufacturing has scaled up during COVID. And so, I guess the question is when one group that had been working, I'd estimated, you know, \$60 billion a year to keep ever more manufacturing in place. I think our committee did not include that figure in our reports. But are we prepared as a global community to really assure the level of demand in the non-pandemic years necessary to sustain the level of manufacturing to be able to deploy when pandemic hits? And I don't see that level of political limit yet, but we have to find some ways to make this work. And I think this report is starting to go in that direction. Phyllis probably will have a more articulate version of this.

PHYLLIS ARTHUR

Not at all, Amanda. That was brilliant because I think you hit on that key issue in the second half of your comments, which is, however, we do this manufacturing expansion. And I think that governments and Joe's industry all agree. We need a level of sustained increased manufacturing and certainly committed to geographic diversity, partly because it allows you to get product closer to where it's going all at the same time. And that's certainly one of the issues we learn about COVID. But I think we have to make sure that between in that intra pandemic period, this particular manufacturing capacity is working on something, and that's key. It needs to be sustained. Biologics manufacturing, in particular, actually is a series of very important incremental improvements that allow it to be more efficient. Even if you look at what happened with the COVID vaccines over the last two years the two primary manufacturers went from estimated doses of 1.5 billion or so to three billion to further, not just by expanding the partnering that they did with manufacturing, but by continuously improving the manufacturing process.

And that's the power of good, high-quality biologics manufacturing is that you can get those efficiencies that give you more output. So we need to think about how we do this in a voluntary way, such that you're having geographic partnerships that are incentivized by governments, by the various world banks, so that companies all over the world are partnering to have manufacturing partners everywhere to make sure they can make those very easy or not easy to make those transfers and continue that working relationship on the biologics improvements between themselves as the originator company and the places that may be partners to that technology. So it's not a once and done, it's a continuum of improving manufacturing over time.

AMANDA L GLASSMAN

And I just do want to recognize that the administration announced yesterday actually...

PHYLLIS ARTHUR

An RFI.

AMANDA L GLASSMAN

Exactly, a plan to produce approximately an additional 100 million mRNA doses a month against COVID. And importantly, they said, or other pandemic viruses. So far, a lot of it's been mainly about domestic supply, but obviously this has implications for global supply as well, and you can imagine providing such financing for distributed manufacturing all over the world, too. So I thought that is a really good news item. And the question is, how global will that be in its scope? Thanks.

DANA KORSEN

Thank you for those comments. Next question. My concern is that this addresses only respiratory transmitted viruses. Don't you think perhaps the infrastructure that you propose would be better in adapting in all-hazard approach for pandemic diseases may be further addressed?

AMANDA L GLASSMAN

I think Devi should answer it.

PHYLLIS ARTHUR

Me, too.

DEVI SRIDHAR

OK.

PHYLLIS ARTHUR

I was thinking the same thing.

DEVI SRIDHAR

I'm happy to take it and also to flag that, Alex, I'm going to be coming to you in a moment to talk about the PIP framework and what it can and can't do. So I'll give you a couple of minutes to get your thoughts on that. Yeah, I mean, I think already it's been a big move to move from looking at purely influenza, which has been built up in an exceptional way to looking at respiratory pathogens as a whole and take it even further to anything that could be a pandemic. We could, of course, consider, I mean, the same thing of having to get the sequencing and hopefully being able to build a vaccine quite quickly enough. If that is the ultimate solution for that pathogen, I think we've been had other outbreaks. We constantly have outbreaks, but they haven't reached pandemic potential because the way they spread. So I

remember just last week at a conference in London and the room was full of 200 people and no masks required now in England. And I said actually that if it was Ebola and someone had it, it would be unlikely anyone else would be infected in the room.

And that's how we can contain it quickly. Whereas with respiratory pathogens, very unlikely quite a few people would be infected in that room because of how it spreads. And so I think with respiratory pathogens, there is something about the transmission mechanism, which makes them more difficult to stop using, let's say, public health measures of trying to get towards elimination or eradication, which is kind of the gold standard. But we'd rather do, which is not have it circulating at all. With respiratory pathogens because they're so difficult to stop, that leads you to thinking about actually what are the kind of more scientific exits from a pandemic which has led us to kind of looking at this from beginning to end. So I think that's why we have this focus on respiratory pathogens versus everything as a whole because of the transmission mechanism and because of what that means in terms of your public health response. And I don't if I want to turn maybe to Alex, talk a bit about PIP because I think people might be interested in knowing what is the framework, what can it do and how it needs to be expanded, which was a core part of our discussions.

ALEXANDRA L PHELAN

Yeah, absolutely. So the Pandemic Influenza Preparedness Framework, or PIP framework, is a non-binding international instrument that member states adopted back in 2011. And what's really unique about the framework is it's a statement or an agreement non-binding agreement between countries and the WHO about how to prepare for and respond to pandemic influenza. And it is really limited only at this point in time to pandemic influenza in humans. It is coupled with a series of template contracts that mean pharmaceutical manufacturers. So vaccine, therapeutic and diagnostic manufacturers can be under contracts to provide an amount of real-time and lump sum doses of vaccines, diagnostics or therapeutics in the case of a pandemic. And that's in exchange for access to the Global Influenza Surveillance and Response System, which is a network that's been around since 1952 of sharing influenza virus samples around the world and national influenza centers around the world for influenza surveillance and response.

Part of that agreement also includes financing through a partnership contribution about 50% of businesses operating costs. So it's a really unique public-private structure under international law. And there's been some reviews are being conducted over recent years to look at how the PIP framework could work, how it could be expanded. And there are two really key areas that we discussed in this committee. The first is there's been talk about expanding it to seasonal influenza, that there is a need to when you are sharing these virus samples. That's not necessarily an understanding of whether a sample is going to be a seasonal flu, whether it's going to be a pandemic flu. So to increase that surveillance and also to increase that distribution potentially of seasonal influenza vaccine. The seasonal influenza burden is, under described in many countries around the world. And so the distribution of seasonal influenza vaccines is also perhaps an area that we can improve public health whilst also sustaining capacity.

So when we do have a pandemic, we can switch our capacities to pandemic flu vaccine production. The second area is genetic sequence data. COVID 19, I think, has really demonstrated the power of genetic sequence data in not only genomic genetic epidemiology for tracing, how the viruses are mutating and changing and where, but also for the development and testing of vaccines, diagnostics and therapeutics.

And we've seen some proof of concepts really come to the fore and actually happened during COVID 19 that hadn't been seen before. The PIP framework mentions that the topic of GSD needs to be addressed. And there have been a number of studies that WHO has done looking at what are the potential options for including GSD in the PIP framework. But it's a challenge because sequence data is not a physical sample. And so that balance of how you get that commitment from vaccine manufacturers and you build up your potential supply for equitable distribution based on public health need. That leverage is changing.

And this is all operating within a global environment of updates to the Nagoya Protocol, which is about accessing genetic resources and equitable sharing of benefits. And so there's a lot of scope here for thinking about where the PIP framework can be expanded and what model might of other pathogens that I think invariably ties into also any international negotiations for treaties or amendments we see going forward. I think that the report does go into some of our particular recommendations, but I think at the forefront really the consideration of genetic sequence data and how we need to think about that now and how our current instruments might need to be updated to address that is really a priority.

DANA KORSEN

Thank you so much. Our final question for this part of this morning session is with the ongoing revision of the IHR where are the key opportunities for other efforts like the global health security agenda to augment the IHR and improve preparedness for future health emergencies?

ALEXANDRA L PHELAN

So I can respond. And usually on that one. So I think, we are hoping that there is some IHR amendment there is plenty of scope from COVID-19, but that's also in parallel to discussions about the new treaty. And so we'll see at the special session with the World Health Assembly at the end of this month where that goes and whether the IHR revisions will occur in parallel. I think the global health security agenda is an incredible example of investment around the world to build up that capacity and core capacities under the International Health Regulations. But there's definitely been a sense in many of the reports from the independent panel and different international bodies that we need some form of assessment mechanism that is updated to include matters like governance and legislation and more metrics and target of capacities has been. But also some form of accountability. So whether that is a binding process or a compulsory process tied under, say, a pandemic treaty or under the IHR.

And there's move towards taking lessons from, say, the human rights law regime where we have universal periodic review. So it WHO has set up a group to start trialing and piloting universal reviews under that system. And I think that culture of accountability in that norm building is really critical for governance. And so I think, it'd be interesting to see where the GHSA ends up fitting within that. But I think there's definitely quite clear arguments to be expanding where attention focuses, particularly on governance and the others might have all sorts of (UNKNOWN).

DANA KORSEN

Any other comments?

AMANDA L GLASSMAN

I mean, maybe just to say that the whole area around pandemic prevention and preparedness and the governance of that is evolving and the global health security agenda is an initiative of a coalition of the willing. And the question is how would this evolve over time? How much is governed under a new treaty

or a revision to the IHR charter? And how much of the global health security agenda also becomes a financing mechanism? Because, famously, over the past couple of years prior to COVID, the GHSA did a great job conducting external evaluations of countries levels of preparedness and also developed a national plan supporting countries to develop national plans, which had a whole list of items to do and investments to make. But these were not financed for the most part. And so the question is, can we put some real financing behind these country plans for preparedness and surveillance? And here again at the US government has been at the forefront with Norway, South Africa, some other nations in the G20 process talking about a new financial mechanism and more financing for preparedness, particularly for country level surveillance and preparedness and quick detection of outbreaks.

But that has not become concrete yet. So I think what happens in the next couple of months is going to be really important for the future of this area.

DANA KORSEN

Thank you. And with that, we will close this first part, so thank you to our committee members for this thorough discussion on the Global Coordination Report.

VACCINE RESEARCH AND DEVELOPMENT TO ADVANCE PANDEMIC AND SEASONAL INFLUENZA PREPAREDNESS AND RESPONSE: LESSONS FROM COVID-19

DANA KORSEN

We'll now move to the second half of this morning session with a discussion on our report on vaccine research and development. I'd like to introduce one of the co-chairs of that report, Enriqueta Bond who is founding partner in QE Philanthropic Advisors. So, Dr. Bond over to you.

ENRIQUETA BOND

Thank you so much. And good morning, everybody. I think you're going to hear a lot of the same themes echoed in our report that you just heard. I'd like to say thank you to the Office of Global Health Affairs for the privilege of carrying out this study. We know you have a lot of expertise, but we were delighted to participate in your efforts, ongoing efforts. Next slide. So, we had a diverse, well-rounded committee that covered basic clinical manufacturing and regulatory science. Unfortunately, we lost one of our members along the way. And I want to shout, do the same shout out to our excellent staff, without whom we would never have been able to conduct this study. Next slide. So, our statement of task, next slide. First, we wanted to assess how lessons from COVID-19 and other prior epidemics have change the research and development ecosystem, and explore how these advances could be applied to pandemic and seasonal influenza. Secondly, we were asked to review the need for novel vaccine development platforms beyond the traditional processes that is the egg-based vaccines.

Three, we were to discuss the implications of the existing seasonal flu response ecosystem on future flu pandemic, and consider how emerging technologies can be applied to management of both seasonal and pandemic influenza outbreaks. Next. Fourth, we were asked to recommend actions to strengthen and diversify the use of vaccine production facilities and novel vaccine technologies covering the gamut of various technologies and business strategies that could be sustainably and rapidly adapted. Fifth, we were asked to consider the effects of issues such as viral drift, repeat immunization effects, seasonal flu vaccine effectiveness, and intellectual property on the technical, regulatory, and policy feasibility of

recommended actions. Next slide. Six, we were asked to recommend ways to build capacity for accelerated vaccine development and delivery against pandemic influenza viruses. And finally, to consider mechanisms to better coordinate and integrate research and development processes for newly developed vaccines with cohesive vaccine distribution and post-approval surveillance efforts.

And these considerations include streamlining vaccine and drug discovery, clinical testing, intellectual property management, and other international policy barriers that may impede or delayed development. Next. So, our committee took the following approach, our feeling was that the rapid development of COVID-19 vaccines really has demonstrated what is possible when researchers have the necessary resources and novel technologies to conduct and apply their research. And with rolling review by regulators and public-private partnerships, as well as extensive data that was a striking and leading lesson that we learned. And during our initial committee meeting, it was decided that the issues fit within four dimensions. And those were used to structure our meetings, and also our reports. So, you will see that we have chapters on basic and translational science on clinical science, on manufacturing science, and regulatory science. Next. So, before I delve into the recommendations for each of them, let me just pull out a few of the themes that I heard in the first presentation that you will again, hear through our presentation.

First of all, influenza and COVID differ, but influenza preparedness efforts have facilitated COVID vaccine development and now we can take lessons from COVID development to improve and expand the influenza preparedness efforts. Second, as one of the questions demonstrated in our last presentation, most experts believe that influenza will be the next pandemic because of past pandemics and the genetics, re-assortment, global distribution, and its respiratory aspects. As we heard work to develop a universal vaccine is ongoing, but the goal is not been reached. Next. Influenza vaccines are now largely produced from inactivated virus grown in chicken eggs and are not very effective. We need faster and more platforms such as RNA and recombinant protein platforms. But the presence of a cheap and approved vaccine are a barrier to development of other platforms without adequate sustained investment. As we saw from slides in the previous report, most manufacturing capacity is in the developed world.

Lower, middle-income countries do not vaccinate for seasonal influenza due to other health priorities. And we would need many more doses than are currently produced for seasonal influenza in a pandemic situation. And very importantly, we need global regulatory and surveillance systems to facilitate combating a pandemic. So, here go our recommendations which follow through on some of the themes that you've heard in the past. HHS through NIH-NIAID, BARDA, and DOD as well as other corresponding governmental and funding agencies domestically and abroad should invest proportionate to the enormous cost of pandemics in basic and translational science, that we can deliver a diverse array of influenza vaccines using different platforms, viral targets, adjuvants, and delivery systems to optimize the control of influenza across diverse settings and phases of pandemics and epidemics. One figure that is quoted in our report is that the global cost of a pandemic is \$570 billion. Whereas control of a pandemic would require something like \$4.5 billion of investment which is the World Bank estimate.

Next slide. So, for basic and translational science, as I mentioned, continuous funding for vaccine R&D is vital for preparedness, but it's often not sufficient. COVID-19 has resulted in a paradigm shift in vaccine technology presenting benefits for rapid development of pandemic vaccines and improving seasonal influenza vaccine effectiveness. As seasonal egg-based influenza vaccines have low to moderate efficacy

and require annual updates so these infrequent funding is needed to develop more novel platforms and technologies that may lead to vaccines that are more efficacious. And this will require building additional production capacity to include accommodating regions where capacity may not be limited, maybe limited sorry, or it is limited. This will also implicate greater application of assays that induce immunity through mechanisms other than strain-specific neutralizing antibodies and validating correlates of protection, which are currently used by the FDA, which means there isn't much incentive to move beyond.

Next slide. So, as it relates to the sort of findings, the recommendation to two is the WHO working with multilateral stakeholders, for example, CEPI government's funding agencies in the vaccine industry and philanthropic organizations should advocate and build global capacity for robust and internationally comparable preclinical, clinical and immunologic assays of influenza vaccine candidates, including novel candidates that use other structures, targets and delivery systems to potentially broaden or improve what is limited protection at this time. Next. Recommendation to three international research networks supported by governments and funding agencies, WHO, and the vaccine industry should support and conduct multicenter international clinical trials and field studies to compare these emerging vaccines that we believe are needed with standard egg-based vaccines in geographically, demographically, and immunologically diverse populations so that they have the data to inform rational and situation based use and manufacture of an extended array of vaccines.

Next. Recommendation to four national regulators to engage with the vaccine industry and academic researchers in the development, standardization and implementation of assays to evaluate vaccines that induce immunity through mechanisms other than strain-specific neutralizing antibodies and establishing validating correlates of protection. Next. On the clinical side, we felt that the expansion of clinical trials globally, particularly in low and middle-income countries can decrease the risk of such large investments and fill clinical funding gaps. That clinical studies of influenza vaccines need to represent the diversity of the population study and early study should prioritize high risk groups. Population based studies should measure differential effects in subpopulations with consideration of characteristics such as racial, ethnic, social, economic, age, pre-existing medical conditions, and diversity within and across countries. And that coordinated global pharmacovigilance systems are needed really to ensure vaccine effectiveness and safety data are timely and complete.

This will reassure the public and enable approvals. Next. So, with these findings, our first recommendation under clinical science was that the WHO in collaboration with national public health agencies should conduct burden of disease studies in low and middle-income countries to understand their health and economic burden of influenza illness and barriers to immunization in adult populations. We need to really build the infrastructure and capacity in these countries needed for pandemic vaccine development and implementation. And if we have cost-benefit analysis, that include additional economic productivity losses due to delayed access to a vaccine in a pandemic, this will enable better use of vaccines. Next. So, the international coalition of medical regulatory authorities and WHO in partnership with national regulatory, and public health agencies should invest on a global level and data infrastructure and capacity building to conduct those real-time sentinel sites surveillance of vaccine safety and effectiveness of the different vaccine products to avoid for use of both in epidemics and pandemics in diverse populations, including a plan to ensure coordination, collaboration and data sharing across the sentinels surveillance science.

I think, sites as we heard in the previous presentation, this is a great need. Next. Again, the international coalition of medical regulatory authorities and WHO should ensure international coordination and collaboration on timely and transparent review of vaccine safety data during epidemics and pandemics to support the real-time decision-making about the use of these vaccines. Safety data should be made available to support country-level benefit-risk assessments because each different population and country are going to have a different benefit-risk assessment particularly in low and middle-income countries relying on regional data from sentinel sites conducting safety surveillance. Next slide, please. So, findings under manufacturing science, we found that expanding manufacture capacity in low and middle-income countries can help avoid the delayed rollout of vaccine and LMICs that it's vital that these models not only be sufficient but self-sustainable to ensure that production can keep up with the urgency of demand and pandemic conditions.

Public sector investments and improvements to data sharing infrastructure can aid manufacturing centers able to mobilize quickly during the pandemic. Financial aid may also incentivize vaccine manufacturers to assume more risk in building infrastructure. This was certainly critical on COVID. An eligibility for such funding should be contingent upon participation in R&D, data sharing, technology adaption, and training activities within our national partners. So, with these findings... Next. Next slide, please. Recommendation for one was that HHS and WHO should develop a plan for sufficient global supply of influenza vaccines for pandemics which includes convening, supporting and encouraging vaccine manufacturers to benchmark, prioritize and harmonize the influenza vaccine manufacturing. And enhancing and expanding support of the global influenza vaccine manufacturing network, creating manufacturing hubs for greater collaboration and building capacity to address the challenges in manufacturing in LMICs.

Next. Vaccine manufacturers should take that risk-based approach for pandemic influenza preparedness that would include participating during research and development, data sharing, technology adaption, and training activities with international partners. Growing international capacity to assess the production needs and their risks. Using scientific evidence to design strategies to reduce risks such as WHO pre-qualification licensing, marketing et cetera. And formalize technology transfer, the scale-up, and scale-out activities, taking into consideration timeliness and the outcomes for equitable costs, access, and distribution. Next. For regulatory science, our findings which drove the recommendations were that regulators should develop comprehensive and transparent guidelines for how to conduct preclinical and early clinical trials between pandemics and developed pathways for rapid review of vaccines for pandemic strains. That such efforts should include provisions for optimizing passage through regulatory pathways, including improved understanding of correlates of protection, which was certainly in place for COVID and was a great facilitator that regulatory agencies should work closely with public health to ensure that the public receive accurate and streamlined messaging about vaccine development and approvals.

As a gesture of goodwill vaccine manufacturers are encouraged to share vaccine trial results and updates in regulatory review. So, with that, our recommendations follow. Next. The FDA and other national regulators working with the scientific community and pharmaceutical industry should establish comprehensive guidance for the development of influenza vaccine on novel platforms through emergency use authorization to full licensure. This guidance should provide pathways for both seasonal and pandemic influenza so that there might be a way to use the seasonal influenza to develop the platforms that are needed for the pandemic. Next. The FDA and other national regulators should

commit to transparency in the oversight of clinical trials review of data authorization, and approval of pandemic influenza vaccines, including the release of facility inspection findings, clinical trial protocols, and clinical data that are the basis of decision making. Regulators should convene independent advisory committees to build public understanding and confidence prior to the authorization or approval of novel vaccines.

Next recommendation. The WHO and the international coalition of medical regulating authorities should facilitate coordination between regulatory and public health agencies when announcing different decisions on the same or similar vaccines to explain the different underlying circumstances and judgments. I think we saw a lot of confusion during COVID and we need to be sure that the risk-benefit of different or similar vaccines in different circumstances in different populations is well understood by the public. Next. Vaccine manufacturers should adopt a code of conduct for press releases and other communications regarding vaccine trial results and other matters, which emphasize the critical role of regulatory review. Next recommendation. So, as a summary, overall summary of our recommendations, I think there are two takeaways. One is that having vaccine earlier and ensuring they're widely and equitably available, including through building vaccine production and distribution capacity and lower and middle-income countries in a future influenza pandemic could significantly reduce both the burden of disease in the social and economic consequences, both domestically around and around the world.

And we believe that we've provided a blueprint that the world can leverage what has been learned so far from the COVID-19 pandemic to effectively prepare for the next influenza outbreak. I'd like at this time to ask my Co-Chair, Kanta Subbarao to add any of her comments to this summary.

KANTA SUBBARAO

Thank you Queta, I don't know if you can see me, but it's been a real pleasure to work with this committee and discuss these diverse issues. The only thing I would add to what Queta said is that influenza is unique in some ways. I mean, there's so much that we can learn from COVID-19 but the lessons sort of go both ways. There was a lot from the influenza experience that informed COVID-19 and the converse is true as well. So, what's unique about influenza is that we have vaccines, we have these phenomenal network for surveillance, international collaboration, we've got excellent interactions with the manufacturers, we've got an increasing diversity of vaccine platforms that are available, but there's still room to improve. So, we do need better vaccines. And we need to be able to move into using or investigating some of these, and certainly, having sustained and proportionate funding to be able to support this. And the other challenge with influenza is because we've got an existing influenza vaccine, there's a bit of a hurdle in trying to take a new concept through to clinical trials.

Q&A

DANA KORSEN

Thank you both for those comments. Again, Dr. Bond was joined by her co-chair Kanta Subbarao, Director of the WHO Collaborating Centre for Reference and Research on Influenza. And now we'll begin our Q&A session. Simply type your question into the chat box below the video frame to submit a question. And let me first introduce other committee members who have joined us to help answer questions. We have Maria Elena Bottazzi, Associate Dean of the National School of Tropical Medicine and Professor of Pediatrics at Baylor College of Medicine, Co-Director of the Texas Children's Center for

Vaccine Development, and Co-chair of the Vaccines and Therapeutics Taskforce for the Lancet Commission on COVID-19. We also have Annette Fox, Senior Research Scientist in the Collaborating Center for Reference and Research on Influenza at the World Health Organization. We also have Grace M. Lee, Professor of Pediatrics at Stanford University School of Medicine, and Joshua M. Sharfstein, Professor of the Practice in Health Policy and Management at Johns Hopkins, Bloomberg School of Public Health.

Thank you all for joining. So, let's get started. First question is with a wealth of data from COVID-19 immunization efforts, are there lessons for future outbreaks related to cost benefit analyses of vaccinations at the country level?

GRACE M. LEE

I'm happy to take this. First, I want to thank our chairs for steering our committee through these really rich discussions. It's been really wonderful and wanted to especially call it also Hoda Sultani, who's been amazing to work with. In terms of individual country level cost benefit analyses, I think the rationale for it is twofold. You know, one being that we need to continue to make the business case, as was mentioned in the prior session, for the importance of building the infrastructure that's needed for vaccine development and delivery of these vaccines. And the health and economic impact has been tremendous. But in many ways, it is really difficult for us to continue to invest in prevention as an important effort. I really appreciated also, Phyllis Arthur's comment that in many ways, we don't question the investment of preparedness when it comes to defense. But it is really hard for us to invest that same level of both capacity building as well as, you know, financial investment in health prevention.

And so we hope that this will actually provide direct evidence of benefit to countries about the importance of this investment, recognizing that there are many priorities that countries face.

DANA KORSEN

Thank you. Does anyone else want to add anything to that? Alright, next question. Would prioritizing some sectors or ages across countries have a greater impact than others?

KANTA SUBBARAO

Yeah, I think I could try to take that one. So, I think that we know with seasonal influenza, that there are certain age groups and sectors that are at greater risk of, of disease, and you can focus on them in your initial rollout of a vaccine. But with pandemics, I think we have to watch and see what the epidemiology is, and be able to tailor the response. So for example, with the 1918 pandemic, there was a use a W shaped curve, where in addition to the two extremes of age, there was a lot of disease and mortality in the young, healthy adults. But that same curve does not did not apply in all the subsequent flu pandemics that we've had in the last 100 and few years. So, I think that the, for instance, in the 2009 pandemic people over 50 were largely spared, because there was a virus that had circulated in the 50s. In the 1950s, that was somewhat similar. And there were some residual immunity that protected the elderly from severe disease. So, I think we do have to wait and watch even though we can create some guidelines based on prior experience and based on seasonal influenza, but we have to have the ability to pivot and to modify.

DANA KORSEN

Thank you. Next question is, how close are regulators to accepting a standardized measure of cellular immune responses as correlates of protection? Joshua, can you take that?

JOSHUA M. SHARFSTEIN

Sure, I would say, not that close, as far as I'm aware, I don't know. I would say all the details, but there are certain, you know, correlates that are accepted, particularly where the response to the protein that is now the major antigen, but cellular immune responses, I don't think so it's one of the things that we talked about in the report that it's really important to develop new correlates of protection, perhaps even better than the ones that we have, and particularly, as they relate to novel vaccine platforms. And being able to do that is the difference between having to do a huge study every time and being able to do a much more efficient study just focused on the correlates of protection at in the case of a pandemic. So, there's a lot at stake with being able to develop new bullets and protection, and we think it should be a big emphasis.

KANTA SUBBARAO

If I could just add a little bit to that. It's one of the things we've talked in our committee - about the need to standardize assays. And there's a tremendous need to do that. And there are several consortia, including some public private partnerships that that have made a lot of inroads in standardizing assays including some assays for cell mediated immunity to influenza. So, one example is the FLUCOP which is a correlative protection consortium in Europe.

ANNETTE FOX

I would also say that some assays are more amenable to standardization. I mean, the flow cytometry based assessments are very tricky. There's a huge variation in results between groups. I think, you know, there's for the basic sort of absolute counts of lymphocytes that came along way with HIV, absolute counting platforms came up and international standards or international quality assessment schemes have been put in place, so it's not impossible. But some other essays such as ELISpot, I think FLUCOP, and others have done quite a bit on working on that. And that probably has some prospects on the T cell side. On the B cell side, I think that's also really important that we get a handle on the memory B cells, and how well they are induced by vaccine and maintained because they can provide a rapid source of protection even when antibody levels are low. Yeah, so I think there hasn't really been a lot of effort on that front. And that's something that we would really want to invest in a lot more.

DANA KORSEN

Thank you. Next question is manufacturing mRNA has more difficult cold chain requirements than egg derived vaccines, what new bottlenecks would be created in the move to mRNA to control a pandemic? Clinical, it is a big hurdle, ethical and statistical to demonstrate incremental efficacy improvements compared to a partially effective flu vaccine. What can regulators do to reduce this hurdle?

MARIA ELENA BOTTAZZI

Maybe I can start with the first part of the question and speak towards you know, indeed, you know, the challenges to bring new technologies as we've seen with manufacturing of our mRNA for COVID-19. And I think the key here as we highlighting that report, is to really involve the manufacturers very early on in the participation of learning and ramping up the know how building the human capacity, that workforce that can understand, you know, the nuances of bringing in into the manufacturing skills, how to produce the RNA technology, and therefore then, you know, explore the opportunities of how can you not only scale them, do it in a certainly affordable manner with the right reagents and supplies, but at the same time, evaluating the ability of creating them in a way that it can be accessible within, you know, for example, that cold chain requirements. So I think that, you know, the bottlenecks are primarily related

to, it will be a steep learning curve for the manufacturers. But if they participate early, as we are recommended to in R&D activities in data, sharing activities in how to adapt the technology, and bring it in such that it makes sense within their capabilities in their structure, I think that will be something that will really advance the field.

And then, of course, have the opportunity of transitioning them into appropriate clinical trial designs. Maybe I can transfer the second question to another committee member.

JOSHUA M. SHARFSTEIN

I'd just like to jump in very quickly and say that there are statistical designs like non inferiority designs that allow you to do a comparison to an existing vaccine that can be done practically. So, I think that it sometimes requires a few more patients. But it doesn't make trials impossible to do. One of the key points in our report is that we can do this during a regular flu season. So, you can bring up a new technology, and you know, have a big trial during a regular flu season, work on establishing correlates of protection, really understand the efficacy of a new technology, and then be in a really good position for a pandemic, and just waiting for the pandemic. And trying to do all this right then is going to be much harder than taking advantage of the fact that we have annual flu season.

GRACE M. LEE:

And I wanted to just perhaps add one thing, which is, you know, now with the COVID-19, vaccines, the mRNA vaccines, we were really fortunate that the pediatric formulation is more refrigerator stable out to ten weeks, which I think, you know, took us a while to get here. But this is a very different situation, at least for our ability to deliver these vaccines, compared to where we were in December 2020, with the ultra cold freezer temperature requirements. And so we'll just continue to encourage the innovation and development that needs to happen with the end goal in mind, which is really thinking about what are the delivery requirements in different countries? And how can we maximize our ability to vaccinate large populations under different implementation conditions.

ANNETTE FOX

I think one of the other points of the need for having larger clinical trials and putting more investment into clinical trials was even if we are trying to trial universal vaccines that may not reach the same high or same level of efficacy as a strain specific vaccine, at least it will give us an indication of what efficacy they may have against a completely novel strain. And it will also give us an opportunity to develop correlates of protection for these types of vaccines that we currently lack. So I mean, yes, we would need large studies with seasonal influenza as a clinical endpoint. But you know, that investment would give a lot of return in terms of pandemic preparedness.

DANA KORSEN

Thank you. Our next question is why does the report say a universal flu vaccine is the quote ultimate prize?

KANTA SUBBARAO

Sure I'll take that one. So, the reason we think that universal influenza vaccines would be the ultimate prize would is that they add in, you know, different people define universal influenza vaccine differently. But a truly universal influenza vaccine would obviate the need to update seasonal influenza vaccines annually and would provide protection against a novel influenza strain that emerges. So, being able to vaccinate and get good coverage and good protection from virtually any influenza virus to make it, you

know, would be a real game changer. Presumably also it would make the costs of vaccine less burdensome because you have one vaccine that can do it all and you don't have to each year gear up and try to get the next one. So you'd have a thing, you know, the system in place to really go just crank it out.

DANA KORSEN

Thank you. Our next question is, if it is accepted that vaccine pressure changes viral ecology favoring increased prevalence of escaped new mutants, is their interest to fund as a research model study of influenza vaccine impacts on the viral ecology of enlarge livestock populations? For example, how does influenza vaccination of swine populations impact the variability of circulating influenza variants?

KANTA SUBBARAO

So, I can try to take that one and see if anybody else wants to jump in as well. So there are some studies that are conducted. So there's influenza surveillance, in swine populations, and there's depending on which part of the world you live in influenza, the swine herds are is the livestock are vaccinated, pigs are vaccinated. And in China, they're vaccinating poultry, with a vaccine to protect and to prevent age five, and h seven influenza viruses. So, in China, they were very, very successful in controlling H7 and H5 infections on poultry. So, we haven't seen any H7 and H9 human infections for about two years ago. And we do see some we've been seeing an uptick of H5 and H6. So again, just like with seat human, seasonal influenza, they have to update they may have to update their vaccines. But it's a good question. I think that it's not likely that vaccine pressure is driving all of the antigenic drift because there's not enough vaccine used globally, to for the vaccine to be responsible.

But vaccine induced pressure could play a role. And so that it would be, you know, a good system to study in animal populations as well.

DANA KORSEN

Thank you. Our next question, is unprecedented data and cost sharing between manufacturers allowed for the scale up for COVID vaccines without the same urgency? Do you ever see this being copied for seasonal vaccines? And how do we make that scalable?

MARIA ELENA BOTTAZZI

I can try to take that question. So I think we do highlight that indeed, what we need is to keep the momentum and then and incentivize the manufacturers to be able to continue with the ability of participating and collaborating amongst themselves, especially during the normal business as usual times, right, you know, during, you know, even the years where we just have to advance not innovation in the seasonal vaccine design. But I think that it will be important to indeed give them that incentives and that's why in our recommendations, we call for the actions from organizations such as World Health Organization, and of course, you know, the U.S. government agencies to provide a path towards bringing all these manufacturers together so that they can continue seeing the ability of collaborating and feeling that need to continue collaborating and sharing their challenges and of course, looking for solutions that then can be very rapidly adopted in the event of course of a pandemic influenza situation.

So it is clearly a group effort that will require the agencies to really be the framework where they can call for the ability of meeting and sharing the information and make bring the incentives for them to be able to participate.

ENRIQUETA BOND

Josh, do you want to add to that? No, hold it. Maybe Kanta? Yeah, sorry.

KANTA SUBBARAO

Yeah, no, I don't really have anything to add. I think that that's, you know, that is.

ENRIQUETA BOND

Yeah, I think the example, Kanta that you told us at the committee about we already have tried to develop other platforms. But without that sustained funding, they really haven't gone forward to fruition. Or they don't compete well, with the current egg-base vaccine.

KANTA SUBBARAO

Yeah. And I think the other example is really that in when there have been efforts to diversify the manufacturing to countries that weren't previously manufacturing influenza vaccines, some companies have had difficulty in sustaining a market. And so that's one of the reasons why doing studies to define the burden of disease would help as well, to sort of keep those players alive.

JOSHUA M. SHARFSTEIN

Just re-emphasize that the urgency of pandemic preparedness should be helpful here. I mean, as much as we can make the case for seasonal flu, the ability to do this is really important for pandemic preparedness, and that should hopefully drive more support, collaboration and progress.

DANA KORSEN

Thank you. Our next question, can you expand on the recommendation five to on increasing transparency in clinical trials? What's the best way to do that?

JOSHUA M. SHARFSTEIN

I'm happy to jump in, I think there are different dimensions of transparency. But one of them, you know, you can see from the good work that the FDA did that there were clear standards for the clinical trials, that key data was shared about the clinical trials, there was an advisory committee that discussed that data publicly, this did not happen in every country, you know, for example. So, I think those things are very important. There are also some, you know, basic details about clinical trials, when they start, when they're halted. Why they're halted? That are really kind of basic things that I think if the regulator is able to be transparent about then it avoids the possibility of, you know, misunderstanding, which can really undermine the confidence that people have in product development. So, I think all across from the origins and the standards all the way through the results and the decision making. Transparency, I think is really important these days. Because we know that even like a day of confusion can lead to 1,000 theories blooming on the internet that really can confuse people.

And just also say that we ultimately support the idea of sharing and some of the key underlying data to the extent the extent possible, and that probably can't be done in real time, you know, all of the data in real time, but key data in real time can be shared. And we saw that happen, I think, very successfully in this country.

GRACE M. LEE

I might chime in that in addition to the importance of transparency and public confidence in both the process as well as the recommendations. You know, I think in many ways, it also enables efficiency by essentially creating these standards or articulating them and recognizing that they may change over

time. But it allows not only manufacturers but I think the public to better understand, you know how vaccines are being judged in terms of safety and efficacy. And I will emphasize again, Josh's point about having federal advisory committees. I do believe, you know, for example, a Virbac deliberating on the regulatory sort of needs that they felt were important for vaccines in various populations, I think has been really helpful to have those discussions and open in public and it allows us to be able to ensure that diverse perspectives are heard and also that the public can watch those meetings and understand sort of how these decisions are made. So, the rationale for these decisions, I think is important and transparency is a part of that public process.

DANA KORSEN

Thank you. Next question. So this is in reference to one of the conclusions that says low and middle income countries have disease burden studies performed, vaccination rates are improved. So, given that what is the best way to incentivize burden of disease studies in low and middle income countries?

KANTA SUBBARAO

So, I can take the first part and have my colleagues jump in after. So I think I will, I was referring to this, in part because we've had the experience in the past, we are following the first recognition of avian influenza viruses circulating and the 2009 pandemic. So, there was an effort that the WHO led to try to bring developing country manufacturers into the space and to develop homegrown influenza vaccines. And some of these companies of companies have actually struggled to have a find a market because the local policymakers, and actually, the local population doesn't necessarily recognize the need for influenza vaccines. So, the WHO is doing some of this, but it means that we certainly need a lot of support to do burden of disease studies in low and middle income countries so that people can recognize the importance of influenza, there are so many competing priorities in countries with a heavy disease burden caused by many other things. And so that we do need to incentivize this with funding.

And so to make funding available, and potentially work through the WHO, because they've got, they've already set up protocols and can actually talk through the design that would allow the burden of disease studies to be compared to other countries. So, there are tools available. So I think the real reality is that we need some funding support for it.

GRACE M. LEE

And maybe I'll just add, that I think, to reflect a perhaps a broader definition of burden of disease, just recognizing that, for example, I'm a pediatrician and in children, it's not just the health impact of the disease, but it's really, you know, what is the educational impact, the impact on social emotional functioning, the financial burden that causes because of workforce capacity issues. So, I think that we also need to not only think of it in its traditional sense of burden of disease, but we need to go beyond health to really understand the full impact of some of these infections that I think, at least for COVID-19 is clear, it has had long term consequences. But I also believe that those impacts translate into influence.

DANA KORSEN:

Thank you. And I believe we'll move on to this - our last question. On the last recommendation on code of conduct, and press release, can you expand how the companies can do this and what guidelines they should adopt?

JOSHUA M. SHARFSTEIN

So, I think that one of the concerns that a number of people had, including a number of public health

officials is that sometimes people were learning about key information from company press releases without a lot of information, and the regulators weren't talking about it at all. And that wasn't just about, like the great news about a trial but also about what was happening behind the scenes when the trial got stopped, and if that wasn't a press release, it might have even just been like a comment to investors. And, and so you know, when that happens, it undermines confidence in the regulators, it leads to a lot of confusion. I was on a different national academy meeting where health officials were saying, you know, a company would say something, we would get 100 questions, and the regulator couldn't say anything. And we had no idea where to turn and it just undermined our ability to know what was going on and to provide leadership in the middle of a pandemic. And so I think the idea is that there should be, you know, opportunities for companies to talk about their products, but it should be well coordinated with the right later and that every communications really emphasize the role of regulatory reviews.

So people don't, you know, hear a result ago, like, why can I get this today? It seems like I should get it today. And then I'll automatically be angry before there's even any, you know, chance to review. And we've seen that when review happens, even, you know, in a pandemic, there are all kinds of things that that get identified. And sometimes the result isn't exactly as it was originally at the forward. So, I think that the goal for this recommendation is to put this kind of thing on the radar screen, I don't think we presume to say, here's exactly the code of conduct the company should adopt. But the principle is that we should be communicating and communication should really be geared towards the overall outcome of good information for the public in a way that doesn't create more confusion and undermine trust in public health and regulatory agencies. And we hope that this recommendation starts conversation that can lead to a responsible code of conduct for industry.

DANA KORSEN

Any other comments? Alright, well, those are all the questions we have for today. Thank you to all of our committee members, and for all of you who joined us this morning. Again, the four reports that are being discussed today are available for free download on the same page where you are viewing this video. And also a reminder that the next session, which will begin at 1:00 pm Eastern, will cover the studies on public health interventions and supply chain. So, have a great rest of your morning and we hope to see you back here at 1:00 pm.

SESSION 2

WELCOMING REMARKS

STEPHANIE MICELI

Good afternoon, everyone, I am Stephanie Miceli, and I am a media officer at the National Academies of Sciences, Engineering and Medicine. Thank you all for joining us this afternoon for part two of today's public briefing on four reports that were just released yesterday as part of the National Academy of Medicine's Advancing Pandemic and Seasonal Influenza Vaccine Preparedness and Response Initiative. If you have not already, you may download copies of these reports and other supporting materials at the links you'll see on your screen. And for those of you who are not familiar with the National Academies study process for each requested study, committee members are chosen for their expertise and experience, and they serve pro-bono to carry out the study statement of task. The reports that result

from the study represent the consensus view of the committee, and they must undergo external peer review before they are released, as did these four reports. I will now briefly turn it over to Dr.

Victor Dzau, who's president of the National Academy of Medicine, to kick us off this afternoon.

VICTOR DZAU

Thank you, Stephanie. And welcome all of you to the second session of the public report briefing for any initiative on pandemic and seasonal influenza vaccine preparedness and response. For those of you who join us this morning, welcome back. And for those who could not join us this morning, welcome, and I'll give you a little background about the initiative. You know, this initiative is an important and timely effort to distill lessons learned from COVID-19 that could be critical advancing future influenza preparedness efforts. This initiative is timely, because the world has focused on combating COVID 19 pandemic, but seasonal and pandemic influenza remain an imminent global health threat. We have also seen how viruses have potential to disrupt the world and because of global preparedness, response and the willingness to rapidly use these capabilities to counter new threats. So these four reports were developed with that in mind to underscore that preparedness has to be an ongoing commitment.

It can be from year to year a crisis of crisis. And as we learn from COVID 19, experience, surveillance, supply chain and research infrastructure as the well-resourced before and not in the midst of the next pandemic. So with this background we have assembled, should International Committee with a wide range of expertise in global public health across all sectors, government, academia, industries, civil society and international global health organizations, may show the first line. So this is the international committee, and they are going to review for you this statement of task and the recommendations. And I'm very grateful to all of them that truly, as you can see, international next slide. And next slide shows you the full consent study, which you see listed, they are countering the pandemic threat to global cognition, vaccine of influenza imperative vaccine research and development to advance pandemic and seasonal influenza preparedness. Response lessons from COVID 19, public health lessons from non vaccine influenza interventions.

PUBLIC HEALTH LESSONS FOR NON-VACCINE INFLUENZA INTERVENTIONS: LOOKING PAST COVID-19

STEPHANIE MICELI

Thank you, Dr. Dzau. And now I would like to introduce Dr. Penny Garcia. She is a professor at the School of Public Health at Cayetano Heredia University in Peru. And she's also a member of the National Academy of Medicine. Dr. Garcia served as our committee Vice-Chair for the report titled, 'public health lessons for non-vaccine influenza interventions, looking past COVID-19'. She'll be our primary presenter for today. And I'll turn it over to you, Dr. Garcia. Thanks for being with us.

PATRICIA GARCIA

Thank you, Stephanie. So next slide, please. First of all, I would like to thank you, all the members of this committee that work very hard during this time to put together this report. And also, I would like to thank the National Academy staff that you can see there in the PowerPoint. Next one, please. So our statement of task was to review and come out with recommendations related to public health lessons for non-vaccine influenza interventions, based on what we have seen in COVID-19, which means that there were so many things that we had to review and it was really challenging. Next one, please. So, first

of all, we work, we had to analyze the evidence of the effectiveness of these key non-vaccine measures. And we're talking about masks, indoor air quality, and ventilation that had been developed across different disciplines, and include also novel or existing diagnostic tools that could be adapted and optimized to mitigate respiratory infections. The second thing that we had in our as part of our tasks was to explore the social and political context that could underlie the effective implementation and optimization of those public health measures and diagnostics.

So one is effectiveness and the other one is how could we implement it in the right way, taking into account the contextual factors. Next slide, please. Number three was to review promising COVID therapeutic approaches, like antiviral, monoclonal antibodies, host-directed responses, plus the supplies that are needed also for these therapeutic approaches to be implemented. And try to see which ones have demonstrated some effectiveness and could give us some critical opportunities to be used during seasonal or pandemic influenza. And number four was to highlight innovations around the world during COVID, as well as other seasonal and Pandemic Influenza events, particularly that were related to surveillance, and rapid, transparent data sharing that can lead to best practices recommendations from for notification, contact tracing, testing efforts. And that could include and should include the digital technology and data science. Next slide, please. Finally, the number five was to analyze some prominent research agendas, the existing research initiatives, and the knowledge gaps that were identified from the response of COVID and other outbreaks to outline some priority actions for future research efforts related to seasonal and pandemic influenza.

So we have these five tasks. Next one, please. And actually, we decided to organize these five tasks into these five chapters. But so you can follow me better when I presented chapter two, basically, because we thought that this could make more sense was going to be related to these best practices and innovation in surveillance and data sharing. So the first chapter had to do with surveillance and data sharing, chapter two. Chapter three goes into effectiveness of these key non-vaccine measures. Chapter four had to do with implementation and the social and political context. Chapter five, therapeutics. And finally, in chapter six, we had some concluding thoughts that includes several of the different things that have been taught. And in these different chapters, we were including also some priority actions for future research efforts. So next slide, and let's start talking about each of these. So given the study timeline and the scope of the committee's charge, the committee largely chose not to focus on workforce training or capacity.

Interventions for health care workers, as opposed to general population, which all most of the recommendations have to do with and with vaccine hesitancy. So these are the areas that we decided not to include in this report. Next one, please. So the report recommendations next one. So chapter two had to do with surveillance and data sharing, the first recommendation 2.1 had to do with the institutions like WHO, the World Bank, National Centers for Disease Control, should all work collaboratively with countries, particularly those with a high degree of animal-human interfaces to build sustainable. And we would like to highlight this word sustainable capacity for routine surveillance in animals. And this includes wildlife, livestock, and domestics, and develop and support inter agency One Health platforms. Next one, please. And this graphic that is part of the report is trying to highlight this multi-scale and multi-step process of pandemic emergencies. So, we have tried within the recommendations to direct some recommendations to these pre-emergence as a stage, which means we need to have good surveillance at this first level to catch things early, but also to keep moving into what to do when we start having the peaks or the outbreaks.

And finally, what to do when we have the global emergence. Next one, please. So recommendation number two had to do with the incentives that need to be built into systems for more rapid reporting of surveillance data from all countries to WHO and to the One Health Tripartite to more quickly be able to identify in that, at the bottom of that figure that I just show, which one's the origin and the spread of novel agents and strains. And these incentives and barriers to reporting should be removed. So this is a critical issue, we need to have a more rapid reporting surveillance data system from all countries. Next one, please. So recommendation 2.3, countries should institute surveillance as the backbone of their health care systems. So that's why this recommendation goes to national authorities with the advice and assistance of regional and global public health agencies, who should establish these robust surveillance systems that will give true timely and comprehensive risk assessment that will help to inform policy decisions.

Our recommendation also, it's directed to epidemiologists that should be alerted to potential ascertaining biases for such biases during the analysis and interpretation of the data. That could happen so they could be able to alert authorities and take into account those biases and improve the surveillance methods to achieve better representativeness and sufficient geographical coverage. Next one, please. Recommendation 2.4. WHO, the regional disease control agencies, European Center for control, Africa Center for Disease Control, for example, should work with countries, and national governments should be working also with supranational entities to harmonize, coordinate, and optimize surveillance activities, data collection and sharing. Next one, please. So from surveillance and data sharing, we are going into effectiveness of key non-vaccine measures. And the recommendation 3.1 had to do with the World Health Assembly. And we discussed that it should be a change in the international health regulations to allow countries to use border measures during a pandemic of influenza or other respiratory viruses.

Recommendation next one please, recommendation 3.2. At the global state and local public health agencies and other entities should mandate wearing face masks that comply with WHO's guidance. There is enough evidence and it's all in the report that a really a points into the importance and the effectiveness of the use of face masks. And in the case of influenza, we added that when justified by the incidence and the severity of influenza. Next one, please. Recommendation 3.3, in collaboration with other expert bodies, WHO should develop and disseminate technical recommendations on how to create ventilation conditions in various settings that will reduce the transmission of respiratory viruses, and should promote this widely and assist countries in implementing them. And we think this is a critical issue, ventilation needs to be taken into account as one of our weapons to fight transmission of respiratory viruses. Next one, please. Recommendation number 3.4, the WHO, CDC as well as regional, national, subnational public health authorities, should recommend against the use of plexiglass barriers, or the use of face shields without face masks.

Next one, please. Recommendation 3.5., and this has to do with research, right? What we have seen is that there is research done in the medical fields and research that is more in the area of the scientists. And what we are calling here is that there needs to be an incentive for more integration of the research among these two groups, scientists, medical fields to inform investigations on transmission, prevention, and treatment of influenza and other respiratory viruses. Such integration should include standardizing and sharing language across sectors and mechanisms in order to share relevant data. Next one, please. Now we go to the other component that we have realized that is quite important, is not only to know that something is effective, but how can we make it effective in real life? How can we implement it well,

and for that, the context is critical. And we have realized that social and political contexts are quite important. So in recommendation 4.1, we're calling for global and regional public health agencies, and national governments, including the local and the state health agencies, to adopt policies that are tailored to each affected population, taking into account its' social, economic, and cultural characteristics.

They're needs, the resources, and other contextual factors, including its norms, values, and beliefs in order to optimize the implementation of public health interventions, especially those interventions that rely upon individual behaviors. Next one, please. In recommendation number 4.2. Governments, leaders, and departments of health at local state and national levels as well as elected and appointed government leaders should take the systemic factors, including race and socio-economic characteristics that affect the health of affected populations into consideration when developing and implementing public health interventions. Demonstrate in their behavior, other Institute's adherence to non-vaccine measures to prevent influenza in order to promote public trust and uptake of these measures, which means that the governments and the leaders should be showing that they also believe and they adhere to these measures. So people will follow. There is a need also to engage the community in the decision-making.

And we have to be careful in their choice of words, utilizing more positive communication. And this is something that has been seen during the pandemic, instead of physical distancing, and social solidarity, let's talk about instead of physical distance, we use physical distance, instead of social distancing. And instead of individual isolation, we can use social solidarity. So we have words matter, and we need to be sure that we are using the right words. Next one, please. And recommendation 4.3, funding agencies should create mechanisms to support the rapid application of data and Implementation frameworks during an influenza pandemic, as well as to enhance these similar mechanisms during the inter epidemic periods. We need to invest on understanding how to better implement, measures that are in the in-control conditions work. Such mechanisms can be used to support implementation research on non-vaccine control measures for influenza. Next one, please. National governments as well as local, state, and global public health agencies should develop readily and demonstrably implementable intervention plans for outbreaks of influenza and other respiratory diseases.

And we want to highlight implementable intervention plans. That's why these plans include embedding the 30th collection and use of data in all interventions, taking into consideration the needs of a population affected. Again, with a special attention to needs of marginalized groups. That means that we have to incorporate within the research not only numbers but also behavioral and social sciences. And these from the beginning of the pandemic, planners should use proven scientific frameworks in order to guide and improve the implementation of non-vaccine influenza control measures. Next one, please. Now we go to our chapter five, which have to do with therapeutics. Recommendation 5.1 calls for national governments that should mandate that the appropriate authorities, ministers of health, or comparable governmental agencies should conduct periodic inventory evaluations of existing stockpiles on both therapeutics, including antivirals and supportive care treatments like oxygen, and anything that is needed for delivery, for example, the protection the personal protection equipment.

And also it's not only to create the stockpiles but also assess if they have them with what they have the availability to produce versus what they would need to procure. And secure an adequate, reliable supply chain in order to appropriately respond to an outbreak of pandemic influenza. This is a critical issue that

we have seen, especially in low-middle-income countries, which we were not used to stockpiles, we were not able to produce. OK, so we have really to have these periodic inventory evaluations. Next one, please. Recommendation 5.2, the government agencies responsible for public health guidance in each country should develop a framework to guide, use, and how to prioritize treatments that can be flexible with changing evidence during a respiratory viral pandemic. And, again, let's highlight flexible, let's highlight evidence and changing because this is an ongoing situation, this framework should be able to be adjusted depending on the pathogen, taking into account its transmission mode, the at-risk populations, and associated morbidity and mortality rates.

Next one, please. In recommendation 5.2, I mean, this was a little long, there were some important considerations that we wanted to highlight, OK. So WHO will evaluate guidance from global and national health organizations and from professional societies in order to define evidence-based treatment guidelines. Who will evaluate this guidance? How guidelines for treatment, selection, and delivery will be communicated with the states provinces, and regions in the country? How suitable are places to administer the care that will be selected? Which populations should be the focus of the therapeutic? And how to distribute the treatment modality equitable throughout the country and among patients? Next one, please. In recommendation 5.3, global and regional health organizations should collaborate to determine how therapeutics and the resources needed for their delivery can be shared between countries to ensure equitable distribution and control pandemic spread. Next one. In recommendation 5.4, governments and private companies should focus their efforts on researches, strategies, and platforms that were shown to be particularly effective during COVID pandemic.

Q&A

STEPHANIE MICELI

And with that will now begin our Q&A session, just a reminder, you can simply type your question into the chat box below the video frame if you would like to submit a question. And I also want to acknowledge Dr. Garcia is joined by several fellow committee members to help answer your questions. As she said earlier, we are joined by Mr. Alex Capron, who is the chair of this committee, and a professor at the University of Southern California, where he teaches public health law and policy bioethics and torts. We also have with us today Dr. Adolfo Garcia Sastre, who is director of global health and emerging pathogens and professor of microbiology and medicine at the Icahn School of Medicine at Mount Sinai. We have Dr. Raina MacIntyre, who is a professor of Global Biosecurity, a national health and Medical Research Council, principal research fellow and head of the biosecurity program at the Kirby Institute in Australia. We have Dr. Linsey Marr, who is Charles P. Lunsford, professor of Civil and environmental engineering at Virginia Tech. We have Mr. Tolbert Nyenswah, who is a senior research associate with the Department of International Health at the Johns Hopkins Bloomberg School of Public Health. We have Dr. Rosanna Peeling, professor and chair of Diagnostics Research at the London School of Hygiene and Tropical Medicine and director of the International Diagnostics Centre. And we have Dr. Marybeth Sexton, who is assistant professor of infectious diseases at the Emory University School of Medicine and medical director of Antimicrobial Stewardship at Emory University Hospital, and epidemiologist at Emory Clinic. And with that again, we will start the Q&A. We do have first question for you all, which is, why did the committee recommend against physical barriers?

PATRICIA GARCIA

So I would like to invite Linsey to answer that question.

LINSEY MARR

We see these types of barriers everywhere, but there is extremely limited evidence to show that they work and face shields are really barriers intended to block spray by large droplets. And they actually would not work for aerosols in the same way, we did find limited evidence that they can potentially be harmful. For example, there was a study of schools where they found that there was an association between the use of plastic barriers on desks and a higher incidence of COVID 19 symptoms. There was also a study, but there it has been a newer study showing that the barrier does reduce exposure to aerosols in a situation where you have two people directly across from each other for a brief period of time. But it doesn't account for increased exposure to people who are on the same side of the barrier or somewhere someone who might come in right afterwards. They can block proper ventilation of a space which is critical for removing aerosols, and thus we recommended against them.

STEPHANIE MICELI

Thank you. Our next question for you all is can you clarify the circumstances when countries should be allowed by the International Health Regulations to close their borders during a pandemic?

PATRICIA GARCIA

Raina.

RAINA MACLINTYRE

Yeah, that's an interesting question, and I think the origin of that recommendation, the International Health Regulations, and the recommendation of WHO not to close the borders is more around concern about trade than around health. And in the end, closing the border is a national decision. And countries that did use that strategy, ranging from Australia and New Zealand to small island nations with very weak health systems like Samoa, manage the pandemic very well last year with maintaining essentially a zero or minimal COVID scenario. And economic studies subsequently have shown that, that was actually more beneficial both economically and health-wise.

ALEX CAPRON

May I add a word about that? I think it's important to understand that the use of such a limitation at the border or complete closure at the border depends upon the nation not already having community transmission of the virus. It's not an effective strategy otherwise, so it's a relatively limited situation. Moreover, we were sensitive and discussed the reason for that being part of the IHR this general prohibition on using border controls. And that is, it's important that nations not be discouraged from quickly reporting outbreaks that could become a pandemic to allow other processes to kick in and decide what the global response should be. And so it's important that when they do that, that they not be singled out. And there were experiences, obviously with COVID of focusing on the process of singling out, and it was very unfortunate. So, therefore, it's important that this notion of closing is in circumstances where it would be possible to allow the country to have much better control because it isn't already subject.

And the closures are global. They're not directed at the country that made the report and with that we thought the reasonable balance was to have the IHR adjusted to recognize that there will be circumstances where that is a good public health countermeasure.

STEPHANIE MICELI

Thank you. And as a follow-on to that, doesn't the recommendation that the International Health Regulations be amended to allow countries to close their borders run contrary to the recommendation to eliminate disincentives for countries to report outbreaks of pathogens with pandemic potential?

ALEX CAPRON

Well, Stephanie, as I tried to suggest, we think that would not be the case, that there would be a contradiction between those, we think it's very important that incentives exist at the local regional national level in making reports, including that final level between the nation and the global institutions. And you can avoid that if any response by closing borders does not single out that reporting country, but rather or countries, but rather is instituted at a time when the country wanting to make that limitation could have a very substantial benefit and it is doing it worldwide, recognizing as was certainly true in COVID, that this spread of the virus, the respiratory virus is likely to be wider than whatever is perceived at that moment. And so they have to be very certain that they're in a situation where they're not having community transmission, in which case the border closure would be ineffectual and set of bad precedent, and that they are doing it as to the rest of the world, rather than as to a country that has done the responsible act of quickly reporting an outbreak of the novel virus that could have pandemic potential.

STEPHANIE MICELI

Our next question for the committee is, could you please explain more about what role you are recommending for the World Health Organization in getting countries to adopt standards for ventilation? That would be more protective of people indoors.

PATRICIA GARCIA

Linsey.

LINSEY MARR

We are asking the World Health Organization to develop guidelines for ventilation. There is some material out there now. I think there's a lot we've learned and a lot that can be done to further emphasize ventilation and provide some numerical targets for ventilation rates that will appreciably reduce the risk of disease of transmission.

STEPHANIE MICELI

Thank you. Our next question is in recommendation 4.2, you mentioned leaders should model good behavior. Did the committee talk about what to do to mitigate the impact of that behavior?

PATRICIA GARCIA

Anybody that would like to answer that? One of the things that we realize is that by the time we were starting to work on this report, which has to be based also on evidence, most of the evidence was just being collected and most of the studies that had to do with the leadership and the context were starting to be done. People, even researchers, have been very busy trying to fight COVID. So this is an area that definitely needs more data, needs more research. We need to learn and that's why we were highlighting also the importance of doing research, behavioral research, social sciences to try to understand how to better work together and how politicians, the community leaders, how their behavior could potentially be critical on how the populations will take the interventions. Legitimacy and trust are two issues that are critical in this area.

ALEX CAPRON

You know, a related aspect of that, Patty, that I think you mentioned very important is allowing the recommendations which must be based on the current evidence to reflect changes in the evidence without undermining trust. And this is an extremely we talked about. This is extremely sensitive matter and having that consistency by the leadership, the political leadership, which is not in a position to make the judgments necessarily in the first instance about the evidence, which is an expert matter reflecting when those judgments need to be made, reflecting what the evidence shows. And you know, the old saying when people say, do what I say, not what I do, when we say that as a joke because we recognize it's very hard to have trust in a recommendation that the recommender isn't following. And so ideally, as was exhibited in some countries, very well. The political leadership communicates to the public that we're making changes not in an arbitrary way, but because we now have evidence, the evidence, for example, on the effectiveness of face masks develop in the early period of the pandemic.

And it required a different message, not masks are not a primary tool, but masks are a primary tool along with several of the other countermeasures. And that understanding developed inside of the role of the political leaders is to overcome people's skepticism when recommendations change and communicate we're changing because we know more now than we did last month or last year, and there is a solid reason for changing, and I'm going to follow that. I'm going to put on the mask, I'm going to socially distance, I'm going to avoid indoor meetings and so forth, having crowds of people come to indoor events. That's not the time for that, and I'll show that in my own behavior. And without that, it's very hard for the scientists who are carrying out the studies, making the interpretations to have a full understanding of the public. Because of course, when things change, there's a natural inclination to think. People are being inconsistent. No, they're being consistent with new evidence, and that's what we were trying to emphasize in that recommendation.

STEPHANIE MICELI

Thank you. Our next question is the report mentions global health security index preparedness scores did not always accurately predict pandemic response. How much weight should we give to this finding? Does the report offer advice on how we can define preparedness or should that be adjusted?

PATRICIA GARCIA

Marybeth, would you like to answer that?

MARYBETH SEXTON

Sure. So we looked at with respect to defining preparedness. Looking at that, particularly from the therapeutic and allocation of therapeutic perspective. And so in recommendation 5.2, we laid out that list of ideas that should be addressed ahead of time and then adjusted as needed. But things like how are you going to make decisions about which guidance you're going to follow? How are you going to make decisions about who is prioritized? How do you assess your supply chain ahead of time and then how do you execute on your supply chain in the moment? How do you ensure that that is all done equitably? And so that degree of preparedness, I think we really learned from COVID is critical. And I think we'll have a lot to do with how we attack an influenza pandemic in the future, because a lot of those issues will be the same about how to allocate therapeutics, where to allocate therapeutics and what the supply chain looks like and what to do when it's disrupted. So I think with respect to existing scores of preparedness, it's not that those should be disregarded because they contain a lot of other inputs into how those are calculated that go beyond some of the preparedness aspects we addressed

with respect to non-vaccine interventions and including into the vaccine realm, which some of the other study groups have addressed.

But I think it's important to remember that as good as some of those indicators can look, how you're going to be able to shift depending on the pathogen, the mortality rate, the transmission modality, and how contagious something is, that your ability to pivot in the moment and to address some of those challenges and your ability to address a supply chain that globally may be impacted may not be picked up as well on existing metrics and are things that we need to be able to prepare for in advance.

RAINA MACLINTYRE

I might just add to that that probably, you know, I think all the indices that go into something like the Global Health Security Index are good and necessary, but looking at lessons from the COVID pandemic, the three things that probably weren't accounted for that should be accounted for in subsequent iterations of such indices are culture, leadership, and universal health care. And those three things could explain, for example, why relatively affluent countries did badly last year.

ALEX CAPRON

We also noted other social factors very much related to what Dr. MacIntyre just said, which is if there are equity issues in the implementation that certain parts of the population will face particular difficulties in following the recommendations, if housing is insecure or food is insecure, or if there's a lack of replacement income and so forth, you have equity issues in trying to achieve people distancing, staying at home and so forth during the early spread of a pandemic and we, therefore, noted that as a barrier to implementation. And unfortunately, those kinds of disparities exist in high-income countries as well as low-income countries. And so we saw a good deal of that. Does any other member of the panel want to comment on any of the other failures of the predictive scores?

PATRICIA GARCIA

Well, one. I mean, I think we all agree that the predictive score didn't work because there are other aspects that we have just realized that are important. But even with a predictive score, several countries had a very low score and nothing was done. So it's not enough to have this scoring, but we need to think globally, how do we approach and how do we help countries? Or how do we, as countries really take the responsibility of changing those issues. So I have to say that I mean I know about several Latin American countries doing this questionnaire is voluntary and we knew what were our weaknesses, but nobody, especially at the political level. This was not a priority. There are priorities that are fighting between each other, but I think for it, this might be the moment right now when we still have fresh what is going on with COVID to think it's not only measuring, but what are we going to do with those measures? So with those numbers, what are the kind of things that need to change and how to improve?

TOLBERT NYENSWAH

So I want to jump in a little bit on the index score and all of that, and for full disclosure, our member of the panel of experts on the index. And so I know we've done a lot of adjustment on some of those things that Raina and Patty now have mentioned concerning, especially political leadership and the importance of that and cultural issues, social determinants of health and all of those things I've been taking care of right now. By December, another report is coming up very shortly that incorporate all of those issues. Thank you.

ROSANNA PEELING

And I just like to add that I think through this pandemic, we've learned that public health, unlike what we thought we used to do well in public health, we need the public to be part of public health. We cannot simply just tell them what to do and they will do it. So I think with this pandemic, we've learned that, no one safe until we're all safe and that we need to give the public the tools and the data, the knowledge in order to act responsibly, and that it's something that we should think about for the Global Health Security Index for countries, how much they can establish what John Nkengasong, the head of Africa CDC, said should be the new public health order.

RAINA MACLINTYRE

May I just add to that the issue of culture that public health measures for epidemic control or pandemic control are necessarily draconian because you have to stop people contacting each other and whether it's face masks, which you know, there was no culture of face mask-wearing in Western countries or movement restrictions or density limits or lockdowns. Countries that have a very highly individualistic culture, it'll be much more difficult to implement those sort of measures, whereas countries that have a more collective culture would have greater ease in implementing those kind of measures. So I think those are some of the culture is really important and then universal health care. You know, if you've got to pay for a COVID test and we know how important testing and identifying cases is, you're not going to get good rates of testing. You know, it's got to be free and easily accessible.

STEPHANIE MICELI

Thank you. Our next question is a two-part question about diagnostics and therapeutics. The first part of that is just the report addressed specific recommendations about therapeutics for influenza, any potential future research priorities. And then the second part is when we asked everyone to get tested for the flu, as we did for COVID 19, or would we not recommend everyone get tested if they have like symptoms?

PATRICIA GARCIA

Rosanna, would you like to take the lead on that one?

ROSANNA PEELING

OK, so I think for testing for our report, we didn't find enough evidence to say whether we should do more testing for flu and less testing for COVID or the other way around. First of all, COVID is a new pathogen. So that's why at the beginning of the pandemic, the director-general of WHO said test, test, test, because we need to do all the testing we can to know how the pathogen infects people. What are the common clinical syndromes so that we could refine the clinical definition of a case? And also, we want to identify cases early, be able to do contact tracing, and stop the spread. So, so that is why we have testing centers. We urge everybody who has COVID-like symptoms to get tested. But I think as we know now more about the pathogen, we know its way of transmission and we're more able to control the disease, especially with vaccines, then we are looking to see whether this virus would become endemic. And once it's endemic, then it would be very important to start adding COVID to the surveillance that we have in countries.

And then, you know, I think that at that stage when COVID becomes endemic and it's just all a part of a seasonal cause of respiratory infections, then countries may be better able to use their resources to do our strengthened surveillance and track emergence of variants of concern, et cetera. And so right now, it's too early to tell one way or the other. So the story is to be continued.

ADOLFO GARCIA-SASTRE

Maybe I can add something about therapeutics. So for influenza, we have some drugs available, we have Neuraminidase Inhibitors we have Endonuclease Inhibitor. But these drugs still need to be taken very early on during infection in order to make an impact. They may cause an impact for people that are hospitalized, but the impact is more limited there. And we know very little about how to treat severe disease, which is also one of the few stuff we found with COVID 19. The use of dexamethasone, the use of anticoagulants these seem to help some individuals, but not all the individuals. So there is still a lot to be learned about how to treat severe disease for both COVID 19 and influenza. And there is also the issue of potentially resistance to already existing antivirals for influenza, and therefore the need for more broad-spectrum antivirals for influenza that may not lead to development of resistance. So, but especially in the area of treating the host according to symptoms, there is certainly a lot of things that need to be done.

Still, we know that both from COVID 19 and for what we have already available for reports that we still we need to do quite research on that is clear.

MARYBETH SEXTON

And I think along those lines, one of the things that we tried to call attention to in the report is that more than direct transition of therapeutics for COVID 19 and influenza, because we know that some of those do not cross. Some of the guiding principles of therapeutic research that we learned to adopt this point to focus on during COVID 19 may have applicability to influenza. So things along the lines of going after some of the host inflammatory response to disease and how does that apply to severe disease with influenza things like dexamethasone, tocilizumab, baricitinib that we've used with COVID 19? Are there similar avenues to address with influenza? And so looking at some of those areas of crossover on the general principles of the research on therapeutics.

STEPHANIE MICELI

Thank you all, and I know we're coming up on the hour, so this question will be our final one. And it's like you've stated in the study lab studies randomized controlled trials and observational studies demonstrate that face masks are effective for both COVID 19 and influenza. However, as has been seen in the US especially, some of the best measures for protection have been highly politicized. How do we reverse this and communicate to the general population that mask-wearing may be here to stay?

PATRICIA GARCIA

That's exactly what we are trying to introduce in Chapter four. When we are talking about the context. OK, so those measures that depend on the behavior of humans need more research to understand why humans act the way they do. So one of the goals is we need really to do more research, social sciences and behavioral research to understand how to change those behaviors, how to better communicate. Alex was talking also about having the models, the leaders that could become role models for the use of these measures. I think disseminating better the information that we are that we have right now is not going to be enough, OK? We know from the history of HIV and other diseases. I mean, we know that condoms work, but people don't use condoms. OK, so I think there is a lot that needs to be there. But having right now, the scientific evidence is the first step we need to work also on how to communicate that better. But we need to understand how to better act on the behavior of people. Changing of their behavior.

It's very difficult cultural norms, as Raina was saying. I mean, for societies that are more individualistic is more difficult for us. People are using masks, but the problem is that they don't... And I'm talking about Latin America. We're very social. We don't respect distance, social distance. We want to be very close together, right? So these kind of issues need to take into account. So it's not enough to have a directive measurements. We need to understand how to implement that better. And for that, we need all the sciences working together.

TOLBERT NYENSWAH

In that line this is where the bottom-up approach is very, very much critical. Engaging your community is critical. Thank you.

STEPHANIE MICELI

Well, thank you all.

ALEX CAPRON

Thank you.

STEPHANIE MICELI

Thank you to Dr. Garcia and to all of our committee members who participated during that Q and A and for very thorough discussion on the Public Health Interventions report.

GLOBALLY RESILIENT SUPPLY CHAINS FOR SEASONAL AND PANDEMIC INFLUENZA VACCINES

STEPHANIE MICELI

Will now move on to part two of today's session with our discussion on the supply chain resilience for influenza vaccine studies. And for that, I'd like to introduce our chair of that report. We'll be hearing from Dr. Ravi Anupindi, who is professor of Operations Research and Management at the Stephen M. Ross School of Business at the University of Michigan. Welcome Dr. Anupindi and I will turn it over to you.

RAVI ANUPINDI

Thank you Stephanie. Good morning, good afternoon and good evening wherever you are. It's my pleasure to present to you findings and recommendations on global resilient supply chains for seasonal and pandemic influenza vaccines. Next slide please. So first of all, I would like to recognize my co-chair Prashant Yadav as well as the committee members who came from vetted backgrounds with lots of deep experience from industry as well as academia. And really appreciate their taking time from their busy schedules to participate in our meetings. I would also like to recognize the academy staff who really worked extremely hard to make this possible. So I really appreciate that. Next slide please. So what I'll do is, just like the other committees walk you through the statement of task first and then outline how the report is structured and walk you through some findings and recommendations. Next slide please. So we had a fairly extensive statement of task broken into about seven pieces. Number one was to review recommendations for pandemic vaccine manufacturing following SARS, H1N1, Ebola, COVID-19 responses, et cetera.

The second was asking us to identify what was all the enabling factors for national vaccine distribution readiness that facilitate equitable distribution and efficient use of resources, including in low-resource

countries, to talk about, cold-chain infrastructure, immunization frameworks, et cetera. Next slide please. The third item in the statement of task was to identify critical gaps in vaccine delivery, which gets into details of supply chain, about managing inventory, managing resources like cold-chain, et cetera, and what kind of delivery platforms are there for actually doing the immunizations. Task four was around manufacturing of vaccines itself. That is what are some of the critical inputs that go into influenza manufacturing and what are some of the existing mechanisms for tracking these inputs? It's not enough just to have the final stage of production, we need to look at all of the components that go into vaccine manufacturing. So that was statement task four. Next please.

Now statement task five asked us to identify novel technologies and advances in translational research and science derived from the current pandemic that can be adapted to scale-up and sustain influenza manufacturing and distribution. So going from research to manufacturing, that interface. How do we look at that? Statement task six asked us to identify what were some of the barriers for the scale-up of manufacturing going from clinical trials to scale manufacturing for pandemic vaccines, and what strategies could we recommend? So while six asked us to identify the barriers, seven then went one step further to say what kinds of incentives could be devised to effectively encourage investments in vaccine manufacturing. So these were fairly extensive set of tasks that we had. Next slide please. Now I just want to make some highlights of the nature of the task that we had. We were asked to look at previous SARS and H1N1 kind of epidemics. But here, now the lessons derived after COVID-19 experience, and the challenge was that we are still learning lessons through this because it's not over yet, including all of supply chain and manufacturing.

Number two, the committee really tried to balance off the lessons learned and to balance off the roles and responsibilities of United States and global actors. It's not always easy to identify the global actors because we're still living through this as we manage the COVID and the experience of COVID is really very new. The final part on the recommendations is that, from a deployment distribution of vaccines perspective, this is going to be getting to in-country. They are very context-specific and there is a lot of heterogeneity across countries. So we didn't get into specifics of each country but stayed at the high level in terms of what kind of frameworks and what kind of common issues arise as we think through this. So that's kind of at the high level the summary of recommendations. Next slide please. Next slide please. So before I discuss the recommendations in this webinar, I just want to say that we had seven items in the statement of task. The way we organize this around in terms of chapters, there are six chapters.

Chapter one there's summary. Chapter two gave some introduction of the vaccine manufacturing and distribution as overall. But Chapter three to six is where we get into findings and recommendations. What we started from left to right if you think about from vaccine manufacturing, so Chapter three focuses on all of the inputs that go into vaccine manufacturing and the recommendations around those. Chapter four then gets into distribution issues globally as well as in-country. So those are the physical distribution (INAUDIBLE). Chapter five then focuses on what kind of preparedness frameworks exist, what needs to be done, where are the gaps, et cetera. So that's Chapter five. And finally, Chapter six gets into the issues around barriers and incentives to ensure scale-up of vaccine manufacturing and sustainability of vaccine manufacturing. So that's how the different chapters are organized. Given the extensive nature of the shipment of tasks, we had quite a few recommendations. Obviously we'll not be able to cover all of those in this webinar.

So the numbers that are listed there are select recommendations that I will cover in this webinar. And of course, you have the report accessible to you to look at all of the recommendations. Next slide please. So switching to Chapter three which is focused on the critical components. Few key findings that global vaccine manufacturing requires timely access to hundreds of items produced by several manufacturers across dozens of countries. So this is truly a global endeavor to get all of the inputs together. Which means that the components must be defined, identified and managed for both seasonal and pandemic influenza to ensure uninterrupted and timely equitable vaccine supply. This is where the set of countries that have this production capacity of inputs as well as vaccine manufacturing, trade barriers and other kinds of interruptions could put a dent in how we can ensure vaccine supply. So what is needed is a well coordinated global body with an inclusive governance structure that will play the role of orchestrations. We emphasize the word orchestration, of such a globally distributed supply chain to produce influenza vaccines.

So these are some of the key findings coming out of the Chapter three which was focused on vaccine manufacturing. Next slide please. This is just a graphic to show you illustrate different components that go into vaccine manufacturing and highlighting the set of countries where the capacity exists. And just to highlight the global nature of it. And therefore any disruption in production of any of these inputs will hamper our ability to produce vaccines. Next slide please. So the very first recommendation that we make is that G20 should constitute what we call a global pandemic manufacturing supply chain task force. And this task force as a permanent structure governed by a globally inclusive body with technical responsibilities to ensure global pandemic influenza manufacturing and supply chain preparedness and response. So this is task force whose main focus will be around ensuring that all of the inputs into vaccine manufacturing, as well as the vaccine manufacturing (INAUDIBLE) capacity is well orchestrated so that we have sufficient supply of vaccines.

Such a task force will include in the governance structure, both relevant agencies United States as well as international governmental agencies, but also will include industry associations, private philanthropic organizations and international NGOs as well. So that's recommendation 3.1. Next slide please. In the rest of the chapter, we're going to highlight some of the recommendations and call out some specific actions for United States agencies to provide technical and resourcing support to the committee's recommended task force. The idea for this task force is they need to develop a comprehensive pandemic preparedness and response capability framework. What should that framework have? Typically three things. We need to have end-to-end visibility of all the critical inputs produced across the globe, different countries. And once we have visibility into those inputs, how much capacity this will produce is what? The second task would be to do an assessment of resiliency. Where do we have capacity gaps, where we have bottlenecks?

And once we do that analysis, then this body can then think about what are some mitigation measures that can be done ex ante as part of a preparedness task. So the third capability should be thinking about preparedness, thinking about response, as well as structures for global coordination across all of these different players for inputs as well as vaccine manufacturing. Next slide please. As we thought about critical inputs in our community, we thought that not just physical inputs but workforce is an extremely critical input for ensuring that we have sufficient capacity to produce vaccines. So this recommendation is focused on that about what the government agencies, commercial entities, academic institutions, et cetera, need to do to ensure that we have vaccine manufacturing and technology development hubs where training can be conducted. And then we are asking that the HHS as well as technical agencies,

including non-governmental partners such as PATH, to develop and implement a medical countermeasure university for training a vaccine manufacturing and delivery critical workforce.

So the idea is that we recognize that workforce in addition to physical inputs are extremely important. So we had a strong recommendation just highlighting that. Next slide please. There's been a lot of talk even in the other committees if you were there in the morning as well about the need to have a globally distributed network of vaccine manufacturing capacity. While we did not make specific recommendations about what such a manufacturing network would look like, but what we are calling out is this task force that we have asked in recommendation 3.1 that they should look into evaluating the feasibility, the structure, and sustainability of such a network. Technology is changing quite a bit. We have legacy technology, we have new technologies. Each of those technologies have different characteristics. And therefore what this network would look like still needs to be determined as we evaluate these different technologies. So that's recommendation 3.5. Do some research to figure out what this network should look like.

Next slide. So now we wrap up Chapter three which was on manufacturing and we get into distribution and delivery. So the key findings here really four levels if you think about this, first is the resources needed for distribution and delivery depend largely on the vaccine characteristics. As we have seen, the resources needed to distribute mRNA is very different, that requires ultra cold infrastructure, et cetera, versus the other vaccines. So recognizing that the design of the vaccine itself has a huge impact on what people need downstream in distribution (INAUDIBLE). Second finding was that countries need access to a broad portfolio of vaccines to adopt because they know best what is suited for their populations and the distribution infrastructure that they have, and therefore access to a broad portfolio becomes very important. So if you think about the first one is around design, the second is portfolio, third gets into the physical infrastructure. And what we have seen is the main bottlenecks are cold chain logistics and transport capacity, are the primary bottlenecks in vaccine distribution.

So once a country knows which vaccines they're going to deploy, they can review and assess how much of cold chain infrastructure and transport capacity they would need. But in addition to the physical infrastructure, we need the information architecture as well. So there is limited data on global vaccine distribution, how it contributes to challenges in vaccine planning. So bottom up in terms of what's happening on the ground in terms of distribution, how can data be captured to further up, to inform better planning, both at the country level as well as global planning in terms of how much vaccines we produce. So these are some of the key findings, recommendations are structured around that. Next slide please. So this is more of a broader recommendation to highlight the need to recognize a systems approach to design and development of vaccines for feasible distribution and delivery in various global context and support relevant innovations. So I want to kind of emphasize the committee wanted to emphasize the systems approach that is the first finding that design of vaccine impacts downstream distribution delivery issues.

So the follow up recommendations from this recommendation 4.1 was around how do we make the different stakeholders aware of these challenges? Or what does it mean for funding vaccine development? How do we kind of get that surfaced during clinical trials? What kind of investments need to be made to think about stabilization and delivery platforms? Because that's beyond vaccine development that could be done. So these are different ways to think about how do we ensure feasible distribution delivery. This is what is encapsulated under what we call a systems approach. Next slide

please. We move on to Chapter five which focused on what are some of the frameworks, tools and innovations for distribution readiness. Some of the key findings our Committee had was many countries lack frameworks for pandemic preparedness and vaccine introduction. Existing frameworks do not look to be suitable for mass vaccination campaigns. We also need improved tools for in-country allocation, distribution, administration.

And finally, trying to think about how to engage the private sector for planning could advance pandemic preparedness. Because what we are going through in the COVID is not only is COVID an impact in the health sector, it is impacting the entire country's economic infrastructure that impacts the private sector. So private sector has a lot of capabilities that could be leveraged both in planning and preparedness. So this was some of the things that we discussed in our committee. Next slide please. So the first recommendation in Chapter five would be these global agencies to come together, periodically convene... It's not like one time convening, periodically convene to identify challenges in global preparedness for influenza, as well as overall preparedness for emerging pathogens, benefiting from lessons learned. So the outcomes of these meetings should be to inform national authorities on approaches and best practices to prepare and periodically update the national preparedness plans. It's not just enough to have preparedness plans once done, but to have a periodic (UNKNOWN) to update them based on new information that comes in, new technology that comes in, et cetera.

Of course this will require technical support from different agencies. We need to ensure that plans are of high quality, they're granular, relevant, and actionable. And finally, we also call for national authorities should be encouraged to engage with the private sector for pandemic preparedness and response. Next slide please. One of the things that we found during COVID-19 is that it's not just the classical health agencies or this WHO, UNICEF and Gavi that engage in this, but you also have the financial institutions that are engaging. The World Bank, the IMF, other development finance institutions, regional organizations, everybody is coming together to help solve the problem. And yet sometimes what you see is there needs to be coordination across these agencies, coordination in terms of how do they do assessments of country readiness, et cetera. So what we're calling for is an independent convening to get all these agencies together to share their best from evaluating the tools used to respond to COVID-19 vaccine rollout.

Identify current capabilities, constraints, and gaps, and to harmonize country assessment methodologies relevant for different stakeholders. The last thing we want is a country to respond for one set of assessments to the World Bank or a different set of assessments to WHO or somebody else. So to the extent that this can be harmonized it makes it easier for the country to abide by some of these assessment methodologies. Next slide please. So here we go one step further. Some of this discussion has come up in the previous webinars about countries are sovereign. We can give guidance in terms of what they should do in terms of preparedness. How do we ensure that they will actually do comply? How can we incentivize country compliance? So recognizing that a pandemic, just like what we are going through right now, has much broader impacts than in the health sector. Not just health sector for COVID itself, but COVID has disrupted the delivery of other health services as well. So what we are calling out is other programs that the US government has through USAID or PEPFAR programs, that US Congress should authorize government agencies and programs to include pandemic preparedness as an input into country funding proposals.

That is, it should be everybody's task to think about whether the country has the preparedness plans or not for various health programs. And if there are gaps identified, then those deficiencies should be supported through technical assistance and financial support. Even in other programs and not just for pandemic influenza. Similarly, when global institutions like the World Bank, IMF or IFC, they are doing their development initiatives with the countries, they should integrate country preparedness assessments into their country economic assistance programs because economic development is also at risk when we have a pandemic. Next slide please. We were asked to look at some of the innovations that came out of the pandemic, of course still ongoing. We do identify some in the report, but we ask that there needs to be a comprehensive review of the innovations developed. Some of the innovations at the global level are well-documented already but there are lots of innovations happening at regional level and local level that still requires systematic review and capturing some of those innovations.

To also see where the gaps are for a future pandemic preparedness and response. Next slide please. When we come into barriers, incentives and innovation for sustainable mechanisms, a few key findings we have is that novel vaccine technologies are needed to produce more effective influenza vaccines in shorter timeframes. Because we have limited time in a pandemic (INAUDIBLE) and therefore we need to figure out new technologies that can get us there quickly and the vaccines are more effective. The second finding was that liability and risk faced by manufacturers, along with the lengthy regulatory review, are also barriers to innovation. So what can we do to somehow mitigate some of these liability and risk that manufacturers' face? And finally, transparency of clinical trial process is important for increasing vaccine acceptance and therefore demand, because if there is a challenge in terms of vaccine acceptance obviously that impacts demand. So these are some of the key findings and recommendations that are structured around these findings.

But I will only capture a few of those in the webinar given the time constraint I have. Next slide please. So coming up with this liability mechanism (INAUDIBLE) liability mechanism, et cetera, we reviewed what the current structures exist. And there are three structures that we currently have. The factors include - how are they funded, who is eligible for this, what is the eligibility criteria, how are they administered and what elements of compensation are being captured? So that is what this table kind of highlights. But what we recognize as a committee is that a low fault compensation mechanism is really a key tool to reduce the risk taking on by manufacturers doing vaccine development, especially when using novel platforms. So while we review these three systems here, in one of the recommendations we call out is that there needs to be some global indemnity mechanism, regardless of how the country actually sources or procures those vaccines, which mechanism they used to procure vaccines, whether it is the COVAX facility or in a bilateral arrangement, there needs to be one standard global indemnity mechanism that they can use that could mitigate the risk for the vaccine manufacturers.

That will incentivize the vaccine manufacturers to quickly scale up vaccine manufacturing. Next slide please. So I'll just close with just one recommendation. Of course Chapter six has many recommendations, I'll highlight one of the recommendations which is, given a lot of the new technologies that have come into effect during this COVID-19 pandemic, what we are calling for is a competitive assessment of all the available and potential manufacturing technologies for influenza vaccines. So the metrics for assessment could include, speed - how quickly can this technology be scaled? Complexity of scaling that technology - how scalable is it? How much flexibility exist, recognizing there was a lot of talk in the earlier webinars as well about sustainability. If the platform is flexible that could make other kinds of products as well, that helps in terms of sustainability. So we need assessment

of these different technologies for mass production. Once we have this assessment done, that should inform a decision making framework not only for future investments in those technologies, but going back to recommendation in the context of Chapter three that I talked about earlier, that would then also inform what kind of distributor network do we need to build globally.

Because the technology capabilities inform the nature of the distributed network that we need to build. Next. I think that's the end of my formal presentation, I would like to now invite my co-chair Dr. Prashant Yadav to offer some comments. Prashant over to you.

PRASHANT YADAV

Thank you Ravi, and thanks first of all to all of you who are joining and also to our committee members who like Ravi said come from deep expertise in different aspects of manufacturing, regulation, funding of research for manufacturing. I will hear from some of them in the Q&A session in a few minutes. I want to stress three points. One is that when we in this committee talked about what all needs to go into building resilience in influenza vaccine manufacturing and supply chains, and both pandemic and seasonal influenza, but also more generally for vaccine manufacturing and supply chains, we thought that it starts with good data on a number of things. It requires systems thinking, and systems thinking implying, regulatory, quality, critical inputs, lots of things that you would see appear in the recommendations that Professor Anupindi just described. And along with that, a very well coordinated risk management structure. You also see that the enablers for making such resilience occur in vaccine supply chain, those enablers include things such as indemnity or (INAUDIBLE) plants, or some areas where you might say, "well, this is getting into financing." Indemnity is one particular example.

But the reason we got deeper into some of those areas was that unless the enabling environment for the supply chain was in place, it would not be feasible to talk about a sustainable resilient vaccine supply chain. So we did delve into some of these areas which are in a way adjacent or auxiliary to the core remedy we're focusing on. I also want to remind us that there are many parts of this which are dynamic, especially because the global structure for pandemic preparedness, financing, manufacturing are involving and lots of discussions are in play currently. So in places where there are ongoing discussions such as what will be the future of new task forces that have been established or what is the nature of new financing that will be used? How will it be organized? Other structures that are evolving for global coordination partnerships, including for vaccine manufacturing preparedness. So I think at times the recommendations of this committee will have to be viewed in recognition of the idea that there are aspects of structure that are involving or financing that are involving.

Q&A

STEPHANIE MICELI

Thank you to you Professor Anupindi for that presentation and for your comments. I will now move into that Q&A session and just a reminder for our audience. If you would like to submit a question, you can just simply type that into the chat box below your video frame. And we're also joined by several other committee members for this Q&A period. We also have with us today Dr. Matthew Downham, who is with the Coalition for Epidemic Preparedness Innovations in the UK as the sustainable manufacturing

lead. We have Dr. Noreen Hynes, who's a physician, trained and board certified in internal medicine and infectious diseases with additional tropical medicine and epidemiology training. She also serves on the faculty at the Johns Hopkins University School of Medicine and Public Health. And finally, we have Dr. Jennifer Pancorbo, who is director of industry programs and research at the BioManufacturing Training and Education Center. So our first question for our panel is how did the committee decide that the G20 would house the proposed manufacturing task force?

And what would this entity look like?

RAVI ANUPINDI

Prashant do you want to respond to that?

PRASHANT YADAV

I'm happy to have you, but I think Matthew might be good to talk about this as well.

MATTHEW R DOWNHAM

That's fine, thank you. Thank you very much Prashant, and hope you can hear me all OK. So indeed, the suggestion was that the COVAX manufacturing task force that's been existence now for about four months, such be housed under the G20. Particularly given some of the activities that the COVAX Manufacturing Task Force is engaging on, particularly thinking through to one of the particular work streams co-convened by the WHO to support vaccine manufacturing capacity capability across low middle income countries. And this was felt to be aligned not just with the G20, but also with the G20 initiative in terms of supporting, for example, geo-diversification of vaccine manufacturing moving forwards, particularly to ensure improved public health security provision for those particularly in underserved or regions of the world that don't necessarily have vaccine supply currently. So the sense was the alignment, particularly like the say between the COVAX manufacturing task forces. We met objectives, its vision, its mission and how that aligned with the G20 accordingly.

Hope that addresses the question properly.

PRASHANT YADAV

One thing I will add to what Matthew said was, I think the committee deliberated quite a bit on the idea, what's the right hosting entity and structure for this task force. And the two ideas that we took into account in our deliberations for it has to be hosted in a place where the membership is consisting of countries which are currently or likely to be vaccine manufacturing countries. And we also took into account that if it is hosted by a structure which is all member states, then we may not have the kind of governance that is needed for something which is very specific, a technical task that requires very intense coordination. So I think that's those two points led the committee to think about the G20 as the structure for hosting.

STEPHANIE MICELI

Thank you. Our next question for you all is recommendation 4.3 discusses commissioning studies on demand forecasting and uptake. We know that demand varies. So is there more context on feasibility and how this can be improved?

RAVI ANUPINDI

Yeah, I can offer something and then maybe have other people jump in. I think it's, yes, demand is uncertain, but, you know, also influenced by local issues in terms of demand uptick, etc. So therefore,

getting a good sense of what are the factors that are impacting demand, whether it is, you know, hesitancy issues prior experience with health systems, there are many factors that go into that. So having and that could also be those factors could be country and region specific. So therefore, we are calling for research to kind of capture some of those that will influence that will impact how demand forecasting can be done. And that then filters up and aggregated such that our vaccine manufacturing network will figure out how much capacity to invest in etc. Anybody else wants to add something? Yeah.

PRASHANT YADAV

One thing I will add to what Ravi said, and then, sorry, Jennifer, is the idea that we have to make a start with better forecasting for seasonal flu vaccine. That will get us closer to having better forecasts for pandemic influenza. Because we are talking about influenza vaccines, I think the stock has to be... we can do much better on seasonal vaccine, seasonal flu vaccine or seasonal influenza vaccine forecasting and then from there build and contribute to the capabilities for pandemic. But Jennifer and others have probably thoughts too.

JENNIFER PANCORBO

I think your question, if I may add one of the other rationales that we entertain was the idea that we need to somewhat incentivize organizations and countries to look in to taking manufacturing, production and tracking of components that are important for vaccine manufacturing, influenza in particular. But others in general, and by looking into the demand and the need that different regions may have, then we can open up potential solutions and open up incentives for organizations to engage in manufacturing and by expanding the manufacturing capability, then going to solving some of the other issues as well.

RAVI ANUPINDI

And Noreen.

NOREEN HYNES

One of the things that certainly has been discussed in other groups and was discussed by (UNKNOWN) has to do with in an LMIC influenza might not be traditionally seen as an important problem when there are limited resources that you need to spend other things on. However, in the setting of the current pandemic, which is, of course, a respiratory virus, it will be very interesting to see what impact or change in demand this has, as people wish to prevent other potentially serious respiratory diseases. And if we can marry up with that, we might be able to get some better sense of the inputs that go into demand in different countries and in different settings, and that the uptake might be improved.

RAVI ANUPINDI

Thank you, Noreen. Matthew, anything you want to add?

MATTHEW R DOWNHAM

No, I think it's all very nicely been said, take the opportunity. Thank you.

STEPHANIE MICELI

Regarding recommendations 6.5 on agreeing to inspection and only exporting emergency use listing or pre-qualified vaccines, how did you decide to recommend a treaty as opposed to other mechanisms to do this?

RAVI ANUPINDI

Who wants to take that up the shot? Noreen.

NOREEN HYNES

Thanks. I will take a stab at based upon our discussions, but the important thing is that a treaty has much different impact than a recommendation would have from WHO. And in light of the fact that we have seen during the current pandemic the release of vaccines, perhaps before their time, that is, before there was sufficient data to understand what was the efficacy of a vaccine, which could have dissuaded population uptake. So we were thinking that something that was codified in a way that countries agree to and there could be the carrot and stick associated with this. We might have a more adherent group to following the necessary guidance for releasing a vaccine that essentially can be accepted globally under an emergency use listing.

PRASHANT YADAV

So to add to what Noreen said, I mean, I think we have a quite intense discussions in the committee about how do we ensure that, you know, quality standards are stringent and they are upheld? And we talked about a combination of incentives and disincentives, and disincentives to make sure that there is some way to discourage manufacturers from bypassing good practices, adherence to good manufacturing practices. And one of the ideas was that you could do that by the Global Indemnity Program, which is the only manufacturers who would be allowed to be a part of the global indemnity program would be the one to go through a proper WHO pre-qualification or emergency use listing. But then we said there are still going to be requirements for the need to conduct. Independent audits and quality inspections and housing all of this under an existing treaty or the treaty that was that is being discussed and gives it the farthest reach and creates the right balance of incentives and disincentives for quality audits, and that was the driving factor in putting 6.5B under a treaty like recommendation.

STEPHANIE MICELI

Thank you, Dr. Yadav. Our next question is the findings and recommendations from this study seem applicable to the supply chain for PPE in general, for example, high filtration masks, medical gloves and rapid result diagnostic tests. This has been a roller coaster of supply, and demand and lack of high quality PPE was a key factor in community spread of SARS-COVID at the beginning of the pandemic. What are the committee's thoughts on this?

RAVI ANUPINDI

I can take a shot, I mean, we didn't discuss, obviously, this was not part of our strategy to discuss other public health countermeasures. But you're right, I think, you know, the question that the structures are similar structures would be definitely relevant for, you know, whether it's PPE or ventilators or other kinds of things, because we have seen similar chaos happen in scaling up of the manufacturing of drugs. So this comes under the broader idea of this is where the recommendation 3.1, which is and then what Prashant was talking about in his comments, saying good data systems thinking and a coordinated risk management structure. I mean, that's in some ways a universal kind of thing if you want to think about resiliency of supply chain for any critical work. But we didn't in our committee focus on the other. I would say that the structures, I think, would be relevant for much more broadly. Anybody else wants to add to that? Matthew?

MATTHEW R DOWNHAM

Yes, I mean, certainly, I think the PPE is as an illustration of how the pandemic has hit, the COVID

pandemic has impacted multiple supply chains and supply aspects, that have impacted not just health care, health major control provisions, but also the vaccine industries. And so there's a certain thought behind how supply chains need to be managed, particularly in future from the surge demand perspective. So there's that aspect as well. And certainly, I think the issue regarding the PPE illustrates the pressures put on systems when pandemics emerge and how they may impact other vaccine products like influenza, etc. that are used on an annual basis. It's a good question.

RAVI ANUPINDI

Jennifer and then Prashant.

JENNIFER

Thank you. Thank you Ravi. And if I may add to what Matthew just mentioned, we actually did discuss extensively PPE in the context of manufacturing because a lot of the same components that are utilized in care and in health are (UNKNOWN) by manufacturing facilities and the gowning that are required to access clean rooms and manufacturing facilities. And this or this objective is definitely all encompassing. And like Matthew indicated, PPE is an example of the many components and then we try to address.

RAVI ANUPINDI

Prashant.

PRASHANT YADAV

Yeah, I was I was going to say two things, one is along the lines of what Jennifer said, which is that the manufacturing network that we're talking about, which is going to get expanded will have new sites. We did talk about the need to have safety in place for workers in those manufacturing plants, so that is dependent on having PPE. The second is that I would like to conjecture about the supply chain for PPE in that sense is somewhat simpler than what we faced for flu vaccines, partly because the strain and the strain matching and those things have to be done each year, whereas for PPE, it's in that sense a somewhat more standardized product. So the planning processes are a little bit more complex and depending upon information getting revealed much closer to the season. And I think therefore we think this is more complex than the supply chain for PPE or other medical products that were.

RAVI ANUPINDI

Right. Yeah. Thank you, Prashant.

STEPHANIE MICELI

Thank you. Our next question is two parts. So how can we ensure that low and middle income countries don't get left behind in the rollout of a potential pandemic influenza vaccine? And then how can LMIC's be more engaged in the manufacturing?

RAVI ANUPINDI

Once you get back. Matthew. Yeah.

MATTHEW R DOWNHAM

Thank you. Yes. I mean, obviously from (UNKNOWN) but closely involved with the COVAX facility, that is, of course, trying to support ensuring the middle income countries are not behind in terms of the COVID pandemic currently, that drive to ensure equitable access to vaccines across the COVAX facility, which of course, is (UNKNOWN), GAVI, UNICEF and WHO. And such a mechanism, I think is really illustrated how groups have to pull together to facilitate getting vaccines to support LMICs, but also the complexity of

distributing vaccines into low middle income countries. And so in terms of the question in terms of also, how can the LMICs be more involved and not left behind? I think there's a call here to have more Geo-diversification of vaccine manufacturing and establish footprint in the middle income countries, low middle income regions such that vaccine distribution can be more accessible, more rapidly in an agile sense provided from directly within specific regions, rather than having call centers globally where vaccines are currently inarguably distributed from.

So there's a whole piece of work around how to ensure lessons learned. Let's say the current COVID pandemic, but LMICs are better served better provided for. And some of that speaks to, like I say, Geo-diversification. Improving vaccine manufacturing capacity capability maybe exists today and needs to be expanded or countries where it doesn't exist and needs to be established from the ground up. And that's some of the motivation, like I received, (UNKNOWN) and of course, COVAX, and I can see Noreen is (UNKNOWN) to speak. So I'll stop. Thank you.

NOREEN HYNES

Thanks, Matt. And we also discuss the whole issue, remembering the very nice diagram or pictorial that Ravi showed. You know, there are so many component parts that go into a vaccine, over 100 things that are needed. And we did also discuss the importance of regionalization. But also it could be an ultimate goal for a country, a low or low middle income country to become a vaccine manufacturer. But it can also begin with becoming a manufacturer of critical component parts that become part of this and that within a regional hub, they feed into it with a one or more regional manufacturers in an area. So it isn't a solution overnight. It's building capacity in a progressive manner.

RAVI ANUPINDI

Prashant and then, Jennifer.

PRASHANT YADAV

So I think we had multiple discussions, I think the precise recommendations in the committee's report that touched on this issue as far as I recollect are two. One is what focuses on asking this new taskforce to explicitly look at the value of decentralized manufacturing, to what extent can it be put in place, evaluating the economics and technical aspects of more decentralized manufacturing? So I think the committee isn't recommending a full fledged go to decentralized manufacturing. It is saying that this task force needs to get into that more deeper. The second is that where the committee is making a specific recommendation is around the area of workforce development for vaccine manufacturing. And that's an area where I think there is an explicit asked that Health and Human Services and other agencies should look at how can we develop a stronger workforce for vaccine manufacturing, which can then contribute to more localized manufacturing emerging over time.

RAVI ANUPINDI

Jennifer?

JENNIFER PANCORBO

Yes, if I may add the following what Noreen said, yeah, that this is something that will be develop over time kind of takes back to one of the first questions we had about demand and understanding demand. So using that knowledge will help us build up that understanding and then evolve the situation in terms of low and middle income countries. We learn through our investigations that depending in the region and somebody who's a very open and really engaging influenza vaccine, vaccination and orders are not

so much for a number of reasons. And so understanding that demand and how that pools will eventually help us develop a more strength in the hope and what interaction within the between the manufacturers and the various organizations involved.

RAVI ANUPINDI

Noreen.

NOREEN HYNES

And also building on what Jennifer has said and Matt and Prashant, and Ravi has to do with another thing that we spoke about and certainly would be under the umbrella of a G20 task force that's created is providing other incentives that would assist new actors in the field of vaccine development across the spectrum of the needed supplies. And that would be particularly when you get to manufacturing because of the difficulty going from small scale to large scale. Part of, one of our recommendations was that for these newer developers and small biotechs that as part of a contract, at least within the United States, and this could be something that the task force could examine or even under treaty, that you would need to identify a successful manufacturer to partner with to help you get across the finish line. And of course, would in fact be a step in building further capacity.

RAVI ANUPINDI

One last thing I would add, Stephanie, is that I think the government structures we call for it to be an inclusive government structure. So for example, the developing country vaccine manufacturing networks have representation there. So I think the other way to get the voices heard, both from manufacturers perspective as well as country perspectives is to have more inclusive governance structures. Thank you.

STEPHANIE MICELI

Thank you. Next question is about recommendation five, specifically the mechanism to evaluate preparedness plans. How did you envision this compared to other efforts like the US General Service Administration's plan? And how would these work together or are they completely separate from each other?

RAVI ANUPINDI

Yeah. We didn't get into details about how we would evaluate preparedness, but the idea that a lot of discussion in our group was that the preparedness plans are not granular enough. Countries are not obligated to submit their preparedness plans to the quality needed. So we need to develop, you know, what, give technical support as well as, you know, structure incentives to ensure that the preparedness plans are robust enough. So that was kind of the idea. And the second one was that it's dynamic. So that is why the recommendations 5.1 is talking about a periodical convening and updating based on lessons learned. You know, what we had a preparedness plan before is that still relevant? Are there gaps? So I mean, how do we know? So we didn't get into details about how actually to measure preparedness, but the idea of doing mock drills, et cetera, tabletop exercises are one way to ensure that our country is prepared. Anybody else who wants to add to that? Yeah. Noreen.

NOREEN HYNES

We did we did discuss the fact that there is at least under the global health security agenda, the joint external evaluation process that does look at preparedness planning. However, it is unusual for any of those plans to go so far as to look at their manufacturing or elements of manufacturing capacity. It really

has to do with a traditional Ministry of Health Preparedness Plan being ready to respond to additional surveillance, which we heard earlier today. It's very, very critically important, but it has not gotten into the manufacturing and supply capacity in many of those plans, and not all countries participate. So it's an idea that can be embellished as, for example, when the G20 task force could look at this further.

RAVI ANUPINDI

So I think, I suppose, you know, you raised the issue about the question, Prashant raises the existing kind of frameworks. I think part of this convening also is to begin to understand, OK, where are the gaps? And are existing frameworks good enough? What has been your experience from, you know, countries experiences from managing the COVID 19? If there are gaps that is rather theoretically committing to upgrade them or maybe develop a new set of criteria for what preparedness actually means.

STEPHANIE MICELI

Thank you. And since we are nearing the end of the time, it looks like this may be our last question. And we would love to hear from all of you, looking again at recommendation number five on real time global data to inform manufacturing, the World Health Organization is working on efforts to develop large scale levels at a, dashboard or hub that takes in information from companies to inform drug supply chain efforts. Is this similar to what this committee was envisioning for influenza vaccines?

RAVI ANUPINDI

Matthew, you want to take this one?

MATTHEW R DOWNHAM

In simple terms, yes. And so that the WHO hub is largely leveraging off the directors influenza program in terms of rapidly sharing data, for example, the database gives aid leveraging off the cancerous infrastructure. That upgrade shows through a network of laboratories globally that are monitoring and tracking the disease and its value. It's epidemiological and development, all of which feeds into the manufacturing strategies and decision making process. So that means, you know, that that exists today and has been in existence close to 70 years, certainly was the kind of template. And certainly, as I say, the (UNKNOWN) thinking forward to using that kind of model for future activities to monitor and track diseases and inform manufacturing accordingly. So I say sometime is yes, but obviously open to my colleagues for the feedback.

PRASHANT YADAV

So again, I wasn't sure, you know, WHO has, the World Health Organization has two or three initiatives which are probably fitting to what was described in the question, if it is about the influenza, just say it works as Matthew's describing hopefully he did, but it's also very well be about WHO work on building a control tower, demand and supply matching to for essential COVID technologies. And if that's the one that is being referred to in this question, I think it is structurally like that. But I think what we are recommending goes one level farther and it says a planning methodology which brings together what is the current supply, what is the, what is the currently installed manufacturing capacity and what is the demand and what tool allows doing that planning for influenza vaccines, both seasonal and for scenarios of pandemic.

RAVI ANUPINDI

Thank you. Anybody else? I think, I'd just like to add to that, Stephanie, I think the, also, what we

discussed in the committee is bottom up, there's lots of the country specific situation varies. And as dynamic as the changing, is there are there mechanisms or tools to be developed that can capture some of that? And of course, you know, there'll be data sharing restrictions that countries may have. But whatever level is needed for global planning, instead of mechanism or platform to filter some of that out so that for a global supply perspective, one is getting a better picture of what the time phase demand might look like. Anybody else? No, I think that's all we have.

STEPHANIE MICELI

Thank you so much to you, Dr. Anupindi and to you Dr. Downham and for all of the fellow committee members and to our audience, some of you have spent the better part of today with us for these presentations. So thank you for that. And just a reminder, once you exit this webinar, you'll be redirected to the main study page, and from there you can download all four reports and the related material. So again, thank you. Have a great rest of your day.