Clinical Laboratory COVID-19 Response Call
February 22, 2021

Agenda

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JASMINE CHAITRAM: Hello, everyone. Thank you for joining the Clinical Laboratory COVID-19 Response Call I'm Jasmine Chaitram. I'm with the Division of Laboratory Systems at CDC. The Division of Laboratory Systems has been hosting this call since March of last year. And we host them every other week. And we hope that there are useful to all of the laboratories and public health partners that are out there that are dialing in.

I wanted to tell you a little bit about our division before going forward with our agenda, because there are probably new callers, participants, that are calling in today, because we sent out a LOCS message to a bigger distribution than we normally do. So the Division of Laboratory Systems has been working with and supporting clinical and public health laboratories before COVID in the areas of biorepository, informatics, quality and safety, data science, and training and workforce development. We've also been working in this with these laboratories in preparedness and response activities. And we continue to do so during the COVID-19 response.

Our division is serving as a liaison between the CDC Emergency Operations Center and the clinical and public health laboratory community. We have these calls, as I mentioned, our agenda is showing. The agenda changes with each week, based on topics that are most relevant to the issues of the day. And we also take suggestions for topics for future calls. And I'll tell you how to do that in just a minute.
Before we get into the actual meat of the call, I wanted to cover a few housekeeping items, especially for those of you that are new. First of all, I just wanted to clarify that the slide decks may contain material from panelists that are not affiliated with CDC. And that the views that are presented may not necessarily reflect CDC's official position.

Also, as I kind of mentioned already, we have a new way of distributing messages for our Laboratory Outreach Communication System. We're using Adobe Campaign, which allows us to reach a larger audience than before. If you have already received a message from LOCS, Laboratory Outreach Communication System, then you don't need to do anything. But if you got this information about this call from a friend or colleague, you should click on this link. And you can opt-in to receive messages in the future.

Also, wanted to mention that the CDC Science Office has weekly summaries of new COVID-19 related studies on topics like epidemiology, clinical treatment and management, laboratory science and modeling. And to receive these updates, you can visit this page and enter your email to sign up for the COVID-19 Science Update.

As I'm talking, there are folks that are helping with this call. And they'll be dropping important links into the chat for all of you. Also on these slides are important links to resources for laboratories on the CDC website pages. We've put them here on the slides. So they are easy to find and to get to. We, the Division of Laboratory Systems, have a DLS Preparedness Portal. And this is like a one-stop shop for the information we provide to the laboratories.

It includes an archive of all of our LOCS messages, as well as the audio, and transcripts, and slides from all of our calls. So the slides that I just showed you, where there were important links, you can go to this website and download those slides to access those links if that helps you all. There's other information here on this portal and links to other CDC pages that are of use to all of you.

As I mentioned already, these calls are every other week. The next call will be on Monday, March 8 from 3:00 to 4:00 PM. We'd like to hear your opinion on any training and workforce development needs. And you can send those to LabTrainingNeeds@cdc.gov.

And then also, especially for those of you that are new, I just wanted to give you a little bit of information about how to ask a question. So in the Zoom system, there is a feature. It's a Q&A button at the bottom of the screen. We prefer that you use that to submit your questions to us. And do not submit your questions in the chat box.

By putting them in the Q&A, it allows us to track the questions that we receive. We are not going to be able to answer all of the questions we receive during the call. It's just a lot of questions. And we only have an hour. We want to give you as much information as possible and try to be as responsive as we can to your questions. It's just not possible.
What we will do, though, is after the call, for any questions that have not been answered, if you provide your email, we will follow up with you and give you a response if we can. Or as I mentioned previously, we might use that information to formulate an agenda for a future call. I do want to thank those of you that have submitted questions in advance of today's call. Once you received the email, you probably submitted a question to our LOCS mailbox.

And we did get those. And some of those will actually be answered offline because we don't have the appropriate subject-matter experts on this call to answer them. But we will be working on answering those questions for you. And we will continue to do the same thing for any questions that are submitted today that we're not able to get to. And just a quick note, if you're with the media, please send your questions to media@cdc.gov. And if you're a patient, please direct your questions to your healthcare provider.

And I believe that we are now ready to go ahead with our first presentation. It will be from Greta Massetti. She is with the CDC Community Interventions and Critical Populations Task Force. And she'll be talking about the operational strategy for kindergarten through 12th grade schools phased mitigation plan. And Greta, I'll just turn it to you.

GRETA MASSETTI: Thank you so much. And thank you for having me. So I'm just going to share with you, in the next few minutes, a high level overview of our K-12 operational strategy that was released on February 12. We actually had two documents that were released. One is a science brief that is focused on COVID-19 among children and adolescents and transmission in schools. And that science brief summarized the evidence on COVID and transmission in schools and served as the scientific backbone for our operational strategy.

The operational strategy is intended to support schools in safely reopening for in-person instruction. A lot of these reviews of the science found that many K-12 schools that have implemented mitigation have been able to safely open for in-person instruction and remain open. And so the strategy is intended to serve as a pathway, to provide a pathway to schools to open. And for those that are already open, to remain open through mitigation. Next slide, please.

So the strategy presents, essentially, three elements, what we call the essential elements of safe in-person learning. The first is consistent implementation of layered mitigation strategies. And that includes masking, physical distancing, cleaning, and maintaining healthy facilities, hand washing, and respiratory etiquette, and contact tracing, in combination with isolation and quarantine. That's the first element.

The second element is this idea of indicators of community transmission. So that school leaders are aware of the amount of disease circulating in the community. And the third element is bringing those together and providing a phased mitigation plan to help inform school leaders at what levels of community transmission safe in-person instruction is possible.

There are also two additional layers of COVID-19 prevention. And those include testing and vaccination for teachers and school staff. Today, I'm just going to mostly talk about the testing component. There are lots more information about the essential elements in vaccination on our strategy online. But I'll talk a little bit more about testing. Next slide, please.

Next slide. Oh, there you go. OK, so this is the second essential element, this idea of levels of community transmission. We provide two indicators of burden. Those are total new cases per 100,000 persons in the past seven days, and the percentage of tests that are positive in the past seven days, and different

thresholds for community transmission from low to high. This information is really intended to help leaders, school leaders, district superintendents, principals, decision-makers at the school level, understand what is the likelihood that a case will be introduced into the school setting, and what level of vigilance should they have to assess presence of virus in their community. Next slide.

So the K-12 operational strategy, testing is framed as an additional layer of prevention in schools. And with that in mind, all schools, regardless of whether they do screening testing or not, all schools are recommended to have a plan for diagnostic testing. What that means is, essentially, they should know if there's an individual in the school environment that has symptoms, a student or teacher, they should have a plan for how to handle that situation and how to offer diagnostic testing.

Do they establish collaboration with the local public health department? Do they refer to the individual's provider or some combination? But all schools should be prepared to know how to handle people who are symptomatic in the school building.

Then, some schools may also choose to implement screening testing as an added layer of mitigation to identify cases and prevent secondary transmission. It's not intended to replace other mitigation strategies. It's intended to supplement what schools are already doing, related to masking, distancing, and so on, and so forth.

So next slide, I'm going to just jump right in, because it provides more details. So the strategy provides a table based on the levels of community transmission, where-- and you can see from this table, at the top, it says all schools implement mitigation. And all schools provide, at all levels of community transmission, provide or offer diagnostic testing referrals. And then, schools that implement screening testing, we recommend doing routine screening testing of teachers and staff at least once per week at all levels of community transmission. And then, at moderate, substantial, and high levels of community transmission, we recommend routine screening testing for students, at least once per week.

There's also recommendations related to in-person instruction and sports and extracurricular activities. And I'm just noticing, by the way, that second row, there's a mistake. That routine screening testing of teachers and staff is repeated. It should say students in that second row, under screening testing. Apologies for that. We'll get that fixed. Next slide, please.

Recognizing that there may be limitations in availability of testing supplies, when schools have to make decisions about who to prioritize for testing, we recommend prioritizing teachers and staff first, then high school students, and middle school students, and then elementary school students. So essentially, we're providing recommendations to schools to make decisions about how to prioritize.

Schools may also choose to prioritize access to testing or implement screening testing in those schools that serve populations that have experienced a disproportionate burden of disease relative to population size. So for example, schools that are in communities with moderate or large proportions of racial and

ethnic groups that have experienced disproportionate high rates of COVID-19 and schools in geographic areas with limited access to testing. Next slide, please.

The strategy also talks about the elements needed for screening testing, the feasibility, and considerations, and ethical considerations in implementing screening testing. And these include things like having a dedicated infrastructure, staffing and resources to support testing. A discussion about CLIA certificates and waivers, mechanisms to report all testing results that needs to be established in advance of offering a testing program, timely reporting of results, ways to obtain parental consent, physical space, and plans to do confirmatory testing. Next slide, please.

So that's all that I have. That's the overall overview of the testing component. I am happy to include the link. I'm going to include the link to the operational strategy in the chat if it hasn't already been added. So that you can read the full operational strategy.

JASMINE CHAITRAM: Thanks so much, Greta. And thanks for the presentation. I do have a question for you. And the question is, in regards to K-12 testing guidance, we are seeing many schools set up COVID testing as a screening process for asymptomatic students or staff using either antigen testing or even some saliva-based screening that does not currently have an EUA. What is the CDC's position on the necessity or efficiency of asymptomatic testing, I think it's supposed to be asymptomatic testing, on a weekly basis at schools?

GRETA MASSETTI: So there's certainly a lot more detailed discussion in the strategy. And then we also kind of refer a great deal to FAQs on the FDA website. The strategy does recommend, or we recommend, that for schools that are implementing screening testing, that there are benefits to offering screening testing to asymptomatic students, and teachers, and staff. That's assuming that an emergency use approval has been obtained.

JASMINE CHAITRAM: OK, thanks. Here's another question. I've got another one for you. HHS has provided 150 million Abbott BinaxNOW antigen tests to be used solely for schools, K-12, as part of the mitigation strategy. What part, if any, does PCR testing play in this strategy, confirmation of positive or other needs?

GRETA MASSETTI: Yeah, so there is, I think, in my slide, I mentioned that there is a consideration around having a plan to confirm results, both for-- and we don't necessarily indicate that-- we don't even necessarily provide an example of the confirmatory plan. But we do recommend that a plan be in place. And then, just in terms of the recommended types of tests to be used.
The key emphasis, based on modeling that we have done and that other groups have done, the driving component really seems to be the how quickly test results can be returned. And in particular, anything beyond 24 hours seems to lose effectiveness or usefulness and actionable information in a school setting. So regardless of the specific tests being used, the most important consideration is how quickly can test results be returned.

JASMINE CHAITRAM: OK great. And then another question is—

GRETA MASSETTI: I'm sorry. I have a webinar at 3:30. And I have to jump to that right now. I'm so sorry.

JASMINE CHAITRAM: Oh, no problem.

GRETA MASSETTI: But I'm happy to answer any additional questions. If you want to send them by email, we can provide an answer.

JASMINE CHAITRAM: Sure, sorry, I forgot about that time crunch for you. And I do appreciate you taking the time to be with us today.

GRETA MASSETTI: Yeah, thanks so much. Sorry.

JASMINE CHAITRAM: OK, all right, we will continue on in our agenda and move to our next speaker, Vivien Dugan from the CDC Laboratory and Testing Task Force for the COVID-19 response. And Vivien has joined us for the last two calls to give updates on what's happening with the variants. And she will continue to do that as a standing agenda item, probably, several weeks into the future. So here she is today. Vivien, thanks for being here.

VIVIEN DUGAN: Thanks, Jasmine. Hello, everyone. Thanks for joining us today. Appreciate this time to kind of go over where we are with some of the variants. And most of this data is publicly available. But I just want to kind of give you a high-level overview. So you can see some of the things that we're tracking. Next slide, please.

So this is our emerging variant cases in the United States. It's a map that we have online. And it is updated on Tuesdays, Thursdays, and Sunday evenings around 7:00 PM. We're tracking, right now, B.1.1.7 variants, those are the variants that were originally found in the United Kingdom, the B.1.3.5.1 variants, those are the lineage variants that were originally found in South Africa, and the P1 lineage variants, which are the variants that were initially discovered in travelers from Brazil and Japan, but primarily from Brazil.

And since they were first detected, most of these variants have spread to a number of countries. So here's where we are with the US. So these data, I think it's important to note, that the data that's on our website represent sequencing confirmed variants, which is the primary, and mostly, the only way that you can detect-- at least the B.1.3.5.1 and P1 variants, through a lot of different sources.
So public health labs are doing a lot of sequencing. And so you'll see a lot of their data put into the public domain. CDC is performing the sequencing through our national SARS-CoV-2 strain surveillance network, where we're receiving approximately 750 primary specimens coming into CDC, which get sequenced. And then, often, are selected as a subset for virus characterization through laboratory activities.

Also see a lot of the data also coming in and being put into the public domain for those efforts, as well as some of the contract laboratory partners that CDC has funded, Illumina who is partnered with Helix, and then LabCorp, and now Quest Diagnostics, which is our most recent award that we expect to have data coming in to CDC and then being put into the public domain again. But any variants that are detected through sequencing, we don't need to wait to put them in the public domain. We act immediately on them. And so we will notify state partners and jurisdictional partners when a variant, any of these three, are detected within their jurisdiction.

So this data was updated on Sunday evening. We have a total of 1,688 variant cases. And this is not comprehensive. It's not everything. And again, the data are coming in from a lot of different sources. So it's challenging to put a denominator on this to understand the full prevalence or the spread of where these variants are right now. But we do have some published modeling data on B.1.1.7s that we can share in the chat, that we posted and published in January.

So for the B.1.1.7s, we have a total of 1,661 reports in 44 US jurisdictions. For the B.1.3.5.1s, there are 22 of these variants (351s) in 10 US jurisdictions. And then for the P1s, with five P1s from four US jurisdictions. Again, this map's going to be updated on Tuesday evening. So check back there. And you can see how the numbers are changing over time. Next slide, please.

OK, so this is another public site that we have, where we are tracking the data that is either generated by CDC for sequencing or the data that is generated by the contract laboratory partners that CDC is funding, to put data into the public domain. And so when we first started the National SARS-CoV-2 Surveillance Program, it was about mid-November. And so we have since scaled up considerably, as well as starting all the sequencing contracts, which first were awarded, the first one was awarded in late December.
And so you can see that these are all the data that we're putting into the public domain. Our last big deposition of data into NCBI and GISAID, so we submit to both, was on to 2/20. So these dates represent the week ending, which many of you may be used to from a lot of our epidemiologic reporting, where we track by the week ending in a certain date. And so you can see there, the week ending on February 20, we sent in over 9,000 sequences into GISAID and NCBI. And just for awareness, we're not counting our submissions twice as we're submitting two public databases. They're de-duplicated.

So you can keep track of this. Again, you can just go to GISAID and go to NCBI and look for the data there. They are publicly available. The red line shows where we're projected to go, in a cumulative number, and then the yellow line shows, again, the cumulative number of where we were. But with each week, our single depositions will be showing up there, with our overall goal being around 7,000 sequences on a weekly basis.
So this is about 6,000 from the contracts that we're working with, and then about 750-ish from our national strain surveillance. Again, those are public health labs actually submitting specimens to the CDC, where we're sequencing and characterizing viruses. This data is updated on Sundays once a week. Next slide, please.

So this shows some of the US sequences available in public repositories. We've got, again, NCBI National Center for Biotechnology, otherwise known as GenBank, and then the US sequences submitted to GISAID. And these represent US public-- US labs that submit data, so US specimens.

You can see here that we are increasing quite a bit in the overall numbers that are going into the public domain, which I think is a really good sign that we are catching up and truly trying to fill that database with useful data, that will have many, many uses, so from diagnostics, to different studies, to research communities looking at the vaccine and looking at the impact of how the virus is changing over time, and how it changes and affects, and may impact our public health tools and mitigation efforts. Next slide, please.

Again, this is on the same page. It's called our Genomics Dashboard on the CDC's website. This shows just the total sequences that were submitted to GISAID. This map is a static map. But what you can do is, when you go to it, you can hover over each state. And it'll tell you the number of sequences submitted to GISAID for each state, by state, total per state, as far as the collection location on a state level basis. And so this gives a kind of general picture of where we are with sequencing overall.

And then the next slide shows the percentage of cumulative cases sequenced by a percent based. And so this is calculated, again, also it's updated on Sundays, on a weekly basis, based on the number of sequences per state, based on the collection date and the data that's publicly available. And where we are, you can see it'll really change by the number of cases and number of sequences, with some of the more heavily sampled areas being in Maine and in the Pacific Northwest.

There's a lot of sequencing going on in those areas, as well as lower cases in some of those states, like Maine, from what I can remember from where I looked at cases the last time. Again, this is updated on a weekly basis. And I think that's the last slide. Is that right, Jasmine? Yep. So happy to take questions or try to answer any questions that folks may have.

JASMINE CHAITRAM: Thank you so much, Vivien. I do have a few questions for you. The first one is will rapid tests need to be updated to pick up the new variants of the virus?

VIVIEN DUGAN: Yeah, that's a good question. And I think we FDA has joined us today. So I'd probably defer to them. I can say that, certainly, the different rapid tests, I mean, there's a couple of different kinds out there, right? So there's going to be the rapid antigen test and then a rapid PCR test. And I think that the antigen test, we're working and partnered with FDA to look at the B.1.1.7 and its effect on some of those rapid-- or some of the antigen tests in general.
The nucleic acid tests, or the PCR tests would certainly have an opportunity to, as the virus changes, to affect how those tests work. And some of that we've sort of started to see, but it actually worked in our benefit. So the B.1.1.7 variant, that's the lineage variant that was first detected in the United Kingdom, there's a deletion in the spike gene of that particular virus.

And so when you run a couple of specific assays, again, PCR assays that have multiple targets, not just the spike, we will see this kind of characteristic S gene target drop out. So that specimen will be negative for the spike, but positive for the other two targets within the genome of the virus. And so that's one way that, certainly, the UK has used as a proxy for detecting B.1.1.7 variants.

I think there's such diversity, so far, in the United States that we have seen from our perspective many specimens that have shown this kind of pattern, where the S gene target is negative, but the other two targets are positive, but when we've sequenced the virus, it's shown that it has not been the B.1.1.7 variant. But again, I think that's very regional. And it depends on where people are located. But that said, I think I'll let FDA answer. But I believe there's a lot of efforts going on to monitor the sequence data and to keep an eye on different thresholds and different proportions of sequence data, representing viruses changing over time, and ones that are increasing to look to ones that may impact current diagnostics.

JASMINE CHAITRAM: Thanks, and I'm pretty sure FDA will cover that when they give their update. So another quick question, I think, for you is are there any plans to sequence COVID through wastewater testing to get a much broader picture of variant spread?

VIVIEN DUGAN: Yeah, I think, I'm not as familiar with some of those activities. They're not really in our particular team. But I think there are some efforts that are happening, maybe at more regional levels, but also from CDC activities. And I can probably follow up on that unless anybody else on the call has information on the wastewater work.

JASMINE CHAITRAM: OK, great. And then another question, do we need to be prepared for a new surge, secondary to variants? If so, when are you anticipating this to happen? Do we need to do genomic sequencing in our positive patients?

VIVIEN DUGAN: Yeah, I mean, certainly I would encourage, if there's no sequencing occurring, and you have the opportunity and the capacity to have specimens sequenced, I would certainly encourage that. Also, if you don't have the opportunity to or the capacity to sequence, I would recommend contacting your local public health lab or your state public health lab to potentially have specimens sequenced either there, because again, there's a lot of capacity at the state level, and also in submitting as part of our activities here at CDC.

That said, it's really challenging to predict the spread of these particular variants. I think we're still really learning a lot about them. The B.1.1.7, there's some modeling data that has been put out, where, at least from our analysis at CDC, and I can put the MMWR in the chat, the current modeling prediction, again, based on the data known at the time, and a lot of very complicated mathematics, would estimate that may see the B.1.1.7 variant as the predominant virus in the US by around March.

That said, there's still a lot of other variants circulating. And so I think it's very challenging to predict how quickly these variants will spread. We still have very limited data on the B.1.3.5.1 variant, which, originally, was found in South Africa. And then the P1 variant, we have even less information on that. And

so we're working very hard and as quickly as we can to, as these new variants are detected across the country, to get the specimens and to start really characterizing the phenotypes of these viruses. How do they behave in culture? How do they react to sera from vaccinated individuals against sera from people who were exposed to or infected with a classical, I guess, strain of SARS-CoV-2? And so I think as time goes on, we'll get a better understanding of the viruses and look into transmission and pathogenicity. But I think we're still kind of in the early days for being able to predict the spread. But that said, I think the mitigation efforts that we've already been implementing and trying to reinforce, we know that they work against these variants. So if anything, you're doubling down on current ways to mitigate, which is masking, handwashing, vaccinating, social distancing, of course, are effective tools that we have right now.

JASMINE CHAITRAM: Thanks, Vivien. I know you're super busy, too, so if you're able to stay on for the call for a little bit longer, there are several questions in the chat that you could probably address. But before you go, could you just make some general comments about how laboratories that have sequencing capacity or are doing sequencing, how they can contribute to this effort or submit sequences into the public domain, things like that?

VIVIEN DUGAN: Sure, yeah, I mean, I think there's a million different ways to sequence. And certainly there are lots of different technologies and platforms out there. One option is to think about working with public health labs at the state or local jurisdictional levels to understand how they are approaching sampling and what the current needs are, because I think it's going to depend on where you are and what kind of questions you're trying to answer.

Are you trying to get a picture of the overall diversity of what's circulating locally? Are you trying to target variants and particularly focus in on areas where it might be more hot spots versus areas where it may be less concerning, depending on what's already there and what's already known? But certainly, any effort to sequence is certainly encouraged.

And the way to really contribute to that is by putting the data into the public domain. And so, again, the two main repositories that are public that we contribute to are NCBI, which is GenBank, and then GISAID, which has a lot of the sequence data available. And I think those links may be on our website, as well, to get them.

Submitting can be challenging. And so there are some decent instructions that are available on those sites. NCBI, I think, has a lot more detail on the kind of specimens and how to submit them manually, versus kind of bulk upload. But that's really the best way to help the total effort, is to get the data into the public domain. So that across the government, across academics, and a lot of public health labs, who are all monitoring the data, and watching, and analyzing it, we can really see what's going on.

JASMINE CHAITRAM: Thank you again so much, Vivien. And we look forward to having you on future calls. In the interest of time, we're going to move to our next agenda item. But if you are able to answer some of the questions in the chat, we would appreciate it.

Our next topic for today is going to be the CDC testing and travel order. And we've got two speakers that we'll be covering this, Nicky Cohen and Pam Diaz from the Global Migration Task Force. And I'm not sure which speaker is going to go first. Is that you, Pam?

NICKY COHEN: Hi, thanks. This is Nicky. Thank you for giving us the opportunity to speak on this topic. So can I have my first slide, please? So just by way of background, not a lot of people are aware that, in addition to being an advisory agency, CDC does have some regulatory authorities. And one of the places that these authorities are available to us are in measures to prevent introduction and spread of communicable diseases into and within the United States.

And we have basically two buckets of regulations, 42 Code of Federal Regulations part 71, which are the foreign quarantine regulations, which deal with international travel arriving into the United States. And then 42 CFR part 70, the interstate quarantine regulations, which deal with travel between states and territories.

So we issued an order in December after the first UK variant was identified, that required testing of air passengers arriving to the United States from the United Kingdom, specifically to address that particular variant. And in January, recognizing, firstly, that the UK variant had spread to many other countries, and that there were other variants being detected in other countries around the world, and also just generally, because of the spread of SARS-CoV-2, and continued introductions into the US, we issued an order in January that expanded the testing requirement to international travelers arriving from any foreign country into the United States.

And the regulations that these were issued under are listed on the slide. One is part 71.20, which is public health interventions, public health prevention measures to detect communicable diseases. And we have a fairly broad regulation under 71.32, which applies to persons, carriers, and things, and allows the director to take actions for those categories – persons, carriers, and things – to prevent introduction of communicable diseases. So next slide.

JASMINE CHAITRAM: And Nicky, just before I get to the next slide, we've had a few people tell us that they're having trouble hearing you. And for me, I can hear you, but you're going in and out a little bit. So if you can either speak louder or move a little bit closer to your microphone, we'd appreciate it.

NICKY COHEN: And actually I think what I'm going to do is I can switch to the computer. I was using my headphones. I can just switch the computer microphone if that's better.
JASMINE CHAITRAM: Yeah, it sounds better to me. So thank you.

NICKY COHEN: Can you hear me?

JASMINE CHAITRAM: Yes, you're good.

NICKY COHEN: Hi, can you hear me? I think I'm having some speaker issues. Can you hear me now?

JASMINE CHAITRAM: I can hear you. I don't think you're able to hear me, though, for some reason.

NICKY COHEN: OK, well, I'll try to speak up. And hopefully people can hear me. OK so I think I kind of covered some of this already, that in addition to the concerns around the variants, which have been covered already by the previous speakers, so I don't think I need to go over them again, the concerns we have around travel and COVID-19 are really two-fold.

One is the risk of transmission during travel, so that a person will be infectious and be on, say, on an airplane, and transmit disease to other people on the plane. And then the other concern is what we call translocation of virus to destination communities. And what that means is that if there's virus present in one location, that a person could then travel to another location and introduce the virus there. And that is very much a particular concern with the new variants that are circulating around the world, and also in the United States. So next slide, please.

So the testing order that we issued requires that before boarding an international flight to the United States, all air passengers who are two years of age or older must present to the aircraft operator either a negative result of a viral test, and we define viral test as either a NAAT or an antigen test that was performed no more than four days before the-- three days before the flight departs. Or if the person has recovered from COVID-19 in the previous three months, they can show documentation of their positive viral test results, as well as a letter from a licensed healthcare provider or a public health official indicating that they completed their isolation period and were cleared to travel.

And the order has limited exemptions that include crew members on airplanes, if they're following guidance that we issued jointly with the Federal Aviation Administration that includes mechanisms that the crew members are being monitored, and also mechanisms that they would take to prevent exposure to SARS-CoV-2.

There's an exemption for federal law enforcement officers who are traveling for the purpose of law enforcement. An exemption for humanitarian purposes. So if somebody needed to travel very rapidly for reasons of health and safety, if they were not able to obtain the testing before they needed to travel.

An exemption for military personnel on official orders. But the reason for that is really because we expect that the Department of Defense will have similar requirements that are at least as restrictive as CDC. So we're basically just allowing DoD to manage their own personnel. And then we have separate guidance for transporting people who have tested positive for COVID-19 and are still considered infectious. So obviously we're not going to require those people to test negative. But they do need to be transported in accordance with our guidance. Next slide, please.

So the testing requirement is only a single component of our overarching travel protection messaging. So in addition to the requirement for people who are traveling to the United States to be tested before travel,

we also recommend that other travelers who are traveling get tested before travel. So these would include domestic travelers and travelers who are leaving the United States, going to other countries. And we're not requiring the testing for either of those groups. But we do recommend that they also get tested before travel.

And we also have recommendations to prevent spread during travel, including social distancing, wearing masks, hand hygiene, et cetera, which are similar to the recommendations for preventing spread in other settings. And we have post-travel recommendations, which include getting tested with a viral test three to five days after travel combined with a stay home period for seven days if they test negative. And then for people who are not tested after travel, we recommend that this period be extended to 10 days.

We also recommend that people who have traveled avoid being around people who are at increased risk for severe illness, whether or not they were tested. And we also always remind people to follow state and local recommendations and requirements as we recognize that some state, territorial, tribal, and local health authorities have issued their own travel recommendations and requirements. So I'm going to hand the presentation over to Pam, who will review some of the data that we-- or the modeling data that we use to develop these recommendations.

PAM DIAZ: Sure, thanks, Nicky. Just to begin, early in the pandemic, symptom screening was used at airports. But it subsequently proved to be ineffective because it missed mild, afebrile, asymptomatic, and presymptomatic infections. And because of the lack of data, early in the summer, we turned to CDC modelers, led by Michael Johansson, to gain some further insights into this.

And using a mathematical model based on three distinct models of infectiousness, they characterized relative infectiousness over time and some testing strategy. So in this slide, and the next couple afterwards, I'm going to use, these are figures from the manuscript that describe some of these efforts and illustrate the findings.

So this first slide here looks only at reducing the risk of transmission during travel. And it represents a seven-day exposure window before a one-day trip. So the trip occurs on the far right at day 0. Symptom monitoring alone, which you can see in the yellow bar on the far left, symptom monitoring alone, which we defined as isolating individuals when symptoms begin, before or during their travel, there's a 25% to 35% reduction in risk of transmission during travel, if those individuals who are symptomatic get isolated and, essentially, removed from the travel window.

When testing is added, then the greatest reduction of risk occurred when the specimen for that test was collected closest to the time of travel. If you look at the blue bars, those represent testing alone. And testing alone on the day of travel resulted in a 35% to 60% reduction in transmission risk. Whereas, if you back it up and look at testing prior to travel, three days before travel, it's about 5% to 10% reduction. Now, this is with testing alone. When it's combined with symptom monitoring, which is seen in the green bars, you get a higher overall reduction in transmission risk for both of those time frames.

If you look at the next slide, it uses-- can we move to the next slide? Uses the same time-specific patterns and assesses the impact of different types of test sensitivity, here, an 80% versus a 95% test sensitivity. Obviously, the higher sensitivity test giving a higher reduction in transmission risk when it's used at the same time. However, the importance of sensitivity and timing is really intertwined. The lower sensitivity test was as effective or more effective than a higher sensitivity test if that lower sensitivity test was performed closer to this time of travel than a higher sensitivity test.

For example, a test with 80% sensitivity that's performed one day prior to departure was 35% to 45% effective in reducing transmission while a test with 95% sensitivity performed three days prior to departure was 8% to 10% effective. Hence, the testing can provide added benefit. But it's contingent on the timing and quality of the test.

And the outcome here is specifically related to, again, reducing transmission in the 24 hours after departure. And for longer timeframes, the magnitude of this effect shifts downward. But the trajectory is somewhat similar. A test 48 hours prior to departure is better than one at 72 hours, et cetera.

We also looked at the relative reduction in transmission risk of multiple tests being conducted before travel. And although not shown specifically here, the slide does kind of help illustrate that multiple tests prior to travel have little added value. It's really the test closest to travel that has the most effect.

When we assess the effects of symptom monitoring and testing and quarantine on reducing risk of transmission after travel we can see in this next slide, please, where we looked at a variety of testing strategies, including the number and timing of tests and the effects of post-travel testing, in combination with and without symptom monitoring, and varying lengths of quarantine.

This slide has a lot of data on it. So I'll just direct you to a couple of points. The results can be found in the paper. But here, I'm going to just focus on those that are most closely aligned with CDC post-travel recommendations. This slide looks at the relative reductions in risk after travel. And first, look at the yellow and the orange bars on the left, which do not take testing into consideration at all. Here, we find that a seven-day quarantine, combined with symptom monitoring, is very effective in reducing the risk of transmission post-travel.

The importance of quarantine in these measures is illustrated by these findings. And in the paper, but not presented here, we found that a post-travel quarantine for seven days or more, just on its own, was more effective than testing and symptom monitoring without quarantine, regardless of when a test might occur. So the point being that the post-travel quarantine or stay-at-home period is extremely important.

Optimally, though, we found that a single test conducted three to four days after arrival with symptom monitoring and a seven-day quarantine or self-quarantine reduced risk of transmission by 95% to 99%, compared to the 14 day quarantine alone, 96% to 100%. And you can see this in these further bars on the right, looking at testing alone in the blue bars, and then the added addition of testing plus symptom

monitoring in the green, and then onward to the magenta, which includes the full testing plus symptom monitoring and self-quarantine, which is in our post-travel recommendations.

This three to four-day window is optimal, because it balances the reduced risk while someone's in quarantine with a higher test sensitivity for individuals who might remain infectious near the end of their quarantine. We also looked at quarantine adherence, and I'll direct you to the paper for information around adherence to quarantine.

And just note that, in summary, pre- and post-travel strategies, including symptom monitoring, testing, and quarantine, can be combined in multiple ways, considering different trade-offs that include feasibility, adherence, effectiveness, cost, and adverse consequences. And as data becomes more available, we are beginning to look further at testing strategies to further reduce the risk of transmission both during travel and at the destination. Thank you.

JASMINE CHAITRAM: Thanks so much, Nicky and Pam, for joining us today. And in the interest of time, I'm only going to ask you one follow-up question. Although, there are a lot of questions in the chat-- sorry, in the Q&A box. If you have time, and you can answer some of those live, I'd appreciate it.
We did get several questions around if an individual is vaccinated, and they have proof of vaccine, do they still need to be tested before travel, or after travel, or tested at all?

NICKY COHEN: Hi, this is Nicky, so we are still-- yes, so the answer is yes, that the order does not have an exemption for people who were vaccinated as an alternative to testing. So people who are vaccinated are still required to show a negative test or provide documentation of having recovered from COVID-19. With regard to travel, whether testing is not required, we are still recommending testing, even if people were vaccinated. And we have not changed our travel recommendations at this time, although discussions are ongoing regarding travel guidance for vaccinated people.

PAM DIAZ: And I'll just add our travel guidance really takes into account many factors, which includes around travel, including the variants of concerns that are circulating globally, the importance of testing to detect asymptomatic infections, and the challenges of maintaining safe distance and crowding during travel. Thanks.

JASMINE CHAITRAM: Thank you both again very much for being with us this afternoon. The last agenda item we have is our normal, or standing item, from FDA, an update from Tim Stenzel with the Food and Drug Administration, Tim.

TIM STENZEL: Thanks, Jasmine. Hopefully you can hear me just fine. Today, the FDA issued an immediately in effect guidance policy for evaluating the impact of viral mutations on COVID-19 tests. So there were also similar guidances issued for vaccines and therapeutics. I'll just briefly cover what the test guidance went over.

So this guidance provides information on evaluating the potential impact emerging and future viral genetic mutations, which, of course, form the basis for viral variants, and the impact on tests, design considerations, and ongoing monitoring. Of course, in early January, the FDA already issued a safety alert. It was on January 8.

That alert also went into what we had been doing from the very beginning of the pandemic, which was working with test developers to assess, in silico, the variants and mutations that were occurring at that time, to see if there's any impact on tests. We then moved into the summer and began an active search for those tests that have been authorized, because for molecular tests, we have-- for authorized tests, we have their primer and probe sequences.

So we could scan the known genetic databases. We mostly scan the GISAID database for any prevalent mutations and/or variants, and then do a separate search among those prevalent mutations or variants for any impact on any specific tests. We then, if anything is noted by FDA reviewers that could be impactful on a test performance, we reach out to those developers, ask them to continue to assess the situation, alongside the FDA.

And we mentioned three tests in that safety alert from January, the Mesa Biotech assay, the TaqPath assay, and the Linea assay. TaqPath and Linea had an S gene drop out for the UK variant. And that was very convenient to try to enrich for cases that might be representing the UK variant. But it doesn't, at this point, perhaps still doesn't, clearly identify the full variant, just one of the mutations that can be seen within the variant.

The Mesa Biotech had a different impact, it was a three base pairing impact. There was a slight change in apparent LOD. But probably no change in overall performance. But out of abundance of caution, we did mention that test as well. Our search continues for molecular assays. We're doing it on a weekly basis now. And whenever something of significance is noted, we will update our communication for any other tests. But to date, overall, the molecular tests, we believe are not significantly impacted by the mutations and variants.

Now, sometimes, that's due to the fact that many of the tests have multiple targets. And that is a mitigating design strategy to be able to use multiple targets to prevent any single target dropout from impacting the overall performance of the test. So we've seen that, we've seen that, actually, occur more. But fortunately, overall test performance is fine. We don't know how long that might last.

So the other thing new about this guidance is that we're asking the developers of tests, both premarket and postmarket to pay more close attention to this. And especially postmarket, after authorization, to have an ongoing plan to assess the impact of variants. And this goes beyond just molecular tests. It goes into antigen test and serology tests.

So with antigen and serology, it's a little bit more difficult to measure the impact. We are currently looking at amino acid changes that are prevalent in the mutation databases. And then we do have some idea

where the antigen and serology tests target the virus and are able to reach out to those test developers and engage them. Please take a look at that guidance. And happy to answer any questions if there's any one-minute questions here. I know we're close to the end of the hour.

JASMINE CHAITRAM: Thanks, Tim. We are very close to the end here. And we didn't actually have any other questions for you at this time. So I appreciate you being on the call as always with us, going on almost a year now. Thank you.

So just to wrap up, just to wrap up, I just wanted to remind you all that our next call will be on Monday, March 8. And we are glad that you were able to join us today and continue to submit those suggestions for our future calls. You can send those through our LOCS mailbox, LOCS@cdc.gov. And we just want to thank you again for all the hard work that you're doing out there and hope that you continue to stay safe. Thank you.