

**Agenda**  
**Clinical Laboratory COVID-19 Response Call**  
**Monday, March 21 2022 at 3:00 PM ET**

- **Welcome**
  - Jasmine Chaitram, CDC Division of Laboratory Systems (DLS)
- **Antigen Testing Guidance Update**
  - Reynolds (Ren) Salerno, CDC Division of Laboratory Systems (DLS)
- **HHS Reporting Requirements Update**
  - Jason Hall, CDC Data, Analytics, and Visualization Task Force
- **Key Findings for SARS-CoV-2 Testing Using Rapid Antigen Tests from RADx Clinical Studies Core**
  - Apurv Soni, University of Massachusetts Chan Medical School
- **FDA Update**
  - Tim Stenzel, US Food and Drug Administration (FDA)

**JASMINE CHAITRAM:** Hello everyone and thank you for joining the Clinical Laboratory COVID-19 response call. My name is Jasmine Chaitram. I'm the Associate Director for Laboratory Preparedness in the CDC Division of Laboratory Systems. We're glad that you could be here with us today.

I'm showing our agenda for this call, but I do have a few things that I want to go through before we get into our first speaker. So first up is, I do want to do a little reminder of who the [Division of Laboratory Systems](#) is-- and showing our vision and mission statement here. But importantly, just want to mention that we support clinical and public health laboratories in several different areas, and those are in quality and safety, training and workforce, preparedness and response, and accessible and usable laboratory data. And we've been supporting laboratories specifically in preparedness and response by hosting these calls, which we've been doing since March 2020.

Our [Preparedness Portal](#) has all of the information that you need. It's a one-stop shop. It links you to [CDC COVID-19 web pages](#). It also links you to the [archives](#) for all of these calls with the transcript and the audio and slides.

It also has all of the LOCS messages that we've sent out previously-- that's the [Laboratory Outreach Communication System](#). If you're not a recipient of the LOCS emails, please send us a message at [locs@cdc.gov](mailto:locs@cdc.gov), and we can add you to our distribution list. All of our previous LOCS messages are here as well as other information that you might need related to the response.

Big change that I want to announce today, is that our next call will be Monday, April 18th from the same time, 3:00 to 4:00 PM. We were having these calls every two weeks, but now we're shifting as the response activities are slowing down a little bit. And we also know that you guys continue to be busy with other things.

We are going to be shifting to once a month. So our next call will be on Monday, April 18th, and then the third Monday every month after that. And so we will have a LOCS email that will come out announcing this change in our schedule, and hopefully this will not be too disappointing for those of you out there that tune in to us on a regular basis.

And as always, we want to continue to hear from you. So please send your suggestions for training and workforce development to [labtrainingneeds@cdc.gov](mailto:labtrainingneeds@cdc.gov). And as a reminder of how to ask a question during these calls, we really appreciate it if you use the Q&A box in the Zoom features, and not the chat. This allows us to record your question, to get back to you if we're not able to answer it on the call today.

Sometimes there are more questions than we can get to. Sometimes there are questions that are not related to any of the subject matter experts that we have speaking. We do want to remind people that these calls are related to clinical laboratory testing, so if you ask questions about vaccination or masking guidance or anything like that, we probably won't ask those questions during these calls, as these are really focused on the clinical lab testing issues.

We do also-- you may still ask a question about clinical lab testing issues. I know we've received questions about billing, but we need to go back to CMS to answer those. So those are just some of the examples of questions that we've received that we sometimes are not able to answer. If you include your name and email, we can get back to you.

I have previously said don't submit things into the chat. But today I'm going to change that just slightly and ask you if you have any particular topics that you want to see covered on future calls, to please actually drop those in the chat today so that we have some ideas as we plan future calls, of things that you're concerned about or that you'd like to be hearing about. And it doesn't necessarily have to be COVID-19 response related.

As I mentioned, we're transitioning away from the heavy focus on the COVID-19 response as things slow down. And we would like to broaden these calls to cover other topics that are preparedness and response related for laboratories. So please keep that in mind and give us your suggestions in the chat box.

And then the last thing I just want to remind you of, is that the presentations are sometimes from panelists that are not affiliated with CDC. So we do post the slides after the calls on our preparedness portal. But just a reminder in general, that the presentations from external panelists in the slide decks that are presented on our website after the call, are not necessarily reflecting CDC's official position. So just want to make sure you all remember that. And with that, I'm going to turn it over to our first speaker today to cover updates to the antigen testing guidance, Dr. Ren Salerno, the Director of the Division of Laboratory Systems. Welcome, Ren.

**REYNOLDS SALERNO:** Thank you, Jasmine. Good afternoon, everyone. I'm Ren Salerno, and I'm presenting on behalf of CDC's Expansion of Screening and Diagnostics Task Force. And today I'll provide an update on CDC's guidance for health care providers who perform antigen testing. Next slide, please.

This [guidance web page](#) was first created in August 2020 and is intended for health care professionals who order or perform antigen testing in laboratory settings, or at the point of care. It focuses on the diagnosis of new infections and is not meant to serve as self-testing guidance for the public. While most but not all self-tests or at-home tests are indeed antigen tests, the audience for the two guidance pages-- the antigen testing guidance and the self-testing page-- those guidance pages are different.

At present, FDA has granted 50-- I'm sorry-- has granted emergency use authorization for 48 unique antigen tests that include laboratory-based or moderate or high complexity tests, point of care tests or waived tests, and self-tests, or over the counter tests. Antigen tests have been widely used for diagnosis, screening and surveillance of SARS-CoV-2. Even though antigen test reporting is incomplete, in 2022, we've seen over 6.5 million antigen test results reported through the COVID-19 electronic laboratory reporting, or ELR, across health care settings, including hospitals, physicians' offices, and skilled nursing facilities nationwide. And 18.5 million of these test results have been reported across all settings.

Therefore, it is necessary for CDC to maintain and update this antigen testing guidance for health care providers. The current guidance web page has received a lot of traffic this year already, with over 643,000 views. This is significantly higher than the number of views at this same point last year. Next slide, please.

The need to update this antigen testing guidance became clear as soon as CDC updated the [quarantine and isolation guidance](#) and based on the much wider use of antigen self-tests at the end of 2021 and early 2022. To distinguish this guidance page intended for health care providers from the self-testing guidance for the general public, we've updated the name of the web page to specify health care providers and revised the key points to include a link to the [Self-Testing page](#). A current web page can be seen on the right with the updated title highlighted above.

The guidance for antigen testing in congregate settings, and the guidance for processing and handling SARS-CoV-2 clinical specimens, have been removed from this particular page. This information was removed to streamline this page, and because this content is available on other CDC guidance pages. Future updates to those guidance pages will thus be reflected here as well. We now provide links to settings-specific guidance for testing in congregate living situations, such as [long-term care facilities](#) and [homeless shelters](#), and to [biosafety guidelines for specimen handling](#).

We've made two principal content updates to the antigen testing guidance web page. The first update addresses when to consider using confirmatory testing after an antigen test result in symptomatic and asymptomatic individuals. Confirmatory testing could be warranted for positive or negative test results depending on the circumstances, and the guidance provides details on these specific situations. The revised antigen testing algorithm provides an overview of the updates. Next slide, please.

What you see on this slide is the new antigen testing algorithm for health care providers. It has been modified to reflect the updated quarantine and isolation guidance, as well as to be more suitable for

standalone interpretation. For example, we know health care facilities print out this figure as a reference guide in clinics and other testing venues.

This version now includes more detail within the figure itself, and only a few relatively simple footnotes. In the previous version, there were many very detailed technical notes that made interpretation more difficult. The algorithm flows from symptom status at the top, to test result, to recommended action along the bottom. Color has been used to represent the level of caution that is recommended based on the test result and the testing situation.

In this new version, we have added guidance based on vaccination status and whether the person has had close contact with a known case of COVID-19. This reflects CDC's quarantine and isolation guidance updates. Given our current knowledge of antigen test performance, the figure suggests that a positive antigen test result does not need confirmation. But it includes a footnote that outlines when confirmation of a positive test result may be appropriate.

We've also added more detail on the need to confirm negative antigen test result, when the patient is experiencing symptoms of COVID-19 and indicating that follow-up testing could be either a confirmatory nucleic acid amplification test or by serial antigen testing. The goal of this web page and algorithm update is to ensure that health care providers and testing professionals have a resource to aid in their interpretation of antigen test results, to know when and how to perform additional testing, and to understand what level of caution to prescribe. Thank you very much.

**JASMINE CHAITRAM:** Thank you very much, Ren. Looking in, I don't see any specific questions for you right now in our Q&A box here. So I guess, thank you very much for joining us.

**REYNOLDS SALERNO:** Sure, happy to be here. Thank you.

**JASMINE CHAITRAM:** All right, we will go to our next speaker, Jason Hall from the CDC Data, Analytics, and Visualization Task Force, and he is going to talk about recent updates to the HHS reporting requirements. Jason?

**JASON HALL:** Thanks, Jasmine. So I'm Jason Hall. I work in the National Center for Emerging and Zoonotic Infectious Diseases. I've been on the response for a few years now, leading lab data for the Data, Analytics, and Visualization Task Force for CDC.

I want to briefly review today the [updates to the federal requirements for test reporting to public health](#). So this is Section 18-115 under the CARES Act, is where these guidelines are published. These were first put out, June 4th, 2020.

And when they were put out, it was a blanket requirement. So all facilities that are performing testing for COVID-19 report all results for all test types. So that's antigen, NAAT, and serology. But over the past year, we've been working on trying to produce updates to this in response to the changing needs for

public health through the pandemic, but also balancing with the burden that data collection and reporting places on the facilities, and also on the receiver's public health.

So we have finally come to some updates that are going to take effect on April the 4th, moving away from the blanket reporting requirements to more nuanced requirements. Jasmine, if you'll go to the next slide. So we want to highlight what's changing here, and there's a couple of big changes.

The first is, the new guidance no longer requires reporting of negative results for non-laboratory based NAAT test. So that means all rapid tests, regardless of setting-- whether it's a CLIA waived setting or a CLIA certified setting and it means antigen tests writ large. So even if the antigen test is being performed inside of a CLIA-waived facility, say a high throughput one, still positives only is what the federal requirement is now.

So the other big change is on antibody, serology. And I think this affects a lot of this audience. So moving away from a requirement to report these data to public health along with NAAT and antigen data, to no requirement to report. So that means they are optional.

So again the two big changes-- positives only for non-laboratory NAAT test. That means positives only for all the rapid tests and for antigen test period. And no requirement to report serology data.

It's important to note that this is a floor. So Section 18-115 is federal requirements for COVID testing data reporting, and it's the floor, it's not the ceiling. So state, local, tribal, territorial, they may impose additional data requirements for collection and for reporting above what is in Section 18-115, but this is the minimum.

Um-- sorry. To reiterate in another way, what has not changed is the requirement to report all lab-based NAAT tests, so all of the medium and high complexity lab tests that are NAAT-- so all the PCRs. So all the facilities that perform those tests need to continue to report all the results for those-- that's negatives, positives, inconclusives.

Two other-- actually three other things that I want to point out that's in this guidance. One is sequencing. So we do address sequencing in the text, but it's really to just state that it's not covered here. There's no requirements placed on reporting sequencing data or lineages determined from those.

What we do put in there is an encouragement for facilities that are performing sequencing to report the lineages determined from the sequences to the appropriate public health departments. And there is technical guidance for how to do that. I'm sure some of you are already doing this, but we can send the website out. It's been updated I think as of today-- or yesterday, with an updated technical spec-- to update the codes that are used to help you all package lineages that you determined through sequencing and regulate ELR messages to public health. But there is no requirement under Section 18-115.

Another thing to note is, self-administered testing, self-test, over the counter prescription test, all the-- you know, all of these are the same. It puts no requirement on individuals performing these tests to report the data. What it does is, it reiterates an encouragement and a desire for the manufacturers of these tests and the developers of these tests, to incorporate ways of collecting the data and transmitting the data for public health purposes.

A lot of these are laid out in the EUAs that these devices were authorized with. But it is doubling down on that aspect of it, building these data pipelines out for future needs. But there's no requirement being placed on individuals using these tests to report.

And then the last thing again, there is a section in there-- it's very short but it's re-emphasizing the fact that this is a floor, not a ceiling. And that STLT's could have-- that's state, territorial, tribal, and local public health authorities-- they could have additional requirements above these. Jasmine, if you want to go to the next slide for the summary table.

So this is a way for us to try to summarize it. And there's a few nuances in here that make it a little tricky, and we'll have FAQs on the website. But again, it shows that for NAAT testing for the medium and high complex labs, everything's required, all the test results.

And then for all other testing, except antibody, positives are required. The negatives are optional. Check with your states. And for antibody testing, it's optional, period. But again, check with your state. Some of them may still want it.

And I believe that's all that I wanted to cover there. The other thing I was thinking of, is related to the states. They have expressed certain burdens for processing these. We've heard from facilities that are expressing it. I don't know how many are going to be asking for facilities to continue this, and some may be asking for them to go below this threshold. But what we've got here now is meant to be the floor. So with that, I can take any questions.

**JASMINE CHAITRAM:** Thanks, Jason. A couple of things-- I think it was a little bit confusing, how it was phrased. But in summary, just want to emphasize that what we're saying is that any laboratory based NAAT, the facilities will continue to report positive and negative results. And then any other testing, aside from serology, it's positives only that are required. And for serology, it's neither. It's optional reporting in general.

And so just want to-- because I know there's a few questions that came in that they seem to still be confused a little bit about what we mean by non-laboratory based NAAT. So just wording that a little bit differently. There was a comment about showing the information as a table instead of bullets, and so we have that up here. And so hopefully that's providing some clarification.

Also there was a comment in the chat that HHS hasn't officially changed this guidance, but it is actually changed. I know that we put out in our LOCS message that it was posted as of March sometime-- I think early March. But it will be effective on April 4th. Can you say a little bit more about that?

**JASON HALL:** Yeah. April the 4th is the effective date. And we consulted with states and our partners, and also with our sister agency CMS, to make sure that any other things that needed to be altered, or the preparations for guidance that they had that were ancillary, they had time to update those. So it goes into effect on April the 4th.

The HHS website, I think, has a link now to a CDC-hosted [PDF](#). That's a little bit in response to CDC moving to take more of the lead role in this area. This CARES Act was authorized per the Secretary's direction, and the CDC has been shaping that direction since, and has taken the lead role in it with this. So we published the update, but HHS's website should link to it. So this does take effect April the 4th. It has been cleared and approved by all the agencies and by HHS.

**JASMINE CHAITRAM:** Hey, Jason, here's another question. The new reporting plans will decrease our detection of new outbreaks to uptick of SARS-CoV-2. Are you worried about this?

**JASON HALL:** So not as much. I mean again, we adjusted this based off of what we've learned in the past two years. And not just on burden, but we wanted to keep in mind the burden as well. There is significant burden when we're talking about rapid tests. These are all manually collected and manually transmitted. It's a pain.

But what we have learned as we've tracked-- like Ren was alluding to earlier-- millions of antigen data tests that we've gotten through, is that the huge amount of NAAT testing that's going on in the CLIA certified facilities has tracked really well. There's not huge deviations, writ large, in the antigen testing in this. So as long as we're having good supplies of the NAAT testing that's still ongoing-- at a still elevated level even now-- we feel like we have ways that we are going to be aware of the situation coupled with other data sets.

I mean again, CDC's guidance on levels of transmission in the community is centered around severe disease, hospitalization. So we have ways that we track cases with states, we have ways that we track hospitalizations, we have ways that we track visits to emergency departments. So all of these data are being used in conjunction as we continue to evolve the surveillance for the response. So we're not as worried.

With the data pipelines for the self-administer, that's where we're trying to be a little forward-looking. We didn't put a requirement in there, but we really want some of these pipelines to be built. So as we can all imagine a day where a lot of those tests-- or those tests make up a lot of the volume, we want to have ways to convey the data so they can be available for public health use. Over.

**JASMINE CHAITRAM:** Thanks, Jason. And I think there's still some confusion out there so I'm going to ask you-- waived PCR testing, like the BioFire test-- that's the point of care test?

**JASON HALL:** Yes.

**JASMINE CHAITRAM:** Do the negatives have to be reported?

**JASON HALL:** No. So like the Abbott ID NOW-- and I think there's a few other devices in this area that are PCR tests. They aren't antigen tests, but they are used in waived settings like urgent care centers and emergency departments and doctor's offices. Those are all done manually, they all have the same burden, so we removed the requirement for all the rapid tests to have all tests reported. So it's just positives for rapid tests, regardless of the type of test it is, NAAT or antigen.

**JASMINE CHAITRAM:** Great--

**JASON HALL:** And again--

**JASMINE CHAITRAM:** Thanks Jason.

**JASON HALL:** Yeah, go ahead, Jasmine.

**JASMINE CHAITRAM:** I was just going to ask you another question but go ahead and finish your statement.

**JASON HALL:** I was going to say-- and again, we are going to try to make it even as clear as we can with updated FAQs. We are-- CDC, our comms team is going through and website by website, attachment by attachment, and making sure that we have everything updated by the April 4th start date.

**JASMINE CHAITRAM:** OK. What is a clinical lab to do if the state health department states that they will not accept negative NAAT results?

**JASON HALL:** So the federal requirement-- that is the floor-- still requires you to send them to them. We know of at least one state, and really only one state right now, that has asked for this. They believed that they had been given leave to move ahead with this. But the reality was, I think there was a misunderstanding between enforcement and what's required to be sent under the appropriate regulatory authority.

So they thought that the state was able to override this. And again, I've told the states I'm not a constitutional lawyer. But I believe that the federal reg takes precedence over the state regs in this case. So you're supposed to continue sending them.

We have told states, and we will tell them more if there are more states that try to move into this area. If they would rather not process the negatives, we can work with them on alternative ways for the federal authorities getting de-identified data that are the negatives and easing the processing burden on the state. But as of right now, you're still supposed to continue reporting those.

And for anybody that's in that situation, I would be happy to know if there are certain states that are moving this way. Because we've only heard of one. It's not that anybody's in trouble. We just want to be aware if there's states that are telling you these things, as the feds are telling you what the actual requirements are. Over.

**JASMINE CHAITRAM:** OK, thank you, Jason. There's another question in here. Many monitoring rules are based on percent positive, but we won't be able to calculate that now after removing the reporting of negatives. What metrics do you see being used for monitoring and triggers of preventative measures going forward?

And I'm going to just respond to that, Jason. And then I appreciate your two cents on that. I think you already mentioned that we're still tracking set positive through the reporting of the laboratory-based NAATs, where there's both positive and negative results coming in.

And then the second thing is that CDC has announced-- we have a web page that we're putting in the chat-- the ability to look more at community levels of burden rather than community transmission specifically. And I encourage all of you to look at that. So there's a focus now on hospitalizations and deaths as a determination of the burden of disease on the community. And so there's less focus on percent positive, but we do still have that information. Jason, anything to add?

**JASON HALL:** That's it. We still are tracking it. Again, the NAAT tests that are all still required from the medium and high complex labs that aren't rapid, those have shown to be really good indicators-- as accurate as we've had. When we compare them to the antigen data over time, when we look state by state, they seem to be really good indicators still.

So we have them. But what we're using for community transmission is not the percent positivity now. We still have it; we still will track it.

**JASMINE CHAITRAM:** All right. Thank you so much Jason, for your time on our call today. And because we are running a little short on time and we have more speakers, I'm going to go ahead and thank you and dismiss you for now. If you want to hang on and we have time at the end, and you can take a few more questions, that would be great.

**JASON HALL:** Little bit.

**JASMINE CHAITRAM:** Before we move to our next speaker though-- thank you, Jason. Before we move to our next speakers, we did have a couple of questions that came in after Ren Salerno finished his piece.

And I do want to go back and just address those very quickly. And Ren, if you're still there, the first question is, what does serial antigen mean as far as frequency?

**REYNOLDS SALERNO:** Right. So in the guidance there is a paragraph that's titled Serial Antigen Testing. So I would direct folks to that particular part of the guidance. But serial testing really means repeat testing with the same test.

So with serial antigen testing, it would be using the same test again after a certain period of time. And so, depending on the test, there may be instructions that indicate whether the test should be used in the event of a negative result again, 24 or 48 hours later. Sometimes the guidance on a CDC page might say two to three days later, a repeat antigen test should be performed.

So serial testing is different than confirmatory testing, which in general uses a separate test to determine if the first test was accurate. So we often talk about a NAAT test confirming a prior antigen test result. That's how I'd answer that question, Jasmine. Do you want me to hit the other one as well?

**JASMINE CHAITRAM:** Yes, please. Given sensitivity issues with the antigen test, if someone has symptoms and exposure, shouldn't they repeat the test before considering alternative diagnosis, and stay isolated?

**REYNOLDS SALERNO:** Right. So I think our guidance-- it does say if you are symptomatic, and you receive an antigen negative result, and we recommend a confirmatory NAAT or serial antigen test at that point. And if that second test is also negative, and you've had close contact, then you should consider alternative diagnosis, as well as quarantine for at least five days. So I hope that answers the question. But I think we've covered that in the algorithm.

**JASMINE CHAITRAM:** Thanks so much, Ren. OK, we are going to move to our next speaker. Dr. Apurv Soni, from the University of Massachusetts Chan Medical School, has joined us today to talk about the key findings from a SARS-CoV testing using rapid antigen tests from RADx clinical studies.

**DR. APURV SONI:** Thank you, Jasmine.

**JASMINE CHAITRAM:** We are ready when you are, Dr. Soni.

**DR. APURV SONI:** Sure, thank you. Hi, everyone. I'm humbled here to be representing our NIH-funded RADx Clinical Studies Core, and I'll be here talking about findings from the ongoing studies we have, trying to understand rapid antigen testing and generating real world evidence. Next slide, please.

In terms of agenda for today, we'll describe some of the findings from ongoing studies which demonstrate performance of rapid antigen test with Delta and Omicron variants. Another study that demonstrates timing of rapid antigen positivity in relation to PCR positivity among those who self-report having a close contact. We also would present ecological analysis that we have been doing for NIH and CDC-funded

Say Yes! COVID Test programs, which has distributed a large volume of rapid antigen tests throughout the previous year and continuing to do so in select communities.

More specifically, would describe the association in one community of the program that distributed the rapid antigen test and number of new cases during a subsequent surge, as well as a discussion that preceded this reporting behavior. So far people who and beneficiaries of the Say Yes! COVID Test program that we were able to track anonymously. Next slide, please.

So the first findings come from an ongoing study called Tests at Home Study. And the primary purpose of this study is to understand how rapid antigen tests performed for asymptomatic screening. The findings from this study are-- we're working with FDA for final analysis. But we were able to use data from this study to answer the question of, how does rapid antigen test work for Delta variant in comparison to Omicron variant?

And before diving into those findings, I wanted to orient the audience on how the study was performed. So on the left are participants who are enrolled in the study. And because of the purpose of this study being understanding asymptomatic screening, participants had to be asymptomatic at the time of enrollment. They also could not have tested positive for SARS-CoV-2 in the three months preceding their enrollment.

We also were enrolling all comers. So the only approach we took to make sure that we had enough participants that test positive, is by using a digital platform that allowed us to enroll anyone from across the country who were eligible for this study. But beyond that, we were not refining enrollment by choosing close contacts or enrolling from areas where there is likely to be high prevalence.

Participants after enrolling, sign up for the study by providing their mailing address, and receive a rapid antigen test as well as at-home PCR collection kit. And once they confirm that they have received a series of two boxes, with both rapid antigen tests as well as self-collection kits, they start testing in the schedule that's shown here in the bottom, which is every 48 hours, or every other day, for seven times. And then an extra rapid antigen test was performed at the end of the study. Next slide, please.

This more provides a more visual representation of why we were able to understand rapid antigen test performance for Delta and Omicron variants. So the graph on the right shows enrollment in the study, starting on October 18, and which is shown on the top left in terms of number of cases in West, Midwest, South, and Northeast. At that time cases were low, and we were able to follow the Delta and the Omicron surge and track geographic areas where cases were rising, and make sure that we were able to adapt our digital platform and enroll participants from the hotspots, which allowed us to be able to enroll enough participants that tested positive for Delta and Omicron variants.

Eventually we were able to use wait lists to make sure that we were balancing our cohort in terms of age and racial demographics. And so towards the end, we ended the study at about 7,400 participants. Next slide, please.

So the findings for comparing rapid antigen test performance for Delta and Omicron comes from the set of participants that are shown here. I would draw your attention to the left, which is a concert diagram. 7,300 participants had enrolled by the end of January. Out of them, 5,700 had started testing by the time we performed this analysis.

321 participants tested positive on PCR. 105 of them were Delta variant, 216 were Omicron variant. However out of those 321, only 153 were PCR-positive participants that were observed during the study. What that means is, they started the study with a negative PCR test and then had a positive PCR test during the study.

So we're defining that population as population A, shown here in red rectangle. We also observed that among the people that tested positive, there were two patterns of PCR positivity. In gold or yellow is population B, which are participants who tested positive, and continued to test positive for 48 hours on PCR. And that was the vast majority of those participants, more than half of 153 were population B.

However, we had a pretty sizable amount of participants called population C, which is shown here in blue or teal, which tested positive for the first time during the study. Meaning that 48 hours prior to testing positive, they were negative. But this population, 48 hours after testing positive, were again negative on PCR test. So these singleton PCR positive participants, we observed about 20% of them, both during Delta and Omicron phases.

And then population D are the ones where we did not have a repeat PCR test, and we cannot classify them as population B and C. On the right is positivity for rapid antigen tests on the y-axis, for Delta which is shown as blue point, and Omicron which is shown here as red point, and then overall which is shown as a black point estimate. The two populations shown here is population A, which is all of the participants where we saw positivity during the study.

On the same day-- which is the first data here-- as PCR positivity, we observed only a fraction of participants testing positive on rapid antigen test. That proportion went from around 24% overall to 55% within 48 hours, with a slightly higher proportion of those infected with Omicron variant testing positive, in comparison to Delta. However, the error margins are shown here and they overlap, suggesting that the difference was not statistically significant.

Contrast that with the subset of participants that continued to test positive on PCR for 48 hours. And even though on the same day, the number of participants that tested positive on rapid antigen test was roughly 1 in 3 overall. Nearly 90% of them tested positive within 48 hours. In comparison, none of the singleton PCR positive participants tested positive at any point during the study. Next slide, please.

And this is another way of looking at predicted probability-- the same data but shown here as predicted probabilities. On the left is what predicted probabilities for testing positive or with antigen test as a

function of PCR CT value. The CT values were derived from Roche assay. And for Omicron variant, the predicted probabilities are shown in red, and for Delta variant it's shown in blue.

What I would draw your attention to is, as CT value decreased and R decreased below 26, the probability of testing positive with a rapid antigen test was more than 80%. And the difference, although it was seen here qualitatively, the error margin suggests that difference is not statistically significant.

Referring to the question posed earlier about serial testing, on the right is the concept of serial testing shown graphically and as predicted probabilities. So x-axis is showing what the first PCR positive CT value was, and y-axis is demonstrating the probability of testing positive on rapid antigen test within 48 hours. Here again we observe the same phenomena. But the point to highlight here is, overall probability of testing positive increases even at higher CT values with serial testing. Next slide, please.

And then for this study, we used three different FDA EUA authorized tests. And using the same methodology, we were able to see that there was not too much of a difference in terms of positivity as a function of CT values for each of these three rapid antigen tests. Next slide, please.

So this is a busy slide, but where I want to focus your attention on is the red boxes which is-- one of the questions that we started to ask ourselves is, this population C, which is the singleton PCR positive. Is there something different about them, in that they're more likely to be vaccinated or more likely to have a booster dose? And comparing population C is shown here with population B, which are the consistent PCR positive, we did not see a statistically significant difference between their vaccination rate and the proportion of participants who had received three or more vaccination doses. Next slide, please.

Where we did see a difference is in the CT value between population, B which are positive PCR followed by another positive PCR, in comparison to singleton PCR positives. In singleton PCR positives, all of the participants that tested positive had a CT value of 30 or higher. Next slide, please.

Building on the platform that I showed before and recognizing the questions that were emerging with the Omicron variant, we did a sub-study where we asked a different set of participants to test daily for 10 days with rapid antigen test, and daily for seven days with molecular comparator or a home collection PCR test. Enrollment for this study happened at the end of January, and we were able to use the infrastructure to rapidly enroll 600 participants in a matter of five days. Next slide, please.

These participants were predominantly the ones that reported close contact, so a little different population than in the previous study. And on the right, it shows where the participants were recruited from. By the end of January, given that the pandemic had shifted to the Western part of the country, most of the participants we enrolled were from Washington and West Coast. Next slide, please.

And this is a little bit of a different representation, where we're showing on x-axis, days since self-reported close contact, and on the y-axis, proportion of participants that tested positive on antigen as well as PCR test. PCR positivity is shown as triangles, and antigen positivity is shown as circles. As we get further

away from day of close contact, the proportion of participants that tested positive on PCR test increases, as does proportion of participants that test positive on antigen tests.

And we see that the difference between the two is not statistically significant until we're more than two weeks removed from close contact. And at that point, there is this small difference seen between antigen positivity in comparison to PCR positivity. But even in this population, 80% of those that are PCR positive are detected by rapid antigen tests. Singleton PCR positives in this population continue to suggest that rapid antigen tests don't work as well among the subgroup of people who only test positive on PCR on a single time point. Next slide, please.

And then these are analyses shown from the Say Yes! COVID test program from Michigan specifically, where we distributed-- this should be 500,000-- test kits, 25 per family from June 7th through August 11th. The tests were distributed in Washtenaw County in Michigan in two different townships-- one shown here highlighted in yellow, which was the Ann Arbor community-- younger, more tech savvy, which is relevant given that this was online direct-to-consumer ordering-- and Ypsilanti community, which is more representative of the rest of the Washtenaw County, both in terms of demographics, as well as vaccination rates.

On the bottom here is the population in Ann Arbor, Ypsilanti, and overall rest of the West Washtenaw County. And the vaccination rates prior to the intervention program was lower in Ypsilanti than the rest of the Washtenaw County, but higher in Ann Arbor. And those differences continued throughout the intervention, which is when the tests were distributed, and afterwards as a Delta surge emerged in this community. Next slide, please.

And so the two graphs here show comparison of-- on the top panel is Ann Arbor and Ypsilanti, number of cases that are standardized for daily cases in the pre-intervention period, during the intervention period, and then post intervention period. And what we were able to see is that Ann Arbor and Ypsilanti had a lower number of cases in the post intervention period as the Delta surge arrived in these communities.

And so rapid antigen testing was associated with a lower number of cases. Separating Ann Arbor and Ypsilanti out, black line here shows Ann Arbor number of cases, and this blue line shows Ypsilanti's daily cases, that are standardized in comparison to the control communities, which is West of the Washtenaw. And we see a bump in Ann Arbor around September, which likely suggests students coming back to the college town.

But overall, as we advanced our observation window, Ann Arbor and Ypsilanti both had a lower number of cases, which were estimated as 40 lower cases per day in terms of both joint Ann Arbor and Ypsilanti. And separate modeling showed roughly equal number of cases, say 22 and 23 in Ypsilanti. It's important to note that this is data based on publicly reported data, which in most cases is Ann A(rbor) and Ann A(rbor) reporting.

And this is data based on modeling work, and we will be submitting this on preprint servers and peer reviewed journals later today. And I believe the next slide shows reporting behavior. If you can advance-- oh. Or perhaps not, so I'll pause there for any questions.

**JASMINE CHAITRAM:** Thank you so much, Dr. Soni. One of the questions that we did get was, what were the intentions about publishing this work, and I think you just answered that. So thank you very much for that. Another question we got was, can you explain what a singleton PCR is?

**DR. APURV SONI:** Yeah. And so in both of those studies that I mentioned, the singleton PCR positives, we defined as participants who tested positive on PCR, after testing negative either 48 hours or 24 hours preceding the first PCR positive, and then subsequently tested negative on PCR within 24 or 48 hours. And the reason why I have two different time horizons is, both of those studies did different frequency of testing. But in very layman's terms, those are participants that tested positive on PCR only once during the study.

**JASMINE CHAITRAM:** Great, thank you. And also thanks for all the slides and all the data you presented. I think folks are still a little bit confused, and maybe you could help out by doing a summary of some just really basic top-line conclusions from the study.

**DR. APURV SONI:** Sure. And also I recognize Dr. Stenzel is on the line as well, so he may also provide some medical realization. But the top-line summary for rapid antigen tests is that they work similarly for Delta and Omicron variant, in that on the day of first PCR onset that was observed, the sensitivity was low. But it's rescued by serial testing.

That rescue, we observed was much-- well, all of the detection by rapid antigen testing is among the cases when participants and when people test positive for PCR for more than one day. If they only test positive for PCR at a single time point, or the blips which has been seen in other viral infections, rapid antigen tests do not pick it up. What the data doesn't show is whether or not those blips, or those singleton PCR positives, are infectious or not. We don't have the data to be able to support or refute that statement.

And this graph here shows that there is an association when we performed ecological analysis of mass distribution of rapid antigen tests in a community, and number of cases, especially during surges. The key difference, in terms of drawing inferences from the findings that are shown here, and its implications for the federal initiative to distribute a number of rapid antigen tests throughout the country, is the number of tests we distributed in this community were 25 per family. However, the way of distributing the test was similar for the most part, which was people going online in this community and ordering the tests. But there's a key difference in the number of tests that were distributed.

**JASMINE CHAITRAM:** OK, thank you so much, Dr. Soni. And Tim is up next, so if he wants to add anything, he can add it then when I introduce him. But thank you so much for joining us today. Appreciate the presentation.

**DR. APURV SONI:** All right, thank you.

**JASMINE CHAITRAM:** OK, next up we do have Tim Stenzel, Dr. Tim Stenzel from the US Food and Drug Administration. Tim, go ahead.

**DR. TIM STENZEL:** Yeah thanks, Jasmine. Hopefully you can hear me. And gratitude to Apurv for going through all of this data. It does highlight some very important things, namely in the serial testing study that he went through in detail. This was testing done every other day on purportedly asymptomatic patients. It was community based and I think, a really well-done study.

And it very much highlights the importance of doing serial testing when you have at least an initial negative result. If you have a positive result, especially when the virus is circulating, then I think you can pretty much count on the positive predictive value of antigen tests in that setting, and you can act accordingly. But I think where the real caution needs to come in, is if you have a positive result-- and I mean a negative result. And especially if you're symptomatic at that point, and you're wondering if you have COVID.

The importance of serial testing is clear in that the first day of positivity that coincides with PCR positivity, with antigen tests, is on average in the 30s. And it only-- to 40s, depending on whether you include the singleton positive-- singleton positives being that they only had one positive PCR test in the study.

And PCR testing is done every other day, the same thing as for antigen tests. So even with the singleton tests of patients thrown out of the study, the first day positivity with antigen test was well below 50%. And it was brought up significantly with serial testing. So it just underscores the importance of serial testing when you're negative, to want to know if you're truly negative with antigen tests.

OK, if there's time-- there isn't much time, I guess. But I think there's enough for me to run through a couple of the pre-prepared questions that the FDA received. One is-- the first question is, is there an advisory posted somewhere for folks to avoid off-label testing with current antigen tests? And so first off, the FDA does obviously advise all fit to use tests as authorized, follow their instructions-- and including at-home users.

There has been a lot of discussion out there about, should you use the throat swab instead of an anterior nasal swab? But none of the antigen tests are authorized for throat swabs. And the NIH RADx Variant Task Force team did a study of throat swabs versus nasal swabs during Omicron, I believe. And it did not show a clear advantage of throat swabs. And since there is potentially added risk for doing self-collected throat swabs, the recommendation from that group-- and I believe they're in the process of publishing that, if they haven't already-- is to continue the test as labeled.

Also I just got through saying how important serial testing is in there, and there's multiple tests. Basically almost all of the antigen tests that have screening claims for asymptomatic have a serial testing portion of

that. A few do not, but the one's here do. And as just expressed by myself, and shown by Apurv with this data, it's really important to continue to do that.

The FDA has issued a number of safety communications around rapid antigen tests. And I did put a link into the chat for this meeting. I did put three different links-- one was on [safety communications](#), the second one was on [at-home diagnostic tests](#) just for common understanding. So and then I put a third link in for all the [EUA authorized tests](#). So the way that someone can tell if something is on label or not is, is it in the FDA authorization? And the FDA makes that information available, and hopefully easily on the FDA website.

The second question-- last question is, it OK to use a proctor to test like for travel or work or other events? Does the EUA have to say a proctor is authorized in order to do that, or is that considered a modification of the EUA? Would that require the labs to apply for an LDT? Can the proctor be in another country outside the US?

So probably one of the biggest reasons for proctored tests right now is for travel. Somebody travels outside the US, brings a kit with them. Before they come back in, if there is a requirement to test before coming in, that they do a proctored test and get a result that can be used for them to be cleared into the country.

So there are potential other uses for proctored tests, and that is just to make sure that somebody does it right. There is also the case where OTC tests can be given to individuals the day before they go into some situations. And although it's not really proctored, there can be observers watching people perform the test, and whether or not they perform the test. And then the result could be shown after the individual interprets-- says, I'm positive, I'm negative. You know, here's the result, that sort of thing.

So clearly though, if a proctoring is going to be directing how somebody performs the test and is going to aid or read the test at the end of it, then the FDA wants that proctoring to be part of the EUA authorization, and for there to be data that shows that that proctor situation-- usually telehealth, usually over video, which may have some challenges. And to make sure that the instructions and the test reading, and the test interpretation and communication is all accurate. So if there are any questions about this, I did put an email address into the chat. That can be used by any test developer or proctor organization, or anybody else, like a lab, that wants to ask a question about EUA tests.

They can send their questions to the FDA, and we will do our best to respond relatively quickly. And with that, we're a little bit over. Apologies, but that's what I had today, Jasmine.

**JASMINE CHAITRAM:** Thank you so much, Tim. And sorry, we ran out of time for your updates. And apologies to everybody else for going over. But I do want to thank folks that put topics into the chat. We will take a look at all of those and see if we can get those on future calls as part of the agenda and have speakers to address some of those suggestions. So thank you all and hope you all have a good day. Bye.