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Call Agenda
Welcome

Sean Courtney, CDC Division of Laboratory Systems

SARS-CoV-2 Viral Shedding and Rapid Antigen Test Performance – Respiratory Virus Transmission Network, November 2022–May 2023

Sarah (Lizzy) Smith-Jeffcoat, CDC Coronavirus and Other Respiratory Viruses Division

Situational Update and Response to the Highly Pathogenic Avian Influenza A(H5N1) Outbreak in U.S. Dairy Cattle

Charles (Todd) Davis, CDC Influenza Division

Call Transcript
Sean Courtney: Good afternoon, everybody. We apologize for the delay. Unfortunately, we're having an issue on the technical side of this, and I think it's a licensing issue, because it's limiting the amount of individuals that are able to join our call, unfortunately. So we apologize for that, and we'll try to make sure we get that fixed for our next call. But let's go ahead and get started with today's call.

So again, good afternoon. I'm Sean Courtney. I'm in CDC's Division of Laboratory Systems. And on the screen is the agenda for today's call. But before we get started, I just want to cover a couple of housekeeping items and some announcements.

As you've heard on previous calls, DLS is the CDC division that works closely with clinical and public health laboratories across the country to support laboratory emergency preparedness and response activities. We've been hosting these calls since March 2020. DLS supports this work across four goal areas: quality, workforce and training, preparedness and response, and informatics.

One of the announcements for our call today is regarding the DLS ECHO Biosafety Program. This is a community of practice that looks to address biosafety challenges in clinical and public health laboratories. The next ECHO session is scheduled for Tuesday, June 25th, and we'll focus on *Support: Communication and Documented Information*. These monthly sessions are tailored for laboratory biosafety professionals and provide a platform to bridge gaps, build a community practice, and enhance biosafety. You can scan the QR code on the slide to register for the next session. To view upcoming sessions and access resources for past sessions, please visit the ECHO Biosafety Program website.

And so, as always, we want to hear from you. Our Training and Workforce Development Branch is interested in hearing more about the education and training gaps that you're currently experiencing. And we invite you to send your feedback via email to labtrainingneeds@cdc.gov.

In addition, if you have topics that you'd like to hear on this call, we'd like to hear about those as well, and we would welcome your suggestions for future LOCS Calls. As always, and especially today, we'll be sharing the slides from today's call along with the audio and transcript, and we will post them online hopefully within the next two weeks or so. You can find them on CDC's Laboratory Outreach Communication System page at the link shown at the bottom of this slide.

And if you have a question, we ask that you please use the question-and-answer function in Zoom so that we can address it during the call and do not use the chat function. We'd also like for you to please include your email so that we can follow it up if we're not able to answer it during the call. If you're from the media.

We ask that you please contact CDC Media Relations at media@cdc.gov. And if you're a patient we ask you to please direct any questions to a healthcare provider.

And lastly, I'd like to remind everyone that these slide decks may contain presentation material from panelists who are not affiliated with the CDC. Presentation content from external panelists and may not necessarily reflect CDC's official position on the topics covered.

And with that I would like to introduce our first speaker. Today we have Dr. Todd Davis from CDC's Influenza Division, and he'll provide us with an update on influenza. Todd, I'll hand it over to you.

Todd Davis: Hey, thank you, Sean. Just double-checking you can hear me okay.

Sean Courtney: Yes, we can. Thank you.

Todd Davis: Okay, thanks everybody and thanks for the invitation to speak today. I'm going to talk a little bit first about just a situational update on the H5N1 outbreak in the U.S. and dairy cattle, and then focus a bit on some of our public health response and specifically enhanced surveillance over the summer months. Next slide.

Great. So as of June 13th, and this slide is already a little bit dated, just to be sure that this went through our clearance process. But as of today, really, we're up to more than a hundred dairy herds that have been confirmed across 12 states by the U.S. Department of Agriculture. The map hasn't changed, but there has been a slight uptick in the number of dairy herds since June 13th.

So we've also, through partnerships with USDA - and they're posting this information on the weblinks below - been notified of additional animal species that have been impacted by the dairy cattle outbreaks, and that includes wild birds and several different species of mammals.

And we've also been working with partners, and with USDA in particular, to understand how some of the testing mandates are also now being applied for taking lactating dairy cattle to agricultural fairs and exhibitions. I think folks are aware this is the beginning of the summer season for a lot of the county fairs, state fairs, as well as exhibitions with livestock. And so Wisconsin and Minnesota have declared that they're going to be testing or requiring a negative H5N1 result prior to dairy cattle being shown at those fairs and exhibitions. Next slide.

So in response, you know, the CDC and other partners have been actively monitoring exposed persons. This begins with active outreach to states where there have been positive cattle herds identified. And this is something that we've done for quite a few years because of the outbreaks that occurred in poultry related to H5N1.

And so, there have, of course, been poultry outbreaks that have occurred since February of 2022. We monitor those individuals that are exposed to infected birds for at least 10 days after exposure and to date, there's been almost 10,000 people that have been monitored after those exposures, and at least 350 people that were tested for novel influenza A viruses and of those only one individual, the individual from Colorado that was positive for H5 back in April of 2022, is the only case associated with poultry outbreaks.

But since the dairy cattle outbreaks started, we've also been monitoring individuals exposed to infected dairy herds. Currently, we've been monitoring more than 550 people, and more than 45 persons have been tested, and of those 3 cases have been identified and all recovered. There's information on the right-hand side of the slide that will also point you to the updates that are made to CDC's monitoring pages related to the dairy cattle outbreaks as well as avian outbreaks. Next slide.

So, as I mentioned, there have been 3 human cases confirmed for H5N1 associated with exposure to dairy cattle. The first occurred in Texas, and then there were two additional cases that have been

detected in Michigan. All of these were in adults that were working at commercial dairy farms. They had no relationship to each other, and they were all working on different farms.

Two of them presented with conjunctivitis, and in the most recent case, had mild influenza-like illness. But no one was hospitalized. All of the individuals recovered in isolation of those individuals, was recommended. In each case, there's been no evidence of human-to-human transmission. And if you want to hear more about some of the genetic information and some of the additional virologic testing that's been done, there's a couple of links on CDC's web pages, as well as a link to a recent publication describing a bit more of the epidemiological investigations, as well as the virologic characterization of these individuals. Next slide.

Something else that CDC has been actively doing is working on epidemiological investigations to learn more about the public health risks associated with dairy cattle exposure. So we're working with health and agricultural partners at the local, state, and federal levels, especially those on affected farms. We've been looking at whether or not there's evidence of H5N1 infection in at-risk populations and specifically focused on those that have exposure to infected dairy cattle.

We want to know more about what the spectrum of illness is and whether there are potential asymptomatic infections as well. So we're looking at what types of exposures there are of these individuals on dairy farms and hoping these epi investigations give us more insight into that something else we're actively doing is working on surveys that will allow us to collect this type of information to glean a bit more about the risk associated with both symptomatic as well as asymptomatic infections. Next slide.

In addition to that monitoring and those epidemiological investigations, we're also enhancing our summer surveillance efforts. So as I mentioned, looking closely at workers and others that are exposed to H5-infected animals, conducting outreach and education among those that exhibit animals. So we have quite a lot of experience with swine exhibitions, and the exposures to swine that occasionally lead to novel influenza infection. So, applying those applying those lessons learned, and how they might also impact exposure to livestock that may be infected with H5.

We're also working on more samples coming into our state public health labs. I'll talk a little bit about that in more detail as we go. One other area that we're focusing on is looking at severely ill patients or patients that are hospitalized or in ICU, to making sure that if they test positive for influenza A that we're also doing subtyping of those specimens. We're also looking at investigations of unexplained clusters of respiratory illness, monitoring data for unexpected patterns or data anomalies that might be associated with novel influenza A outbreaks. Next slide.

So one of the things that we do throughout the influenza season is working with our National Influenza Reference Centers, AKA NIRCS. There are three in Wisconsin, New York, and California, as well as our Influenza Sequencing Centers in Colorado, Florida, Hawaii, Massachusetts, Minnesota, and Texas.

And by coordinating with the state public health laboratories, we're able to not only receive and collect additional specimens, but also conduct next-generation sequencing of those viruses. And so that gives us approximately 6,000 samples that come in to CDC through those partnerships.

And that's a very effective method of conducting genetic surveillance and neurologic surveillance across the influenza season. But this summer through our partnership with the Association of Public Health Laboratories, we're maintaining steady state operations of the NIRCS and the ISC so that they'll maintain their sampling and their testing throughout the summer months, in hopes that that will also give us a wider net to identify any novel influenza A infections that might be detected in the U.S. Next slide.

This also includes making sure that commercial laboratories that are receiving and testing specimens are also able to subtype those viruses. So a routine part of the process with commercial laboratories, of course, is anytime a sample tests influenza A-positive but is subtype negative, that the samples are quickly submitted to a state public health laboratory for additional subtyping, or if they get an interesting

result. For example, if they detect influenza A(H1), but not A(H1)pdm09, and their assays that those are also subtyped or characterized with additional testing to be sure that we're picking up those potential novel influenza A infection. So those are fairly routine procedures that are coordinated between commercial laboratories and state public health laboratories and that includes submission of samples that can also be tested using CDC's A/H5 assay - upper respiratory specimens, lower respiratory tract specimens, and now paired nasopharyngeal and conjunctival specimens. I'll talk a little bit more about that in a minute.

But in addition to that routine processing, we're also asking commercial laboratories to submit influenza A- and influenza B-positive specimens that have not undergone influenza subtyping to be sure that we're not missing any novel influenza A infections and those types of samples. So CDC is currently working with commercial laboratories to determine what the appropriate number of samples would be for them to submit those to state public health laboratories, or the NIRCS or ISCs, for additional characterization, making sure that those samples meet established cutoffs for our testing algorithm and making sure that those are done in a timely manner so that we can get subtyping results on those samples. Next slide.

So part of this also includes working with FDA. One of the more recent things we have been able to do with FDA is to request and receive enforcement discretion to now allow state public health laboratories to use conjunctival swabs for a diagnostic test using CDC's H5 assay. These have to be paired with a nasopharyngeal swab per the criteria of the enforcement discretion. And there also has to be in-house verification performance studies per CMS guidelines at the state public health laboratories that are performing this testing. But that's given us a number of additional samples - a sample type that previously was not permitted for testing using CDC's H5 assay.

Something else that just has recently changed is the USDA/APHIS exemption of H5 avian influenza viruses as a Select Agent. So for the next 3 years, according to this temporary exemption, H5 is not considered a Select Agent virus. And so that's also allowing us some flexibility to be able to ship materials that are confirmed H5-infected without having to follow select agent shipping regulations, as well as other things like transfer and destruction of those materials that are confirmed to be H5-positive. So that's some good news and should offer some flexibility to everyone that's testing for H5.

Another area that CDC is very much focused and is prioritized is working with private industry to consider development of additional H5 tests. So the CDC's H5 assay is distributed to state public health laboratories for subtyping, but there's no commercial test available to subtype specifically for H5. And so we're working with commercial companies to be able to think about how they might achieve the goal of developing and seeking FDA regulation for an H5-specific subtyping test and one of the ways that we've approached this is a recent call to industry from just last week, where we've now asked companies to submit proposals through another transaction authority that would allow those companies to develop commercial H5 assays for some criteria that CDC has been working on for the past couple of weeks. So I encourage everyone to have a look at that specific link here - will provide that in the chat as well. So that you understand what that OTA looks like and what those deliverables are.

And then finally, a few other things that we're also working on. We've had some requests from quite a few public health departments to provide recommendations and specific protocols on actually collecting conjunctival samples from individuals. And so we're working on some graphics in a specific SOP that we hope to be able to distribute very soon.

And last, but not least, also working with FDA to consider adding universal transport media as a sample collection matrix as opposed to only virus transport media in order to use a broader subset of media for use at use in CDC's H5 assay. So something that's in the works, and hope to be able to provide some more details on that soon. Next slide.

And I'll stop there. Again, happy to take any questions but appreciate the attention. Thanks.

Sean Courtney: Alright. Thank you, Todd. I appreciate your update today. And again, and I just want to apologize for the licensing issues that we're having. But thank you for the update on influenza. Got a couple of questions, I'll start with one. You spoke about it earlier with the 2022 outbreak and you mentioned monitoring cases out to 10 days. How long do you monitor for this outbreak? How long are the cases being monitored for this outbreak?

Todd Davis: Yeah, we follow the same monitoring strategy for 10 days. I think it would – keep in mind in the case of poultry outbreaks, you know poultry flocks are culled after they're detected. And so we have really a day one for those individuals that have been exposed to those flocks after the culling has taken place. It's a different scenario with the infected dairy cattle where they're allowed to recover, and so it's a little bit harder to gauge exactly when that monitoring period begins.

Sean Courtney: Okay, great. Thank you. Looking at the Q&A, I see a question there. And it is, is there evidence that people can develop avian influenza from dairy cattle and remain asymptomatic? If, yes, are these people considered contagious?

Todd Davis: So currently, we don't have any data to suggest that there's asymptomatic infections out there. And that's something we hope to learn through these epi investigations.

Sean Courtney: Great, thank you. Another question I have actually is around the test itself. Is the test considered presumptive or confirmatory?

Todd Davis: So the tests that are performed at the state public health laboratories are considered presumptive. And then CDC will do the confirmatory testing.

Sean Courtney: Okay. So when the specimens are sent to CDC, that's when they're confirmed.

Todd Davis: That's right.

Sean Courtney: Perfect. Great, thank you. Alright, so another question just came in. It says, how can they find out information for sending a PCR sample for subtyping?

Todd Davis: Yeah, yeah, we do have some links on CDC's web pages. I'm happy to drop those links in that have some specific information and contact for those that are able to receive those samples.

Sean Courtney: Great. Thank you. Alright, well, I do not see any other additional questions at this time, so I just want to thank you again for joining our call. And if you have the time if you could stick around, if any additional questions pop up in the Q&A feature you can just type the response in there. If not, we'll try to get them over to you so that we can get them, answered as best as possible. But thank you, thank you for joining our call. Appreciate it, Todd.

Todd Davis: Thank you. Bye.

Sean Courtney: Alrighty, and with that we're going to move on to our next speaker. We have Lizzy Smith-Jeffcoat from CDC's Coronavirus and Other Respiratory Viruses Division. She's going to provide us with a presentation on SARS-CoV-2 viral shedding and rapid antigen test performance. Lizzy?

Lizzy Smith-Jeffcoat: Hi, I'm an epidemiologist with the Outbreak Response Community Transmission Team here at CDC. This analysis was recently published in MMWR, so I will be walking you through the analysis. Next slide, please.

Rapid antigen tests tell us if a patient is acutely infected with SARS-CoV-2. They detect the presence of virus-specific proteins called antigens from patient specimens. These tests were developed and rolled out broadly early in the COVID-19 pandemic, with the hope of quickly expanding this rapid diagnostic to aid and transmission prevention at a time when there were long wait times for PCR results. Next slide, please.

Previous studies of rapid androgen tests for SARS-CoV-2, most of which were conducted during circulation of Delta or pre-Delta variants, have shown that while RT-PCR is more sensitive, antigen tests correlate more closely with viral culture and may be a better proxy for infectiousness.

As SARS-CoV-2 variants and population immunity have evolved, the role and performance of rapid antigen tests and diagnosing SARS-CoV-2 have been questioned. I think there's an animation to the slide if you can click one more. Yep.

So our objective was to reevaluate the performance characteristics of SARS-CoV-2 rapid antigen tests with those of RT-PCR and viral culture tests during early 2023, a period with greater population immunity and more recently circulating SARS-CoV-2 Omicron variants. Next slide.

The data included in this analysis come from a sub-study at five sites within the Respiratory Virus Transmission Network within the United States. This network uses a case-ascertained household transmission design briefly symptomatic or asymptomatic persons who tested positive for SARS-CoV-2, along with their helpful contacts, were consented and enrolled within a week of index onset.

Participants collected daily nasal swabs and completed daily symptom diaries for 10 days following enrollment. Starting in November 2022, households could choose to be part of the rapid antigen test sub-study. Study enrollment ended in May 2023. Next slide, please.

Sub-study participants collected two nasal swabs each day for 10 days. The first nasal swab was tested, using automated PCR via the Hologic Panther Fusion SARS-CoV-2 assay, and an aliquot from the same specimen was cultured. The second nasal swab was used to perform an at-home antigen test, using the Quidel QuickVue test, which the participants interpreted themselves and reported the results in the daily diary survey. Next slide, please.

Using these data, performance characteristics were evaluated by viral shedding curves and antigen test sensitivity as follows. We defined onset as the first day of symptoms, or, if the individual is completely asymptomatic, their first positive test. Viral shedding was visualized as the percentage of positive rapid antigen, RT-PCR, and viral culture results each day relative to onset, along with 95% confidence intervals, calculated using the Wilson score intervals.

Antigen test sensitivity was calculated among paired samples collected two days before to 10 days after onset, using two references. The first was the same-day positive RT-PCR result and the second was the same-day positive culture result.

Sensitivity estimates were stratified by symptom status on the day of specimen collection and cluster-robust bootstrapping was used to calculate 95% confidence intervals to account for within patient participant correlation. Next slide.

So on to the actual results. Among the 354 participants in 129 households who reported at least one paired rapid antigen and RT-PCR result, 236, or two-thirds, tested positive for SARS-CoV-2 by RT-PCR, and were included in the next pieces of the analysis. Next slide.

Participants had a median age of 36 years. They ranged from 2 months old to 83 years old. 59% were female, 56% were white, non-Hispanic, and 29% Hispanic/Latino.

The median social vulnerability index, which is a measure of vulnerability to disasters based on where one lives, was 0.43 on a scale of 0 to one, which means our households were slightly less vulnerable than the national average. Nearly half of all participants reported at least one chronic medical condition, and 93% reported at least one COVID-19 symptom, so a lot of symptomatic illness.

43% had self-reported or serologic evidence of previous SARS-CoV-2 infection and 40% reported receipt of a COVID-19 vaccine less than or equal to 12 months before enrollment. Next slide, please.

This figure shows the percentage of tests that were positive and 95% confidence intervals each day sent symptom onset, or if asymptomatic, their first positive test. The gray solid line represents RT-PCR. The dark gray dash line represents viral culture, and the blue dash line represents rapid antigen tests. RT-PCR proportion positive peaked at 83% three days, post-onset. Rapid antigen test positivity peaked at 59% three days post-onset, and viral culture positivity peaked at 52% two days post-onset. Next slide.

Next, we'll move on to rapid, instant test sensitivity. So this forest plot shows the rapid antigen test sensitivity 95% confidence intervals against the two different reference groups. Compared to the same-day RT-PCR on the left, antigen test sensitivity was 47%, compared to the same-day viral culture on the right, antigen test sensitivity was much higher, 80%. Next slide.

However, when you stratify by symptom status on the day of specimen collection, antigen tests had a much higher sensitivity on days when symptoms were present, especially days where fever was present. Next slide.

So among these participants were studied during a period of increased disease and vaccine-induced immunity and when circulating viruses differed antigenically from the ancestral SARS-CoV-2 strain, antigen and culture tests detected a similar proportion of SARS-CoV-2 infections. But detection by RT-PCR was higher than that by either antigen or culture.

Similarly, paired antigen test sensitivity was low compared to RT-PCR, but relatively high compared to culture. The sensitivity of antigen testing was higher when symptoms were present on the test day and peaked on days when participants reported fever. Although viral culture is not an absolute marker of transmissibility, this pattern suggests that positive antigen test results could indicate transmissible virus. Thus, antigen tests might aid persons with COVID-19 in determining when they are no longer infectious once symptoms begin to resolve. Next slide.

The findings from this investigation remain similar to those reported and studies from earlier in the COVID-19 pandemic, during the pre-Delta and Delta variant circulation. However, we are in a very different world. We have high population immunity both from vaccines and prior infections, and in turn, hospitalization and death rates from COVID-19 have decreased.

This is also partly due to access to outpatient antiviral treatments, for those are at higher who are at high risk for severe COVID-19. Minimizing false negative test results is now even more important to facilitate access to these lifesaving medications.

Antiviral treatments for SARS-CoV-2 infection should be started as soon as possible, and within 5 to 7 days of symptom onset. Therefore, persons who are at higher risk of severe illness and eligible for antiviral treatment would benefit from a more accurate diagnostic test than an antigen test.

In most clinical scenarios in the United States this approach means a SARS-CoV-2 PCR test. That would be a better diagnostic test to minimize the risk of a false negative result or delaying due to multiple tests needed to increase your positive predictive value. Alternatively. If RT-PCR tests are not available or accessible, clinicians and patients should follow FDA serial antigen testing recommendations to help optimize the diagnostic test performance. Next slide.

I think that's it. Thank you.

Sean Courtney: All right. Thank you very much for that presentation today, Lizzy. I think that was a really-- great information shared. And so I see a question now. It says, if the participants were collecting their own samples for both tests, how are you able to make sure that the samples were collected correctly and not being contaminated with anybody else in the household? So I guess it's around contamination control and specimen collection.

Lizzy Smith-Jeffcoat: So we cannot exactly know that. But the nasal swabs were collected in VTM that did not inactivate the virus, and the coordination centers, for each of these sites had very close rapport

with each of these households, and so there was a lot of handholding to onboard each of the household numbers. There's a lot of follow-up every few days, you know. How's it going? Do you need any help? And they physically come and pick up the swabs every, I think it was like two to three days, from the household. So if there's any issue that they're seeing with how they're storing them, or how they're collecting them from that first collection, then they'll try to correct those actions.

Sean Courtney: Great. Thank you. That makes sense. Okay, well, I do not see any additional questions at this time. So I'll just go ahead and say thank you again for joining our call and providing this presentation for us. One more just came in as soon as I was saying that. Were these results parsed by vaccination status? So did you know the vaccination status of the participants during this investigation?

Lizzy Smith-Jeffcoat: Yes, actually we have very detailed information about their vaccination history. I mean that there was a preliminary look that I did, and we did not find any significant difference by vaccination status. But that was not part of this report.

Sean Courtney: Okay, great. Thank you. And another question came in it says, given the antigen sensitivity was lower compared to PCR, is there a need for better quick diagnostic tests if the -

Lizzy Smith-Jeffcoat: That'd be great.

Sean Courtney: Yeah. Let's see, sorry. Trying to read the rest of it, I apologize. I'm not sure if that one we can answer it. I can say to you, I'm not sure if you'll know it. It says, so if the patients come in with symptoms and signs of COVID-19 and have a negative antigen test. What about treating them empirically with antivirals? And given that antivirals are not likely to have severe side effects, would you check for drug interactions with Paxlovid and take precautions if - I can't even pronounce it.

Lizzy Smith-Jeffcoat: Molnupiravir.

Sean Courtney: There you go. Yeah, sorry. Apparently, this is not my side.

Lizzy Smith-Jeffcoat: So I think Hannah is on. She's my team lead and a clinician, so can give her opinion. But I'm not a clinician, so I'm not going to -

Sean Courtney: Sure I think - there she is. Thank you, Hannah.

Hannah Kirking: I'm here. No problem. It's a very astute question. I think if someone came in and had a negative antigen test, but had signs and symptoms of COVID, it's a little bit of a clinical, as well as to some extent, access to Paxlovid, kind of call as to whether or not you would treat them empirically. By all means, if they're high risk and would qualify and benefit from treatment. If you have a PCR test, that would be great, but you could opt to go ahead and treat empirically on a negative antigen test.

The other thing that we don't frequently recommend and it's a little bit complicated. But for anyone working in public health, we're kind of aware of when we have COVID surges, and so that also might be kind of a key extra tool in the toolkit for a clinician to use when trying to decide to do that.

But yeah, the other thing we are considering here at CDC, just for the upcoming respiratory season, is kind of drilling down a little bit more on how to offer more specific guidance on testing across different respiratory viruses and or getting a little bit more into the empiric antiviral treatment. You know we regularly do it for antibiotics and bacterial infections. We do it less for virals, so we're talking more internally on that for the future. Hope that helps in terms of contraindications. By all means, if they've got contraindications, we would probably not recommend impaired treatment, but that's up to kind of clinical discretion.

Sean Courtney: Right, alright. Great! Well, thank you. Thank you for hopping in and joining the conversation and joining the call today.

So I will move on here and remind everybody that our next call is scheduled for Monday, July 15th at 3 PM. As a reminder, that's the third Monday of each month. So that'll be the 15th. And again, please let us know if you have any suggestions for future topics that we can discuss on these calls. Anything around your laboratory's testing and community needs.

And, as mentioned, we apologize for the licensing issue that we had. And so we'll try to make sure that we get the audio, the transcript, and the slides from today's calls on the website as quickly as possible since we were kind of limited in participants, unfortunately.

As always, you can find CDC on Facebook, Instagram, LinkedIn, and X, or Twitter, I guess, is what us old people still call it? So please follow and stay up today with the latest news and recommendations. And again, thank you for joining our call and thank you for our speakers that we're able to join today. And we continue to be grateful for all of the work that you do, and we will talk to you guys again on Monday, July 15th. Thank you.