Hello and welcome to the GeneXpert: Examples from the Field webinar. I'm Kelly Musoke, the Director of Education at the Curry International Tuberculosis Center. Today's webinar is the second in a two-part series, so we'd like to welcome back those of you who participated in last week's webinar. And for those of you who were not able to hear the presentation about the consensus statement, we will be posting the recording soon on the SNTC website and hope that you will find it useful.

We have almost 800 participants joining us from across the U.S. today, and we know that many of you are viewing in groups. This is a collaborative training between the National TB Controllers Association, the Association of Public Health Laboratories, the Southeastern National Tuberculosis Center, and the Curry International TB Center. We'd like to provide the websites for all the partner organizations in case you wish to learn more about any of us. And today's webinar was produced by two of the five RTMCCs.

We always like to ensure that everyone knows that while the RTMCC in-person trainings and clinical consultation are divided by region. All of our products and webinars are available to a national audience. Since this training has many new participants listening in, I'd like to highlight that each RTMCC provides free clinical and programmatic consultations to U.S.-based clinicians. Responses are generally provided within one to two business days, and you can find out more information about that on the Center's website.

We'd like to thank all of today's presenters, as well as the members of the planning committee. All of today's faculty members have signed a declaration of disclosure and have indicated that they have nothing to disclose, and these are the learning objectives for this webinar, outlining the key points we hope to touch on. But now let's move straight into our session today.

It's my pleasure to introduce today's facilitator, Dr. Neha Shah. She's a field medical officer with the Centers for Disease Control and Prevention, assigned to the California Department of Public Health. Prior to coming to California, she was the TB controller in Chicago, and did her EIS training with the Global Aids Project. She is part of the MDR TB Consultation Service at the California State TB Control Branch. Neha.

Thanks, Kelly. It's a pleasure for me to be on this webinar today and facilitate this important webinar. We've had a lot of questions, and I'm hoping that as we go through our presentations -- I'm sure we won't answer all of our questions, but we will try to do our best to answer as many questions as you guys all have in relation on how to implement this new Xpert FDA label for discontinuing airborne isolation.

I'm going to start off with a brief recap from last week's webinar. It seems some of you, or most of you were on that webinar. I'm not going to go into great detail regarding the whole consensus statement, as we reviewed that last week, and as Kelly mentioned, that should be available for people to listen to and look at on the website. As mentioned, I don't have any disclosures.

As a reminder, traditionally we have used three negative sputum smears as a criteria to release someone from isolation. In addition to not being very sensitive or specific, the release from isolation usually took sometimes up to about five to seven days, sometimes even longer. The other problem with being in isolation for up to a week is that hospitals have limited number of isolation rooms, so we were always in a bit of a hurry to get people out of there. And patients in isolation had a tendency to be seen less often by a health-care worker, had an increase in adverse events, a negative perception of their health care, and had delays in getting proper procedures. That briefly brings us to the topic today, which we're talking about.

In February of 2015, using some new data and some old data, the FDA revised the Xpert label to allow it's use for the aid in discontinuing airborne isolation for patients initially suspected of having pulmonary TB. And following that release, there was a MMWR put out by CDC to announce that this label change had happened.

How did this label change come about? Again, I'm not going to go into detail, great detail today. And there are more details in the consensus statement, which is available online. I'm just going to focus on some of

the most recent data that influenced the label change. In general, the Xpert has had improved sensitivity and specificity versus the sputum smear. Compared to two or three AFB specimens, one Xpert can identify 97% of all smear and culture-positive specimens, and when you do two Xperts, it can identify 100% of them.

The negatives, a NAA from one or two sputums is predictive of two or three AFB smears being negative. In addition to the increased sensitivity and specificity, there is a cost savings, because it reduces the time in isolation and the overall length of time in the hospital. Using these data, and, again, some older data that are outlined in the consensus statement, the FDA approved the use of either one or two specimens as an alternative to the examination of serial smears to aid in the discontinuation of airborne isolation for patients suspected of having pulmonary TB.

When we look at the FDA label change, we saw it was a little bit challenging to interpret from a practical standpoint what that label change meant. So together the NTCA and APHL, and a lot of other participants, put together this consensus statement with the purpose of provide guidance on how to discontinue airborne isolation using Xperts.

What the statement does not address is the diagnosis of TB and when a TB patient or TB case or subject can be released from the hospital. It is meant to help predict infectiousness and to help determine clinical appropriateness to be removed from isolation. Now in reality, we recognize there's considerable overlap of these issues. But, again, let's keep in mind that our main goal was to help understand the FDA label change and how to determine when to remove someone from isolation using Xpert results. We're going to try to, throughout this webinar, show you examples of how that might happen and hopefully in the panel discussion, if those sorts of questions come up, because I know it's a murky area, we can try to address them to the best of our ability.

Here is the main algorithm in the consensus statement. I'm going to walk us through this a little and then let our other two speakers better illustrate how this can be used in a clinical setting. If you have positive Xpert on the first specimen, the algorithm would say TB is likely and to continue isolation. I think that one's pretty straightforward.

Next, I'm going to go to the invalid results. If you have an invalid result, which should happen fairly rarely, about 1 to 2% of the time, and often labs will repeat and an invalid result. So you should not be in the situation that frequently. But if you have an invalid Xpert result on your first specimen, what the algorithms says is that infectious TB is not excluded, go to step two. And I'll review step two in a moment. If you have a negative Xpert, then TB is not excluded then you should continue isolation and go to step two.

Step two: Step two says collect another specimen. If your second specimen is positive, then TB is likely, and you should stop doing extra testing and continue airborne isolation. If your second specimen is negative as well, the algorithm would say that infectious TB is not likely. But in terms of discontinuing isolation, make this decision in conjunction with clinical data, which could include smears. If your second Xpert is invalid, you should continue isolation and use smears with a first Xpert results in clinical judgment to discontinue isolation.

If you continue through the consensus statement document, there is another appendix, separate from what we reviewed, that looks at how to interpret two negative Xperts with smear results. In a setting of two negative Xperts, if you have positive AFB smears, then the interpretation is that TB is not likely and most likely this is a non-tuberculosis mycobacteria. If you have two negative Xperts and two negative smears you can interpret that TB is not ruled out and continue your other diagnostic evaluations such as cultures and X-rays if you need them. If you have two negative Xperts, one positive smear, one negative smear, then, again, TB is not likely and this is more likely to be a non-tuberculosis mycobacteria. In all cases though, cultures should always be followed up.

So I know that's a lot of absorb, and I know it's not as clear cut as we always like it to be. I am going to -- I know this is just a brief overview. But what I'm going to do is turn this over to our next presenter. Dr. Regina McDade. She's a native of Miami, Florida, and she obtained her Bachelors of Science in nursing

from Howard University in Washington, D.C., and she got her Master's of Public Health degree with a concentration in Health Promotion and Disease Prevention from Florida International University. And she has a Doctorate in Education, with a concentration in Adult Education and Human Resource Development.

She's currently at the Jackson Health System Department of Infection Prevention and Control, in the office of TB control, and she's been working in the TB control community for 22 years, so it's a pleasure to have her here. She's going to share her examples -- she's going to share her experiences from Florida. Dr. McDade.

Thank you. Good afternoon everyone. It's a pleasure to share our experience and activities that we have here at Jackson Health System here in Miami, Florida. As mentioned in the previous webinar, Dr. Ashkin talked about the nosocomial outbreak of multidrug resistant TB, and as a result of being one of the hospitals, actually hospital A, we implemented a program here where we followed the CDC recommendations, the administrative respiratory protection and engineer recommendations to control this outbreak. And what we did was, of course, we had a partnership with our County Health Department here in Miami-Dade County, and at the time, the Health Department had a team physically located onsite here at Jackson Memorial Hospital. And the other part of that they hired a tuberculosis control nurse, myself, in 1993.

In addition, we established a respiratory clinic, which was geared toward managing those patients that are co-infected with HIV and tuberculosis, in partnership with the hospital. And we also implemented direct therapy for these patients. And the patients were followed by an Infectious disease doctor in this clinic, along with collaboration with the department of health.

Also, we have a tuberculosis controlled beeper where there is coverage 24 hours 7 days a week to help the staff or anyone with any questions concerned about tuberculosis. And as part of that program, we partner with our Microbiology Lab, where there's frequent communication, both via phone and in person, where if any patient has a first-time positive, if the smear, culture, or PCR, the laboratory will notify the patient care unit if they're in-patient. If they're outpatient, they would notify the physician, and they will also call the tuberculosis control beeper to ensure that the patient is placed in airborne infection isolation.

And today the Health Department is no longer physically located here at our hospital, but we do have a weekly case conference meeting over at the Health Department, where there is a team of supervisors who manage the patients that are followed here, but they provide direct services to those patients. We discuss all patient issues. If we have any exposures or contact investigations, all of that is discussed during that meeting.

And here at the hospital we also have at the time we had a tuberculosis subcommittee that was a multidisciplinary team, and that committee made recommendations, helped with policies and practice and education, and that committee reported up to the Jackson Memorial Hospital Infection Control Committee. The committee is no longer in existence, but all TB activity is still probation reported to the Infection Control Committee.

One of the policies that was developed was the Airborne Infection Isolation Policy. And this applies throughout our system. Our system now consists of three hospitals, Jackson Memorial Hospital, Jackson North Medical Center, and Jackson South Community Hospital. In addition, we have a correctional health component. We have outpatient also. So this policy can be implemented at ER, triage, or any point of entry into our system. So if the patient comes in with the clinical suspicion of TB, the staff are authorized to isolate that patient, meaning at triage they'll put on a surgical procedure mask, and the patient will be placed in the airborne infection isolation room while they're waiting for the physician evaluation.

Also, if a physician orders a sputum or a gastric washing for AFB smear and culture, that means automatic airborne infection isolation. And, of course, there are some exceptions to this, example, children under four, et cetera. As part of the infection control, this training throughout the system, this

training begins, in new employee orientation is a part of that. It's done annually online and in person, and it's also done as needed in any of the units or requested areas of the hospital.

We work closely with the employee Health Office, and what we do, we have a biannual TB control employee health office report that goes through the hospital infection control committee. And we report out based on an employee TST data, serial testing, which was based on our risk assessment of each hospital. So some units are tested more frequently than other units. And also, in the Employee Health Office, they're the ones who monitor the testing and also the Respiratory Protection Program, where all employees are fit tested for the N95 respirator.

During the education, we always encourage our staff throughout the system to call if there are any questions, any concerns, or if they want to know the patient history, or if there is a potential exposure, the workup, or any questions, we encourage them to call. And also case management, here we case manage the patients, those that are the in-patients and with the Health Department and those that are outpatients. They're case managed from diagnosis until cure. And they're both numbers, phone numbers are always listed for employees to call us throughout the system, either by office phone or pager.

So discontinue: As was mentioned before, airborne infection isolation beds are very limited. So even though we have them throughout our system, we have them in the ERs and the respiratory clinics, in-patient units, a couple in ICU, but there is always a need for these beds. And we also have an airborne infection isolation cells over in one of our medical housing units as one of the local jails.

So currently, in order to discontinue airborne infection isolation, the physician must order three AFB sputum smear and cultures. And we have a PRN order for induce sputum as needed. And to discontinue, we require three negative AFB sputums collected 8 to 24 hours apart, with at least one early morning specimen to DC airborne infection isolation.

So with the new change in practice, we're encouraging the physicians to order two induced -- and I emphasize induced to them, induced sputums for AFB culture and two GeneXperts. And we encourage them to do at least one eight hours apart. And preferably get an early morning sputum, we get that to discontinue isolation.

Our Microbiology Lab will process the specimens for us twice a day. We have a morning cutoff time, and we have a late afternoon or evening time cutoff time, so twice a day. They will process it seven days a week. So during the planning stage of making this change, we had meetings with key stakeholders, of course, infection prevention and controls, and infection disease attending, pulmonary attending, the Microbiology Lab, Information Technology, Nursing, Respiratory Therapy, and Department of Health, which we all have the support from all these different disciplines to implement this change in practice. This policy, about two weeks ago, the change in practice was presented to the hospital -- the Jackson Health System Infection Control Committee, and it was discussed, voted, and the policy change was accepted.

Also, as part of this change, our IT Department, they developed an order bundle. So automatically an order will populate for airborne infection isolation, order sputum for AFB smear, culture, and GeneXpert times two, and respiratory therapy will induce sputum. Right now our IT go-date is pending, but we have some physicians who are aware of it as a result of the committee meetings who started implementing this practice.

And of course, once we implement the change, and down the line we plan to evaluate this through our utilization of the airborne infection isolation beds, we're going to look at our ER admission to see if we prevented some in-patient admission, decrease the length of stay for those that are admitted to the in-patient unit, examine the cost effectiveness, and, of course, we're going to monitor to see if there's any change in our TB exposure incidents, monitor employee TST conversions to see if we missed any.

So now I'm going to talk about how we implemented the change in some of the cases here at Jackson Memorial Hospital. The first case was a 60-year-old Haitian female presented with a cough for eight days,

and night sweats. She reported at age 17 she was treated for TB in Haiti for one year. Medication regimen was unknown, but she did state the physician told her she was cleared of disease. She has a history of hypertension, hypothyroidism, hyperlipidemia, polymyalgia, rheumatica diagnosed one year ago, and on steroid therapy. Her social history includes she moved to the U.S. from Haiti 13 years ago. She lives with an adult son and is employed as a housekeeper.

So, as part of the workup, the physician did order airborne infection isolation, sputum for acid fast smears and cultures times three. And part of the workup for her chest x-ray was abnormal. So, during the course of the first smear collected, it was negative and the culture pending. And I got involved with this and spoke to a physician to order GeneXpert, and times two, and if it was negative, they weren't so sure it really was TB with her. So the first GeneXpert, the sputum was collected and the smear was positive, but the GeneXpert was MTB complex not detected. Currently culture is pending. The identification is pending.

The second sputum smear was positive, and the second GeneXpert revealed MTB complex not detected. Again, there is Mycobacterium growing, but it looks like it's maybe a rapid growth. So that physician did discontinue airborne infection isolation. And her length of stay, she was decreased.

So this is an example of step two of the algorithms, where we collected a second sputum specimen at least eight hours from the first specimen. The negative Xpert result MTB complex not detected, so specimen infectious TB is not likely. So the physician made a decision to discontinue airborne infection isolation based on her clinical symptoms. It was a clinical decision, along with the negative GeneXpert, to DC airborne infection isolation.

Case two is an inmate, and this inmate was in the medical housing unit of one of our jails. And he complained of a cough for two weeks. He denied other symptoms, but he did have an abnormal chest x-ray, and his history revealed that, upon arrest, in April 29, 2016, a TST was performed, which was positive. But later it was found in history that he did have a positive TST eight years ago, and he was treated with INH and vitamin B6 while in prison. And so the physician ordered airborne infection isolation to rule out TB. Two sputums were induced for acid fast, smear, culture, and GeneXpert.

The specimens were transported from the jail to Jackson Memorial Hospital Microbiology Lab onsite. So the specimens, there's a delay in transport. One day for the first specimen. The second specimen was transported on the second day, so actually two days instead of the eight hours, which we would do in the in-patient setting. So the first sputum was collected and the smear was negative, and MTB complex was not detected. The next day the second sputum collected was smear negative and MTB complex not detected, and that physician felt that it was not TB, and he discontinued airborne infection isolation.

And that is how we are implementing change, and it's still an ongoing change. And what I'm doing is I get calls, I recommend these changes, and some of the team members who are part of the Infection Control Committee, along with infectious disease attending are informing the staff and educating the staff on this change in practice. And we'll continue to educate our staff. And as soon as we have our IT go-live date, then we'll go out to the units and educate the staff on this change. And thank you.

Thank you, Regina. That was really helpful. And it was great to see how you were using the algorithm for those two patients. I really appreciate you sharing that with us.

Next up we have Dr. Julie Higashi. She is the former tuberculosis controller for the San Francisco Department of Public Health and the Santa Clara County Public Health Department and faculty for the Curry International TB Center. Dr. Higashi is the past president of the California TB Controller's Association and former board member of the National TB Controller's Association. She is currently an area medical director for the Community Health Services Division of the L.A. County Department of Public Health.

Julie, great to have you on the webinar. We miss you up here in San Francisco. It's all yours.

It's an honor to be here and a real pleasure to be able to revisit what was implemented in San Francisco. And just as a disclosure speaking as the former controller, these are my own personal opinions, and there's a lot that has changed since I left. There's a new hospital. So, again, this will not necessarily apply to what the program does in the future. So I am going to advance the slides.

One thing I wanted to point out is that the San Francisco TB program has been using NAATs and GeneXpert for a number of years, and the Healthy People 2020 NTIP target for NAAT use is to really have a goal of TB diagnosis by NAAT within 48 hours. In 75% of specimens that's a goal for 2020. And even in San Francisco we did not have -- what I'm talking about today is really the real-time implementation of NAAT in the county hospital. But before then, we had been using NAAT for several years in the actual TB clinic and transporting specimens from the hospital. And even without the real-time implementation we were meeting this target. And so I think implementation and embracing NAAT, even if you can't do it in real time, can definitely yield diagnoses in a quick turnaround, meaning days rather than weeks.

I'm just putting this slide in to remind myself that there is a handout, which was really what was disseminated on our web and posted around the hospital in different areas of the hospital, in the emergency room to really assess staff in understanding what we were doing with implementation of this real-time GeneXpert in the hospital, and included the parameters of who we were wanting to test, how we were doing, how to collect sputum. And I just point out that that was a very useful document.

So this was definitely partnership between the hospital staff and the UCSF physicians, and the Public Health Department in San Francisco. And we're very lucky to have the TB clinic co-located on the San Francisco general campus. So it made it easy for us to coordinate and work together.

And, really, on the hospital side, I think when I went and embarked on this project, I had no idea, really, the extent to which many of the processes would have to be changed. And I think Regina did a really nice job of laying out all that work that has to be done, and certainly, from the local program perspective, expanding to a hospital really, really does require that complete buy-in from the hospital from multiple areas. Those included, in San Francisco, a combination of pulmonary and emergency medicine teams, and there was always a lead physician.

We had some challenges, which was the ED really did not have a great way of collecting the sputum safely. They did have some airborne isolation rooms, but there were concerns about the level of the air flow in those rooms, and so we needed to implement sputum induction tents that were disposable, and also trained staff. And that was one of the solutions early on, that the pulmonology and emergency medicine teams just sort of did the troubleshooting and the implementation.

The hospital laboratory needed to be able to staff and train their staff to process these NAAT specimens in real time, and we had to set some parameters about what that turnaround time was going to be during business hours and after hours, so there had to be some reasonable expectations. And then actually to implement, there needed to be creation of order set in the electronic health record, which was taken on by the pulmonologist.

There was the indication of the health staff and the other staff in the hospital we have. It's a teaching hospital, and so it there's a lot of rotation. We have residents coming in for one month, two months, three months, rotating in fellows, new faculty, and so it's a constant refresher, this is the process in the hospital.

For this project there was a 24/7 pager that was staffed by the pulmonologist. There's also a 24/7 hotline for the TB Control Program for questions, and so just for the division of labor between those just having somebody, a physician, kind of on call as we went into this project as we went into this project was really important, and then I talked about the educational fire. And then the Pulmonology Group really was the group that spearheaded just the funding and the evaluation of this pilot and committed to the data collection, analysis. They were also able to secure funding for reagents to do the NAATs.

So what did we do on our program side? And our job was really to set the policy for the clearance from the hospital to the community. So I really was hands off about what the policy for removing patients from isolation in the hospital was. I left that to the physicians in the hospital. But I needed those -- those criteria were a little bit different than those that we use to discharge patients to sensitive locations like skilled nursing facilities, corrections, dialysis, long-term care, psychiatric settings, and those involving our homeless population.

And then we also committed that anybody discharged from the Emergency Department we would accept a referral. We have a walk-in referral clinic, the TB clinic, and we wanted to know about all the people who had been tested through this mechanism just so that we'd have another way to review and find out who had been tested, to understand whether or not we thought that they had gotten an adequate number of specimens before being discharged. So this provided a safety net for tracking patients, and we also have field staff that we could send out to facilitate evaluation in some of these patients.

We also had, on our side, the Public Health Laboratory who was now years into running the Xpert tests, and they had the capacity and reagents to run confirmatory testing on specimens from the hospital. We have a very long established relationship with the hospital. So with all these things, we felt really comfortable going forward and created this algorithm for, really, what was use of the test. And it's much more complicated than the actual consensus statement and something that I couldn't really carry around in my head, because it was involved.

But essentially for low clinical suspicion patients, an average of two specimens, which included two Xperts, and two cultures associated with these were adequate for considering discontinuation of isolation for low clinical risk or low clinical suspicion. For higher clinical suspicion we wanted three. The combination of three tests, either three sputums and cultures or an Xpert, but that would be three total specimens to get that information from.

I just want to point out -- I'm going to get my arrow up here -- that this did not include information about initiating treatment, and the buzz word for well you should maybe think about initiating impure treatment is call TB control to discharge. And that was where we just thought putting treatment, impure treatment into the algorithm made it too complicated, and then the other reason for the complexity had to do with our local situation, which involved a very robust homeless shelter screening program, and because of that, for homeless folks that were lower clinical suspicion, we did not require as many specimens, so they were on the lower end if we had low clinical suspicion, we had ways to track our homeless population.

And so this was part of being able to say to the city, you've invested a lot in our homeless shelter screening, so we can actually be able to get these folks through the community with fewer specimens, and they are considered lower risk. So this is a very special situation. And, again, these algorithms have to be locally driven.

So what happened? We implemented this pilot real-time Xpert, and it was immediately very, very popular. People wanted it and were using it. And in the end, what happened was that this pilot immediately was transitioning to the point where we were considering how we do this implementation going forward sustainably. And so we're able to secure resources to continue the NAAT after the pilot, with plans to try to implement it into the actual hospital operational structure and budget.

There was incredible demand. The pilot was supposed to be started in the Emergency Department, and within one day of implementing, it had been expanded. It got expanded to the hospital floor. We were able to make some early diagnoses of active TB in the Emergency Department and that helped patients get into the airborne isolation on medications much more quickly. And so within the first two months, we had at least two early diagnosis in the ED, which were really, really gratifying to everybody who was participating in the project.

A number of corrections patients, we were able to evaluate in the ED alone and avoid admission to the hospital, and this was because they were super low clinical suspicion. An example that comes to mind is a patient with HIV who was being evaluated for headache and got a lumbar puncture for meningitis, had a

normal chest x-ray, and we just recommended doing an Xpert because we weren't sure whether this could be TB. And so she was able to be evaluated with the two specimens and sent back to corrections.

We didn't have any major misses during the pilot. What Xpert did not detect, our clinical suspicion was so high the patients went on empirical treatment, got additional specimens, and we were able to make the right call from an infection control standpoint.

So what are some of our lessons learned? The algorithm, as it is laid out, is complicated, and so I personally, being one of the people who developed it, could never really answer a question without looking at it. And so, you know, going forward, it would be great to be able to simplify it in some way.

I forgot to include dialysis on the algorithm as a special circumstance, and so early on we had a couple folks that were considered lower risk that ended up getting only two specimens, and we would have wanted three. So that's just another reminder that dialysis settings are another special circumstances.

The initial group of tests of sputum, we actually had a very high rate of no-test because of poor specimen quality, and this was because the Emergency Department was not experienced with collecting specimens. They weren't used to doing this routinely, and so, I mean, if you're going to be doing more specimens or collecting more specimens and training staff to do it, you need to expect that there's going to be a learning curve to understanding what a good specimen is. We also noted early on that direct specimens, which don't have a smear and culture associated to them, were less sensitive. And so therefore, in general, they don't carry as much weight.

Testing in the Emergency Department dramatically reduced after our attending who is our champion moved on from San Francisco General. So it is important that there is some point person in each of the areas that you're trying to target for implementation so that you can continue to have a champion there on the ground.

So I'm going to go into some cases, and I think what's really nice is that all these cases, when you look at the new consensus statement, the consensus statement really addresses all these scenarios.

So case one is a 30-year-old bartender who was assaulted and found down on the way home from work. This is a guy who just goes and tends bar, and these are not specified locations. He was brought into the Emergency Department and had everything taken. So he was in a very bad mood. He wanted to leave AMA.

This is his chest x-ray, and I'm using this as an example of a very classic active TB suspect or we suspect this patient has TB. There is infiltrates. There is cavitation. And so this is a case that meets high clinical suspicion. He was asymptomatic with a chest x-ray like that. U.S. born. But he had very high risk for exposure TB because he had spent eight years living in Korea recently.

And so our program sent over one of our disease control investigators to talk to the patient and set up follow up, because we knew from just looking at the chest x-ray, we were going to initiate anti-TB treatment. He was our first patient, and we decided, hey, let's use this point-of-care test for MTB. Here's another example. You can see the cavities on this cut. And, again, more evidence of the cavities and infiltrates.

So of course this is what happens. The GeneXpert, the direct specimen is negative. Well the patient had already been told he would be treated regardless of the test result, because we just knew that we needed to be very clear that we were going do be collecting multiple specimens and that we were going to be doing treatment. He went home and he returned to clinic the next day.

One of the specimens collected in the ED came back smear positive. We were able to do Xpert on that concentrate, which confirmed MTB. And, of course, you know, this being our first patient, I get a call from infection control, "Are you sure you want to keep doing this?" And I had to say, "I know. I know this is not a good way to start, but we should keep going." And so that's an example of the limitation of specimen

quality and the need to get multiple specimens. And so with Xpert consensus statement, you know, you need to get multiple sputums.

Case two is an example of airline travel clearance, and this was a 21 foreign-born Asian. He was a college student going to college out of state, and he was interning at a tech company downtown San Francisco. He had homothesis in which urgent care, they did a chest x-ray and he had a cavitation, and that initiated collection of sputum, got referred to our clinic and was worked up as an outpatient. We were able to get specimens. They were all smear positives. And generally our practice in the clinic had been to get at least one Xpert on anybody who came in with clinical suspicion for TB, and he was initiated on anti-TB treatment.

Well, he was with us for a period of just, I think, a few weeks. And it was near the end of summer, so he lets us know, "You know, my internship is almost over. My housing is going to be done in about a week, I have to fly back. Fly back to my college. So we need to clear him -- needed to clear him for travel. We didn't believe this was tuberculosis because of the first negative NAAT, and so we decided, okay, let's collect two more specimens and do Xpert testing or make sure we get two more Xperts and show that he's negative. Normally we might not have to do that, but in this case because we were going to be releasing him to another jurisdiction, we wanted to have as much information as possible.

We called the local TB program where the college was to coordinate the transfer, and they agreed this is not TB. We continued the treatment plus Azithromycin. And we were really lucky in that the local TB program consultant also happens to be the college student health physician, and so was very comfortable with the student going back to campus housing. And he had clinically approved on treatments, and that was one of the reasons why we did it, stopped treatment, and his culture ended up growing M. Kansasii. So this is a nice example of a smear positive specimen with a negative Xpert which was MTM.

Case three is a 58-year-old Asian man. He had been one of the San Francisco TB clinic patients, had completed treatment for MTB five years prior to presenting with cough and fever for a few weeks, and he was found to have a new cavitation on his chest x-ray. AFB smears and cultures were collected, they were negative times three, but one of his Xperts was positive for MTB. We initiated him on anti-TB treatment plus Moxifloxacin because we weren't sure whether this was relapsed TB versus something else.

So we continued anti-TB treatment with Moxifloxacin. And thinking maybe this could be lung abscess, we reimaged him within about three weeks, after initiation of treatment, and he did show improvement. His cultures, we continued treatment with anti-TB treatment just because we were just not comfortable yet that we could call this a lung abscess. The cultures ended up being negative times three. He ended up being able to show resolution of the cavity, and we had an evaluation of his teeth with dental, and they confirmed he needed almost a total tooth extraction, and so with that, we gave him a diagnosis of anaerobic lung abscess and stopped anti-TB treatment after two months. And we attributed the MTB from the Xpert as bacteria that were still lying around from the previous treatment, and then continued to follow him like at 6 months and 12 months, after we had finished, just to make sure that we on the right track.

So where do we go from here? And I think that the consensus statement that has come out has really given us the tool to say, you know, you need a certain number of specimens to make an assessment of whether or not airborne isolation can be discontinued. And it's in a form that is user friendly and easily applied, unlike that other more complicated algorithm, which really fits the hospital's needs right now.

And so the clinician, you still have to make decisions, because the consensus statement doesn't really address this to initiate empiric treatment when, despite negative Xpert results, the clinical suspicion for TB is high enough. And if you're able to partner these two things, then you're going to end up with making good decisions.

I really think it's very, very important, and it's kind of difficult sometimes, but to continually evaluate the test performance. In order to feedback to the users, and also to improve, you know, good use of the test, and so in San Francisco now there's a new hospital. And so sputum induction and getting sputum

collection in the Emergency Department is easier now than it as been before. So now is a good time to go back to the ED to say, "What's going on? Are you guys actually doing this real-time testing," and have that person, that liaison to kind of keep thinking TB in the Emergency Department.

So I wanted to acknowledge these are really the key players that put together the initial pilot, and helped keep it going. And some of them are carrying it forward today. But it is a very much a group effort, and just thanks so much.

Thanks Julie. Those cases were very helpful. I think they really illustrate some of the murkiness of how to put this all together.

Next we're going to have Dr. John Bernarndo. He's going to give us a bit of a summary and wrap up an overview of how NTCA came about to put out this consensus statement. He's a Professor of Medicine and Biochemistry at Boston University School of Medicine and he's the TB Medical officer for the Massachusetts Department of Public Health. He was the NTCA co-chair for this Consensus Statement Workgroup. And he may not remember, but he was one of my attendings when I was a resident Boston Medical Center, so great to have you on the webinar, John.

Well thank you, Neha, and I remember well, and I am pleased to see you where you are and what you're doing. Well, thank you for having me back. We spoke last week about the algorithms, and I just want to summarize here. The previous speakers did a great job of going through clinical applications and how this might fit into the rhythm of what programs do every day.

Stepping back, as Neha pointed out before, this test was approved for this indication in February of 2015. The FDA labeling change, however, was sufficiently vague; that we were concerned that there may be some problems interpreting this. So this led to the publication of this consensus statement, because basically the laboratory folks are doing the tests and those of us in tuberculosis control felt that clinicians needed more information about how to use this technology appropriately.

And, in addition, this gave us an opportunity to improve the process. Since we have new technology we can put it out there and get it right this time. So to maximize the yield of this technology, we decided to put this statement together to offer detailed guidance in how to develop the assessment so that it maximizes the performance of the technology.

The statement is not a diagnostic algorithm, although it uses a diagnostic test, and that's what appears to be the center of a lot of confusion here. As pointed out by Regina and Julie, these tests are good diagnostic tests, but what we're looking for here is a negative answer. You're looking for a negative test to help make a decision to remove somebody from airborne isolation.

A positive test gives us the answer, and you can stop. So what we're really looking for is the negative test to take the place, in essence, of the negative smears on our long-time three negative smear crutch that we use to make a decision to get people out of isolation. We now have a more sensitive and specific test to be able to help us make these decisions, so we need to make the best use of this.

At the same time, we need to establish a diagnosis, because we're doing these tests on people who are real TB suspects. So sputum smears and cultures are still necessary for identification of the organism, drugs, susceptibility testing, and for genotyping. What hasn't been said is that nucleic acid amplification testing, in general, should not be used to monitor response to treatment or to release a newly confirmed TB patient from airborne isolation.

The use of the NAA in this context was pointed out by Julie in her last case, with the patient with positive NAAT who was really being treated for a lung abscess. What you're measuring here is nucleic acid, you're not measuring viable organisms. And so you have to remember that this test should be used for this purpose in this context when you're trying to make a decision to remove somebody out of airborne isolation.

And, furthermore, this is not an endorsement of Xpert or any specific product, the statement reflects the new FDA approval of nucleic acid amplification and technology that applies only to the Xpert MTB/RIF system and to this specific indication. As other applications develop, we're going to have to adapt this recommendation. But for the moment the Xpert is the only platform for which this technology is approved in this indication.

And as pointed out by the other speakers, this is not a rationale for delaying the start of empiric treatment when TB is suspected. A negative Xpert does not fuel a decision to, well let's back off. It's negative. We're not going to treat him. If the patient is clinically suspected of TB we need to start treatment.

What this is, is it's a series of recommendations on how to interpret GeneXpert results in this context. It's a document that stresses the difference between diagnosis and infectiousness of TB. It provides what we think are easily followed instructions and protocols for sputum induction, and for the operational implementation of this technology. It contains a flowchart that you can customize to adapt to your own policies and use onsite at your institutions.

And we also have to remind people that this is an important technology, but it needs to be applied in the context of the public health regulations, your local and/or state where regulations may have to be accommodated by your interpretation of these results.

Any new clinical algorithm must be adapted to the rhythm of patient care in order to be most effective, in order to optimize the performance of the technology, and to optimize patient care. As both of the other speakers pointed out, communication and coordination between patient services is essential. These include dietary. Yeah, you don't want somebody to miss breakfast because their NPO for a sputum induction. Nursing and respiratory therapy, physicians, nurses, laboratory, IT reporting platforms, infection control, these were all pointed out in the clinical examples that were given by the previous speakers. And then, again, recognition that this process is independent of the diagnostic protocol. Smears, cultures still must be obtained and followed up on.

But in the end, this is just the beginning. We need to collect data and analyze it to determine and evaluate the effectiveness of your institutional methods to determine this chart from airborne isolation. And periodic analysis of the performance of your protocol is essential and should be used to improve and or modify policies and procedures as needed.

And, in the end, we can help. As with any paradigm shift, early implementation of your experiences are important to document. So we're encouraging people to send questions, comments, success, challenges to the NTCA -- and I have the website shown here on the slide -- so that we can use the information you give us to help us adapt the statement as necessary. And we're going to put up a frequently asked question site so people can exchange information on this indication and the application of the Xpert.

And lastly, I just need to acknowledge my working group and others who were involved with the development of the statement. Thank you very much.

Thank you, John. That concludes the formal presentations for this webinar. What we're going to go into now is a question-and-answer period with our panelists. So in addition to our presenters, who you've heard them today, myself, Dr. Regina McDade, Dr. Julie Higashi, and Dr. John Bernarndo, we also have two of our presenters from last week joining us again today. Dr. David Ashkin, he's a medical director and co-principal investigator for the Southeastern National Tuberculosis Center. He trained at St. Luke's Roosevelt Hospital in New York during the outbreak of MDR TB and did his pulmonary fellowship at the University of Miami during their TB outbreak. Whether that's a coincidence or not, I will let you all decide. Dr. Ashkin also serves on Florida and national advisory panels for the elimination of TB and was recently instrumental of restructuring the Florida TB program to better address TB in the state.

We also Dr. David Warshauer joining us. He is a chief bacteriologist and deputy director of the Communicable Disease Division of the Wisconsin State Laboratory of Hygiene. He currently serves on APHL's infection Disease Committee and is chair of the APHL Subcommittee. He's worked on several

national workgroups that develop CDC guidelines for the use of nucleic acid amplification tests for the detection of MTB infection, and for the use of interferon gamma release assays. He was also one of the co-chairs for the NTCA consensus statement.

So welcome to David Ashkin and David Warshauer, and back to having all the rest of our panel here with us as well.

We've had a lot of questions that have been coming in, and so I'm going to try to start by just triaging some of the general questions we've been having regarding this consensus statement. And certainly as more come in, I will try to address as many questions as possible. I would say there have been some questions about specific individual patient situations. I would suggest for those situations, if you could e-mail any one of the panelists or your RTMCC consultant, that would probably be best so that we don't have any personal information shared over our large webinar.

So I think one of the questions that I've heard frequently and that comes up quite a bit is this question about this is a consensus statement but this is not really CDC changing guidelines or states officially endorsing a new statement? Are they changing their guidelines? So I was wondering, Julie, Regina, if either of you can speak to the fact that this is not necessarily a new CDC recommendation. It's a consensus statement. How does that affect what your program did? Did it limit what you could do? If you could talk a little bit about that, that would be helpful.

So I'll talk about -- because the consensus statement actually is coming out after we've did the implementation, I think what it does is provide some structure in order to actually streamline what the specimens are that we would -- the basic number of specimens you need to make an evaluation of removing a patient from airborne isolation. So I think it was nice. It's kind of like an affirmation by, you know, subject matter experts across the country to say in should be -- these are the types of specimens you need to make a good evaluation. And I think that's very helpful.

Did either of you feel that you needed to have the state that you are based in endorse this or get some sort of approval before you could implement this algorithm or your version of an algorithm?

I think what happened, really, my opinion, was when the FDA notification came out, that was sort of the open the gates for moving toward Xpert without sort of contextual understanding by the community hospitals about how you use the test. And so, you know, in San Francisco we actually -- the pilot and this Xpert and the FDA sort of labeling came out kind of simultaneously. So we were in a situation in San Francisco where we at least had something ready to go. So we were moving the direction anyway to real-time testing, and the actual driver was that the hospital itself was constantly on divert. We're trying to think of ways to reduce the number of beds, and that's all patient movement, which is isolation, you know, release from isolation, and so this one was one of the ways that the hospital is trying to improve their patient flow. So with an independent process, and all I can say is that there was pressure even without the validation that this test -- how can we -- what are ways that we can do to improve our understanding of how infectious somebody is and whether or not we can remove them from isolation.

Yeah this is Dave Ashkin. Just to comment from a TB program, state TB program perspective, you know, one of the things that, you know, we were being asked for at the state level was some guidance from the hospitals so that they could implement it. Because most policies and procedures that are utilized usually refer to another quote, unquote, guideline of consensus statement. So, you know, we felt this was very, very important, and it really helped us as a state to kind of craft our guidelines so this way we could pass it down. So at least from our perspective, I think these guidelines, or at least these consensus statements, from our perspective, seeing in Florida hospital staff utilized them so that they can draft their own policies and procedures.

Thanks. Thank you, David. This's really helpful.

And this is John. I don't know if you can hear me. But one of the concerns we had was that since these tests are very dependent on the quality of the sample that's provided, we wanted to make sure that it was

the best sample being used for the testing. So we wanted to make sure that sputum collection was done in the standard way and in a way that might maximize the yield and the performance of the tests. So that was another factor that helped drive our decision to go on with this.

Yeah. I think it provides necessary context and validation from a group of experts that are experienced with this type of a decision-making. And also I think that statements regarding, this is a separate algorithm that doesn't include the decision to empirically initiate treatment is important also.

Well, that's right.

Yeah, I think those are great points that actually bring up some of the other question that have been coming up. And going back to what you were saying, John, there has been a lot of questions about laboratory questions. And Dave Warshauer you're on the line, I would like to pose some of these to you. There are a few questions, one on time between specimens, what if it's not fully eight hours apart, does that make a difference? Induced versus spontaneous sputums and (inaudible) versus concentrated specimens. So I was wondering if you could talk a little bit -- I know you went through some of this last week, but if you could touch a little bit on some of those questions. They've come up a few times.

Hi. This is Dave Warshauer. As far as the use of the raw estimates versus using a concentrating sediment, really, it's not an early significant difference in the sensitivity or specificity of the testing in that regard.

And what about with the eight hours apart? What if it's not fully eight hours apart between specimens?

The data is very soft, whether the eight hours apart; that is a recommendation as of now. But I think some experts will say that, really, that is not critical, critical timing, and that perhaps getting specimens closer together will provide similar results. So I think that's something that needs to be looked into more to determine if that, really, eight-hour criteria is important.

Yeah, that's helpful. I don't think I'm as familiar with the actual eight-hour number and where that came from. So it probably does deserve a second look.

Yeah, this is John. I agree.

Sorry, go ahead, John.

No, I agree. The data are very soft on that. And I just want to emphasize, though, that one of the specimens should be, if you can get it, a first-morning specimen, since that tends to be the best yield. And I know in the consensus statement itself, there is a whole section of laboratory specimen and quality of the specimen. So there are more details on the consensus statement for those of you who have more detailed questions.

Julie, one of the things you brought up, which has come up a lot and has come up on the Q&A section a lot, is this kind of gray area between using this algorithm for discontinuing airborne isolation and whether you can use it in other environments. Can we use it in outpatient settings? Can it be used to determine whether somebody we think is a TB suspect can go home? I think all of you can probably comment on what you think about using this algorithm in different ways. It's a bit of a gray area, but it comes up frequently.

So I think that it is -- so you're saying that -- I mean the consensus statement algorithm can be applied to the hospital setting, as well as ambulatory settings where you may be saying to the patient, "Don't go to work until we're done with this evaluation, until we collect your two or three specimens."

Exactly. Can we use it in that sort of setting as well? Or do you think it -- is it only for in-patient airborne isolation? You know, again, I think what we meant it for as really an FDA interpretation. But I wanted to

read that to the programs to share your experience of how you've maybe used Xperts for other types of isolation questions.

So I think that, generally, it can be -- it is applicable, but there are just some slight differences, I think. Basically it would be you have the patient in the community already and it's whether or not they're allowed -- do they have to restrict their activity. And I think if you look at it that way, yes, there are similarities, but I don't want to just go ahead and say, it's exactly -- you know, you can just take this one situation and apply it to the other. I think you have to think it through a little bit. But, yes, the same general principles apply, I think.

Yeah, this is John. Yeah, this is John. The statement was drafted in response to the specific FDA labeling, which refers to the use of the test to make decisions to take people out of airborne isolation in health-care facilities. So how people adapt that is what they're going to be doing. So I think you're free to do that. But recognize that the FDA labeling is such as it is. I agree the test is better than the smear, so if it's done properly, and it's almost idiot proof. So if one must substitute Xpert for smear in making decisions whether to send people out of an Emergency Department, for example, it's really up to them in context of the public health regulations. And remember, we take care of most of our TB patients today as outpatients anyway.

Dave Ashkin or Regina, any other comments?

I think John really did, you know, a good job. I think, you know, the big issue is to realize that this is just a tool. It's a tool to try to help us assess infectiousness. So it's like John said, I think you really have to put it into context of the patient situation. So, yes, we are using it in Florida to make such decisions. But it's also in context of where the patient's going to go.

I mean, I think you'd agree that when you look at the hospital situation, or let's say the correctional facilities, the thing that makes this very, very interesting and the risks are so great is that the patient's going to be released into a potentially very, very, you know, susceptible population. So that's where like in the hospital you're really looking at a diagnostic tool that has to be very good as far as predicting infections, not diagnosis.

And I think the same thing goes in the community. It really depends not only on the patient, but, you know, what kind of situation the patient's going to go into. And, again, the bottom line is, is that the consensus statement was really meant in the context of hospitals because that's what the FDA was really talking about. But at the same time, I think like everything else, it's a test and it needs to be interpreted in the context to the patient. There's always a clinical input that needs to be done.

Yeah. Thank you, all of you for that input. And I would agree with you. I think you're right. The consensus statement and the FDA label was really meant to help determine airborne isolation. However, we used NAATs and GeneXperts to help us with diagnostics all the time, and I think there is definitely a rule for using these diagnostic tools and determining other questions, such as whether you have a TB case? Do you want to start them on treat? Do you want to send them home? Where are you going to send them to? But this particular consensus statement, I think as you all have pointed out, was really meant to help with airborne isolation, and its continuation. But certainly -- and I think that's where we allow a little bit of room for programs to also figure out how to use it in their local setting and whether it applies to their TB program in an outpatient setting or not.

One of the other things I think that has come up or I've gotten questions for is the question of one versus two specimen. And I know we talk a lot about this when we put the consensus statement together. And, John or Dave, do either of you want to talk a little bit more of how we decided on two specimens versus one? The FDA label says one or two. I want to know if either of you can speak to that.

Yeah. This is John. We were nervous. The decision the FDA made was based, at the time, on an, as yet, unpublished study. This study shows it's been published, and it showed excellent results. But the sputums were collected under study conditions. There were some 638 U.S. patients in the study. There were other

studies using the Xperts, and other platforms that supported the use of the test for the syndication. But we were concerned that programs would take this recommendation, as insufficiently detailed as it was in the labeling change, and apply it very loosely. So we wanted to make sure that we had good specimens, and then analyze data as it comes in and see how we can adapt this further. So we wanted to make sure that we got the best results, and were a little nervous about going with one sputum sample.

Yeah, I think with the vagaries of sputum collection, you know, it's unwise to just hang your hat on one specimen. And, you know, as far as -- I just also wanted to make a point about the direct specimens. Because you have only the NAAT results and you don't have any other sort of information like the smear results or the culture results of that one specimen, it just has less information attached to it. When you have a specimen that has a sputum smear and culture and a NAAT, you at least know if it's smear positive. Well this might be a better specimen that I'm going to get -- that the NAAT is going to tell me, we're going to get more information from the context of both the smear and the NAAT. So I just think because sputum collection is not necessarily going to be consistent, even within the same patient it's wise to get -- I think it was great that you went with two.

This is Dave. I also agree with you 100%. But I think it's also important about that it's very local, because, you know, the whole TB issue is not the same throughout the United States. There's areas of this country that really have not seen TB in a long time. So to make those areas say, hey, we're going to do two all the time, then, you know, I think that's not correct. I think it really also depends on the prevalence in not only the area that you practice but also the patient, you know.

So I think something that's really important that we touched upon but needs to be constantly touched upon is pre-test probability. You know, base theorem is that the accuracy of the test is definitely dependent on the prevalence of the disease in either the area you practice or in the patient. So I think, you know, the consensus statement was meant to kind of give a little lee way to the clinician. But the bottom line is I think it is going to vary, at least in my opinion, from area to area, as well as patient to patient, just like you said.

Yeah. No, sometimes it's hard to, like what if you get a patient of high clinical suspicion and a low prevalent area, it's just, you know, the two colliding.

To a degree you're favoring, just like you said, you're favoring more, you know what I'm saying. You're definitely going to favor more specimens. And, again, it's a clinical call.

Right.

And I don't think was meant to be a one-size-fits all sort of guideline the consensus. It's really meant to outline what would be the things, what would be the things you should be thinking about when making that decision. You're a hundred percent right.

This is all a good discussion.

I think it's important. I think each institution has to determine if one specimen works for them. For example, if you have a facility where you're having induced sputum or you're having very good instruction and giving good instructions to the patients and observing that patient provide an excellent specimen, that you may be able to reduce from two specimens to one specimen if you look at your data over time. In some other facilities they may need two to get to increase that percentage of positive NAATs that they will not get with just one specimen. And keep in mind, it's a really difficult for the laboratory to determine the quality of the specimen. Many patients with TB don't have purulent sputums so we can't reject specimens based on the lack of white cells. So it's important that the person collecting the specimen observes that, yes, this was a good specimen, good sputum specimen. And then you may only have to use one specimen.

Practically speaking, I have to say that's really hard to achieve in the general hospital setting, but I think that your point about reevaluating the quality over time to determine whether you need one or two is really important.

And, Dave, just because you're on line, there was a question about the quality of using stored specimens and whether that has an effect on the results and the quality.

You know with the NAAT testing, if the specimen is refrigerated, it can be used for several days from the time of collection, which is obviously not a good thing to be delaying the testing, because you're defeating the purpose of the rapid result from the NAAT. But if you look in the package insert of the Xpert, specimens that are refrigerated can be held for I think up to, oh, a sediment can be held for seven days, and a raw sputum for several days. I'd have to look up exactly what that time is. But they can be stored.

And what about specimens from broncs?

Go ahead, John.

No, go ahead, Dave. Go ahead.

The test is FDA approved for sputum expectorated and educed sputum. It is not FDA approved for broncs.

Right.

So you cannot apply.

I will point out that it is also not approved for individuals older than -- 18 and older, so adults.

Correct. All the data submitted was from a population with 18-year-old or older, is that's what the test is approved for.

John, were you going to say something?

No. Dave said it all.

There were a few specific -- we have about ten more minutes, and there were a few specific questions, Regina, for you, and I'm going to open the lines to have people ask a few more questions. Two questions for you, Regina. One was were physicians included in your employee fit testing, and then what is your baseline, IGRA TST in your staff?

I'm sorry, what was the first question?

Are physicians included in your employee fit testing?

Yes, physicians are included in our health office fit testing. And for the second question, for our system, we're still using the tuberculin skin test, since we have such a large amount of employees right now. We haven't -- we're not using IGRA yet. What is your baseline TST IGRA positivity? Or I guess TST, because you're not using IGRA.

Okay. I don't have that data right in front of me, the most recent data. I'll have to answer that question later.

Okay. Great. Thank you. And for everybody else on the line, if there are questions that we didn't get to or were unable to able to answer for you satisfaction, please just send us an e-mail, either to Kelly at the Curry Center or NTCA e-mail, and we will make sure that the panelists and the speakers all are able to respond to your questions.

Yeah, this is Dave. While waiting for a question, I mean I think one of the interesting parts and was brought up in the case before, was, you know, the one thing about in patients with previous TB. And, you know, we always talk about we'll look at the negatives. But, you know, in our experience in using it the positive side of GeneXperts in previous TB patients can definitely cause a little bit of an issue, you know. And, John or Julie, I'm just wondering how you deal with that. So you have a patient who has a positive, you know, had TB before, treated five or six years ago, and now the x-ray -- you don't have a previous x-ray and they come in with symptoms, and now you have a positive GeneXpert, and now they're on isolation. John or Julie, you want to comment on how you would handle that, or how you guys are handling it. We're seeing it quite a bit.

Well Julie's case --

Sure. In situations where I have been able to identify -- you know, this is actually dead bacteria -- is because we had knowledge of the patient's treatment prior. So it's a little bit of a, you know, retrospective scope in that we knew that the patient was treated, adequately treated and then had to look at the clinical scenario. So another case I encountered was one where not only was it Xpert positive, but the risk, it looked like it was risk resistant. And so it was not only the patient was treated before, but now he may have drug resistant TB. And then, you know, after the initial hoopla of trying to reinitiate treatment and think about multidrug resistance, you take a step back and you have to look at what the clinical information is and why the patient came to presentation, and in this other case it ended up being like a congestive heart failure exacerbation in the end with the assessment. So that was a situation where knowledge of prior treatment, knowledge that there might be dead bacteria and the clinical presentation just didn't match a reactivation TB situation, we were able to actually not initiate treatment and continue to just watch the patient and follow as an outpatient post treatment TB patient from two, three years prior.

So it really is the clinical scenario and sometimes you have to empirically start treatment and just see how things go, like that other patient I presented with the lung abscess, and it really just depends upon the whole clinical scenario.

Yeah, this John. The test measures nucleic acid. It doesn't measure viable organisms. And, in fact, the FDA approval only applies to people who are on treatment for fewer than three days or seven days. I think it's three days.

Three day, John.

Yeah, it's three days. So, you know, that may answer the question.

Yeah, I agree. I mean, I think, though, you know, again, as it pertains to airborne isolation, a lot of times where a lot of things I think everything Julie said is exactly correct, but a lot of times you are stuck with keeping them in isolation until you sort them all out.

Oh, yeah. Yeah. Yeah.

I really want to make the point that while I totally agree that the GeneXpert is more sensitive for detecting TB, there are going to be situations where you may have negative smears, but the PCR is a positive and you're kind of stuck in a situation. Again, I think you have to look at the whole clinical scenario, just like Julie stated. I agree with what John said.

We've had some great pickups Xperts for folks that are going to need to be discharged to skilled nursing facilities, and that was an early diagnosis. And we would have actual empirically treated them anyway. But it feels a heck of a lot better having that Xpert information, you know, initiating treatment for somebody who's going out to a skilled nursing facility for example.

Well this goes for --

And help you too. You can make the diagnoses that you wouldn't have made necessarily because a smear is negative.

Yeah, this is John. But this goes for other platforms as well. You know, nucleic amplification testing has been around for a while, and these tests are -- the MTD is still out there. And if I can bring something else up. One of the questions came up a couple of times, that hospitals may be sending samples to other laboratories, outside labs for Xpert testing for this indication that is getting people out of isolation. And if you do that, you may lose some of the time advantages that is, you know, unless you stick it in the taxi cab and run it over there that morning and have a time arrangement with that lab, you may lose some of the time advantages of doing this. So you have to work out a system with your laboratory.

So this is Neha. We're at 11:30, which is close to the end of our time here. I think there was still a few questions left. If we didn't get to your question, please e-mail it to us. I do want to thank all of our panelists and our speakers for joining us today, and I'm going to hand it back over to Kelly to end us out.

Okay. Wonderful. Thank you for everyone. This concludes today's webinar.