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Critical Congenital Heart Disease Webinar
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Presenters: Leilani Russell, MPH and Matthew Oster, MD, MPH

Please direct all comments/questions pertaining to this webinar to Thalia Wood at Thalia.wood@aphl.org or 240-485-2701.

Thalia Wood: Thank you again everyone for getting on the call on time. I think we'll go ahead and get started right away. Amy if you want to go ahead and get us rolling as to what we're doing today, we'll get started with the speakers.

Amy Gaviglio: Perfect, can you hear me?

Thalia Wood: Yes, thank you Amy.

Amy Gaviglio: Hello everyone and thank you so much for joining us on today's call. We are very excited to have our two speakers today, talking about their analysis of the recommended algorithms for pulse oximetry screenings, and analyses such as these are really vital to our effort of achieving optimal results from the screening program. I think this topic is quite timely within the world of CCHD screening, as states and programs continue towards their efforts of implementation and education around screening for CCHD. We, certainly in this group, have continued to discuss the importance of data collection to further asses components, like the effectiveness of the algorithm and the effectiveness of the screening program as a whole. I think this will be a really great talk today, I'm really excited.

With that, I will introduce both of our speakers. I'll introduce them both now and we'll be holding questions to the end of both presentations.

Our first speaker today will be Leilani Russell. She recently graduated from the Colorado School of Public Health, and is currently on the job hunt, so if anyone is interested. Leilani will be talking about their work on the screening protocol within Colorado.

Our second speaker today will be Dr. Matt Oster. He is the director of the Children's Cardiac Outcomes Research Program at Sibley Heart Center in

Atlanta. He will be talking about work on analysis of the recommended protocols.

With that, I will pass it over to Leilani.

Leilani Russell: Hi. This is Leilani, I hope that everyone can hear me.

Thalia Wood: We can. Thank you Leilani.

Leilani Russell: Thank you Thalia. Thank you Amy. Again, thank you very much for that introduction and NewSTEPs and APHL for having me present today. My name is Leilani Russell and I'm going to briefly be talking about possible modified newborn screening algorithm for critical congenital heart disease at moderate altitude. Why don't we begin?

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What we know - I feel that hopefully everyone on this call is very comfortable with what critical congenital heart disease is and the importance of screening for it in newborns, so I'm going to skip the normal introduction I might do. We'll just briefly talk about concerns that Colorado has. This is related to the fact that we are a state of moderate to high altitude. We know that as altitude increases, the partial pressure of oxygen is going to decrease, and this is going to result in lower oxygen saturation. The American Academy of Pediatrics' algorithm has been based on studies conducted at, or near, sea-level. This poses a lot of concerns with false positives, and some of these false positives might just be delays in transition from a fetal to a neonatal circulatory system.

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We see that - You look at sea-level based studies and we look at that false positive rate, we see that it is statistically lower than what we have found in previous studies conducted in Colorado. All of these studies use that recommended AAP algorithm.

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The question that the CCHD study group has had was, "Could we possibly make some modification to the algorithm that lower this false positive rate?", but we still want to make sure that we're catching all of those babies that we can with CCHD. We definitely to do not want to pass any babies that have CCHD, or that we should be catching with the algorithm. Even a modified algorithm.

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Briefly, this was a retrospective cross-sectional study conducted at the University of Colorado Hospital between the states, and only of babies in the

well-newborn nursery. What I have done is taken the recommended algorithm, the AAP, and I've compared it to three modified algorithms. The Tennessee, what I'm going to call the Cone, and a combination of the Tennessee plus Cone. I will discuss these in a little more detail in just a minute. We calculated the failure and the false positive rate for these and compared them.

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I'm going to apologize right now, I feel that Dr. [Dutcher 00:04:56] is going to do a fantastic job talking about the Tennessee algorithm. So I'm going to just briefly show this to you guys, and if you have any additional questions later on, I'd be more than happy to talk about it. Just that these modifications are at the beginning of the algorithm.

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Here we have what I'm going to call the Cone algorithm. What happens here, is that you have a baby who goes through the standard AAP algorithm. At the end, while they are waiting in echo, and they're going to continue to be screened and they're going to be screened every four hours. If they have a passing saturation level, passing the algorithm, then they don't necessarily need an echo and they exit that algorithm. What this has come about from is the fact that the various staff at University of Colorado Hospital have noticed that sometimes they have babies failing at eight o'clock at night, and they no longer have a technician to do a fetal echo, so they have to wait. Thinking, "While we're waiting, why don't we continue to see if their saturations start to improve?" Lo and behold, a few of them do, in fact, improve. This kind of makes us think that there is definitely a delay in transition in some babies, in Colorado, from that fetal to the neonatal circulatory system. They just maybe needed a little more time. Otherwise, they're very healthy babies and they don't need to go on for additional diagnostic testing.

Slide.

Then the thought is, could we somehow combine, hopefully the best of, the Tennessee modifications and the [Keller 00:06:32] modifications? Even improve things possibly more. Is this doable?

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Briefly, here are the demographics of our population. Again, I want to say that this is only well-newborn babies. We did not analyze any baby that was admitted to the NICU, so we're not going to have those babies that we're prenatally diagnosed with CCHD. We're not going to have very premature babies. We're not going to have those that were low birth-weight for estimated gestational age. Here are the demographics for our population.

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What did we find? What we found is that if you were to use the AAP protocol within this population, at the times we did the study, we see a false positive rate of 1.11%. Many people might think, "Oh, that's not that bad." I like to think of it in terms of Colorado has just started planning how we're going to implement CCHD across the state, and if you were to use this algorithm, and let's say Colorado has about 70 thousand births a year, that would be 700 babies that would have a false positive CCHD screen. This can create a lot of problems. It creates stress on the families. It creates stress on the facilities. It also creates stress for the public health department, both local and state. Logistic concerns, we have a lot of rural hospitals and rural populations. If they fail the screen, the question becomes do you automatically transfer them to one of two facilities that could can actually treat CCHD, when we don't know if they have it? Some of those rural hospitals also don't have the capability to do an echo. So, 700 babies going through this system a year, having to do that, when they might not need to is kind of concerning. That false positive, the 1.11%, is kind of a concern. We do see that this starts to improve as we go down the list. When we hit the bottom at the Tennessee plus Cone, it's 0.74%. That is about 500 babies that are going through the system. Which for me, is still kind of high. I would like to see some improvements upon that, if possible.

Slide.

What we see when we compare this to that sea-level, kind of historic rate, we see that the current study, they're all still statistically higher than that false positive rate that you see at sea-level, but we do see a trend downwards when we make some modifications to the algorithm. I also want to say, at this point, that we actually did not identify any baby that's CCHD using the screen. We do feel that the failure rate is a good approximation of the false positive rate. Also, going backwards, we worked with the birth defects registry within the time period at this hospital to identify any baby that we possibly missed. There were none, which is a positive thing.

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Another possibility of an area of improvement, perhaps, is the idea of incomplete screen. If you were to use the AAP protocol, we see a 1.72% incomplete screens. Luckily, we know these babies that have incomplete screen, so far have not presented to the birth defects registry to show that they have CCHD diagnosed later on, or that we somehow missed. So it is good to know that these babies, in this study, at this time, do not have CCHD. But again, if you go down the list, and you get to the Tennessee plus Cone, that proportion of incomplete screens now drops to 0.49%, which is a marked improvement.

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There are some limitations to this study, by all means. There is some incomplete date, incomplete screens. Again, we did not detect any babies with CCHD during this study. It would be good to know if, in real time, we could use any of these modified algorithms to detect a baby with CCHD. It also left us unable to determine the positive predictive value of any of these algorithms. There is a lot of concern, also, because this was done in one hospital setting, of obtaining the necessary information from the electronic medical record.

Slide.

What can we learn from this? While it still is much higher than what you see at sea-level, the Tennessee plus Cone algorithm has both the lowest false positive, and the lowest incomplete rates. We do believe that there is a delayed transition in some of these babies. That they are relatively healthy otherwise, and they just needed possibly a little more time to pass the algorithm.

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Moving forward, what we would recommend - Again, these babies that we studied were only in the well-newborn nursery, and we know that of the 33 babies that presented to the birth defects registry at this hospital, from this time period, all of them were admitted to the NICU, so they were not included in the analysis. It would be good to know could we use any of these in the NICU, or would that not make sense at all. So, evaluation of modified screening algorithms for the NICU. As the state starts moving forward with statewide implementation, there is going to be some concern about [inaudible 00:12:17] using electronic medical records for data collection and analysis by the state health department. It's a fantastic state health department, but it's going to create some problems. There might be some ways to ease this on the point-of-care side at the hospital location side. We'd also really like to see a multi-site, multi-altitude, studies of these modified screening algorithms. When we did this in Denver, Aurora specifically, it's about 50 to 80 or a mile high. Having those sites possibly further up in altitude would be good to see if this makes sense for a larger statewide implementation.

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Here, I would just like to thank the member of the CCHD study group, and everyone who has helped in the data collection, the families.

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Thank you so much for having me talk today.

Thalia Wood: Thanks Leilani, that was some really good information. We'll move right on into Dr. Oster's presentation. Hopefully we'll have a good discussion after. Dr. Oster?

Matt Oster: Yes. Thank you very much for having me--

Thalia Wood: Go ahead, thank you.

Matt Oster: Thanks. Can you hear me okay?

Thalia Wood: Yes, fine. Thank you Dr. Oster.

Matt Oster: Wonderful. I'm grateful. Thank you very much for allowing me to share some of this data. It's still preliminary, some of the things that we've found. We're presenting some of this at the American Heart Association next month in Orlando, as well. If anyone wants to talk more after this, I will be there if you want to come up and chat.

This project is newborn screening for Critical Congenital Heart Defects, optimizing the screening.

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Outline of what we're going to do. There's three commonly use algorithms in the United States. We just heard about the AAP, and the Tennessee, and a little bit about the New Jersey. I'll go into them in a little bit more detail, and then talk about how we compare the different algorithms. How we might want to go about choosing a preferred algorithm if we were to change something. Then what's a false positive? I want to have a little discussion about. You just heard a little bit about trying to decrease the false positive rate, and we'll talk about that in a second. And plans for the future, were do we stand in the area of data collection and how it can inform this project moving forward.

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Why do we have different algorithms? The algorithm that's primarily used in the United States is based on a study out of Sweden that showed that they used an algorithm to detect - They used pulse oximetry and followed with algorithm that they could decrease the rate of misdiagnoses from about 25% to 8%. They showed that it pretty much worked, but they didn't really compare it against other algorithms. They had some data, at the time, form where they had their cut points, but didn't compare it to others with regards to sensitivity, specificity, cost, ease of use, those sorts of things. We wanted to say, "Can we come up with something that might be better in those different domains?"

Next.

First, we looked at the three different algorithms that are currently used. The AAP algorithm, or some people call it the Kemper algorithm since it was first published in the paper where Al Kemper was the primary author. Most of you should be familiar with this one. This is intended for the well-baby nursery, at

about 24-hours of age or older, with the screen from the hand or the foot. With less than 90% from either being a positive screen or fail. If it's 95% or higher, and a 3% or less difference between the two, that's a pass or negative screen. Anything between gets a repeat screen in an hour, and a repeat screen in an hour. The purpose of these repeat screens, is to primarily decrease that false positive rate. This is very similar to what you just heard about with the re-evaluating, over time, to see whether kids who initially have low saturation can come around, and eventually have good saturation.

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New Jersey, when this was rolled out, they liked that proposal, but said a couple of things. One, it might be a little confusing, to say, "Well, either the hand or the foot has to be at least 95, and the difference." They also wanted to make sure they weren't missing any babies, so they said, "Are both the hand and the foot 95 to 100?" That was the first thing there. That's the big difference. Whereas the AAP says either the hand or the foot is 95 to 100, New Jersey algorithm says are both the hand and the foot 95 to 100. This should have the results we would expect of increase in sensitivity, since more babies would fail. Everyone that would fail AAP would still fail by New Jersey, plus some. We wanted to see what that would do with the false positive rate.

Next.

Tennessee came along, and Bill Walsh spear-headed the effort there, and said, "This 3% thing between the hand and the foot, there's very few instances where their foot should actually be higher than the hand." Certain cases of [transposition 00:17:36] in great arteries. There's certain cases of [inaudible 00:17:40] veins [inaudible 00:17:40] streaming. I won't get into the physiology of it all. It's actually very rare for the foot to be significantly higher than the hand. A 3% difference in true ductal-dependent lesions, it's typically that the hand is higher than the foot. They said, "Let's just start with the foot, and if the foot is 97 or higher, you can reasonably assume that the hand will also be 97 or higher." You'll meet those criteria of having 95% or higher on either one of those, and a 3% or less difference. They just start with the foot, and if it's 97 or higher you pass and don't do anything. If it's less than 90, that's an automatic fail, similar to the AAP algorithm. If it's somewhere between 97 and 96, they then basically screen the right hand and revert to the AAP algorithm from there. Just follow the AAP algorithm from there.

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What do we do to compare these?

Next.

We reached out to a number of different institutions and studies, starting about a year ago and going through into the fall. We got lots of data from some public health agencies and many hospitals, and also some previously published reports, both in the United States and in Europe. We wanted to get that data, from the pulse oximetry saturation and what the outcomes were, to compare sensitivity and specificity primarily with the algorithms, while also keeping in mind cost and burden, and ease of use and human error.

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We worked primarily in Atlanta, also at CDC. We had some other people at CDC, a few people at Georgia Tech. All working together to use data from these screening programs to compare the various algorithms through mathematical modeling with the goal of determining the optimum algorithm for screening in the United States.

Next Slide.

As I said, we solicited a number of different agencies and hospitals from around the country. We expanded to the published studies internationally. The requirement is that we needed to have the actual pulse oximetry values that we were going to run things through these algorithms. The ideal that we'd all share information about false negatives. We had about 75 thousand observations from seven different states in the United States, as well as from the United Kingdom. With 57 identified cases of Critical Congenital Heart Disease.

Next Slide.

What do we do to test these algorithms? First, we did the simple let's see what happens if the child were to go through each one of these algorithms. Once we have the actual pulse oximetry values of a child, we can apply any algorithm to that baby and see what the results would have been for that child. Then we added strict, kind of yes/no cut-off algorithms. What if we just said, "It had to be 95 or higher, period, and that's it. Either the hand or the leg,"? Then we played around for different thresholds for each of the algorithms. For instance, if we started with the Tennessee algorithm, and let's say we change the initial cut-off down to 96 from 97, and we were going to accept upper low saturation difference of 5, instead of just 3. Adjust to the lower automatic positive threshold to 85, and change the upper threshold to 95. What would that look like? We did that and we can just, with the mathematical model we can do that with a number of different algorithms, such that we had over 1800 different algorithms that we could do. Fortunately, we did not go through all of these algorithms. We set some criteria for the computer to spit out which algorithms work the best. We went in these basic criteria and said, "This is what our optimal algorithm would look like." First, we wanted it to have an area under the curve of at least .75. We wanted to go in with a low false positive rate, because that was a big concern. With about .003 or .3%. I know in Colorado they

were trying to aim for less than 1%. .3%, which is about one in every 333 childs failing. We wanted the sensitivity to be at least 50%. Anything less than that is really no better than a coin flip.

Next slide.

For the AAP algorithm, there were 560 different variations. I'm showing on the slide these four, which we deemed candidate algorithms for consideration. All the way on the right you'll see the standard AAP algorithm has an upper bound of 95, a lower bound of 90, and a difference of just 3. The sensitivity of that algorithm applied to the same 5000 babies we had was 54%, with a false positive rate, or one-minus specificity, of about .006 or .6%. The AAP is .77.

Next.

The one next to it is, we thought though, was the best of the remaining ones. Where, basically the big difference there is, if you change the difference from just 3%, would be 5%. You don't really lose much in your sensitivity there, go from 54% to 53%, but you do drop your false positive rate by quite a bit, to a third of its current standard, from .006 to .002.

Next slide.

What happened when we saw New Jersey? Again, all the way in the right, for reference, is what New Jersey standard is. With the upper bound of 95, lower bound of 90, and difference of 3. Their sensitivity is 58%. Again, this goes with what we said earlier. We thought that this one would have a higher sensitivity since they have that and requirement for the upper and lower extremities, instead either or. So, sensitivity is 58% instead of 54. But the false positive rate, or the one-minus specificity, was much higher. .009, or .9%.

Next slide.

If we modified that one, just a little bit, changed the upper bound to 94 and the lower bound to 95 and allowed a very big difference of 6, you could bring down that false positive rate without really affecting sensitivity a whole lot. Bring it down to 53% from 58%.

Next.

In Tennessee, we had a number of different variations, 750 of them. All in the right is the standard AAP algorithm, where the first screen zero we're calling it, 97 is a pass, less than 90 is a fail. The standard cutoff of 95, 90, and 3. That had a sensitivity of 53% and a false positive of .003.

Next.

The other best difference, we thought, it changed that if you were to drop the upper bound to 96 instead of 97, and yet allow a difference of 4, instead of 3, you could bring our false positive to .002 without changing your sensitivity a whole lot, but it did go down from 53% to 51%.

Next.

We're left with a few different algorithm, and trying to figure out how do we pick one? What is the best algorithm? This is not an easy question to answer, so after this I'd love to hear any thoughts you people have. Clearly in screening, and typical screening tests, and from a public health standpoint in your screening, you want to have as high a sensitivity as possible. You'd love to have a high sensitivity, but none of the algorithms really had great sensitivity in practice.

Specificity, yes we'd love to have high specificity, or a low false positive rate, to those reasons explained earlier in the prior presentation. Trying to alleviate the burden to hospitals, to families, and the like.

Cost, we want something that doesn't cost as much to do. Both from the actual testing standpoint, plus the [ampliary 00:26:08] testing that comes with seeing your results.

Ease-of-use. We did not get into misinterpretations to your algorithm, but we certainly see that in a couple of publications, of people not necessarily following these algorithms appropriately. Simple is clearly better, if that is an option.

Next.

Here are the six that we're left with to compare. I have up here each of the standard algorithms, then to the left of them, the modification we thought would be the best choice from the modification of that one. We culled it down from over 1800 to about 6.

Next slide.

If you want to look at just sensitivity, they're all pretty similar in sensitivity, with New Jersey having the highest sensitivity. Which is not a surprise. We thought that going in.

Next slide. Specificity, or false positive rate, New Jersey had a highest false positive rate of .009, but we could modify that to get them .003. There are a couple of options you go down to .002. It's unclear what is going to be the best. To be honest with you, I've looked at this many times, and spent a lot of time thinking about this, and I still don't even know what would be the best algorithm based on what we've run here. There's no magic bullet that can maximize your sensitivity and your specificity, while also being easy.

Next.

Then came the question of what's a false positive. This is a very, very important question, which, the more we get into this, the more I hear from different clinicians. The issue keeps coming up. We went into this project looking at a false positive being any child who does not have congenital heart disease, but fails the pulse oximetry test, that's a false positive. We identify the kid that failed, they really don't have any critical congenital heart disease. Yet, depending on the study you look at, anywhere from 20 to 70% of these false positive cases in screenings, could have some important clinical condition that explains their hypoxia. Such as pneumonia, PPHN, pneumothorax, sepsis, Meconium aspiration, or TPN requiring oxygen. These are all important clinical conditions that we would not want to go unrecognized in a baby. Certainly not acutely life threatening as Critical Congenital Heart Disease, but they can be pretty severe, can be pretty debilitating if not picked up promptly.

Next.

The question is, should the algorithm cutoffs reflect these changes? Should we allow for a higher false positive rate, if we change our definition of false positive to mean anything that didn't have any unclear explanation of hypoxia. Now, that's different from the public health standpoint. For screening for Critical Congenital Heart Disease, change our thinking about it. So, from a public health standpoint, yes we're doing a Critical Congenital Heart Disease screening program, and we want to screen for Critical Heart Disease. Any child that doesn't have that, we're not that worried about, we're not going to track. Yet, from a clinical standpoint, it kind of matters. It matters if a kid fails and has a low oxygen level, even if they don't have Critical Congenital Heart Disease, we'd like to find something else. In fact, we're doing a, AP has an expert panel. We're going to be submitting our recommendations soon, for lessons learned from pulse oximetry screening. One of the lessons that we've come up with is that you don't need an echo in every baby. If you can identify a source of hypoxia in a baby, and can treat that source and that hypoxia is resolved, an echo is not indicated.

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With those thoughts, where are we going to go from here? Well, the biggest thing that we've thought is that we need more data.

Next.

Data's been ramping up across different public health agencies. We did not get nearly as much data, or as many people, to submit as we had hoped, but I think that's changing. Recent MMWR said that 19 states are now collecting all the oxygen saturations and times of screenings for all infants, or planning to start collecting it. That data can be very useful in taking this project forward. [Kim Lee

00:30:51] only had about 58 cases identified as CCHD, we'd certainly want more. Is there an option for, or an opportunity to get coordinated data collection? That's an issue that just needs to be discussed in the future.

Next.

Some limitations of our study. Not all babies were going through all the re-screens, so we did our algorithm and ran everything, but we didn't really have the information, every baby, if they were to be re-screened. For instance, if the baby went through the Tennessee algorithm and didn't get re-screened in an hour, because they passed with a 97, we couldn't really use that. Non-CCHD conditions were not well collected, so this false positive question I can't answer, in here, what percentage of these 75 thousand kids had something else. The ones who failed. The false negatives were not well tracked. Again, we had a lot of information from hospitals, not necessarily public health agencies. The hospitals know what happens inside their hospital, but they're not well equipped to figure out what happens when the child's at home. The child who passes the pulse oximetry screening but has a defect, whereas public health agencies are more equipped to do that.

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In conclusion, there are a lot of different algorithms in place. I do not have a clear answer for you, what's the best? Some issues that need to be resolved, is are we doing CCHD screening, which is the public health goal, what's on the recommended uniform screening panel. Or are we doing hypoxia screening? Which is pulse oximetry was invented for in the first place. We're adapting technology to do our CCHD screenings, but there may be important components, or other conditions, that are explaining hypoxia in some of these instances. The bottom line is we need more data. For anyone who's on here, who's interested in helping us do more of this, we are going to continue our data collection efforts. We had stopped for a little bit while we did all this analysis, but I think we've raised as many questions as we've answered, and getting more data from public health agencies would be very helpful in trying to answer some of these questions. I'd be happy to speak more with anyone who's interested in moving this project forward.

Thank you, and I'd finally like to thank all the people who've helped. Regina Simeone, an epidemiologists at CDC, who's helped coordinate this project and collect a lot of our data. Turgay, Pinar, and Cagler are all at Georgia Tech, and they've been very instrumental to me. Analyses and running the different algorithms and the different modifications, determining our output. And of course, all the people who have collected, and shared, data with us. It is very important that we do strong data collection effort, and your efforts have been very instrumental in making this project a success thus far. Thanks very much.

Thalia Wood: Thank you Dr. Oster. That was great. Definitely I would like to have anybody who has a question at this point, just unmute your phone with star seven, or put it in the chat box, because I think this is some important information and we'd like to hear about how the algorithms are going in your state.

Anybody have any questions? Amy would you like to talk about what's going on in Minnesota?

Amy Gaviglio: Yeah, sure I can. We have implemented the New Jersey protocol and I think at this time we probably don't have enough data to truly assess how we're doing with it. I think the questions that you brought up, Dr. Oster, are ones that we have as well. The only other questions that I can think of, that we have been trying to figure out as far as assessing the effectiveness of the algorithms, are how does the effectiveness of prenatal diagnoses maybe change that? Just realizing, which is different for us in newborn screening, is that the value of the screen may be different in different facilities. I don't know if there's any way to speak to that, or whether in an effort to achieve the most effective screen, if it might be reasonable to think that different algorithms might be better in different facilities - I guess those are a couple questions that come to mind - Even within the same state.

Matt Oster: We've referred to the different algorithms, it's very, I found it helpful that we have different things out there. I think that's just a good acknowledgement that what we have there, we're not sure it's the best thing, longer term. I think getting different data from differing opportunities is important. I think it can help them form all this.

I'm curious to know from some of the public health agencies, who are on this call, if this were to be just hypoxia screening, how much harder would it be to collect some of the data regarding non-CCHD conditions?

Amy Gaviglio: Okay, I'll talk again. This is Amy. I think that's a good question. I prefer, personally, to talk about it as a hypoxia screen. I think it makes more sense. I think this is not something new, necessarily, in newborn screening where we tend to call a screen based on what maybe our original target was, but it may be more likely that we pick up other things. Though I think SCID is a good example. We call it the SCID screen, but we're much more likely to pick up things like an idiopathic t-cell, lymphopenia, or a DiGeorge syndrome. I think calling it hypoxia screen makes... Would probably make it easier to, I don't want to say, "sell it," but I think it's more accurate to what we're screening for, truly. As far as data collection of that information, I don't think it would be that much more difficult. I can't speak for each state of course, but we certainly are trying to collect any outcome of failed screens. More than just non-cardiac, cardiac, or nothing. Trying to get some of that information, and it doesn't seem like it's much harder than if we were just doing one or the other. That's our experience, it certainly could be different elsewhere.

Thalia Wood: I do have a question in the chat box, from Kim Van Naarden Braun from New Jersey, "I have comment regarding that question re-screening for hypoxia and challenges in data collection." Kim, did you want to go ahead and address that? Just star seven to unmute your phone.

Kim: Hi, can you hear me now?

Thalia Wood: Yes, thank you.

Kim: Hi, Matt, excellent presentation. I agree, I think it raises more questions than answers, but I think that what you've presented is really so nice. In terms of New Jersey, we have found babies where they, the screening detected early conditions other than CCHD, including other CHDs, but other significant medical conditions. The way we've collected those data, we'd incorporated into our birth defects registry information such that any fail can be reported, and so related to that we get final diagnosis. So, that's cast the net wider than just the birth defects, and a lot of information has been useful to us. I don't know about the flexibility of other systems, but that's been one way in which we've been able to get that additional information.

Debbie: Hi, this is Debbie from Maryland. We have... Just to answer Dr. Oster's question about hypoxia screening, our folks who evaluated, our advisory council in Maryland just wanted to make this standard of care for that reason. We thought it would be a good piece of information to have on all babies. In terms of collecting the data, we've actually found it difficult to get information, or clear information, on diagnoses other than CCHD. We can cross-check CCHD diagnoses with our birth defects registry, but if we have, for instance, children with pneumonia, pneumothorax, or whatever, it's much more difficult for us to consistently get follow up from the hospitals. They tend to put in if there's a CCHD diagnoses, but they don't fill in that slot in our electronic database if there's not a CCHD diagnosis.

I just wanted to echo something that Amy said, I do agree that I think the numbers look very different depending, in terms of sensitivity, depending on prenatal diagnosis rates. Because we tend to have a fairly high prenatal diagnosis rate, and our sensitivity, so far, has been much lower. Particularly in well-babies.

Cindy: Hi, this in Cindy in Vermont. Can you hear me?

Thalia Wood: Sure, go ahead Cindy.

Cindy: I just wanted to follow up on both Amy and Debbie's comments, and give another food for thought about screening for hypoxia versus CCHD. That's wondering if there might be some liability in that if we say we screen as part of our panel for hypoxia, does that imply some sort of liability if we don't pick up something that causes hypoxia? We've had the same discussion as Amy

mentioned, about SCID versus t-cell lymphopenias, and generally it's easier to look for one particular thing, or in the case of CCHD, a constellation of conditions, rather than open it up to something that's so generic and vague, that you could never pick them all up. So, I wonder if there should be some legal input into that discussion. I'd be interested to hear what you have to say.

Matt Oster: This is Matt, and by no means am I an attorney, but I would say that screening for hypoxia, you're probably in a better legal footing than saying your screening for Congenital Heart Disease. The reasoning is this, you're screening for CCHD using pulse oximetry is only 50% sensitive, more or less, based in practice. The estimates where it's going to be about 70, 75. In practice it's only been about 50. We're still missing half the kids who, by 24 hours, haven't declared themselves as having CCHD. That's number one, and number two if you say you're screening for just hypoxia, well, the definition of hypoxia is having that saturation level less than whatever cutoff you say. You can say, for sure, that nope, this child had 97% sat. That's not hypoxia. That path of hypoxia, may have had something else that we, say... We're not going to say we're screening for pneumonia, we're not going to say we're screening for sepsis. You just say you're screening for hypoxia, that's a simple yes, no. You can have CCHD without hypoxia, you can have pneumonia without hypoxia, but to have hypoxia by definition, you need to have a low saturation on you pulse oximetry saturation.

Thalia Wood: That was a good point, thank you.

Okay, do we have anymore comments or questions? Please don't get off the phone, because I do have a poll when we're done with the discussion. I want to ask first if anybody else has any questions?

Matt Oster: I would just add that I expected this question to come up, but it didn't. I didn't put this in the slide show, but if you were to do just on saturation on, say, just the foot and have a simple cutoff. If you were to, say, 95% higher or lower, and that's just it. You just did 95% single cutoff, your sensitivity would be about 56%, which is similar to what we have, and your false positive rate would be about 1.2%. Which is a little bit higher on the New Jersey ones, a lot higher on the other ones. You're not losing much in sensitivity if you just have a single threshold value. I think the big question comes, if you want simple, if you want easy, and good sensitivity, you can get that just by testing one time only, and just in one extremity. You're going to sacrifice your false positive rate. The question, and this is why I brought it up, is that a bad thing, to have a higher false positive rate. As long as we go in saying you don't need to necessarily transport the kid, you don't necessarily need to get an echo if you can identify some other rational for hypoxia that is treatable, or at least explainable for the hypoxia. Is that necessarily a bad thing, to have the higher false positive rate?

Thalia Wood: I think that's a really good point. Does anybody have any comment on that?

Amy Gaviglio: This is Amy. I think that's really interesting. I think I'm still processing it, because we've been talking so much about pre- and [post-ductal 00:45:47] measurements. I would imagine you're right. If you can make sure that when you get a fail, it's not all bells ringing and you go straight to echo or transfer... Very interesting.

Matt Oster: I think even just in our own experience, in our center, when we rolled out screening in our practice, I heard from a lot of our cardiologists that they were worried that they'd be getting a lot more calls at night and a lot more work to do all these extra echos for these kids who are failing. That has just not born out, really not been the case at all. We have picked up a few cases with the screening, but we're not seeing the work overload and the transfers in the middle of the night in the remote places happening in the middle of the night, to be concerning.

Amy Gaviglio: That's good to know, because I was going to ask if you've tested that in rural populations were the attending physicians may be less comfortable doing an evaluation first, before transferring?

Matt Oster: We have not looked specifically at rural populations. Most of the data is just more general and broad-based.

Thalia Wood: Okay, thank you so much. I'm not hearing any other comments. If you have a comment, we'll still be on the call here for a few, but I'm going to put up the poll right now. There's a character limit to the poll, and I apologize for that. I'll have to read this out loud.

What we're wanting to know from the people on the call, is to choose your top three topics that you would like to see in future webinars. I'm going to read what they really are, since I had a character limit. The first one is improvements in pre-natal diagnosis of CCHD, and the impact of pulse oximetry screening detection rate. The second one is discussion of long-term follow up means for CCHD. The third one, best practices related to data collection, short-term follow up and surveillance of screenings. The fourth one, educating families on neural developmental resources available for children with CCHD. I just want to announce that there is a webinar on this, it will be sponsored by AAP on November 12th, at 3 pm eastern time. We will send out more information about that soon. The fifth one is building a framework for evaluating your CCHD screening program. The next one, real quick, is screening issues of the NICU. The last two are common CCHD data definitions and nomenclature. The last one is HIT in newborn screening data collection.

You want to go ahead and choose three of those, everybody that's on the call. As you answer, you will see the answer on the screen here when I go through the results here in just a second. We'll see what your voting looks like. It will help drive the 58C work group as they continue on into the future with new

topics. Just to let you know... We don't have a topic for the next one, do we Amy, at the moment?

Amy Gaviglio: No, I think we were relying on the poll.

Thalia Wood: All right. I'm going to see what the results look like. Well, one of them obviously has... The best practices related to data collection, short-term follow up and surveillance of screenings, looks like the big winner. Go ahead. You can just see it moving on the screen, that just means more people are voting right now. As I said, the CCHD work group will look at this, will look at what your ideas are, and will come up with some speakers and topics then for future webinars as we move forward.

Okay, it looks like it's pretty much done. Amy, do you have any parting comments, or Dr. Oster, any parting comments?

Amy Gaviglio: No, I would just like to say thank you to both of our speakers. I think it's really helpful to see these analyses done, because I think states, unfortunately, maybe with the exception of New Jersey, are not quite there with data collection to do some of this own our own it's really, really helpful to have some resources available to look at how they compare, and help make some decisions on what protocol you want to promote. So, thank you very, very much for taking the time, on a Friday, to share your information with us.

Matt Oster: I would just like to say thank you for the opportunity and thanks for the discussion. If anyone who is collecting data would be interested in helping us out and collect more and analyze more, that would be helpful in us trying to fine-tune these algorithms and what's going to be the best approach to recommend for all involved.

Thalia Wood: Thank you for that Dr. Oster.

Amy Gaviglio: I just also wanted to thank you guys for the opportunity to present today. Thank you.

Thalia Wood: You're welcome. So, if you have any questions for Dr. Oster and you want to send them to me, this is thalia.wood@aphl.org, I can forward them to him, or his contact information. And again, thank you to the speakers. And actually, we ended a little early, so you get eight minutes of your day back. Thank you everyone who was on the call.