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Critical Congenital Heart Disease Technical Assistance Webinar
December 2014

Presentations:

- Pulse Oximetry Screening for Critical Congenital Heart Defects in the NICU: Michigan's Experience—Derek Bair, MD, Neonatologist Oakwood Hospital
- Evaluation of CCHD Screening in the NICU: New Jersey—Kim Van Naarden Braun, PhD, Centers for Disease Control and Prevention, New Jersey Department of Health and Regina Grazel, MSN, RN, BC, APN-C, New Jersey Department of Health CCHD Screening Program

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

Thalia Wood: OK, again, thank you everyone. For the speakers, don't forget to push *7 before you speaking and we will open it up to questions at the end. So now I'm going to turn it over to Lisa Hom from Children's National who will get us started, Lisa.

Lisa Hom: Well everyone to the December Critical Congenital Heart Disease Technical Assistance webinar. We have some wonderful speakers lined up for the neonatal intensive care screening topic and this has been a really interesting discussion amongst the teams in the various states in terms of process.

We know that there's a national recommendation for best practice and a validated algorithm for asymptomatic babies but many states are dealing with whether or not to screen in neonatal intensive care units and specialty care units.

So the first speaker that we'll hear from-

We have two states, Michigan and New Jersey. The first state that will be presenting, both are HRSA grantees, will be Dr. Bair. He's a neonatologist at Oakwood Hospital and he will be doing a presentation on pulse

oximetry screening for CCHD in the NICU base on the Michigan experience. So, he's been the director of neonatology for over 13 years at Oakwood Hospital. So 30 bed levels, three being NICU, that manages over 5,000 infants a year. He is also the chairman of the Michigan Department of Community Health's Newborn Screening Technical Advisory Committee and has also served on the newly-formed Newborn Screening Quality Assurance Committee, representing neonatology for the state of Michigan. Thank you very much Dr. Bair.

Dr. Derek Bair: Thank you. Hopefully everyone can hear me. I've got a phone that normally I can hit, just, mute and de-mute, and I'm good to go. So I'm on a low-tech phone here. Can everyone hear me?

Thalia Wood: Yes we can. Thank you Dr. Bair.

Dr. Derek Bair: Excellent. Now, how do we progress with the slides?

Thalia Wood: Just tell me when you want me to move the next slide and I'll move it for you.

Dr. Derek Bair: OK. OK. Well why don't we go ahead and move to the next slide. I think everyone knows that Michigan looks like a mitten so we're identifiable. What you see in this slide is sort of a layout of the state. As you may or may not know, most of our population is consolidated in southeast Michigan, which is where we are located. We've been having a gradual decrease in the number of births but in 2013 we had roughly 112,000 births with roughly 12,000 NICU admissions nationwide. Just a correction, I don't admit 5,000 babies to our NICU. We have about 460 admissions to the NICU. Our system does about 5,000 births per year and our system just joined with Beaumont and now we will be doing about 13,000 per year. There are 83 birthing hospitals in the state of Michigan. There are 20 NICU's. We are one of the level-threes. There are 20 total NICU's in the state. Next slide.

As was mentioned prior, we are one of the HRSA grantees and we are starting our third year on our grant. Our goals for the program were to increase the number of Michigan newborns being screened for CCHD and we have expanded that to the NICU's as well, just not the normal newborns, and to develop the state infrastructure for collection of that information through electronic record. We do offer, in the state, multiple avenues by which the individual hospitals can report, both those on paper and those that are done electronic. There are eight hospitals in the

state that are using HL7 and six of those eight have reported to the state. We started our screening report- Although it started prior to April 1st, we started effective April 1st, it was mandatory for all hospitals to start reporting for CCHD, both in the NICU, those in normal nursery, as well as those born at home. Next slide.

When we developed our CCHD screening, especially for the NICU, I was involved in that. It was a multidisciplinary approach involving both physicians on multiple sides of the fence, myself being from neonatology, we also had pediatric cardiologists involved in the process. We went through a variety of algorithms and many, many renditions of it, trying to hone down something that we thought would be applicable across the state. I think it's probably still going to be a little bit of a growing phase. So we are finding some things and I'll talk about our experience with that since we've implemented this. MDCH is monitoring all the CCHD. We did develop a final algorithm prior to a go-live date and now we're in the process of getting feedback on how the process is working. Next slide please.

So what you see on the right-hand side of the screen is our algorithm that we use for the state. We had a lot of trouble, or growing pains, as you will, as we were putting this together trying to make sure that we were trying to pick in the ideal time in which to do this and trying to keep with the, as much as possible, the healthy newborns, which was screening at 24 hours of age. We eliminated the babies, if you will, those that had had a echo prior to the CCHD screening or if they had had one in the NICU after 24 hours but they were still on supplemental oxygen or, for some other reason, had not been screened, that they would have the echo and that would eliminate them. And we'll look at some of those numbers in a second. We also looked at these three criteria, if you will, [inaudible 00:06:14]: infants not requiring supplemental oxygen and asymptomatic and screening them after 24 hours of life. Infants requiring supplemental oxygen in the NICU state, screened 24 hours after weaning to room air, requiring no supplemental oxygen or respiratory support. And then those infants going home on oxygen, to consider perform an echo prior to discharging, we had recognized that a large number of the babies who, fit into that category, have bronchopulmonary dysplasia or chronic lung disease and, because of that, many of them are having echoes done anyway just as a baseline for cardiac functioning, looking for evidence of cor pulmonale. I would backtrack to say that the first group, where we had infants not requiring, might be those babies that came in simply for prematurity, or those babies that came in for some form of sepsis

evaluation or had been transferred from another hospital for some other unrelated reason. It was expected that all NICU babies would be screened using these guidelines, if not previously screened or screened prior to discharge from the unit. Next slide.

With respect to screening in Michigan, after excluding units using HL7, such as Oakwood, from reporting pulse oximetry screening results, were reported and then linked to the blood specimen. Now, one of the issues that we are running into, as you can see, is that samples were at 68%, were linked. We do have a problem with linkage. We've run into the same problem with the normal newborns, outside of the NICU setting. We do know that one of the pluses of certain programs, electronic medical records, is that some of them have built-in processes by which to link them, but we don't have this completely ironclad yet. This is through our April through September information. We had roughly 4,200 infants in the NICU. 57% or 2,383 had screening results that were reported and we'll have that breakout on the next slide. Three NICU's reported pulse-ox screening results for >90% of the infants but what should be noted there is that only one of those units had more than 15 infants. Next slide.

So this is the breakout from the data. So, of those 2,383 newborns, 2,015 passed, which represents approximately 15%. 28 of the infants that did not pass were re-screened and two of those failed. Neither of those two that failed were identified by echo to have a CCHD. Of the 28 that should have been re-screened, 14 were re-screened and all of those infants passed. If I throw those into our "pass" category it really doesn't bump us beyond the 85%. 14 of the 28 were not re-screened and, of those, seven simply were not re-screened, six reported as missing, and one had an echocardiogram performed as opposed to a re-screen. They represent approximately half of those that should have been screened. A more interesting category, from my perspective as part of the leadership, is the 380 and 338 that were not screened. You can see the breakout there. I see points of opportunity here. 38 were transferred and we don't know if they will fall out in the HL7 results because we are a referral center, so some of those babies may have, for some reason, ended up in our NICU, which raises the question whether or not there is a process issue or that it may be lost in translation, if you will, between reporting systems. If you look at the nine deaths that occurred prior to screening, or those that had a pre- or post-natal diagnosis, of 23, those represent patients that did not have the screen performed but, rather, were diagnosed with an underlying congenital heart problem prior to the 24 hours. And then we had 67 that had echoes performed. If you pull those out they represent a

good number of patients that fell into the non-screened category. The more concerning population is those reported as "missed", which makes up 159 of the 338 patients and I see that as a process failure. We have also the 32 that fall into the "other" or "unknown" that weren't specified and those do require further delineation to have a better understanding, whether or not they more than likely fell into the "missed" category. Does anyone have any questions regarding those at this point? If not, I'll move on to the next slide.

Speaker 6: Yeah, I'm sorry. Go ahead.

Lisa Hom: Are you taking questions now or should we-

Dr. Derek Bair: Well, I thought if anybody had any particular questions about this particular slide I would try and answer questions while we're on it. If not, we'll just move on to the next slide and we'll ask questions at the end.

Speaker 6: Yeah, these are great data. I have a question about the two fails. So, the two fails, those were two babies with a CCHD.

Dr. Derek Bair: They failed the screen. They did not pass. They failed the re-screen, but on echo they did not have congenital heart disease.

Speaker 6: OK so they were false positives.

Dr. Derek Bair: They were two false positives, correct.

Speaker 6: OK great. That was my question. Thank you.

Dr. Derek Bair: You're welcome. OK, if there are no other questions we'll move on to the next slide.

So the next two slides are sort of answering-

We're trying to answer the question that was posed, which was, "Should we be screening patients in the NICU?" And these were my thoughts. In the NICU you're dealing with a select, high-risk population that, many of them, are still in the process of transition. This is where I have a slight reservation in that NICU's, I believe, maintain a high rate of suspicion and babies that are in the first few weeks of life we're always looking for underlying issues related to congenital heart disease because the majority of the kids that come into the NICU are, because they are a high

risk population, are coming in for cardiopulmonary compromises, one form or another. So we are always trying to delineate that as a possible cause. At the same time, an argument in favor of screening in the NICU would be that we also, in southeast Michigan, have a large population that has limited or no prenatal care, which means those are patients-

We've lost the opportunity, if you will, for prenatal diagnosis and therefore must be monitored closely and would certainly benefit from having the CCHD screen performed.

I apologize, my computer just locked me out. I will read from my slides that I have in hand. With respect to regionalized care, as we all tend to try and move towards regionalized care, there's always the concern of infants falling through the crack and if you remember from a previous slide, we did have 38 infants that, for whatever reason due to transfer, were not screened. And therefore we have to have due diligence and the question is, "Did we truly have 38 that fell through the crack versus did they fall through the crack of a documentation system where we know that we're already having some issues with linkage?" Next slide.

These were issues that we've encountered in the NICU setting since we've started to undergo utilization of the algorithm. We've had, what I'm calling, delays and that's why I put it in italics, where it's at least perceived that the screening process is delayed based on the current algorithm, in that many of our infants aren't being screened at 24 hours or once they're in room air and asymptomatic. When I've asked our nursing staff why it wasn't performed there's been some educational issues on our part, but there's also been the very logical question of, "Well, I didn't screen them because," and the quote is, "because they're normally between 90 and 95%," which means that we would automatically get kicked out on the algorithm. We are usually 90-95% sat. as a normal in our NICU, based on the most recent [VON 00:15:27] Cochrane review that was presented in spring of this year. So we do have babies that, although we are accepting at a 92 sat., we wouldn't necessarily launch into evaluating those kids, looking for a CCHD, just because they're sating between 90 and 95%. The other comment I had on this was whether or not we have a large number of our babies that do have echoes for one reason or another, since we do tend to lean towards the extremely small side of infants. Roughly one-third of all our infants have echocardiograms performed while they're still on supplemental oxygen, looking for things such as PDA's. So we do have a large number that would be kicked out. The last is the concern of pulse oximeter usage

and this is one question I raise by whether or not this is unit-specific. We tend to leave our babies on pulse oximeters from the time they come in, regardless of what issue they came in for, until they are discharged. So, we would readily identify the kids who have unacceptable saturations, but I can't say that that's always true in all NICU's and since we have to fall on the side of being conservative that would be another reason for having CCHD screening, because the sats can be greater than 85 and the child not necessarily pure cyanotic or having increase [work 00:17:00] of breathing, and therefore still fall into the group that would otherwise fail the screen. Those were my thoughts. At this point I would say that we are in favor of continuing NICU screening but I think there's a lot of data [be-it 00:17:13] collected before we can say that we're doing it exactly the right way, or certainly the timing of the evaluations. I'm ready for questions.

Thalia Wood: Well, thank you Dr. Bair. Actually I think we'll hold questions until the end because I'm hoping we'll have some discussion.

Dr. Derek Bair: OK.

Thalia Wood: Thank you very much

Dr. Derek Bair: You're very welcome.

Thalia Wood: Lisa, you want to introduce our next speaker?

Lisa Hom: Certainly. Thank you so much Dr. Bair-

Lisa Hom: So next we'll hear from the New Jersey team. We have Kim Van Naarden Braun. She's an epidemiologist with the Developmental Disabilities Team in the National Center on Birth Defects and Developmental Disabilities at the Center for Disease Control and Prevention. She's also the state assignee with the Division of Family Health Services at the New Jersey Department of Health. She's published over 50 peer-reviewed articles and book chapters and she is joined by Regina Grazel who is the Advanced Nurse Practitioner and Project Coordinator for the New Jersey Department of Health's Critical Congenital Screening Program. So thank you guys very much for joining us on the call.

Kim Van Naarden Braun: Thanks so much and thanks for having us join the discussion today. Regina and I are going to tag team and we're going to provide, just, very brief results from our data collection over the past 3+ years,

specifically focusing on what we found in our NICU population and then share with you a study that we're currently embarking on. The goals, the message and welcome other collaborators and other folks to participate. So I'm hoping that you'll keep that lens in mind as we're talking. Next slide.

Thanks. So over the past, approximately, 3 years we've had a little over 300,000 live births in the state of New Jersey and approximately 99.6% of babies that were eligible in the state to have been screened, were screened. And, as many of you know, in New Jersey our legislation requires that we screen all newborns across the state regardless of their clinical status. Next slide please.

The babies that fail the CCHD screening are reported to our New Jersey Birth Defects Registry and in the registry we can collect information on the clinical characteristics of these babies so that we can put them into two buckets: whether a bay has received and echocardiogram prior to the time of the screen, whether they were prenatal diagnosis, or whether they had signs and symptoms that would have warranted a post-hoc measurement prior to the screen. So these were babies that were already identified, or worked up, and so their diagnostic evaluation wasn't attributable to the screen. So we had, over this time frame, 208 babies that failed the screen were reported to us in the Birth Defects Registry. 111 of these had one of those three criteria such that their diagnostic evaluation happened because of other indicators. There were 97 of which, that the diagnostic evaluation was prompted because of the failed screen. Next slide please.

Of those 97, we identified 14 babies with a CCHD that were identified prior to discharge because of the screen, 12 with CHD, 9 with other non-significant cardiac conditions, 27 where their only finding was a PDA or PSO, and then there were 35 babies where, based on the information that we got from the hospitals, there was no documented reason for the failed pulse-ox. And interestingly, 66% of these babies didn't follow-

Nurses didn't follow the protocol. Next slide please

Of the 14 infants with CCHD that were identified because of the screen, there were five co-arctations, one Ebstein anomaly, two D-transposition of the great arteries, one tricuspid atresia and five PAPVR. Next slide please.

Where we'd like to shift the conversation is to talk about the NICU infants. And what's interesting is that, of our population of babies that were screened, the 208, 62% were actually in the NICU at the time of the screen. So when the screening was conducted they were located in the NICU. So no we'll shift and I'll let Jean talk a little bit more about those results.

Regina Grazel: Next slide please.

So we're going to talk specifically about our findings in the NICU. So of the total fails we had 128 babies who failed their screen in the NICU. And to put this in perspective, Kim shared our overall birth rate is about 100,000 per year in New Jersey and we have 15 level-3 NICU's. So of those we had 128 fails and, again, the same categories. 100 babies failed but they had one of the criteria. They had a prenatal diagnosis or they were showing signs and symptoms at the time of the screen, or they had an echo that was done or planned prior to the screen. So 28 babies, in the category to the right, had a diagnostic evaluation, solely attributable to the pulse-ox screening. Next slide.

Of the 100 infants with the failed screen whose eval. was not attributable to the failed pulse-ox, we just wanted to share a little further. As in a [me-tri-can 00:23:09] presentation, many of those babies do have a prenatal diagnosis or an echo prior to the screen. So we had 69%, so about two-thirds, had a prenatal diagnosis or an echo, but not 100% of them in the NICU. Of those, 27% had the prenatal diagnosis of CCHD and 62% had an echo, prior. Next slide please.

So, of the babies who had a diagnostic [two 00:23:41] evaluation that was attributable, directly due to their failed screen, these are our findings. So we did have one baby with CCHD detected in the NICU. Five babies with other congenital heart defects. Other non-significant, non-cardiac conditions, we did not find in the NICU, which is not surprising. We did find that in the well-baby population. We had 11 babies with PFO or PDA as the only finding. And there were 11 babies with no documented reason for the failed screen. Of those 11, nine had not had the protocol followed. Basically they were not repeating the screen up to 3 times, per the protocol. Next slide.

We're going to look a little bit further into the babies who were detected with CCHD and CHD through the screening. To note, all these babies were term. So this is a population that we have our eye on, in terms of the

term babies in NICU, is that potentially a population that could slip through the cracks. The age at screen ranged from two days to two weeks. The case number one baby was found to have a co-arc. The baby was admitted, obviously a larger baby, an infant of a diabetic mom, baby was admitted to NICU once the sugar problems were resolved. They did the screen and found the baby's had a co-arc that was not identified prior to that. Baby did have a little bit of respiratory problem initially as well, which could have masked some symptomatology but the screening clearly detected the co-arc. The other CHD's are listed there in terms of their pre- and post-ductal results, the number of screens before the baby was deemed a "fail", and what the final diagnosis was. Next slide.

So, just taking a peek at the gestational age and how that affects our results. Of the 100 babies whose eval. was not due to the screen, 60% were term and 19% were pre-term. 21 were in the extremely pre-term. Looking at the 28 babies whose diagnostic evaluations were due to the pulse-ox screen, as is consistent with the prior slide, the majority were term infants. So 75% were term, 21 were pre-term and we did have 4%, a couple babies, that were the extreme pre-term. Next slide.

So, faced with much variability in NICU practices concerning CCHD screening, we know nationally there is a lot of variability and even, anecdotally, within our state. So we partnered with our New Jersey NICU collaborative, to just do a really brief survey on their practices for NICU screening. Next slide.

There were some brief questions about screening. We had 20 respondents from mostly level-3 units and a couple weighted in from the level-2 units. The majority screened at a minimum of 24 hours of age and the timing was variable. And that's kind of what we expected. They're all, by legislation, they need to screen but they are screening sometimes immediately after weaning from oxygen, sometimes right before discharge to the home. So we asked them, "If your timing is variable, then when would you do it?" Next slide. Next slide? Oh, I think we skipped one.

Thalia Wood: This slide, did it have motion in it because sometimes motion doesn't carry well in this platform. I'm not sure which version you wanted. Was it this one?

Regina Grazel: We did that one and now we're going to look at the subset of bullet #2. So then, when do you screen? So, medically stable, without oxygen, they

were screened at 24 to 48 hours. And if they were unstable and on oxygen, then 57% tried to screen as soon as possible when medically stable. Another would be any time after when they were stable without oxygen. And others are, kind of, closer to discharge or one institution did all babies, no matter their clinical condition, at 24 to 48 hours and they repeat the screen when the babies were weaned off. So, again, it really just said to us that we have such variability in practice that we need to form a working group-

Next slide.

-and discuss the results, and say, "What do we want to do? Where do we want to go with this?" So we convened a group of experts of neonatologists and pediatricians and pediatric cardiologists and advanced practice nurses and epidemiologists and we put our heads together, and everyone said, "OK, where should we go now? Do all NICU infants need to be screened?" These were the questions that were posed. Could we apply some exclusion criteria, such that babies who had an echocardiogram prior to the screen or prenatal diagnosis or those really, really tiny babies, could they be excluded from screening at this time. And, if so, what is the appropriate timing for other babies in the NICU. So, after we met pretty much all day and really went around and around-

Next slide.

-the decision was to not make any changes right now and to continue the current protocol. And this is largely based on because we really do not have large population-based data. We don't have a lot of studies about screening in the NICU. So these are some of the publications and some are small. Some are commentary or case studies. And so, really, the decision was to continue the current protocol and then look into further studies. So I'm going to hand it off to Kim who's going to talk about our proposed evaluation of screening in the NICU.

Kim Van Naarden Braun: Next slide, please. The goal of the activity that we're knee-deep in now is two-folds when we have our New Jersey perspective. To inform our best practices regarding CCHD screening in the NICU and, coupled with that, to inform our rules and regulations that would accompany our statewide legislation. So Jean mentioned from the key questions that our working group had talked about and they translated into the objectives for this study. So, to evaluate whether exclusion criteria could be applied to our statewide mandate for infants in the NICU. Whether an

echocardiogram prior to the screen could form an exclusion criteria. Prenatal diagnoses and extreme prematurity. And these are indicators that some, as Michigan, so nicely spoke about, [inaudible 00:31:33] incorporated into their existing algorithm. And because our mandate mandates that all babies be screened we really are hoping to get population-based data to even support going in that direction. And then, secondly, to assess the most appropriate timing for the screening during the NICU stay, and hopefully getting at some aspects of burden associated with different timing options. So, again, the exclusion criteria and the timing pieces are two of the main objectives of our study. Next slide please.

We've developed a multi-stage screening protocol for all NICU infants and for that to be systematically implemented across all of our New Jersey NICU's, in particular, but we are eager to, and welcoming of, any other state or entity that wants to participate as well. We have gone through New Jersey Department of Health IRB and this evaluation was deemed public health practice non-research and we have that documentation and have been working with our other New Jersey hospitals to both rely on that exemption but also working with specific hospitals and how to navigate this as an evaluation. Next slide please.

So I'd like the run through, just step by step, the building of our proposed study protocol that has incorporated feedback from our New Jersey NICU's. It's a multi-stage, as I mentioned, and there are three potential stages when we look at this. The first stage is screening all infants at 24 to 48 hours of age including those on supplemental oxygen. This "stage one" would be following the current New Jersey-recommended algorithm. Next slide please.

Taking assessment of supplemental oxygen into account, if an infant was on supplemental oxygen we're proposing a modified approach such that, if the first set of screening measurements is 95-100% and the difference is three or less, that would be deemed a pass, which is consistent with the New Jersey protocol, or if that first set of screening measurements is <95%, and consistent with clinical profile, and the difference is three or less, not to re-screen. Enter the data in, but continue on in that arm, left of that point. If the baby is on supplemental oxygen and the first set of screening measurements is a difference of four or greater, to then proceed with the re-screen process. Then, if there's a difference of four or greater after three attempts, that's deemed a "fail" but, if after the first attempt, or even the second, the difference is 3 or less, than it's

deemed a pass. Our neonatologist and pediatric cardiologist felt strongly that incorporating this modification could potentially pick up a [Cartesian 00:34:41] where the difference would be potentially missed at that very early stage. Next slide please.

The second stage is applicable to the infants that were on supplemental oxygen. So the majority of babies are going to be screened at stage one. For babies that are on supplemental oxygen the stage two is a screen at 24 to 48 hours after weaning to room air. So similar to the Michigan protocol. But the two stages aren't dependent on each other, they're mutually exclusive. So our optimal protocol is for all babies to be screened at stage one. For babies that were on oxygen to also be screened at stage two. Next slide please.

In discussions with our NICU's, for some of the NICU's it's customary practice for them to do a pre-discharge screen, and that's their current timing. So we don't want to, because this is a public health evaluation of our legislation, by any means dictate changing clinical practice, so we've incorporated into the protocol optional data entry for pre-discharged screening. So that can occur if it already is, or it can be added also if a hospital wants to incorporate that additionally into their current operations. But you can see that it's a dotted line because it isn't formally something that is part of our study design. Next slide please.

In terms of methods of data collection, of transmission, we've created a secure, web-based instrument through Zoho, which is a web-based tool, and we're proposing that the study occurs between a 4 and 6 month window of time. In the web-based instrument, data are entered at each hospital and the data are purely de-identified, such that individual-level data are entered in for each child, a random, unique identifier is automatically added for that child. Only each hospital would maintain the link between that randomly-generated ID and the identifying information for that given infant. So that would be maintained at each hospital. In order to get the information on timing, so the age at the various screens, the age at discharge and age of transfer, the instrument will require, in the front end, to enter in date of birth, enter in date of screen, but then it will calculate the age and only retain the age within the data instrument. So the identifiers of date in any form, whether date of birth or date of screen or date of transfer, aren't being submitted as part of the data collection process. As I mentioned, all the data will be entered at the hospital site and there'll be secure access for each of the hospitals. Each hospital will only be able to see their own site's data. Rutgers University is

the entity that we've contracted with to develop the instrument but they'll also be providing technical support as well as oversight from Jean and myself and NJDOH. The system is a web-based instrument that's secure. So, it is going through a secure portal. And on the end stage of the study, all of the data, because they're de-identified, will create an analytic data set which can be shared with participating sites because it's purely de-identified. That being said, we are developing data use agreements such that any analyst that wants to look at the data has to submit the proposal and the objectives for specifically what they want to look at so that we can work collaboratively and the data can be used appropriately. And then there's also [signings 00:38:39] that, even those these data are de-identified, there would be no attempts to try to identify any infant in the study, even though that is most likely not possible. The other thing that we've now had some discussion about with state is a data-sharing agreement. So there's the data use, which an analyst would sign, and a data-sharing such that, if another department of health wanted to or was able to provide their data that they've already collected, but wanted to contribute to the study in some way, that we could share those de-identified data between departments of health or between this evaluation and the data that's already been collected. So we're trying to be creative in exploring agreements and mechanisms to share data not only to be analyzed but also to contribute to the sample size of the study in various shapes and forms. Next slide please.

This slide lists out the data elements that are a part of the instrument, currently. As I mentioned, the dates of birth, the dates of screening, birth weight, gestational age, clearly those are characteristics that we're going to want to stratify our findings by, all of the individual-level pre-imposed [duct-al 00:39:57] results. And then the age and the time of the screen will go along with that, analytically. The presence of a prenatal diagnosis, echocardiograms and consults, both related and unrelated to the screen. We're trying not only to get there at that, identifying potentially exclusion criteria of the echo and the prenatal, but with the consult and the echocardiogram, trying to assess burden as well. Were there unnecessary echoes and consults done solely in response to the failed screen and was the timing a variable that prompted that? Also, whether the baby was on supplemental oxygen and any information on transfer and discharge dates. Next slide please.

Currently we are working with our New Jersey NICU's to beta-test our instrument and where it stands now, and working on developing worksheets for them to incorporate into the daily workload. So trying to

think about the ways of implementation and then actual data acquisition at the NICU level and then submission into the instrument. We have interest from, indefinite participation from a number of different states. New York. Four hospitals from New York are participating. We've had some discussions with Michigan, California, Texas, and we welcome any others that want to join in this adventure with us. The other thing I just want to mention is the potential for batch submission of data, and that refers back to a data-sharing agreement where, if an entity, whether it be a department of health or a hospital, has the data already collected, it's a matter of matching and formatting the data elements such that a batch submission could be sent off and all the individual-level data don't need to be re-entered into our specific instrument. Our goal for timing is to start data collection in January of 2015 and, it's a moving target as it is with any, sort of, activity, but we're eager to get started and looking forward to having some data to try to help inform our best practices. Next slide.

Again, next step is to convene a conference call with potential participants. Again, we talked to folks here in New Jersey but opening it up a bit wider. Finalizing our data collection instrument based on the feedback from beta-testing and, as I mentioned, starting data collection after the new year. Next slide.

And here's our contact information. Thank you so much.

Regina Grazel: Thank you.

Thalia Wood: Yes, thank you, both Kim and Jean. I appreciate that. We've had a lot of questions come in over here during both presentations so I think I'll just start up at the beginning. Dr. Bair, if you could un-mute your phone again. The first two questions, actually, were for you.

Dr. Derek Bair: OK I'm un-muted.

Thalia Wood: OK thank you. Somebody wants to know where they could find the Cochrane review.

Dr. Derek Bair: Oh, the Cochrane review? I'll have to search that and I can send that on to you. It was presented by the Vermont Oxford. They were the ones that held the presentation and I've forgotten what-

It was in the first quarter of the year that they held the review and did the presentation on the data.

Thalia Wood: OK great. And then the second question is also for you. If the NICU baby is on continuous pulse-ox, do you do right, U, E and foot?

Dr. Derek Bair: I'm sorry. Rephrase? Say that again?

Speaker 7: OK, sure. You bet. If the NICU baby is on continuous pulse-ox, do you do right, U, E and foot?

Dr. Derek Bair: OK, yes. We rotate the pulse-ox on a continuous 4-hour basis. So every four hours the pulse-ox is being rotated so at any given time it will be on an upper extremity, right hand, or it may be on the left, on a foot. I think that's what the question is asking. We don't do continuous, simultaneous, right arm, lower extremity input unless we have a concern of a shunt, like PPHN or something along that line, in which case then we would be looking at pre-ductal and post-ductal on a continuous basis.

Speaker 7: Thank you.

Thalia Wood: OK the next question is for Kim and Jean. How many babies were screened to get the 208 fails?

Regina Grazel: So the 208 fails represents a little over 300,000 infants.

Thalia Wood: OK. And then somebody wanted to know if they could get a copy of the survey tool of the NICU's that you used in New Jersey.

Regina Grazel: The survey tool, meaning the questions about variable timing, or our data collection instrument?

Thalia Wood: That's a good question. I don't know. And again it was [Gerri 00:45:08] who asked that question so she'd have to un-mute her phone to-

Regina Grazel: OK. Well we can share the NICU survey on timing and the data collection instrument is in progress but we're happy to let anyone demo it.

Thalia Wood: The next question was, "Can you clarify how you define full term, premature and extremely premature based on weeks of gestation?"

Regina Grazel: That's a great question. This was based on, again, fails that were-

This was not a study per se. It was based on fails that are registered to the New Jersey Birth Defects Registry. In New Jersey all babies who fail the screening, regardless of their final diagnosis, are required to be registered to the Defects Registry. The Birth Defects Registry has preset categories for term, preterm and extremely preterm. We will be able to, in the prospective study, be able to narrow that a little bit better. In the registry, as it stands now, >37 weeks is term and preterm is just less than 37 weeks and extreme preterm goes by weight and not just age. It's less than a thousand grams. So a little bit of a mix mash.

Kim Van Naarden Braun: Right. And particularly for this study it's imperative that birth weight and gestational age get entered in for each baby.

Thalia Wood: Great. Thank you so much. Somebody also asked me, they said it's something they might have missed, but what is your current NICU screen protocol in New Jersey?

Kim Van Naarden Braun: The same as for well babies. There's one screening protocol for all babies in the state.

Regina Grazel: So it's, screen before they're discharged. It's recommended to screen all babies at 24 to 48 hours or as soon as possible when medically appropriate. And that's left to interpretation of the hospitals and that's where we'd like to find some more guidance, based on the study.

Thalia Wood: OK we have another question for New Jersey. Did you run the proposed NICU protocols past the screeners themselves? It seems kind of complicated and they wondered if there was a concern of misinterpretation.

Regina Grazel: We've had a number of working group meetings where we developed the protocol and it was agreed upon that, at least in theory and on paper initially, that that was going to be easily implemented. Clearly we're going to need to have trainings with staff via webinar to actually go through it as well. One of the hospitals, probably maybe two, that are beta-testing the instrument are going to data test actual implementation. So we'll get feedback on that as well. And what they're going to try to capture as they do the initial pilot, you could say, is not only interpretation but the time and the burden of actually doing it and doing the data collection, because I think that that's going to be really helpful. How burdensome is it to even participate in the study.

Kim Van Naarden Braun: And just another comment. What we presented was all the timing action. So not each site will need to use all timing options but we needed to build it into the study protocol if they wanted to use it. So, for most of the babies it's going to be one screen. And that is going to be, across the board, at 24 to 48 hours. For babies who are on oxygen, we wanted to still have the screen done at 24 to 48 hours and really only re-screen or consider a fail based on the difference pre- and post-ductal. And then we built in the pre-discharge because that is the current policy of some hospitals. So it looks more complicated because we needed to cover all the timing options but most places are not going to be doing three screens, they're going to be doing one or two screens.

Thalia Wood: Great, thank you. And Dr. Hokanson, I'd like you to go ahead and unmute your-

Or Dr. Martin, excuse me. I'd like you to go ahead and unmute your phone rather than have me read off all of your questions over here and raise your concerns.

Speaker 8: So, first of all I just want to congratulate New Jersey. That team has just been marvelous and they are a model state for, not only being first, but for the attention to detail and reporting of data that is really going to help us improve. So congratulations. You guys are all-stars in New Jersey.

Regina Grazel: Thank you for that.

Speaker 8: Number two. I do want to express a little concern about your [pre-me 00:50:22] protocol, or I'm sorry, your protocol for babies on oxygen. You are taking an algorithm, although slightly modified, from data that was collected on babies studied at room air and applying it to babies on oxygen. So, in effect, you're almost doing research on what might you find. It can't be considered a test of the algorithm, number one. Number two is that, given that we're looking at CCHD, there are three real types of CCHD. There's transposition physiology, decreased pulmonary blood flow. Now those kids don't react to oxygen. So probably those kids you're not impacting, but the complete mixing kits, total vein, hypoplastic [latart 00:51:30], [tri-o-tree-sia 00:51:31], single ventricle. Those kits are going to have increased pulmonary venous oxygen content and that is going to increase their left atrial saturations and their ventricular saturations and make the test-

It's going to decrease the sensitivity of that. So you need to be aware of it. It's one reason why we've made the suggestion to wait until babies are off oxygen and perhaps a little bit like Michigan, basically realize that many of those children that have a continued oxygen need are going to get an echocardiogram because they have an oxygen need and it's clinically indicated and wait until they're truly off oxygen. That's been our bias. Not that we know the right answer.

Kim Van Naarden Braun: Hi Dr. Martin. It's Kim. Thank you. These are all excellent points and ones that we've talked about with our pediatric cardiologist and neonatologist. One thing that was really interesting about-

OK a couple things. I think one is that the endpoint, being that it's a public health evaluation of the legislation, I don't think that our endgame is to try to really test the algorithm or recalculate sensitivity, specificity. Matt Oster is doing some really nice modelling in Georgia with data that he's trying to collect to look at various aspects of the algorithm and actually testing it by looking at screening parameters. When we had, [where 00:53:14] kind of the genesis of tweaking that weaning off oxygen in 24 to 48 hours came from, in our group, was the concern of not doing screening at 24 to 48 regardless of oxygen and that babies with the difference wouldn't be identified early. So there was that concern of, "Let's try to see whether you can influence culture," and just having it on the minds of clinicians in the NICU of a cardiac issue that may otherwise wouldn't have been on the radar. So it was an interesting discussion that was driven, in part, by trying to-

What was culture? Clinical culture. I think, and not wanting to miss those co-arcs early on. So I think that your points are definitely well taken. Ones that we've discussed here too and hoping that what we're doing to, we don't have the- (laughs)

But to cast the net as wide as possible at that 24 to 48 hours and not putting any exclusionary criteria on it from the beginning and getting the individual-level data. And all the sats will help us look at this in some way to give us-

Speaker 8: But you're going to-

If you're trying to catch the co-arcs, having them on oxygen is going to be a hindrance. Because, with co-arcs they're going to have higher left atrial oxygen saturations. Many of them have an [HO 00:54:47] left or right

shunt and since you're trying to pick up a right-to-left shunt at the duct, what's going to happen is you're going to increase their PA saturations and you're going to decrease the difference between the upper and lower extremities. So, from a physiologic standpoint, testing them earlier on oxygen is going to be a negative to having you help catch them. And also, most of the co-arcs that have been missed in NICU's have been kids that have been in the NICU for weeks anyway. The ones that have at least been reported in the literature. So, I'm worried about that strategy because I think co-arcs is a disease in progress and I think many of them don't have co-arc when they're first a day old.

Dr. Derek Bair: I'm going to interrupt just for a second, just, it's anecdotal but we did have a case that we received that at 24 hours when the CCHD screen was done the child was sating pre-ductal post-ductal 100%. At two-and-a-half days, prior to that baby's discharge, the baby started to deteriorate and was diagnosed with a critical co-arc, on the third day of life.

Speaker 8: That's exactly right. When the ductus is closed.

Kim Van Naarden Braun: Right. And that's why we're hoping to get both time points to assess the timing.

Speaker 8: Congratulations New Jersey.

Kim Van Naarden Braun: From my understanding it's a tricky group any which way you cut it so trying to get-

I appreciate and I agree with what you're saying, but trying to get some data at least on the group.

Speaker 8: You guys are doing a great job.

Thalia Wood: Thank you for that. We have a couple more questions here to go. What was the failure rate in NICU babies in New Jersey. It looks like it was substantially higher than non-NICU babies.

Kim Van Naarden Braun: Can you back up to that slide?

Thalia Wood: Can you tell me about where it is in the presentation?

Kim Van Naarden Braun: So I think that what's a little challenging with our data right now in terms of calculating rates, we kind of try to steer a little bit away from it, is that we don't have individual-level data on all of our babies.

Regina Grazel: Only fails.

Kim Van Naarden Braun: Only fails. So we don't [inaudible 00:57:11] higher failure rate among the NICU population but we don't have screening results on all the NICU babies. We just have the fails that were reported to us and then we know, of the fails, what their final disposition was in terms of diagnosis. But, of the fails that were reported to us-

Regina Grazel: You can back up one slide.

Kim Van Naarden Braun: -a higher proportion of them were in the NICU. So I think you're correct. I wouldn't necessarily consider it a population rate of failure.

Regina Grazel: Because we had 128 fails in the NICU. But that covered babies that were prenatally identified, babies who already had a [net-go 00:57:49], although babies who, under the current legislation, still need to be screened. So we had 128 fails. Of those, 100 were expected to fail and did not require further evaluation or testing based on their failed screen. 28 required further exam.

Kim Van Naarden Braun: One earlier.

Regina Grazel: Go back one, you might hit it.

Kim Van Naarden Braun: Two more before that and-

Regina Grazel: One more.

Kim Van Naarden Braun: And that's the breakout. So, 128 fails. We kind of did expect more NICU babies to fail only because more NICU babies have one of those three criteria. If that makes sense. They're in the NICU so they have signs and symptoms, they had a prenatal diagnosis or they had an echo planned just because of their clinical course in the NICU.

Thalia Wood: OK thank you. We have one more question we'll go ahead and take here at the last minute. Many hospitals are using continuous monitoring but often it is just hand monitoring. What do you say to them as this is not a screen if a foot is not screened. If you do both hand and foot continuous

monitoring, are you taking data and calculating the screen's outcome if the hand and foot are taken hours apart?

Kim Van Naarden Braun: I think that's a question for Dr. Bair. In New Jersey they interrupt continuous monitoring and actually take a pre- and a post-ductal snapshot, if you will, and record that as a screen.

Dr. Derek Bair: In Michigan, at least in Dearborn, we do both pre-ductal and post-ductal at the same time.

Thalia Wood: Thank you. Well we are at the end of our time. We've had a lot of great questions and a lot of great discussion. Lisa did you want to wrap this up for us?

Lisa Hom: Thank you so much to our presenters, Dr. Bair, Kim, and [jeen 00:59:55]. I think you really highlighted a lot of the considerations for the special care nurses in NICU's in terms of process issues, appropriateness and effectiveness. So thank you everyone for the fantastic questions and to our fantastic presenters. Everyone, I hope you have a great weekend and there will not be a webinar in January but we will look forward to speaking with all of you again in February. Thanks Thalia.

Thalia Wood: Thank you everyone.

Kim Van Naarden Braun: Thank you.

Dr. Derek Bair: Thank you.

Regina Grazel: Thank you.