NewSTEPs
A Program of the Association of Public Health Laboratories™

Short Term Follow-Up Technical Assistance Webinar

July 2016

Presentations: Sharon Quary, MS and Angela Wittenauer, RN, BSN, Georgia State Profile

Cindy Ingham, RN, BSN, Recap of the Cystic Fibrosis meeting

Susanna McColley, MD, Timeliness in Newborn Screening Consideration for Cystic Fibrosis

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

Thalia Wood: Okay, I think we'll go ahead and get started. This is Thalia Wood with the Association of Public Health Laboratories and the NewSTEPs program. Welcome to the July short-term follow-up webinar. I want to turn it over to one of the co-chairs of the work group, Carol Johnson in Iowa, to get us started and introduce our presenters today. Carol, go ahead.

Carol Johnson: Thank you. Good afternoon everyone, happy July. I hope you're staying cool, wherever you are.

Today we're going to hear our state profile from the state of Georgia, and we're going to get perspectives from two different individuals. The first is Sharon Quary, she's the newborn screening coordinator at Northside Hospital, and Angela Wittenauer, who is the coordinator at Emory University.

Sharon, if you'd like to go ahead, that would be great.

Sharon Quary: Thank you. Actually, I was asked to give a bit of how we do follow-up here at Northside Hospital because there's probably not a whole lot of hospitals that actually have newborn screening coordinators. Angela Wittenauer and I are going to tag-team this a little bit. Next slide please.

These stats were pulled from the most recent block grant application that Georgia submitted: our current births approximately 132,000 in [inaudible 00:03:08] 2015. We've calculated that right at 107,000 of our infants were actually matched as receiving at least one screen, so we still have some work to do with our matching algorithms. The number of presumptive positive screens is right at 7,200; and then the number of confirmed cases from those positive screens is 285. Next slide please.

The way that Georgia conducts its short-term follow up, the Department of Public Health actually contracts with the specialists in the various areas. There is a contract list, Emory University- Department of Human Genetics, and they handle all of the conditions except for the hemoglobinopathies. The follow-up for the hemoglobinopathies, the actual presumptive positive disease cases, are divided between Children's Healthcare of Atlanta, which deal with the metro-Atlanta counties. That's the bulk of the population. Then the remaining counties, it's 159 counties in Georgia, so the majority are actually covered by Georgia Regents University in Augusta, Georgia. The two of them tag-team the sickle-cell positive screens, and then those screens that have sickle-cell trait results actually go to the Sickle-Cell Foundation of Georgia. Then they perform follow-up for those cases.

At this point I'm going to turn it over to Angela, and let her talk about our conditions identified and then follow-up with Emory.

Angela Wittenauer: Hi everybody, can you hear me okay?

Thalia Wood: We can, thank you much.

Angela Wittenauer: Okay good, I just wanted to make sure.

I'm Angela, and I'm the follow-up coordinator, as Sharon was saying, through Emory. Just real quick, we have two slides here where I've pulled together the number of kiddos diagnosed with various conditions last year.

As you can see, we have a lot of sickle-cell and sickle-cell trait in our state, but the rest of it is probably shaking out like most other states. This is just a smattering, it's not everything. I didn't include a lot of the secondary conditions, but there are few in here of interest, just in case you're interested in what our numbers look like. Next slide please.

Georgia is a little different; we all think we're all special, right? Of course I think Georgia's special, we do things a little bit different than a lot of states. One is that Emory, and this is probably true in the history of most states, Emory University was very intimately tied with bringing out newborn screening in the state of Georgia and helped to initiate the initial screening for PKU back in the sixties and we started [inaudible 00:06:26] it up.

We are still very intimately involved, even before it was an official contract, although we did establish a legitimate contract with the state of Georgia back in, I believe it was 1978. The contract currently includes support for a wide-range of activities that relate to newborn screenings, most importantly the actual short-term follow-up. It funds me and my team, I have a team of nurses along with some other folks, our day-to-day tasks are to handle calling out all results on the dried-blood spot except the hemoglobinopathies, as Sharon was saying. We call out all those results, whether it's a repeat screen or whether they need urgent care as of yesterday. We handle all of that.

We also get support in that contract for our clinical care; Emory is the only metabolic service in the state of Georgia. It helps support that care that is hard to come by, and honestly hard to fund, supports our physicians, supports our dietitians, has supported metabolic food up until this fiscal year. We're really excited to talk about the fact that we are getting a whole separate project and funding sources to support metabolic foods and formula for our kiddos, we're really excited.

It also supports other specialty consultants, I get expert advice from folks in [CF 00:07:58] immunology, things like that, helps support diagnostic labs if needed, and whole lot of other fun stuff. Next slide please.

Short-term follow-up, again, is coordinated through Emory University, again except hemoglobin, sorry. What I was talking about here really focuses a little bit more on what our relationship is with Northside, because, again, everybody's special, our relationship with Northside is a little special and I'm not sure if any of you all know but Northside, unless this has changed, is the biggest birthing facility in the country. It really gives us a lot of bang for our buck to have good relationship with Northside and a good process with them.

We report all of our abnormal results for babies who are still at Northside directly to their screening office, that's Sharon and her team. That includes all three of their campuses; Sharon will talk a little bit more about what their facilities are like. Regardless of where the baby's located we contact one office with the results and the recommendations for follow-up on that. That gives us a lot of a streamlined productivity on that.

For our critical results, or the presumptive positives, we call those not only to Sharon's office and fax them there but also directly to the neonatologist. That makes sure that we're getting any critical clinical information handled right away in

a bidirectional way. We need to know what's going on with that kiddo but most importantly the neonatologist needs to know what to be watching out for on that kid. There's no delay on that, we tell them right away, and then continue our follow-up through Sharon's office so we can make sure we get access to lab results, can provide any support that they may need, and we can make sure that any paperwork that they need to get their job done in taking care of those kiddos gets taken care of and doesn't get lost in some random fax machine going off to who-knows-where in such a huge institution. Go ahead, next slide please.

Again, those confirmatory results, all those lab results that Northside collects comes back to us through Sharon's office, that way there's not 20 neonatologists and all the hundreds of nurses touching that baby that are responsible for trying to remember to get back to us on that. It's just Sharon and her focused team, they get that back to us and we have one point of contact in case something falls through the cracks; it makes it very simple.

Northside is also great with that team of dedicated nurses and staff supporting us in all this activity, so maybe a baby's been discharged by the time we're calling, they help us find pediatricians if that wasn't listed on the newborn screen card. They will also go ahead and notify us when children are transferred out. They are right across the street from one of our major children's hospitals and Northside does a great job of letting us know when the kiddos have been sent there so we can get follow-up handled right away instead of waiting for the children's hospital to reach out to us.

Having Sharon's office also is really key for us because their hospital has a contract with Mayo Medical Laboratories up in Minnesota, so most of the diagnostic testing happens through there. As you can imagine, it's not next door and can take a minute to get lab results from Mayo. If we need something on a machine today, Emory Genetics Lab can handle that and working with Sharon's office helps to communicate that urgency so that we know "Hey, this kiddo is special and we need to do something a little different". Having that office advocate for the prompt care of those children really helps us get our kiddos taken care of.

I think that's all I have, if you want to go ahead and click to the next slide, I think I'll turn it back over to Sharon now. Is there anything else you want me to touch on with that, Sharon?

Sharon Quary: You're good Angela, I'll take over.

Angela Wittenauer: All right, thanks.

Sharon Quary: A little bit more about Northside and our hospital-based follow-up program. As Angela mentioned, we have three campuses, pretty much in the midst of the Atlanta area. Last calendar year our number of live births was just over 20,000, and my understanding is that our numbers are projected to increase again this year as well.

Our Atlanta campus, which is our main campus and has level 2 and level 3 nurseries, a little over 16,000 births last fiscal year. Our Forsyth campus also has level 2 and level 3 nurseries, a little over 3,000. Our smallest facility, which is a little bit further out of the metro-Atlanta area, but that area is also rapidly growing and they're actually in the process of building a new hospital, so just over 1,000 births. We expect our numbers to continue to increase, and as Angela said, unless it's changed we birth more babies at our 3 hospitals than any other hospital in the country.

My understanding- I've only been in this position for about 4 years- but from what I've been told, Northside had a system in place for many, many years initially worked through their hospital laboratories, but about 10 years ago they decided, or the administration decided, that an actual coordinator was needed to address some of the deficiencies in the system so that we could provide the best care to our patients and not place them at risk, or our organization. It also happened around the time that the state was expanding newborn screening and there just needed to be some further coordination. Next slide please.

Currently, I serve as a full-time coordinator, I'm here 40 hours a week. I actually have 4 part-time nurses, so between the 5 of us we have about 2 FTEs. Our responsibility is to make sure that every baby born at Northside, all 3 campuses, has a screen done at the appropriate time and that that specimen is of sufficient quality.

We also coordinate, we're also for the CCHG screenings and as Angela mentioned we work with our follow-up programs, not just Emory, but also our follow-up programs, the hemoglobin follow-up programs here in the Atlanta area. To report abnormal screening results to our neonatologist for those babies who are still in-house, we actually receive those results, we triage them and we take them upstairs and put them on the babies' charts. If we need to have a conversation with the neonatologist to make sure they get a message we'll do that.

Also, if our babies have been discharged, we take that information, we forward it to the discharge pediatrician, and we send the report to Angela's office every afternoon saying "This is what we've got and this is what we've done with it".

Also, as Angela mentioned the transfers to tertiary centers, we let them know that those babies are no longer here. Depending on what the case is we will also forward that information and then let know Angela and her staff know that we've done that as well.

In addition to the abnormals we also make sure that if there are any issues, say for instance, a baby got out of here with a screen that was less than 24 hours of age, in error, or if a screen was unsatisfactory, or by chance a kid was missed: because we're checking on that every day if there was an issue we assume that responsibility of making sure it gets taken care of. We track all of those. We don't

have the best data system, we do it all through Excel spreadsheets, but we document all of those issues, we track all of those issues so if we get a phone call we can report back pretty quickly about what happened. I think we have a very well-oiled machine. There's a whole lot more I could tell you, don't have time to do so, but we have a very well-oiled machine and we're very proud of our program here at Northside Hospital. Next slide.

Just contact information for our state program, our state laboratories, and Angela's information, JoAnne Beasley who does follow-up in the metro-Atlanta area if you guys have any other questions. And I'm done.

Thalia Wood: Thank you so much Sharon and Angela, that was a great presentation because you do have an unusual program and that was wonderful. We will hold questions to the end, so Carol, you want to introduce our next speaker?

Carol Johnson: Sure. Our next speaker today is Cindy Ingham, from the great state of Vermont, and she is going to do a little bit of a summary of the cystic fibrosis quality improvement and timeliness meeting that many of us attended in Denver a few weeks ago. This is now going to be the theme for the rest of the webinar. Cindy is going to speak first, and then we have Dr. McColley who will speak next, and I will introduce her after Cindy is done.

So Cindy, please go ahead with your presentation, thank you.

Cindy Ingham: Thank you, Carol and good afternoon everyone. I'm going to give you a whirlwind overview of a very productive working meeting recently sponsored by NewSTEPs and the CF Foundation. The purpose was to convene various stakeholders in newborn screening for cystic fibrosis and to identify strategies to assure timely screening through a partnership between CF centers and state public health departments. My challenge is to pack 2 really intensive days into 10 minutes, so buckle your seatbelts.

I want to start with a disclaimer. Some of those on the call today who were speakers at the meeting may recognize slides and information that you presented. I have shamelessly pirated these slides that you gave permission to have posted on the NewSTEPs website, and I'll apologize in advance if I don't correctly represent the information you provided. Dr. McColley, our next speaker, says that such piracy ... Oh, could you go back to the previous? Yeah, we'll stay there for just a sec. Dr. McColley says that piracy is a form of recycling, so think of this as my contribution to saving the environment. I don't have enough time to touch on all the excellent presentations and I really encourage you to visit the website which is listed there under Jack Sparrow's picture for a more in-depth view of the discussions that we held. Next slide please.

There were 40 states represented, comprising a variety of professionals and screening algorithms. Here's a fairly recent map showing distribution of the various algorithms used across the country as well as those participants that were there by

their professional affiliation. Next slide.

The format of the meeting was really well planned to allow for the presentation of topical information followed by smaller breakout sessions to allow programs with similar concerns to focus on barriers to timeliness in screening. The group as a whole would then reconvene to summarize and share suggestions for implementation strategy. Next slide.

The Cystic Fibrosis Foundation recommends that infants with cystic fibrosis should be diagnosed by the 30th day of life and data reported for babies who were born between 2010 and the end of 2012 suggest that the average medium age was 19 rather than 15 days of life. The problem with this is that these data cannot be reliably measured unless we have consistent guidelines followed and definitions used both by newborn screening programs and the CF clinical community in reporting such data. If you go on the website again you can see Marci Sontag posted presentation about data challenges, and I think you'll find that interesting.

With these caveats in mind, it's clear that timeliness of diagnosis and intervention does indeed make a difference in clinical outcome and that states can make positive changes in this area. Next slide.

Carol Johnson, who you just heard from Iowa set the stage with an outstanding description of barriers to timeliness in screening in general, not specifically CF. Next slide.

She reviewed the very real barriers of each step of the process: obtaining and shipping filter papers correctly; laboratory analysis; reporting and follow-up of results through to diagnosis and intervention. It struck me as Carol was talking that hospital staff, midwives, subspecialists, primary care providers, and others would benefit greatly from having a similar introduction to the big picture view of screening, and I've decided that I'm going to include this information in more depth in future orientations and presentations I do for these groups. Next slide.

Yvonne Kellar-Guenther proposed using the process of root-cause analysis to identify specific problem areas and to propose solutions. Next slide.

With that in mind we worked in small groups on a variety of topics. Here is just a few examples of brainstorming by state, who share the same CF screening algorithm, whether it's IRT to DNA, IRT to IRT to DNA, or IRT to IRT. You can see for example we talked about how DNA is run, what to do with babies on whom it's really sort of inconclusive: they have one mutation, what to do with those kids, the availability of sweat testing. This is just a small piece of what we talked about but this is the sort of practical solutions that were developed from these working groups. Next slide.

I am always stimulated and encouraged and excited by hearing about other programs' success stories as well as about ideas that worked better in theory than

in fact. This theme ran throughout the 2-day meeting. I'll very briefly describe some success stories presented on the topics of education and training, courier systems and operating hours, and health information technology. These are just the tip of the iceberg and I encourage you to follow up with any of the speakers whose presentations strike a chord with you. Next slide.

Erica Wright talked about Colorado's pilot project to improve the accuracy, completeness, and quality of specimens being submitted. Next slide.

They focused on educating hospital staff who were collecting and submitting filter papers, and they developed some attention-getting and effective posters. I looked at this one and think "How much more seriously would you take the process if you thought that every time you fill out a newborn screening form you're holding a baby's life in your hands?" Next slide.

Along with this very clear poster describing timing priorities, the Colorado program also developed a chain-of-custody envelope for transmission of the filter papers through each step of the process. The results of these education efforts were very gratifying, if I got this information correct, over a 6 month pilot phase the four participating hospitals submitted no "unsatisfactory" specimens, which is just awesome. Next slide.

Let's talk a little bit about Iowa. Stan Berberich talked about Iowa's successful efforts to improve timeliness in the areas of courier systems and laboratory operating hours, and the results are impressive. Next slide.

Because courier services are offered 365 days a year, the specimens are usually received in the Iowa laboratories that very same day, or that night I should say, weather permitting. The laboratory is staffed 24/7 so that processing can start the same day as collection. That's really fantastic, you can't really get much more timely than that. Next slide please.

Rachel Lee from Texas tackled the topic of how the various health information modalities can effect timeliness of screening. Next slide.

She reviewed the HL7 messaging systems currently in use by 40 of the Texas facilities; these allow for the transfer of data to and from the newborn screening laboratory information management system. Next slide.

She also described plans to improve and expand the Texas web application as well as other aspects of the data transfer process. Now, regardless of what data systems your particular state has in place, HIT is a critical aspect to consider in your evaluation and planning efforts. It kind of strikes me, as a nurse with zero background in this field, that we really need to educate ourselves more than we have done in the past about HIT processes. Next slide please.

On the afternoon of the first day we had state and regional breakout sessions to

identify problems in newborn screening processes. They tended to fall broadly into the category of communication, education, lab processes, and operating hours. After a lot of small group discussion we presented back to the entire group. Next slide.

Here are just two examples of potential barriers to timely screening as they relate to education of hospital staff and primary care providers along with possible solutions. We dealt with turnover, communication, buy-in from hospital staff who are already very busy, PCP offices who may not understand the urgency of reporting. As I say, this is just one very small example, and if you go to the website you'll see these barriers and solutions posted in that portion of the slides. I would encourage you to do that and see what might be appropriate to consider for your state's program. Next slide.

NewSTEPs is offering financial and technical support to assist states in timely reporting of newborn screening results, and some of you, many of you, have already participated in year one of this project. Next slide.

Here are the application mechanisms for either state or collaborative group applications. Note that because some state programs are unable to accept funding, as ridiculous as that seems, it is possible to apply for technical assistance only. Next slide.

The application deadline for year two is very close, August 1st. Please do contact NewSTEPs staff for more information if you're interested. Next slide.

In closing, I'd like to thank the Cystic Fibrosis Foundation and NewSTEPs for bringing together stakeholders who don't usually have the opportunity to collaborate in such a targeted way. I can envision this happening with other specific disorders in the future, that would be really great.

I think I've met my 10-minute goal, phew. I guess we can save questions until the end. Thank you.

Thalia Wood: Yes, thank you so much Cindy, that was a great recap.

Okay Carol, if you'd like to introduce our last speaker?

Carol Johnson: Sure. It is my pleasure to introduce Dr. Susanna McColley. She is currently at Northwestern University and has been a cystic fibrosis clinician with over 25 years of experience. She has served as the CF liaison for the Illinois Department of Public Health Genetics and Metabolic Advisory Committee, and she serves as the vice chair of the Cystic Fibrosis Foundation Newborn Screening Quality Improvement Consortium. Without any further ado, Dr. McColley, we look forward to your talk.

Susanna McColley: Thank you, can everyone hear me okay?

Thalia Wood: We can, thank you Susanna.

Susanna McColley: Thanks, and a shout out to Cindy for the Jack Sparrow slide, Jack Sparrow is my second favorite pirate. My very favorite pirate is the great pirate Roberts from the Princess Bride, who of course wasn't a pirate at all, but great use of a great image for that.

Let's go to my next slide. What I'd like to talk to you guys about today is why it's urgent to make a CF diagnosis early, and this slide really tells the story that the primary goal of cystic fibrosis newborn screening is to achieve normal growth, because in CF, all other health relies on normal growth. There are other important aspects to health and survival in CF, but growth is where it starts.

If you look at the panel on the left side of the slide, these are works published a few years ago in the Journal of Pediatrics that show if you take a cohort of children, longitudinally followed, these children were born between 1989 and 1992, and you look at their growth attainment as weight per age and height per age percentiles that those at the lowest weight and height are much more likely to die before age 20 than those who have better growth. This is incremental, so the best survival is in children who at age 4 have weight and height above the 50th percentile.

On the right hand panel we have a very old article published in 1949 that really just reminds us that without pancreatic enzyme replacement therapy, which allows for digestion of food, CF is fatal early in life, often in the first year of life, historically. Next slide please.

Newborn screening has actually been going on for a while in the United States, although not widely, and Colorado started screening for cystic fibrosis in 1982, and that was really based on the concept that you could avoid having children come in very sick. It was many years before the full benefits were realized and it really took a randomized control trial that was conducted by Bill Farrell in Wisconsin that showed significant and sustained improvement in nutrition in screened versus non screened children. This table shows those results, well it shows the age of diagnosis for the screened versus the control group. The control group was recalled, for those few of you who are not familiar with this study. Note that they looked at the age of diagnosis in weeks, and the mean age at diagnosis was at 13 weeks in the screened group, but with a median of 7 weeks. With the control group, also much larger, some of them came to clinical attention, others were recalled. The reference is here for anyone who would like to read that paper that hasn't had an opportunity to do so. Next slide.

These are the growth data for the Wisconsin study, and what you see here is that in the yellow lines are height on the left hand and weight on the right hand, percentage of patients above the 10th percentile. Remember, that's the real dropping off point with survival in the later study. Both the screened population's in the yellow line, the control is in the blue line, and you see that going between age 1 and 13, height and weight are higher for the screened population, a much

higher percentage achieving that greater than the 10th percentile throughout into early adolescence, with the weight just catching up at 13 years of age in the control population. Next slide.

Another outcome of this was this study that looked at prediction of survival with a number of different modes of diagnosis. You see here that survival probability up to age 60 years and beyond is greater in a screened population, and it's even greater in a population with a positive family history once you get beyond about 20 years of age. Meconium ileus, it does result in early diagnosis of cystic fibrosis, but this is known to be a very severe phenotype that has other associated morbidities. So in summary, screening appears to have a survival advantage. Next slide please.

Early treatment is essential, obviously, to achieve this advantage, so if you have pancreatic insufficiency you want to be started on pancreatic enzyme replacement therapy as early as possible. This is a table from guidelines published for treatment of infants with cystic fibrosis diagnosed through newborn screening, and there's an evidence table here. What you'll note is that the CF Foundation is recommending that treatment for infants diagnosed with CF by newborn screening should start within 24-72 hours of diagnosis. What you see in this guideline is that it really refers to what occurs not only after a positive screen but after a positive diagnosis, and that leads to a lot of variability in how programs may be implemented. Next slide please.

This is seen in this median age at CF diagnosis, which is quite variable between states. Here I just have one bar that shows the median age at diagnosis in each state. This was between 2010 and 2012, and Cindy referred to this as well.

There are some caveats around this because it just looks at date of diagnosis. When we originally did this graph there were several states whose median age at diagnosis was negative, and this has to do with the way the CF Foundation registry has been set up in that a prenatal diagnostic test showing 2 CFTR mutations can be the first diagnostic test confirming the diagnosis in the population. That's why on this graph you'll see that it says "Date of diagnosis greater than date of birth", we took out the babies that were prenatally diagnosed to get more of a glance at the newborn screening process itself.

Even so, as Marci Sontag pointed out at our meeting in Colorado, you'll see at the left hand side of this graph there are states who are reporting that median age at diagnosis is less than 5 days. These data are from CF centers, not from newborn screening programs. We're not sure exactly where this is, if you were just to look at how the newborn screening programs, where the only sign that they may have CF is a positive newborn screen. We hope to make some changes in the registry so that we are more aligned with state programs in the way that this is looked at. The other thing thought, that's important to recognize with this, is when you take out those states where it seems like there's something else going on and not really getting the newborn screening results back in 2 days and then getting a diagnostic confirmatory test 2 days later, that that would shift the median age to longer than

it's showing up on this estimate of median age at CF diagnosis. Next slide.

Our goal, as is already stated, is to have that 15 days, part of it is we think is achievable with current technology. This slide now has identification of state, but it also shows that the methodology used can affect median age at diagnosis in that at this time, and many of these states have changed, at this time the states using IRT-IRT, which requires 2 tests, were having a later median age diagnosis than those using IRT-DNA. Regardless of the algorithm used, bringing it to earlier diagnosis may have some health benefits. Next slide please.

Another thing that is timeliness-related have to do with false-negative newborn negative screening frequency. Babies who have a false negative obviously have a significant delay in diagnosis. This graph shows false negative newborn screens between states in this same three year time period. You'll note that actually many states had none, and that doesn't mean they didn't have any babies with CF, it's possible that none came to clinical attention, but among those who did it was as high as 13%. Again, probably some over-representation using the IRT-IRT technology. Next slide. Or algorithm, I should say.

Another thing to be aware of that can delay and cause false negatives is that CFTR multi-mutation panels that are used in IRT-DNA states are less predictive in minority populations. The top table, this table 2, is from the state of Illinois. We published this in the Journal of Genetic Counselling a few years ago. We have a very high Hispanic population and actually, more than 20% of the newborn screen diagnoses we see at our CF center in Chicago is Hispanic or Latino. We just looked at what mutations were covered by our panel, and as you can see the non-Hispanic Caucasians had both mutations detected over 90% of the time, whereas its only 60% of the time in Hispanics, and the non-Hispanic Caucasians with zero or one mutations much lower and Hispanics much higher. There are also data on African-American and information on provided cases, and there weren't very many of those so it was hard to make firm conclusions about that. In the lower panel we also see that there seems to be a trend toward more minority children, those who are not white and non-Hispanic, in false negative newborn screens. These are preliminary data from the CF Foundation's data registry. Next slide.

One of the things that people say is "What's the rush?" We know that there are clear benefits of newborn screening in this population diagnosed at a median age of 7 weeks in the landmark study by Farrell and colleagues. The strongest argument that I'm going to make right now is that there's evidence of a growth deficit in infants with CF, even with newborn screening diagnoses. I'm going to show you a summary of three recent reports, and I will tell you none of them have been published yet, but I think they're nearing that given how complete the data were when these were presented last fall at the North American CF conference. On the next slide, these are the first two studies.

One is the first study: feeding infants right from the start. This is a prospective study [human 00:44:05] growth and essential fatty status, and inflammatory bile

markers, enrolling infants soon after a CF diagnosis through newborn screening. What has been shown so far in this study is that while weight was at the 41st percentile at birth, it declined quite a bit by age two months, and also there was essential fatty acid deficiency noted in many of these babies. Furthermore, weight but not length were recovered by 12 months of age back to birth percentile. The bonus study is an observational study of infant growth, and they really focused on pancreatic enzyme replacement therapy dosing in this study as well. The bottom line for the purposes of our discussion today is that they also had very similar findings and that length was not recovered by 12 months of age. Next slide.

The final study used the CF Foundation patient data registry, and they looked at the first three years in which all US states were performing newborn screening for cystic fibrosis. They used enzyme therapy as a proxy for pancreatic insufficiency. It's not a diagnostic test, but it's a pretty good proxy. They noticed that even in the CF population, those pancreatic insufficient infants had lower weight and length at birth and were smaller at one month of age, and all of these deficits persisted at 12 months of age except for weight for length. Of course, the weight for length percentile, if you're small and short, you're going to be proportional. Let me just say, for those of you who are not familiar with these data, I did show you survival related to height, but the concept here is that the taller you are, the bigger your lungs are, and having big lungs and not just lungs that are proportionally the right size for your body is predictive of survival in cystic fibrosis. Next slide please.

I will hypothesize that given that growth is sustainably increased by newborn screening diagnosis, and that there are growth deficits in the screened population at 12 months of age, earlier intervention is needed to improve growth and close the gap as much as we can. There's a caveat to that, which is that other than the fact that it makes very good sense to start earlier pancreatic enzyme replacement therapy, we don't know what other interventions are going to help us achieve our goals in the first year or two of life. We still have a lot of work to be done in our community to figure out what these interventions are through research and quality improvement activities. Next is my final slide.

I would like to make the quality improvement case that variability in median age at diagnosis suggests that there can be improvements, in other words shift people to the left hand side of that curve, and that targets for improving this include earlier completion of the algorithm that's used, earlier visits for evaluation and confirmatory testing, which is also an issue in CF newborn screening. Reducing quantity-not-sufficient sweat tests, which are the diagnostic tool used, and not having an adequate sweat test does delay diagnosis. Finally, treating infants with presumptive cystic fibrosis, those with positive screens who may not have a diagnosis, especially who have symptoms, those who have two severe mutations on a newborn screening, blood spot sometimes prior to confirmatory testing. The addition of pancreatic enzymes and salts to an infant's regimen awaiting confirmatory testing has no real harm except for family anxiety and some expense, and so it's a good trade-off in that an infant who can't get to a center or doesn't have an adequate sweat test the first time.

That is my presentation for today. Thank you all very much for your attention.

Thalia Wood: Thank you so much, Dr. McColley. Carol, do you want to see if anybody has any questions? And don't forget, you can put them in the chat box or push *7 to unmute your phone to ask a question.

Carol Johnson: Yes, we are happy to take questions for any of the presenters today. Also, I'm not sure if John was able to be on the call but if we have time we'd also like to here from any states who were present at the CF meeting in Denver: if you plan to, or have already made some changes in your CF processes because of the meeting. So, general questions for the presenters and then comments about changes that you might want make in your program for CF newborn screening. ... *7 to unmute.

Thalia Wood: Thanks Carol. While we're waiting to see if there's any questions, I actually have a question that goes back to the profile that Sharon and Angela did for us, if one of you could answer this question?

When I saw that you had kind of a low number of babies that were ascertained "to be screened", is that because of your matching process? Do you think that other 19% is actually getting screened?

Sharon Quary: This is ... Can you hear me, Thalia?

Thalia Wood: Yes.

Sharon Quary: Okay. It's a little bit difficult for me to speak to that because I am no longer a part of the Georgia program, but from my experience with the Georgia program, the issue is with matching, that they just haven't been able to refine that algorithm so that they can actually match every kid with a screen, but I do understand that they are making strides to increase that or to improve that process. They've had some issues with turnover in staff and that type deal so it's a little bit difficult to make improvements in your program when you're continually having turnover in staff and leadership. It's a little bit difficult to get things done. I don't know if anybody from the Georgia program is on the call? ... Don't think so. That's my understanding of some of the challenges that they're having.

Thalia Wood: Okay, thank you for that explanation, that helps. ...

Once again, anybody have questions for the cystic fibrosis speakers or examples of how you've changed your program or are planning to change your program?

Rachael: Thalia, this is Rachael with the Alabama newborn screening program.

Thalia Wood: Thanks Rachael, yeah, go ahead.

Rachel: I wanted to just comment, and I thank the Colorado School of Public Health and

APHL for giving us the opportunity to attend that meeting in Denver. Since that meeting we have begun a project, I went searching online to see if there were any resources that were available for providers and why they should choose an accredited, or make a referral to an accredited CF center. I did come across some information that was developed by the Indiana newborn screening program. We are in the process of developing our own resource to provide to our providers in our state to include some of the information here that Indiana also provided. They went in to describe, what does it mean to be an accredited center, and what kind of standards they have to meet, so we found this resource very helpful. If there's anyone on the call from Indiana, we thank them for developing this resource, we found it very helpful.

Thalia Wood: Great, thank you so much Rachel.

Carol Johnson: This is Carol, while we're waiting for other people to chime in, one theme that we heard at the Denver meeting from the clinicians that were in the room, the CF clinicians, is that they weren't hearing about presumptive positive babies very quickly from the newborn screening program, or from the PCP, was not making timely referrals. So one of the things that we're going to consider in Iowa is to double contact. In other words, we're going to contact the PCP, but we're also going to contact the CF centers and let them know that there is a presumptive positive baby that will need to be sweated so that we can maybe shorten that time between the PCP and the CF center for the accredited sweat test. ...

Thalia Wood: Thank you, Carol. Does anybody else have any thoughts on changes or possible changes you're making to your program as a result of the meeting?

Karen: This is Karen from Nebraska, can you hear me?

Thalia Wood: We can, thanks Karen.

Karen: Okay, I just wanted to follow up on what Carol just said. We have had a practice of always contacting the CF center at the same time or within a short time period that we contact the PCPs. When we were at the meeting we actually were talking about, and we haven't worked this out yet, but trying to get the CF center or having them in some fashion, maybe by fax or something, reach out to the PCPs simultaneously to sort of let them know that ... Because I usually tell them I'm going to call the CF center, they're going to know this and that, but it doesn't necessarily seem to always motivate them as much as I always want them to be motivated. We're thinking if they reach out and actually send something, like we'll be trying to do these appointments, or frequently asked questions, or something to really get their attention that the CF center is waiting and expects to hear from you right away, that sort of thing sort of gets further into it, into making that referral happen. It doesn't always happen as quickly as the program staff or the CF clinicians want it to happen.

Then the other thing I wanted to say is that I too really appreciated the meeting

from the point of view of having that time with different parts of the system all together. From Nebraska we had someone from the CF center, myself from short-term follow-up, and someone from the lab that we use. Having that time face-to-face to talk about these things: well how does it go? Well from ours, we get to you, from you we get to you, and that kind of thing was really helpful. I think we're having a harder time connecting again now we're back and I'm in Lincoln and the CF center's in Omaha and the lab's in Pennsylvania. Even though we email and talk and that kind of thing it's still harder to get together and work things through compared to when you have that face-to-face time with people who are down in the trenches really doing it. I really appreciated that and I think it's a good model to think about in the future again, to be bringing people together who are in those different positions but working on the same problem.

Thalia Wood: Great, thank you for that Karen, that's wonderful. We have a couple more minutes if anybody has a quick question, otherwise I'll let Carol wrap it up. Carol, I'll just wait a couple minutes and see if we have another question.

Carol Johnson: All right. ... No more questions, anyone? Well we hope that you have found this helpful. The meeting was great and I think this is good to focus on cystic fibrosis. We do hope that we can use this model and focus on each one of the disorders that we screen for in the future. If you have any questions please feel free to contact Thalia Wood, her information is there and she'll help you get to the right person to help answer any questions that you might have. I think in closing, what's our next webinar date again, Thalia?

Thalia Wood: It's in September, it's the week after Labor Day, whatever that is.

Carol Johnson: Okay, whatever that date is. So check your calendars for that and we'll be in touch with more information.

Thalia Wood: All right, thank you so much everyone.

Carol Johnson: Thank you, have a good rest of your summer. Bye bye.

Thalia Wood: Okay, bye.