>> SPEAKER: All right, can everyone hear me okay? All right, I'm going to go ahead and get started, because it's 3:15, but thank you all so much for coming to this talk today. I've really enjoyed this conference so far and having conversations with all of you, if you've stopped by the booth, um, a lot of really great questions about genetic testing, who's really ordering the genetic testing and, when you get questions from families about it, kind of, what have they already heard or what information should they know. So, I'm Tera Quigley. I was trained as a clinical audiologist and worked as a research and clinical audiologist for several years at different university and academic settings and, for the past five years, I've been at Decibel Therapeutics in Boston, Massachusetts, and I work there as Associate Director of Medical Affairs, and a big part of my job is talking to clinicians about genetic testing and their processes for genetic testing, and I quickly realized, after going to a couple different institutions, even within the U.S., that it varies so much, and it changes depending on what institution you're in and, sometimes, depending on what provider you're seeing. So, we did a, um, a study that I'm going to share these data with you today. Before I jump into the data, we all know and, if you don't know, you'll know now that most congenital hearing loss is caused by genetics. So, more than half of all babies that are born with hearing loss has a genetic cause and, understanding this genetic cause can really hope both the family and the clinician, and it can help them because it allows them to, potentially, predict the future, and what I mean by that doesn't have to do with a crystal ball, but, basically, the genetic results could help inform the family and the clinician if this hearing loss is going to progress or if there's other symptoms that may emerge to watch out for, as well as how they might do with the treatment that you're prescribing or providing them. We have all that information. So, it can be really informative, and genetic testing for hearing loss is easier to order than it ever has been. Because of these comprehensive commercial hearing loss panels, and there's also academic dream panels as well, and there's also evidence, like I just mentioned, as represented in one of these papers up here, that clinicians can help the family and the patient have better expectations for how their cochlear implant, hearing aid, or the decided form of treatment is going to work, depending on the genetic diagnosis, if there is one. However, we're still not seeing a huge increase in ordering genetic testing. Thanks to EHDI and a lot of people in this room, we've gotten pretty good at identifying when there's hearing loss present. That's for sure, and that's wonderful and a huge accomplishment, but if you look at the bar graph next to me, and this is actually claims data that was presented last year at this conference, what you can see is that genetic testing, measured in these three-year periods, has just gone from 15 percent of kids getting junestic testing who have severe to profound hearing loss up to 16 percent of kids getting genetic testing who have hearing loss. So, that's not a huge increase, especially if we're seeing such mass increases in identification of these children. So, what's going on? Why aren't these, um, children receiving genetic testing? I'm guessing, I've had a lot of conversations, and you all probably have a couple of ideas from your own work that could be standing in the way, but what we wanted to do was, really, understand, with doing interviews, really what's going on in these different institutions. So, we did something a little unique, at least to my experience with market research, is we did it based on institutions. So, we looked at five different children's hospitals, and those are represented up there in gray, and at each Children's Hospital, we interviewed clinicians involved in that process. So, we interviewed pediatric otologists, pediatric audiologists, geneticists, and genetic counselors, all associated with each institution, so we could get that 3D view, what is the patient really experiencing. Along with the clinicians, we were able to interview some caregivers. So, we interviewed at least two caregivers from each institution or geographical location to further give us that 360 view, along with the clinician's perspective, and we were able to balance that by having half of the caregivers be folks that had accepted and ordered genetic testing for their child. The other half of them had decided not to, to defer genetic testing for their child. So, we'll refer to them as acceptors and deferrers in this context, just for ease of communication, and I also want to say that auditory insight, which is a, um, market research firm, are the ones who, um, conducted these interviews. So, they were independent and blinded and not conducted by Decibel, but we did help them create the interview guides and what they were asking. Important for this study, as you know, the patient journey can look quite different, depending on the severity of hearing loss and some other things that are going on, when they're identified, what type of treatment they pursue, things like that. So, we made sure that when we were conducting these interviews or creating the guides, to only focus on a certain type of patient, so we could get some really clear information. So, we decided to focus on severe to profound hearing loss. So, these are kids who do not have a syndromic hearing loss, and it's also bilateral and symmetrical. So, these are cochlear implant candidates. All right, so, when we're talking to clinicians, talking to caregivers, we're talking about this type of patient or child. All right, so, first, what we were able to do with these data from the interviews is take a nice look at the patient journey and, now, I wanted to preface this, saying we didn't go beyond cochlear implant decision and implantation, so, for this project, we really looked at from the newborn hearing screening diagnosis, all the way up to that CI eval and decision-making. We didn't go with yond that, so, that's what we're going to talk about here today, really, that decision-making process. As you can see, the genetic test journey is separate from the hearing loss journey and, that, we found pretty consistently across institutions, and that's because, after the newborn hearing screening, they follow-up with that hearing loss diagnosis appointment and an ENT work-up, at those appointments, 90 percent of the time, it's suggested, you should probably consider genetic testing. That's awesome. So, I wouldn't even have to be here right now, if that was the case, everyone gets genetic testing, we're good. However, 90 percent are suggested, but only 15 to 20 percent actually make it to thatgenetic testing work-up. So, what's happening within that time period? And that's what we're going to look into today. I know many folks in this room are deeply familiar with the patient journey and the activities that happen along this journey, so I won't belabor those, but we were able to get a clear picture of the influencers for each part of the journey, as well as the barriers experienced and, then, finally, I'm going to draw your attention to this at the bottom, is the timeline that these parents and caregivers were experiencing. So, let's zoom in on that timeline a little bit here. So, the newborn hearing screening and the diagnosis appointment happened relatively quick, and that's wonderful, and a lot of you are to thank for that and for this conference, so, we could celebrate this, yes, but as soon as that first ENT appointment starts, that's when we start seeing a lot of variability on when that appointment's actually happening and, then, the variability grows at the hearing aid trial, the caregiver making a decision to pursue cochlear implants and, remember, in this case, they do. Cochlear implant evaluation also has pretty wide timeline and variability and, then, that cochlear implant surgery happening, at least in the caregivers we talked to, at a maximum of 16 months post-diagnosis. Then, you see at the very bottom the timeline for genetic testing. What's interesting here is the caregivers that we interviewed, that accepted and ordered genetic testing, that decision happened pretty quick. You can see it happened around the same time the newborn hearing screening and the first diagnostic appointment is happening. So, let's just keep that in mind. However, to actually get the results, we see a lot more variability there, and that has to do with a lot of factors, and we'll talk about those as this presentation goes on, but I want to draw your eye to the six months average time that it took to get the results, and that, typically, is happening after the decision to pursue cochlear implants. So, these truly are two separate journeys happening at the same time, where the hearing loss journey is going on, they're deciding what to do as far as pursuing a cochlear implant or not and, then, the genetic testing journey is happening, and those might not converge, it depends on where they're being seen. All right, then I just wanted to quickly mention here that this, um, market research was done, or these interviews were done with parents who did not have children with ANSD, not part of the population, but, as we know, that diagnosis could potentially delay some of these, so, just want to keep that in mind, if they only get an OAE for their newborn hearing screen, they may not be caught, right, may not be detected early enough, and that might take longer, which

would then impact the entire timeline, um, as well as depending on what institution, what clinic you're in, um, there might be a wait-and-see method versus treating right away when you have auditory neuropathy, so, just wanted to mention that as far as this timeline's concerned. I also know that everyone in this room is familiar with emotions that the caregivers experience throughout the journey. So, that's depicted in our patient journey here from these interviews as well and, on the bottom, the gray shading represents the negative emotions and, on the top, the blue represents the positive emotions, and you might not be able to read them from where you're sitting, and that's fine, but what I wanted to point out was there's a lot of negative in the beginning, but, as you can see, as they're moving along the journey and receiving more information, speaking to more people, the positive emotions grow and, specifically, in that center column, looking at the genetic testing work-up, some of the positive emotions that can come from getting a genetic test, including acceptance of the diagnosis, that's what some parents said, as well as reassuring and empowering them to make the decisions. Then some even experience relief, and I know I said I was going to talk about barriers to genetic testing and, I promise, that's coming, one more slide. This, I thought was important to point out when we're thinking of influencers. So, the influencers that were brought up during these interviews were variable, but when thinking only about the clinicians here, and that's what I've put on this board, is the audiologists, they spend a lot of time with these families, and they were found to be the most influential provider to caregivers across this portion of the journey, and it has a lot to do with the amount of time they're spending with them. So, we want to keep in mind that the audiologists have a lot of informational power here. When it comes to delivering these recommendations to get genetic testing or what to do, so, we want to keep that, and I talk to a lot of audiology students, a lot of audiologists at this conference who I've heard the same thing, is that they have, they're trying to understand exactly what their role is in the genetic testing recommendation, and it's a big one. So, let's get into the barriers here. What did we find were the barriers that are really keeping patients with hearing loss from obtaining genetic testing results? So, the number one barrier identified by about 80 percent of interviewed clinicians and caregivers was the soft or no recommendation for the genetic testing. So, they're, often, mentioning genetic testing as an option, and they're rarely communicating the benefits of the genetic test, such as improving the clinician's ability to help care for the patient and family and select the proper treatment option, as well as providing those realistic expectations. So, barriers are also identified throughout the entire length of the journey, as you can see here. There's several in the decision-making process, as well as with the genetic test work-up. So, let's jump into a couple of these. Coming back to the soft to no recommendation from this otologist or audiologist, really, based on the caregiver recall, only 80 percent of the time, or 80 percent of the time, audiologists either didn't deliver a recommendation, or it was very soft and not really emphasized. So, the urgency that clinicians have when delivering this recommendation is very critical to whether the patient or the caregiver is actually going to pursue genetic testing or not, if it's up to them. The caregivers who did not pursue genetic testing were more likely to be in the group that didn't get recommended genetic testing from their audiologist, so, it's critical. So, the take-away here is the clinician sets the tone for this urgency. Another interesting part about this recommendation is that the caregivers were just as likely to ask about genetic testing as the otologists were to recommend it. So, it's not happening a lot in the otologist's office or, if it is, it's not memorable with all the other information they're getting at that time. So, otologists don't have a lot of time with their patients in a lot of clinical settings, therefore it's even more important that others in the hearing loss journey, such as audiologists, or others that are helping families along really work with the parents, so they know the benefits of getting genetic testing and understand the information that it could provide. Some other interesting tidbits that came out when discussing these conversations about genetic tests that were happening was that, majority of the time, it was presented as the caregiver's choice. So, this might make you feel better, this is an option, do with it what you want, that was a pretty common conversation. Coming up a little bit, or a lot less was, really, discussing the management benefits, how this could actually help me as a clinician work with your child with hearing loss and how it could help me give you the realistic expectations for how well this rehab or the treatment might work. Then, finally, in some cases, represented in the lightest color here, some clinicians came right out and said there are actual barriers to this, we don't, it may not be worth pursuing, so, they brought up it's not medically necessary or that insurance may not cover it, so, we'll talk about those in a moment. Half of the caregivers who didn't pursue genetic testing worried about knowing the genes that caused the hearing loss and worried about being to blame for the child's hearing loss. Therefore, if we're presenting genetic testing as the benefit is to find out the cause of the child's hearing loss, some folks are going to shut down, and that might not be enough to really let them know the information that they could gain from it and the positive benefits that they could get from genetic testing results. So, how it's positioned and how you discuss it might be as simple as presenting the benefits first versus talking about the cause, just because that might not always be appealing to the person you're talking to, and the benefits might be, and I'll get into that in a little bit, whether the deferrers really would have liked hearing about the benefits or whether it wouldn't have changed their mind at all. Half of the deferrers felt like they really didn't receive clear direction on the process for genetic testing, and one deferrer quoted here in the green box said I still don't even know what I would do, honestly, to get the ball rolling on that, if we wanted to. So, it was really not clear to them what that would entail, and that could be a huge part of it, especially if the clinician isn't understanding the process to genetic testing enough to explain it to the parent, it might be really difficult for the parent to pursue after that, finding out on their own, especially when they have so many other things to be working with with the hearing loss alone at that time, not to mention everything else that we do in life. Clinicians and caregivers both pointed out that there are long wait times for genetic counselor appointments, as well as for insurance authorization, and that is true as far as what we found with clinicians and caregivers. That happens to still be true in some institutions, depending on how it's organized, that wait time to actually get into genetics, even if the parents are fully ready to do it, might be months and, so, they might have to, again, the journeys separate, they do that on their own, if it happens at all. Similarly, insurance authorization can take time as well, and some institutions require it. So, these are, definitely, barriers, and they're harder barriers to overcome, these structural barriers, but it's good to be aware of as we're talking about how important it is to make the process clear to the parent. Now, some of the barriers, such as insurance denial, is brought up a lot, and it's actually not as high of a barrier as you might think, because, now, it is covered more than it has been in the past five, ten years. It only impacts about 10 percent or, in this study, it only impacted 10 percent of the parents. So, caregivers who got genetic testing for their child typically only paid, max, $300 out of pocket, which can still be a lot for families. However, compared to the thousands that some might be referencing in their mind when they talk about the expense of genetic testing, it's gotten a little bit more reasonable since then, and there are other options as well that I'll cover at the end of the presentation. So, it's worth rethinking some of the barriers that you might already have in your mind or that clinicians might already have in their mind about genetic testing and why or why not they recommend it or not, because things have changed a lot in that field. There were some barriers that the clinician said, oh, the caregivers will definitely mention this one, and it turned out not to come up during interviews with the caregivers. Not to mean that it doesn't impact other parents, and some parents might bring it up, but, in our cohort of caregivers, it didn't come up and, so, I thought it was important to point those out too as things you might just want to check. A blood test concern, now, we know that genetic testing now can be as simple as a cheek swab, but there are some clinicians that said I don't think the caregivers would necessarily want the blood test, so, that would, potentially, be a barrier that would come up. Similarly, regarding the medical record and if caregivers would be a little apprehensive about that, as well

as just core beliefs keeping them from getting genetic testing and, then, finally, some of them said, oh, they might just want to go home and discuss, discuss with other family members before pursuing. All of these items came up with clinicians, but did not come up with caregivers, so, it's worth having those discussions to really understand where their head is at, because, sometimes, assumptions just aren't matching up. One of the most important points that I want to get across here today is that the catalyst for two-thirds of these caregivers who actually accepted genetic testing were because it was going to help the clinician manage the treatment of their child. It's going to help them get clarity on the child's health for the present and, also, help them prepare for the future and the child's future needs. We then asked the caregivers who decided not to get genetic testing for their children, please rank all of these statements with what might have made you consider getting genetic testing for your child. Remember, over half of them didn't even get it acknowledged or they don't remember it being recommended to them at the initial appointment, but when they went through and ranked it, similarly to what I just said about the acceptors, the number one catalyst that they said would have helped them or would have caused them to rethink genetic testing and, maybe, consider getting it for their child was this management strategy. So, being able to say that this will help me manage your child's hearing loss, this will help me tailor treatment to your child would have gotten them to, maybe, consider it more than they had. Secondly, you see that making the process clear is also extremely important. It's more straight-forward now than it ever has been, with comprehensive gene panels, so, it's one test to understand what genes, if any, are associated with the hearing loss, so, that's an important one to make clear, and they said it was very important and, then, the turn-around time of three to four weeks. So, that was interesting to me, that parents are thinking about that, caregivers are thinking of when am I going to get this information. So, if they were able to be promised, oh, you'd receive these results in a month, sounds like some would have considered it. Finally, I mean, the second, or the third to last, the ENT and the audiologist just recommending it would have helped in a lot of these circumstances and, then, finally, at the bottom, which was surprising to me, is that the pay and the cost of the test came up at the end. That was something that was not as important as management, the process being clear, the clinician being onboard, and the turn-around time being quick. So, it's something to think about. So, like I said, in summary, there may be many barriers to genetic testing all across the patient journey, but if you take one thing away from this presentation today, it's that caregivers who get information highlighting the clinical evidence that shows the benefit of getting genetic testing for their child, so, predicting the future, they'll be more likely to pursue this route of obtaining more information about their child's hearing loss than if they hadn't been or if it was just presented as finding out the cause. Secondly, the second bullet, the simpler we can make this process for the parents, the more likely the clinicians are going to recommend it. If we make it complicated, the clinicians are going to hesitate to even offer it. So, there are a couple options, or many options, not a couple, um, for these comprehensive hearing loss panels now. In the green here, the academic panels, so, many different, um, universities have done excellent work to develop these comprehensive hearing loss panels, and they're available many different places, as well as at commercial panels. So, commercial companies typically can turn them around a little bit quicker and, then, we have sponsored programs up here, highlighted in blue. So, sponsored programs, such as ours, Decibel Therapeutics, can actually provide the genetic test at no cost, so, this reduces the barrier of cost. It also reduces the barrier of needing the insurance authorization, so, hopefully, reducing wait time. So, what this entails, Prevention Genetics is a company in Wisconsin, basically, we partnered up with them to cover the cost of the, um, genetic test for patients under 18 with auditory neuropathy, so, what this does is allows any clinician in the U.S. to order genetic testing for an eligible patient, so, auditory neuropathy, um, under the age of 18 is the criteria, and it's a cheek swab, sends it in, and 18 days on average, the clinician will get the result back and, just like normal, will be able to talk through it with the parent, and there is an optional genetic counseling component too that is completely covered by the program. So, if the clinician doesn't feel totally comfortable, um, with the results or even with ordering, they can contact a genetic counselor at no cost. Similarly, when there's a result, the parent or caregiver or patient can have a consultation via tele-health with a genetic counselor, so, they can discuss and be very comfortable with the results. So, this also takes the burden off of the clinician needing to deliver all of the information when they're also doing other things with the hearing loss or may not be experts in genetics. So, if you have other questions about amplify, we do have a booth here, so, feel free to come up. I love talking about it, so, feel free. We also have, should be in your bag, a flier, and we have a landing page as well online that has more information about the program. You can order kits at no charge. So, that is it. Thank you very much for listening today.

(Applause.)

>> SPEAKER: I'll take any questions, if you have any. I don't know how much time we have left.

>> SPEAKER: Curious about the survey. Did you survey any parents who may have had genetic testing done themselves? Or was that a part of the survey at all? And/or do you see parents that may want to test themselves ahead of time, what are their characteristics like, and do they do that usually before they have a child that's identified with hearing loss or, kind of, what's the characteristics there?

>> SPEAKER: That's a great question. For these particular interviews, we did not explore whether the parents had or not. That's a good, I think it's interesting, because it would be interesting to see if that was correlated with the ones that actually accepted it, and we also know that carrier testing is becoming more common, but we did not look into that in this project. It was, typically, at least from what the parents had said, they had not had experience before with genetic testing, so, I don't think carrier testing had been done, but we didn't explicitly ask. Mm-hmm?

>> SPEAKER: You said something about ANSD. I missed it.

>> SPEAKER: Yes, sorry, I went through that quickly. Auditory neuropathy spectrum disorder, so --

(Off mic.)

>> SPEAKER: Oh, sorry. For this program, the eligibility criteria is you have to have auditory neuropathy spectrum disorder or have a history of being diagnosed with it. So, perhaps, it's an older patient that hasn't been to the audiologist in a little while, if they're under 18 still and have a history of diagnosis, then they'd be eligible for this program, and this really came about because we have a, um, program for our gene therapy company, and our first program entering into the clinic this year is for children with otopharyndeficiency, and it presents with auditory neuropathy.

>> SPEAKER: This may be a question I should actually come by your booth to ask you, and I think I will come by there to follow-up, but my daughter is actually 11, and she had some genetic testing when she was a baby. Um, they did find some, I guess, some different genes that were abnormal, so to speak, but they weren't necessarily connected to any type of research or anything, and I know with as fast as the medical community is moving with different things, do you think that's something we should, probably, have done again? Because tests were seen to be, you know, inconclusive then. So, I mean, what would you say about that? And they also took, like, six to nine months for us to get results at that time.

>> SPEAKER: Yeah, no, that's a great question. You should definitely come to the booth and talk with us later. There's also geneticists at our booth that can help out, but, yes, overall, I would recommend, if they have not gotten genetic testing recently, like I said, there's several new panels or new genes that have been added to panels, so there could be new information you could gain from doing a genetic test now, if it was some time ago. So, just depends where you had it, how many genes were included. All of those companies I popped up here, you can usually find a list of genes that they encompass on their website, so if you had that information to compare as well, but, yes, they're changing all the time, so, it's definitely information to keep up-to-date on. Good question. All right, thank you so much.