

Tuesday, January 11, 2005
EHDI Ad Hoc Teleconference
2:00-3:00p EST

Edited Transcript

Jamie: Good afternoon, this is Jamie Elliott from CDC. I'd like to welcome you to this conference call. The call is entitled, *A multi-center evaluation of how many infants with permanent hearing loss pass two-stage OAE/A-ABR newborn hearing screening protocol*. I'd like to thank our speaker Karl White and everyone for calling in. I'd like you to mute your phone when you're not speaking to reduce background noise. If you don't have a mute button on your phone, I believe you can use star 6. And star 6 will un-mute you, also. So, if you need to put your phone on hold, please don't put it on hold. Instead, just hang up and simply call back. We have had a couple of instances where we have gotten music or messages while people have their phone on hold. So, I please ask that if you need to leave the call, simply hang up and call back in. There is a power point presentation available on the web that will accompany today's teleconference and that power point can be downloaded at www.infanthearing.org/checkpoint/2stagescreening.

Karl: Jamie, instead of downloading it, they can also just watch it on the web as the conference call proceeds.

Jamie: Excellent. So today's teleconference is being recorded, and the transcripts will be available on the website in about two weeks' time. As I said, the title is *A multi-center evaluation of how many infants with permanent hearing loss pass two-stage OAE and A-ABR newborn hearing screening protocol*. Again, please make sure your phones are on mute and don't put your phone on hold. And I'd like to introduce today's speaker, Karl White. Karl is the director of NCHAM which is the National Center on Hearing Assessment and Management at Utah State University where he is a professor of psychology. Dr. White has conducted numerous research projects and published extensively about the issues and evidence related to implementing and improving the efficacy of hearing detection and intervention program. He supervises NCHAM's activities related to provision of technical support and training to hospitals and state departments of health interested in implementing EHDI programs. With that I'm going to turn it over to Karl. And thank you for presenting for us today. Welcome to everyone.

Karl: Thank you. I'm delighted to be here, and to be able to present this on behalf of the larger team that actually conducted the study, and CDC, who was very involved in the study from the design phase through implementation and reporting. As Jamie mentioned, there are slides on the web that you can either download or follow as I go through it.

There are fairly complicated numbers being presented here and I think the PowerPoint slides will help you to follow that. In the bottom right hand corner of each of those PowerPoint slides is a number, and I will refer to those as I go through the presentation.

Slide number 1 indicates that the study is investigating how many infants with permanent hearing loss at about 9 months of age pass a newborn hearing screening protocol consisting of otoacoustic emissions and automated ABR, or as some people have referred to it, a little inappropriately, we're looking at whether babies with hearing loss are being missed with this protocol, and I explain later why that's a somewhat inappropriate depiction of the study.

Slide number 2 indicates that I'm presenting these results on behalf of a research team led by Dr. Jean Johnson at the University of Hawaii. The other co-investigators are listed on that slide, some of whom are probably on this call, and will be available to participate in the discussion later.

As shown in slide number 3, the study was funded by the Centers for Disease Control and Prevention, and the consultants from CDC listed there were actively involved in all phases of the project. We express our appreciation to them for their work. Funding came through a cooperative agreement with the Association for Teachers of Preventive Medicine to the University of Hawaii.

Slide number 4 indicates that the findings of this study have previously been presented at several different meetings, and has now just recently been accepted for publication in *Pediatrics*. I mention that in case some of you may have seen this presentation before. What I will present is very similar to what has been presented at those other meetings although there will be some very slight adjustments in some of the numbers.

As shown on slide number 5, the background for this study begins with the National Institutes of Health Consensus Development Panel on Early Identification of hearing Loss which met in March of 1993. After reviewing the evidence about the importance of and the methods for effective early identification of hearing loss, the panel recommended that the preferred model for screening should begin with an evoked otoacoustic emissions test and should be followed by an auditory brainstem response test for all those who failed the first test.

For several years after the panel reached that conclusion ABR technology continued to improve. This led to many hospitals in the U.S. implementing a variation of that recommended protocol that was based on automated ABR. In the mid to late 1980s, there were a number of anecdotal reports to the EHDI team at CDC that the two-stage OAE /automated ABR protocol for newborn hearing screening may be missing infants with mild hearing loss. As a consequence of those reports, CDC issued a competitive Request for Proposals in late 2000 to investigate this issue.

As shown on slide number 6, this Request for Proposals called for a research study to determine whether infants with permanent hearing loss when they were about 9 months of age would not be identified when newborn hearing screening was done using this two-stage protocol in which infants who failed the OAE, but pass the automated ABR, are not followed for subsequent diagnostic testing. The RFP specifically stated that a sample of infants should be recruited from existing screening programs, and that infants who failed the OAE but passed the A-ABR who normally would be considered to have normal hearing and would not be followed, that these infants should be assessed with visual reinforcement audiometry and other audiological assessments at between 8 and 12 months of age to determine their hearing status. Hearing status among this group of infants was also to be compared as shown on the graphic on slide number 6, to the hearing status of infants in the same birth cohort who had failed the OAE, and had also failed the A-ABR, and were consequently referred for an audiological evaluation.

As shown in slide number 7, the team assembled by the University of Hawaii for this study consisted of sites that had been operating successful newborn hearing screening programs using this two stage screening protocol for at least six months. Each of these sites had to have 2,000 or more births per year and to have a historical referral rate of less than 10% for their OAE, and less than 4% for their A-ABR screening. Sites also had to demonstrate that they had been successful in following up 90% or more of the referrals from their newborn hearing screening program in the past. The group of sites selected for this study using these criteria had ethnic and socio-economic characteristics similar to the U.S. population.

As shown on slide number 8, participating sites came from throughout the United States, ranging from Orlando, Florida, in the southeast to New York and Providence, Rhode Island, in the northeast, to Hawaii in the extreme west, and Ohio and Kansas in the Midwest.

Slide number 9 shows that in each of the participating hospitals, infants who failed the OAE and passed the A-ABR were considered to be eligible for participation in the study. Parents of these infants who spoke English or Spanish were contacted. The research study was explained and parents were invited to participate in the study. Those parents who agreed, provided written, informed consent and the study was approved by the IRBs in each of these hospitals as well as the University of Hawaii and the CDC. Parents also provided information about the family and demographic characteristics and information about the health of the infant. Contact was maintained with the family when the infant was approximately 2, 4, and 6 months of age by sending them a post card reminding them about the study and asking them to return a tear-off card with four or five short questions about the infant's developmental status. The post office provided us with address corrections in those cases where the families moved and left a forwarding address. At seven months of age, families were contacted and an appointment was made to conduct an audiologic diagnostic assessment of the infant. These assessments generally took place between 8 and 12 months of age.

Slide 10 lists the type of data collected for each child on the enrollment forms. As can be seen, information about most of the risk indicators specified by the Joint Committee on Infant Hearing for late onset or progressive hearing loss were included in these data.

Slide number 11 describes the study sample. 1,524 infants were enrolled, of whom 973, or approximately 64%, returned for a diagnostic evaluation. For a substantial number of those infants who were enrolled in the study only one ear met the study criteria, thus 1,432 ears were evaluated for the study.

Slide number 12 shows that the 7 participating sites enrolled infants from approximately May 1, 2001, through January 31, 2003. A total of 86,634 infants were born at these hospitals during the enrollment period as shown in the last row of that table. Most hospitals enrolled infants from both the well baby nursery and the neonatal intensive care unit, although hospitals 3 and 4 only enrolled infants from the well baby nursery, as shown here. During the time that infants were enrolled in the study, the participating hospitals averaged a 4.8% referral rate for otoacoustic emissions and 1.0% referral rate for automated ABRs.

As shown on slide number 13, of the 3,462 families circled in red at the bottom who were eligible, only about 2700 were approached about being enrolled. 1,524 of those enrolled, and 1,154 were asked but declined to enroll. An additional 784 eligible parents were not approached because of staff shortages at the hospital, or other scheduling and administrative issues or because they didn't speak English or Spanish. The fact that only 44% of the eligible infants, i.e., those who had failed the OAE but passed the A-ABR, were actually enrolled in the study, should be remembered, because this is important for interpreting the results to be presented in just a moment.

Slide number 14 outlines the audiological diagnostic evaluation procedures that were completed with infants when they were invited back for an audiological diagnostic evaluation at an average age of 9.3 months. As can be seen, this evaluation consisted of at least visual reinforcement audiometry, tympanometry and otoacoustic emissions.

The protocol for the audiological diagnostic evaluation as shown in slide 15, was based on one developed by the University of Washington for a large multi-center study funded by NIH in the early 1990s and reported in 2000 in the journal *Ear and Hearing*. The goal of the diagnostic

evaluation for our study infants was to collect minimal response levels of 15dB HL at 500, 1, 2 and 4 kilohertz. Approximately 32% of the infants for whom diagnostic data were obtained required more than one visit to complete this protocol.

Slide number 16 shows the criteria developed by the research team for categorizing the hearing status of each child based on the results of the audiological evaluation. Although I don't have time to discuss these criteria in detail, a couple of brief examples will be useful in interpreting the results. Let's look at the first row in that table, "not permanent hearing loss". We used that term instead of "normal hearing" although it's a bit cumbersome to say, because we were only looking in this study for children with permanent hearing loss. So an infant was considered to "not have permanent hearing loss" if using the best results from all assessments, minimal response level thresholds of less than or equal to 20dB were obtained at 1, 2, and 4 kilohertz. It will be noted that 500 hertz was excluded from the definition we used to determine hearing loss. Further, an infant would be classified as "not having permanent hearing loss" if the minimal response level was below 20dB at 1K during the first testing session but 2 and 4K couldn't be tested or were above that level, and it was below 20dB at 2 and 4K during a second or third session. In other words, we used the best response across sessions.

For a second example, look at the third row labeled "permanent hearing loss." An infant was considered to have permanent hearing loss if minimal response levels were greater than or equal to 25dB at 1, 2, or 4K, if VRA at those frequencies with the elevated thresholds was done with good confidence. In a few cases VRA data were not available but ABR data were. In these cases, thresholds needed to be greater than or equal to 30dB for us to consider the infant to have a permanent hearing loss. With either VRA and ABR data, to be classified as permanent hearing loss, the infant had to have OAEs that were consistent with normal hearing at the frequency with elevated MRLs and had to have normal middle ear functioning based on tympanometry or to have elevated thresholds using bone conduction. The definition we used for OAEs to be "consistent with normal hearing" was a signal to noise ratio greater than or equal to 3 dB at 1K, and greater than or equal to 6dB at 2 and 4K.

Now turn to slide 17. These are some examples of how those criteria were applied. I won't go through all of these, but again, a few examples will probably be helpful. For example, the first row on this slide, circled in yellow, shows an infant's ear categorized as not having permanent hearing loss. During the first test we were unable to obtain VRA responses for the ear as indicated by the Ds or "did not test," in the spaces for 500, 1, 2, and 4k. But OAEs were obtained, and those were greater than or equal to 6dB at 2 and 4k. As defined by the legend at the bottom of this page, tympanometry results were questionable during the first assessment.

During the second assessment, minimum response thresholds of 15dB were obtained at all four frequencies. The quality of the testing was good. Tympanometry results were normal. OAEs of greater than or equal to 6dB were obtained at 1, 2, and 4K. Thus, this ear was categorized as not having a permanent hearing loss.

Now, look at the ear in the third row; circled in blue, which was categorized as having a permanent sensorineural hearing loss. At the first assessment, minimum response thresholds of 30, 30, and 45dB at 1, 2, and 4K, respectively were obtained for VRA testing which was done with good confidence. Tympanometry was normal and the OAE results were less than 3dB at 1, 2, and 4K. Thus, the first assessment met our definition of permanent hearing loss. However, this infant, as was the case with almost all infants categorized in the study as having permanent hearing loss, was tested a second time to confirm the results. The minimal response levels at 1, 2, and 4K as indicated in the center of that graph, under assessment 2, were still elevated. The quality of this assessment

was good at only 2 and 4k, tympanometry results were normal again. But the OAE signal to noise ratio was greater than or equal to 6 at 1 and 2k. Thus, we classified this ear as having a permanent hearing loss only at 4K since the OAE results were inconsistent with the minimum response levels obtained with VRA.

Finally, in the next row under the blue circle, you see results for an ear labeled as high suspicion. This ear had elevated thresholds at 1, 2, and 4K during the first assessment period, but tympanometry results were abnormal, meaning those elevated thresholds could be due to otitis media. During a second test session in the middle of the graph, minimum response levels were still elevated at 1, 2 and 4K, but the quality of the assessment was good only at 2 and 4K. Tympanometry was normal and otoacoustic emissions were less than or equal to 3dB at 1, 2 and 4K. At this point it could be argued that this infant should be categorized as having a permanent hearing loss.

However, we did one more test and during this final test session the tympanometry results were questionable, but the infant had otoacoustic emissions of greater than or equal to 6dB signal to noise ratio at 1, 2 and 4K. Thus, the otoacoustic emissions were inconsistent with a designation of permanent hearing loss so we placed this infant in a high suspicion category. Even though several attempts were made to get the parents to come back for a fourth assessment which would have been the most desirable outcome, the parents did not return. Because of conflicting information between visual reinforcement audiometry and the otoacoustic emissions, we chose to put this infant in a high suspicion category instead of classifying it as permanent hearing loss. It could be argued this definition of permanent hearing loss is too restrictive. More will be said about this in a few moments.

Slide number 18 shows the results of our categorization using the above definitions of the 973 infants who returned for diagnostic audiological assessment. As can be seen, 79.6% of the 1,432, ears were categorized as not permanent hearing loss with an additional 7% categorized as probably not permanent hearing loss. As shown in the red circle, 30 ears from 21 infants were categorized as having permanent hearing loss, and an additional 19 ears from 16 infants were categorized as having high suspicion of permanent hearing loss. 8% of the infants did not have enough diagnostic evaluation data to make a determination. It's also important to note that only 63.8% of the infants in the study group returned for diagnostic evaluation. Thus, we do not know the hearing status for 36.2% of the infants in the group who were recruited to participate in the study.

Slide number 19 lists questions that should be considered to help us decide about the significance of having 21 infants with permanent hearing loss fail the otoacoustic emissions but pass the automated ABR.

- First, how many infants were identified with permanent hearing loss in addition to those who would have been identified otherwise based on failing the OAE and failing the A-ABR? In other words, how many infants with permanent hearing loss were identified in the comparison group.
- Second, because quite a number of infants qualified to be in the study group because one of their ears passed the initial OAE, and the other ear failed the OAE, and subsequently passed an A-ABR, a substantial number of infants returned for diagnostic evaluations that had passed the initial screening test in one ear. The number of initial passed ears who were categorized as having a permanent hearing loss during the diagnostic assessment provides an important reference point for interpreting the significance of the ears found with permanent hearing loss among those that failed the initial OAE but passed the A-ABR

- Third, from a practical point of view it's important to know how many additional infants we'd need to follow over and above those referred from the two stage screening protocol in order to find this many infants with permanent hearing loss.
- And finally, it's important to consider how many of these 21 infants were likely to have had congenital versus late-onset hearing loss.

Slide number 20 defines the comparison group used in answering the first question. There were 704 infants who failed OAE and failed A-ABR from the same birth cohort. 604 of those infants had enough diagnostic evaluation data to make a determination about their hearing loss.

Slide number 21 shows that of the 604 infants evaluated, 158 children with 204 ears were diagnosed as having permanent hearing loss. This represents a prevalence of 1.82 per thousand in this birth cohort. Remember though this prevalence is probably a little lower than in a general population cohort, because two of the 7 hospitals only recruited infants from the well baby nursery. Consequently, in the data reported here, only infants from the well baby nursery are reported from those two hospitals.

To keep this information in context, Slide #22 is a repeat of a slide shown earlier, which reminds us that in the study group to which these babies are being compared, we identified 21 babies and 30 ears with permanent hearing loss.

Slide number 23 shows the data from both the comparison group, in other words, those who failed the OAE and failed the A-ABR; and the study group, those who failed the OAE but passed the A-ABR. As can be seen here, the prevalence for all hearing loss in this birth cohort of 86,000 plus babies was 2.06 per thousand. 1.82 per thousand from the comparison group and .24 per thousand from the study group. In other words, the 21 infants in the study group represent about 12% of all permanent hearing loss identified in this group of 86,000 infants.

As shown in slide number 24, 71.4% of the infants with permanent hearing loss in the study group had mild hearing loss (i.e., less than 40dB pure tone average), whereas only 19.6% of the infants with permanent hearing loss in the comparison group had mild hearing loss. This is consistent with concerns that led CDC to fund this study in the first place. Specifically, that infants with mild hearing loss, might not be identified with the OAE/A-ABR protocol. In contrast, infants with moderate to profound hearing loss represent only 28.6% of the study group, but 80.3% of the permanent hearing loss in the comparison group.

Another useful reference point for interpreting the results is shown in slide number 25. These are the data from the infants that had one ear that passed the initial OAE screening in the hospital but who received diagnostic evaluation at 8 to 12 months of age because their other ear was in the study group. If a significant number of these babies had been identified with permanent hearing loss, it would cause us to question the significance of the results that I have just presented to you. However, as you can see in Slide 25, none of the ears of babies who passed the initial screening were identified with permanent hearing loss. You will note that this group has a larger percentage of the babies for whom we did not have sufficient data, as shown in the last column in that slide. That happened because when those babies came back, since the testers knew that the other ear was not in the study, they didn't make as much effort to complete the protocol for the ear. But for the 375 ears for which we did have complete data, there were none identified with permanent hearing loss.

Slide number 26 asks the question: How many babies must be screened to find 21 with permanent hearing loss? Well, the obvious answer is 973, the number of babies who completed the diagnostic

evaluations in this study. However, the practical interpretation and application of these data are not quite that simple. If we were interested in following infants who did not pass the OAE, we would probably do a second-stage OAE shortly after the infant left the hospital.

Most programs report that such a second-stage OAE screening reduces the number of infants who need diagnostic evaluations. In other words, we would expect about 90% of these 973 infants to pass a second-stage screen. Such outpatient screening is substantially less expensive than the diagnostic protocol used in this study. On the other hand, it should be noted that such a two-stage OAE screening program, using both inpatient and outpatient screening, often results in substantial loss to follow-up. One of the primary advantages of the OAE/A-ABR two-stage protocol in the hospital is a reduction in the number of infants who need to be followed for further screening. If the prevalence of permanent hearing loss is about 3 per thousand in the general population, one would expect a prevalence of about 3 per hundred in the population of infants needing outpatient screening following an initial OAE screening test.

Thus, if loss to follow-up is likely to be high, a substantial number of infants with permanent hearing loss would probably not be identified following that initial OAE screen, because they did not return for an outpatient screening. Thus, even if we conclude that a two-stage OAE fail A-ABR pass protocol is not identifying some infants with mild hearing loss; we must keep in mind the probability of losing infants to follow-up and thus not identifying all degrees of hearing loss if a protocol consisting of inpatient and outpatient OAE screening were to be used. Such issues must be considered before deciding which protocol is most sensible for a particular hospital.

Another very important question as shown on Slide 27 is, “How many of the ears that were not identified by the two-stage protocol were congenital losses and how many were late-onset losses?”

This study wasn't designed to answer that question. So the short answer is: “We don't know for sure.” However, we can estimate based on the data we have. We do know that if we had successfully followed all of the infants in the fail OAE/pass A-ABR group, who had risk factors for late onset or progressive hearing loss, only 9 of the 21 infants would have been identified. Although these risk indicators have been identified by the Joint Committee on Infant Hearing as being predictive of late onset or progressive hearing loss, we actually know relatively little about how efficacious those indicators really are, nor do we have definitive data about the incidence of late onset loss even though it is clear that some late-onset hearing loss exists. Most of the hearing losses in the study group that were identified were mild which is what would have been expected if the two-stage OAE/A-ABR screening protocol were missing congenital hearing loss. Thus, it is likely that some congenital hearing loss is not being identified by this protocol, but we can't say with certainty exactly how many of the 21 infants were congenital, and how many were late-onset.

Slide 28 poses the question, “Based on the information available in this study, what's the best estimate of the number of infants with permanent hearing loss at about 9 months of age who would fail OAE and pass A-ABR screening prior to discharge from the hospital? Three issues should be considered in making this estimate.

- First, how lenient or strict a criteria is used for determining whether a child has permanent hearing loss.
- Second, because there was a great deal of variation between sites in terms of number of babies identified, we must consider whether all sites should be weighted equally in making this estimate.
- Finally, there are some important demographic characteristics of the study group and the comparison group that may warrant adjustments in making the “best” estimate.

Look at this data in slide number 29 which was shown earlier to remind yourself that there were 21 infants with 30 ears that failed OAE and passed ABR, and were determined to have a permanent hearing loss when they returned for audiological assessment between 8 and 12 months of age. There were also 19 ears from 16 infants who were at high increased suspicion for permanent hearing loss, but did not meet our strict criteria for permanent hearing loss.

Now, as shown in slide number 30, if we include only those infants who met the study's strict definition of permanent hearing loss, there is a prevalence of 1.82 infants per thousand with permanent hearing loss in the comparison group, and an additional .24 infants per thousand that were added to this by including those infants from the group that failed OAE and passed A-ABR. Thus, the total prevalence of hearing loss in this cohort of infants was 2.06 per thousand when this strict definition was used.

It could be argued that our definition of hearing loss was too strict. Certainly those infants who were at high increased suspicion of hearing loss were not hearing normally at the time of the audiological assessment. For example as shown earlier, these infants would typically have elevated minimum response levels of 25 to 35dB, but the quality of testing was only fair and/or there was data from the otoacoustic emission testing at the frequencies with elevated thresholds that were consistent with normal hearing. Given conflicting information from the VRA testing and the results of the OAE testing, our team was not confident enough to categorize these children as having permanent hearing loss. Ideally we would have liked to have had these children return again for additional testing and many efforts were made to do that but we weren't successful. If those children who were at high increased suspicion had been included, the prevalence of hearing loss in the group of children that failed OAE but passed A-ABR would have been increased from .24 per thousand to .43 per thousand. In other word it would have almost doubled.

However as shown in slide 30, we don't believe the data are strong enough to justify inclusion of these infants in the group determined to have permanent hearing loss and so have not included them. But we want to be complete in the data that are presented here.

Next, slide 31 raises an important issue related to variation of outcomes among sites. In conducting such a study, we assume that study procedures were equally well implemented at all of the sites. To the degree that this is not true, data from some sites may be a better estimate than are data from other sites about whether infants with hearing loss could fail the OAE but pass the A-ABR.

Slide number 32 provides information to examine this question. We looked at 4 variables related to the quality of implementation of the research procedures shown in the last four columns on the right.

Those data are percent of eligible infants enrolled, percent of refusals during the recruitment process, percent of infants enrolled who returned for a diagnostic evaluation, and percent of infants with a diagnostic evaluation for whom there was insufficient data to categorize the infant as to his or her hearing status. As you can see, there was substantial variation for each of these variables across the 7 sites. For example, the percent of eligible infants who were enrolled ranged from 18.3% in site 1 to 87.9% in site 2.

As shown by the red circles, site 2 was the best implemented site with respect to the high percentage of eligible infants that were enrolled and that returned for diagnostic evaluations, and that had a very low percentage of infants for whom there was insufficient data to make a categorization. Site 3 had the lowest percentage of infants who refused during the enrollment

process. Using these criteria, we see that sites 2 and 4, which are the sites that identified most of the infants with PHL, were the two best implemented sites.

Slide number 33 shows information about the comparability of the study group and the comparison group. With respect to demographic variables, because the infants in the study group and the comparison group came from the same hospitals during the same time period, we would expect them to be similar with respect to variables such as ethnicity, family composition, income and type of insurance coverage... and indeed, they are. However, there are two other variables that could substantially affect our estimate of prevalence of permanent hearing loss on which the study group and the comparison group were quite different.

- First in the study group, only 44% of the infants who failed the OAE and passed the A-ABR were recruited for the study, and consequently, invited to return for a diagnostic assessment at 8 to 12 months of age. Thus, our estimated prevalence for the study group is based on only 44% of the population. But in the comparison group, the prevalence is based on 100% of the infants who failed the OAE and failed the A-ABR, and were asked to come back for a diagnostic evaluation.
- Secondly, there were different levels of success in getting those two groups of infants to come back. In the study group, only 64% of the infants who were asked to return for a diagnostic evaluation actually returned. Whereas in the comparison group, about 87% of the infants who failed the OAE and failed the A-ABR, returned for a diagnostic evaluation. The obvious question is how these differences affected estimates of the prevalence of permanent hearing loss.

In our opinion, it is essential to adjust for the fact that we only tried to do assessments on 44% of the infants in the study group. Had 100% of the eligible infants been recruited for the study, it is almost certain that additional infants with permanent hearing loss would have been identified. Furthermore, there is no reason to believe that parents of infants who were not invited to participate in the study were any different than those who were invited, and little reason to think that the prevalence of hearing loss would be lower among infants of parents who declined to participate in the study than among those who agreed to participate.

However, the likely consequence of having a substantially different percentage of infants who completed the diagnostic evaluation in the two groups is less clear. Sixty-four percent of the infants in the study group and 87% of the infants in the comparison group returned for diagnostic evaluation. So even though 23% more parents returned for diagnostic evaluation in the comparison group than in the study group, we think it's impossible to say why this happened. It may be that families who think their child has a hearing loss are much more likely to return. If that happened, there would be a higher incidence of hearing loss among those who returned than there was among those who did not return. Parents in the comparison group had also received much more definitive information at the time their infant left the hospital about the fact that their child had failed a hearing screening and needed to come back for a diagnostic evaluation. Perhaps that is why a higher percentage came back. Parents in the study group, however, were told that their infant had passed the screening but they were invited to participate in a research study to improve screening procedures. Thus parents in the comparison group could easily have been more motivated to return, independent of whether their child had hearing loss or not.

Other factors could have contributed to a much lower incidence of hearing loss among those who returned than among those who did not return. For example, the factors contributing to low follow-up rates may be the same factors that increase the risk of an infant having a hearing loss. For example, it could be argued that families who are poor, have single heads of household, are

transient, or have poor health are less likely to return for an evaluation appointment and also more likely to have an infant with hearing loss. To the degree this is true; you'd expect the estimated prevalence of permanent hearing loss to be artificially low in the group that had a lower return rate. Clearly the study group had a lower rate of completed diagnostic evaluations than the comparison group. However, because some variables associated with a lower return rate would most likely lead to an **overestimate** of hearing loss, and some variables would most likely lead to an **underestimate** of hearing loss, we chose not to make any adjustments for these differences between the groups.

Slide 34 summarizes these data. If we base the estimate of how many infants with hearing loss will fail the OAE but pass the A-ABR only on the sites with the best implementation, versus basing it on all sites, there are not dramatic differences as you can see. Basing the estimate only on the 44% who chose to participate, however, results in a substantially lower estimate than if we adjust for what it would have been had we attempted to follow all eligible infants. In our opinion, the best estimate is that 23% of children with permanent hearing loss at 9 months of age would fail the OAE but pass the A-ABR. In other words, adjusting the estimate to what it would have been had 100% of the eligible families been recruited raises the estimate of the percentage of “missed” children from 12% to 23% for all sites, and from 17% to 23% for the “best sites.”

Slide 35 lists the principal conclusions from the study. The data show that a substantial number of babies diagnosed with permanent hearing loss at 9 months of age **will pass** a two-stage OAE/A-ABR protocol. The best estimate is that this will be about .55 babies per thousand, or 23%, of all babies with permanent hearing loss. Most of these babies are babies with mild sensorineural hearing loss, and it's impossible to determine exactly how many of these babies are congenital versus late-onset. However, about 45% of those babies would be identified if all of the babies with risk factors were successfully followed.

Slide 36 shows the recommendations for practice based on the data from the study:

- First, screening for permanent hearing loss should extend into early childhood programs.
- Second, regardless of the screening protocol used for newborn hearing screening, because of loss to follow-up or because some babies may be missed, it's important to continue to do hearing screening in physician offices, early childhood programs, et cetera.
- The data also emphasized the importance of pointing out to families and physicians that passing a hospital-based hearing screening does not eliminate the need to monitor hearing and language development.
- A particularly important implication of these data is that screening program administrators need to be sure that the stimulus levels of equipment being used in the screening program are consistent with the degree of hearing loss they want to identify. In this study, the automated ABR screening equipment used a 35dB click. Thus, we should not be surprised that children who have mild hearing loss would pass that ABR, and consequently not be followed. Unfortunately, this fact may not be understood by many program administrators
- We need to continue to remember the relative advantages and disadvantages of a two-stage screening protocol versus an inpatient outpatient screening protocol in which loss to follow-up becomes a much more significant issue.

Finally, as shown in slide 37, there are a number of issues which still need to be addressed by further research. For example, this study points out the need to continue to examine issues related to late-onset hearing loss so that we have a better way of estimating which babies are congenital versus those that are late-onset. It also points to the need of continuing investigation for various screening protocols, and making sure that the levels of hearing loss that we are targeting with our screening equipment are consistent with what we would like to identify in the screening program. And finally, there is a need for additional work to identify the practicality and cost efficiency of

alternative techniques for continuous screening of infants and young children, be that in healthcare providers' offices, early childhood programs, or other settings.

I'd be happy to respond to questions.

Vicki Thomson: This is Vicki from Colorado. Karl, can we assume that when you talk about your protocol, the OAE/A-ABR, that this is prior to hospital discharge --- Instead of a two-stage screening consisting of inpatient screening followed by outpatient screening?

Karl: Absolutely. The study group was done in-hospital, with both the OAE and the A-ABR screening done prior to discharge.

Vicki: Okay, and not that this would be appropriate for this conference call, but are you able, through the different sites, to identify the manufacturers of the A-ABR used in your study? The reason I ask is that we have one particular piece of equipment here in Colorado that passed 4 complete atretic ears. So, we have some real concerns that some of the manufacturers may have lowered their sensitivity rate and are definitely missing some hearing losses. So I was just wondering if your research would be able to look at the differences between manufacturers.

Karl: Actually, this study cannot compare differences between A-ABR manufacturers, because all of the A-ABR units in this study were from the same manufacturer. In the *Pediatrics* article that has been accepted for publication, we were required to state the manufacturers of the equipment used so I have no problem discussing it on this call. For A-ABR, it was the Natus equipment, and the TEOAE equipment was a combination of Oto-dynamics and Bio-logic equipment. Some of the Oto-dynamics was the Echocheck, some was the ILO88 equipment. However, the study was not designed in a way that allows us to make any statements about differences between types of OAE equipment

I would like to point out that when the Natus equipment was developed, people were not very concerned about identifying mild hearing loss. The fact that Natus set their click stimulus at 35dB certainly has some implications for whether you will identify babies with mild hearing loss.

Unrelated to the type of equipment used in this study is the fact that as more and more manufacturers get into the business with what are essentially "black box" kinds of systems, you raise a very important issue. That was the focus of our second recommendation for research --- specifically, that there's an urgent need to look at what the consequences on identification rates of having different stimulus levels.

Vicki: Great, that's wonderful. Thank you. Another thing, even though it would require much research money, it would be fabulous to know for this cohort of children with mild hearing loss, what are the early intervention outcomes and what the audiologists at these particular sites are doing in terms of fitting with amplification. Clearly it would require another research study, but it would be interesting so thank you to your group.

Karl: I agree completely.

This is [inaudible] from Michigan. Do you have information about the etiology of the hearing loss? Do you find more auditory neuropathy babies for the ones that have passed OAEs but then failed the ABRs?

Karl: None of the babies in this group of 21 babies were diagnosed as having auditory neuropathy. Beyond that, even though we have a fair amount of correlational data, as you saw in those first few slides, we couldn't find any patterns that would say certain types of babies fall into this group versus that group. Furthermore we don't have genetic studies on these babies, which would probably be much more powerful data for determining etiology.

Judy: Karl, this is Judy Widen.

Karl: Hey Judy, thanks for joining us!

Judy: May I add to your answer to her question? By definition, none of the babies in our study could have had auditory neuropathy since a baby with auditory neuropathy would have passed OAE and failed an ABR and by definition all of our babies failed OAE and passed the ABR. So we wouldn't have had a chance to pick up auditory neuropathy.

Jamie: Are there any more questions for our presenter?

Yvonne Sininger: This is Yvonne Sininger from UCLA. I had a follow-up on the issue of auditory neuropathy. If your purpose Karl was to evaluate this protocol, then it would seem to me to be appropriate to follow, also, those infants who had passed an OAE initially who never got to the ABR stage. And in fact, when we did that earlier in the study led by Susan Norton where we did OAEs and ABRs on all the babies and followed all of them, we found also there would be infants that would be missed by OAE. In other words ABR and OAE had an equal sensitivity and specificity. As Judy just mentioned by only looking at those infants who failed an OAE and then passed an ABR, you've automatically not followed any of the infants that probably had auditory neuropathy. And so I'm wondering why those -- the babies who passed the OAE were not followed, as well.

Karl: I'm really glad you raised that issue, Yvonne, because it may prevent people from misinterpreting the results of this study. This study does not even address the question of whether babies are missed with OAE. It begins to address the question of whether babies are missed with the two-stage protocol, but even that is not quite right, because we can't say for sure how many of the babies with hearing loss at 9 months of age were congenital versus how many were late-onset. The reason why the babies who passed the initial OAE were not followed was because this study was a response to a specific question in a specific RFP issued by CDC, which specified which babies were to be followed. I can only conjecture why they did it that way, but I suspect it was because of limited resources. And so this is one study in what should be an ongoing series of studies to examine exactly the kinds of questions you raised, so that we'll have more complete understanding of what happens with all of these screening techniques.

Yvonne: Right, and simply suggesting, though, that a two-stage OAE screening protocol might be an answer to this. I'm concerned a little bit, Karl, that in your definition of "permanent hearing loss" you include the term "absent OAE," and that again is going to take a large number of children who we know have hearing loss with a present OAE out of the mix. I think it's important that we not make the assumption that the presence of an OAE is the same as normal hearing, or the absence of a permanent hearing loss, because we do know that that situation can exist and I don't think it was tested very carefully in this study.

Karl: Yes, you are right and I'm glad you raise those issues, and those questions were not tested at all in this study. If something I said gave the impression that the team is recommending a two-stage OAE screening protocol instead of the OAE/A-ABR protocol, that's definitely not the case.

I used the two-stage OAE screening protocol as an example to show how, because of loss to follow-up, you could lose, or miss, as many babies as were “missed” in this study. I don't think we know what the best protocol is and my personal opinion is that the best protocol will be different, depending on the organization of the hospital and the demographics of the people they're serving. And so we need additional research to answer the kinds of questions you raised, but even right now we need to be very thoughtful about how we implement protocols and consider how successful we are in getting babies to return for follow-up evaluations, what level of hearing loss we want to identify, etc. Although I don't personally agree with them some people are not concerned about identifying a baby with a 25 decibel hearing loss. And so, if a hospital administration makes that decision, then they don't need to be concerned about the babies who are being missed with this protocol.

Yvonne: How many of these infants you identified were unilaterals?

Karl: Judy, do you remember off the top of your head?

Judy: 9 is my guess.

Yvonne: 9 of the 21 or so are mild unilateral hearing loss?

Karl: Yes, there were 30 ears and 21 babies so that gives you the answer, doesn't it?

Judy: It doesn't quite, and I can't quite remember either. It's not obvious, I can tell you.

Karl: I can count them up in a second.

Yvonne: So I guess that leads me to a question. Having sat on the Joint Committee in Infant Hearing we gnashed our teeth over what the definition of the target disorder was. Do we go for unilateral? Do we go for mild or moderate? And definitely there were many discussions along this line, of what is the target disorder? I don't think you'll get consensus at this point that mild unilateral should be part of our target disorder, only because of the costs that are involved. Not because of concern about those children, but simply because of the tradeoffs and the high false positives that would come into place if we began to try to identify hearing loss at 20 or 25dB so those things all need to be considered I think in these discussions.

Karl: Absolutely, and I think this is important to put this study in context, that this is one piece of additional information that we didn't have before that is useful but it doesn't answer all of those questions. And there are another dozen studies that need to be done to begin to answer those.

Vicki: This is Vicki again, I don't have to tell you Karl because you've been at the thrust of this from the beginning, but I would be cautious when this is published in the American Academy of Pediatrics journal; that physicians don't see that “Oops, we missed 21 babies.” And then conclude that these newborn hearing screening programs weren't effective. We worked so hard to try to get this across to the pediatricians.

Karl: Right, and I hope we phrased it well.. By the way, I just counted and there are 12 babies with unilateral loss, 9 with bilateral.

Yvonne: 12 unilaterals, those are mild unilaterals that might have been at 1 or 2 frequencies?

Karl: In the *Pediatrics* article there is a table that shows the details. I can send you a draft of it if you'd like. They weren't all mild ... I think there was one profound and one severe, most of them were unilaterals.

Yvonne: I'm still just concerned, as Vicki is, that using a 35dB stimulus which won't generally catch a mild hearing loss, we know that already, that it was sort of a foregone conclusion that mild loss would not be captured by that ABR and that stimulus, and so it's not surprising that there are some that got through.

Karl: No, I'm not surprised at all by it, but I wouldn't agree that it was foregone conclusion among everyone responsible for operating newborn hearing screening programs. I think these are issues that many program administrators don't consider as carefully as they should. Also, there's a whole body of research showing that once a research study is completed, then everybody looks at it and says well, I knew that already --- but they didn't know it before the study was done.

Yvonne: But the stimulus levels related to what you can identify in an ABR and you can't find a 20dB hearing loss with a 35dB stimulus. That's well established.

Karl: Well, if you talk to the people who are selling the ABR equipment and that's the basis on which many of the administrators are making these decisions I don't think it's all that clear. Many of them claim to be able to pick up mild hearing losses; we can argue about why that's done, but I don't think this finding was obvious to everybody when the study started or else the study wouldn't have been done.

Jamie: I want to thank you Karl for presenting to us today and to your team also and the project you've done. We enjoyed having you, and thank you all for calling in.

Karl: Thank you for the opportunity.

[End of call]