The Voice of the Patient

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Childhood Cancer Hearing Loss

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Collaborators: Children's Cause for Cancer Advocacy, Children's Brain Tumor Foundation, Mattie Miracle Cancer Foundation, Momcology

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The report has not been modified since April 2019. Children's Cause has necessary permissions to submit the report and link to the report from the FDA's website.

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TABLE OF CONTENTS

TABLE OF CONTENTS, continued

Introduction

On September 13, 2018, four advocacy organizations - Children's Cause for Cancer Advocacy, Children's Brain Tumor Foundation, Mattie Miracle Cancer Foundation, and Momcology - hosted an Externally-Led Patient-Focused Drug Development (EL-PFDD) meeting to share with senior officials at the U.S. Food and Drug Administration and other chemotherapy-induced pediatric hearing loss stakeholders (e.g. families, caregivers, and individuals with hearing loss, as well as industry and research institutions) the perspectives of people living with chemotherapy-induced hearing loss, its impact on their daily lives, and their expectations and priorities for current and future treatments for the condition. The meeting was conducted in accordance with the agency's Externally-Led Patient-Focused Drug Development initiative to more systemically gather patients' perspectives on their conditions, and available therapies and treatments. In addition, the recently passed 21st Century Cures Act has emphasized the importance of patient input in the regulatory process, mandating that regulators learn about which outcome measures matter to patients and to consider how patients weigh the balance of risks and benefits of a particular treatment.

More information on the FDA's PFDD meetings can be found at: https://www.fda.gov/industry/prescription-drug-user-fee-amendments/fda-led-patient-focused-drug-development-pfdd-public-meetings

Overview of chemotherapy-induced hearing loss

It is estimated that by 2020 there will be over half a million long-term survivors of childhood cancer in the U.S. Approximately 1/3 or greater can expect at least one life-threatening late effect as a result of their previous cancer treatments. One of these late effects includes varying degrees of permanent hearing loss.

Certain cancer medications and therapies, namely platinum-based chemotherapy drugs, cisplatin and carboplatin, and cranial radiation that involves the inner ear, are ototoxic, with the potential to cause damage to the inner ear that result in hearing loss, tinnitus and balance reduction.

Approximately one third of children with cancer will receive a platinum analog as their first or second line treatment. In the U.S., approximately 5,000 children receive platinum chemotherapy annually. Several pediatric cancers are typically treated with platinum, and these include brain and central nervous system cancers, neuroblastoma, hepatoblastoma, osteosarcoma, germ cell tumor and retinoblastoma.

Approximately 50-60% of children treated with cisplatin and 5-20% of those treated with carboplatin acquire some degree of irreversible hearing loss.

The incidence increases to 80-90% in those receiving cisplatin and myeloablative carboplatin. The prevalence of hearing loss among those who have been treated with radiation is 10-14%, and when a child is treated with cranial radiation and cisplatin, the rate of hearing loss is increased to over 80%.

Age at the time of diagnosis and treatment is a significant risk factor for treatment induced ototoxicity. Children five years of age and under are at a 21-times greater risk for developing hearing loss compared to adolescents. Other risk factors include the platinum dose, both the individual dose per course and total dose, having cranial radiation before cisplatin treatment, and the use of more than one ototoxic medication during treatment. Genetic factors may also affect risk.

The time of onset of the hearing loss is variable but can occur as early as the first or second cisplatin cycle. Ototoxicity occurs typically in both ears and is permanent. The hearing loss first occurs for the high-frequency sounds, increases in degree and spreads to affect lower frequencies as treatment continues.

Hearing loss is a permanent lifetime disability that, in children, has ramifications for speech and language development, learning, social development, employment, and lifetime earnings.

The etiology of chemotherapy-induced hearing loss

Platinum-induced hearing loss results from damage to the sensory hair cells within the cochlea. Cisplatin and carboplatin enter the fluids inside the inner ear from the bloodstream, taken up by several cells within the inner ear. Cisplatin appears to be retained in the cochlea for months to years.

The fluids inside the inner ear have to maintain an electrical charge, the endocochlear potential, to allow this to change sound potentials into signals that the brain can receive. Platinum impairs the function of the cells to maintain this electrical charge. The cochlear hair cells are permanently damaged by the loss of the endocochlear potential, generation of reactive species, while the antioxidant defense mechanisms are also depleted.

Damage begins at the opening of the cochlea, or base, where high-frequency sounds are processed, and then progresses to the apex where low-frequency sounds are encoded. This is why hearing loss starts in the high-frequency range and then progresses to the lower frequencies.

This has consequences for speech development. Children in the process of acquiring language require audibility to 8,000 hertz—across the entire frequency range—to correctly perceive and discriminate the sounds of speech. When the high frequencies are lost, speech sounds such as F, S, T, K, H, P and Sh, are too soft to be heard, and speech becomes difficult to understand, especially when listening to speech from a distance, or with background noise. Much of childhood language development occurs by overhearing the conversations of others, and that requires good distance hearing.

Treatment-induced hearing loss can worsen in the years after therapy is completed. Studies have reported progressive hearing loss in 20-50% of patients who receive platinum chemotherapy and/or radiation.

As a result of the hearing loss, greater cognitive effort is needed to decode speech. Due to the increased cognitive load, fewer resources are available for comprehension and memory. Thus, hearing loss can affect learning and cognition.

One study (Gurney et al) reported that in a group of 137 neuroblastoma survivors who were an average of 11 years post-diagnosis, those with hearing loss had twice the rate of problems with reading, math, attention, learning disabilities or special education needs compared to neuroblastoma survivors without hearing loss.[1] The survivors with hearing loss reported poorer quality of life and educational functions compared to those without hearing loss. In another study of 165 medulloblastoma survivors five years after diagnosis, severe hearing loss was independently associated with declines in cognition and reading ability.[2]

Other studies have reported long-term potential socioeconomic impacts of treatment-induced hearing loss. In one study of 226 childhood cancer survivors who received cisplatin for non-CNS tumors, those with severe hearing loss were at twice the risk for non-independent living, not graduating from high school, or being unemployed compared to survivors without severe hearing loss.[3]

[1] Gurney JG, Tersak JM, Ness KK, Landier W, Matthay KK, Schmidt ML; Children's Oncology Group. Hearing loss, quality of life, and academic problems in long-term neuroblastoma survivors: a report from the Children's Oncology Group. Pediatrics. 2007 Nov;120(5):e1229-36.

[2] Schreiber JE, Gurney JG, Palmer SL et al. Examination of risk factors for intellectual and academic outcomes following treatment for pediatric medulloblastoma. Neuro Oncol. 2014 Aug;16(8):1129-36. doi: 10.1093/neuonc/nou006. Epub 2014 Feb 3.

[3] Brinkman TM, Bass JK, Li Z et al. Treatment-induced hearing loss and adult social outcomes in survivors of childhood CNS and non-CNS solid tumors: Results from the St. Jude Lifetime Cohort Study. Cancer. 2015 Nov 15;121(22):4053-61. doi: 10.1002/cncr.29604. Epub 2015 Aug 19.

Treatments and management strategies

Existing strategies for mitigating ototoxicity are woefully inadequate.

A key consideration in treatments in which hearing loss has been detected is whether or not to continue the offending chemotherapy. For some cancers such as hepatoblastoma, there is little option but to continue treatment in spite of deteriorating hearing loss. In other cases like medulloblastoma, it may be possible to modify or change treatment once hearing loss occurred to prevent further hearing loss. In these cases, caregivers must make an exceedingly difficult decision between preserving hearing and maintaining a better quality of life versus possible compromise of treatment and chance for cure or even survival.

Once hearing loss has occurred, management approaches include the use of hearing technology, such as hearing aids, remote microphone technology, FM systems, or cochlear implants in the case of severe to profound hearing loss.

These assistive devices are expensive. In the U.S., the average cost for hearing aids is $4,600. These have an expected lifespan of 5-6 years and often are not covered by insurance.

There are also educational supports and modifications recommended, including seating accommodations, acoustic modifications to the classroom to reduce background noise and reverberation, special education services, tutoring, classroom note takers, and the use of communication strategies, such as always facing the student when speaking or getting closer.

Survivors with hearing loss also require regular hearing evaluations to monitor for progression of hearing loss over time, and to ensure their hearing devices are working optimally. It is also very important that individuals avoid future ototoxic medications, if possible, and to be very cautious about exposure to noise, using hearing protection whenever exposure can't be avoided.

Meeting Overview

More than 202 individuals registered for the meeting (103 in person, 99 via webcast). Approximately 10 individuals from the FDA and NIH attended the meeting to hear directly from survivors with chemotherapy-induced hearing loss, their caregivers, and other community representatives about the experiences of patients with hearing loss caused by chemotherapy and the available treatments and management approaches for the loss. FDA attendees included Dr. Rea Blakey, the Associate Director of External Outreach and Engagement with the FDA Oncology Center of Excellence, and Dr. Greg Reaman of the Center for Drug Evaluation and Research (CDER). The meeting was also attended by clinical experts Professor Kristy Knight of Oregon Health and Science University and Dr. Gregory Aune of the University of Texas Health, San Antonio-Greehey Children's Cancer Research Institute, who were present to help provide a wider context on the late effects in cancer survivors, including chemotherapy-related hearing loss.

Approximately 60 of the people who attended the in-person meeting were either individuals with chemotherapy-induced hearing loss (25), or a parent/primary caregiver of a child or person with the condition (35). Another 43 individuals with or representing people with chemotherapy-induced hearing loss registered to attend via webcast. In addition, family and friends of those who had lost hearing due to cancer chemotherapy in childhood, and a broad cross-section of representatives from the pharmaceutical industry, academia and patient advocacy organizations also attended the meeting.

After an initial welcome from Cat Paciente of Momcology, who is also the parent of a child with chemo-induced hearing loss, Dr. Blakey spoke to the FDA's efforts in incorporating the patient voice in the agency's activities. As part of the 21st Century Cures Act, one new aspect of this is the Oncology Center of Excellence, the first FDA center creating a cross-cutting interdisciplinary team centered around a specific disease. Another aspect is PFDD meetings, which were developed to generate input from 24 disease-affected communities into the FDA decision-making process. Recognizing that the meetings provided a unique opportunity to hear the patient's voice, the agency invited patient organizations to organize their own patient-focused collaborations to generate more public input in other disease areas.

After Dr. Blakey, Professor Knight—who is also the Audiology Training Coordinator of the Oregon LEND Program at the Child Development and Rehabilitation Center, Doernbecher Children's Hospital—provided an overview on how cancer chemotherapy causes hearing loss and current approaches to its management (the key points of which are summarized in the previous overview).

The main content of the meeting was divided into two topics focusing on different aspects of the patient and caregiver experience. The first was on the burden of disease—including the various ways in which hearing loss impacts daily lives. The second meeting topic explored patient perspectives on current and future treatments, and unmet needs in management of hearing loss. This included treatment benefits attendees considered clinically meaningful and perspectives on the balance of benefits versus risks of current and potential treatment options.

Each session began with a panel of cancer survivors and/or their caregivers representing a spectrum of ages and degrees of hearing loss. These individuals brought their voices and stories to depict the debilitating impact of hearing loss upon their lives. In addition, there was a presentation from Dr. Aune on the challenges in clinical trial design in chemotherapy-induced hearing loss. Each of these presentations helped inform the subsequent discussion..

After each round of panelists, a series of polling questions were posed to the participants at the meeting and, via a live-streaming webcast, across the U.S. and internationally. These were followed by periods of facilitated discussion. Participation in the polling questions was voluntary and included a total of 44 respondents overall, though the number responding to each question varied. The results were used as a discussion aid and to gain a better understanding of the full impact of hearing loss.

To supplement the input gathered at the meeting, a post-meeting questionnaire was sent out for patients and caregivers to provide additional feedback about their experiences. Overall, 29 individuals completed the survey; some were unable to attend in person and some surveys were incomplete. An analysis of the survey results are described on pages 46-57, with the full survey results in the Appendix.

Report overview and key themes

This report is based upon the structure of the meeting and summarizes the input provided by the patients and caregivers during the meeting.

It also includes a summary of comments submitted to the post-meeting survey. To the extent possible, the terms used in this report to describe specific symptoms and treatment experiences reflect the words used by in-person participants and language used in submitted survey responses. There may be symptoms, consequences, treatments, or other aspects of chemotherapy-induced hearing loss in children that are not included in the document.

Topic 1: Burden of disease

The first meeting session, and part of the post-meeting questionnaire, focused on the burden of disease in chemotherapy-induced hearing loss. The feedback during the panelist testimonies, polling and facilitated discussions, and post-meeting questionnaire described a very serious, life-altering condition, revealing a major and underappreciated side effect of the standard of care treatment for many pediatric tumors.

Several key themes emerged:
Most of those with chemotherapy-induced hearing loss were placed on platinum-based therapy in the first several years of life. The vast majority developed at least moderate hearing loss. For most, the hearing loss was moderately severe, severe or profound—and is getting progressively worse.

Starting with loss at high frequencies, the degree of loss varies from mild to profound, but can affect a child's speech development, and, as they age, socialization, learning and academic experiences, employment options later in life, participation in sports, recreational activities, performing arts, and general quality of life. Chemotherapy-induced hearing loss isolates cancer survivors in social situations, poses challenges in trying to keep up at school or interact with colleagues at work—as they either do not hear everything that is being said, or they miss what is being said because of auditory processing delay. Individuals with hearing loss described their frustration attempting to communicate with others.

Many participants in both the externally-led PFDD meeting and the post-meeting questionnaire described severe social isolation and anxiety participating in social situations. Some older children who have experienced hearing loss even expressed a wish that their cancer had not been treated, and at least one current cancer patient was discontinuing chemotherapy in order to preserve residual hearing.

By far the greatest worry about chemotherapy-induced hearing loss is that it would become more severe—and that some might lose all their hearing, or experience tinnitus or balance problems. Consequently, many worried that their social isolation and difficulties with school or work will grow worse, and that their ability to enjoy the activities that they love and maintain overall quality of life will be further compromised. Caregivers also expressed fears that their children will continue to withdraw from the world. Patients and children worried that they might not hear alarms, dangers in the environment, or their own children crying.

Topic 2: Patient perspectives on treatment options

The second section of the meeting focused on the perspectives of former chemotherapy recipients with hearing loss on current and future treatment and management strategies—both to avoid hearing loss while on chemotherapy and to deal with the consequences of hearing loss.

Treatment: There are no therapies available to restore hearing once it has been lost. Although patients use a variety of devices, therapies and adaptation strategies to manage the consequences of hearing loss, the effectiveness is limited and each modality has significant downsides.

For instance, hearing aids are the most widely used intervention and help some—though not all—cancer survivors compensate somewhat for their hearing loss. However, they have significant disadvantages:

- They don't work well in noisy environments
- They are expensive, and few third-party payers reimburse for them
- They can fail due to battery drain or breakage and can become dirty/cause wax build-up
- They can be uncomfortable, both physically and socially
- Many children and young people simply refuse to wear them.

Other devices such as FM systems, educational strategies and environmental adaptive plans are only effective in certain settings and are dependent upon the compliance of teachers and others. Furthermore, they made the cancer survivor stand out further - when they already feel isolated.

Devices such as cochlear implants may work well for some but are: extremely expensive; require the complete destruction of what remains of natural hearing; require batteries; can cause migraines; and can cause skin sensitivity (burning holes in the scalp).

Prevention: Cancer survivors expressed a desire for the development of less toxic chemotherapy alternatives without hearing loss as a side effect, and for other treatment strategies that might prevent hearing loss. A number of cancer survivors represented at the meeting reported positive experiences as a result of participating in clinical trials of sodium thiosulfate (STS), while they were being administered platinum-based chemotherapy. Some reported that after being administered STS, their child did not experience any, or any further, hearing loss.

Participation in clinical trials: More than 4 out of 5 meeting participants did not believe there had been any progress in treatments since they or their loved one had started losing their hearing. Approximately 71% were unaware that there are potential therapy options in development.

What those with chemotherapy-induced hearing loss want from a potential therapy is the recovery of some normal hearing. Short of that, they want to halt progression of ongoing hearing loss.

Most were unaware until after they had experienced hearing loss that there was a drug in clinical trials that might have prevented their hearing loss. Many seemed to have only learned about it during the EL-PFDD meeting. In the post-meeting question, many expressed anguish that they had not been informed that a clinical trial of STS was an option and that the drug had not yet been FDA-approved.

Appendices

The appendices include the meeting agenda, polling questions, meeting attendance data, and the full post-meeting questionnaire responses. Additional information on the meeting has been posted online at www.childhoodcancerpfdd.org.

Benefit-Risk Framework

The patient input generated through this EL-PFDD meeting and post-meeting questionnaire is submitted to strengthen FDA's understanding of the burden of hearing loss on cancer survivors and their perspective on the therapies and accommodations currently used to mitigate hearing loss and its consequences. It is our hope that FDA staff will carefully consider this input as it fulfills its role in the drug development process, including when advising sponsors on their drug development programs and when assessing products under review for marketing approval. The benefit-risk framework (pages 58-60) shows how this input may directly support the FDA's benefit-risk assessments for products under review. This input may also be of value to the drug development process more broadly. Specifically, it may be particularly useful to drug developers as they explore potential areas of unmet need for individuals who experienced hearing loss while on chemotherapy as children, for example in managing psychiatric symptoms or increasing overall symptom control. It could also point to the potential need for development and qualification of new outcome measures in clinical trials.

Topic 1: Most significant aspects of childhood hearing loss and their impact on daily life

The first discussion topic focused on the experiences of caregivers and the cancer survivors describing their experience with hearing loss beginning as children as well as the impact and burden of the disease upon their daily lives. The session began with a panel of individuals with chemotherapy-induced hearing loss and caregiver/parents to children who had hearing loss.

"All of the sounds blend together and become white noise," said the first panelist, a young woman who has suffered from profound high-frequency hearing loss since she was 7 years old. Her hearing loss began when she was 5 years old, as a result of cisplatin and carboplatin treatment after she was diagnosed with stage 4 neuroblastoma at the age of 4 1/2 years. Although her friends try to help her, "I feel like a burden to others if I have to ask them to repeat things for me."

"[He] was 2 1/2 when I knew he couldn't hear me—it was ten months into cancer treatment," said the second panelist, mother to a now 15-year-old survivor of stage IV neuroblastoma. He has a passion for baseball, but his hearing loss has made it extremely difficult to participate in the sport on a team — and at times he has lost interest."

"I've been living with chemo-induced hearing loss for almost 20 years," said panelist number three, a 21-year-old neuroblastoma survivor. During his testimony, he spoke about techniques he employs to compensate for his profound hearing loss. "Not everybody understands that when you have hearing loss you have to focus a lot in order just to even get the most simplistic sentences to make sense," he said.

"After graduating from college and entering the professional world, I began to really understand the difficulties to having a profound hearing loss," said the fourth panelist. The 34-years-old was diagnosed with neuroblastoma when she was 6 years of age, and her treatment included numerous rounds of chemotherapy and full-body radiation.

"He can hear my husband's voice better than mine," said the next panelist, caregiver to her son, who was diagnosed with congenital glioblastoma stage 4 when he was six years old and treated aggressively with chemotherapy. Now 11 years old, he suffers from many late treatment effects that make trying to navigate 6th grade very difficult.

The panelists vividly recounted how the chemotherapy-induced hearing loss isolated them in social situations, posed challenges in trying to keep up at school or interact with colleagues at work, and made it difficult to participate in sports or other recreational activities. Individuals with hearing loss described their frustration attempting to communicate with others. Caregivers expressed their fears for children who appear to be withdrawing from the world, or who might not hear birds singing, cars honking, or alarms or warnings in dangerous situations.

These themes would be echoed in the group discussion.

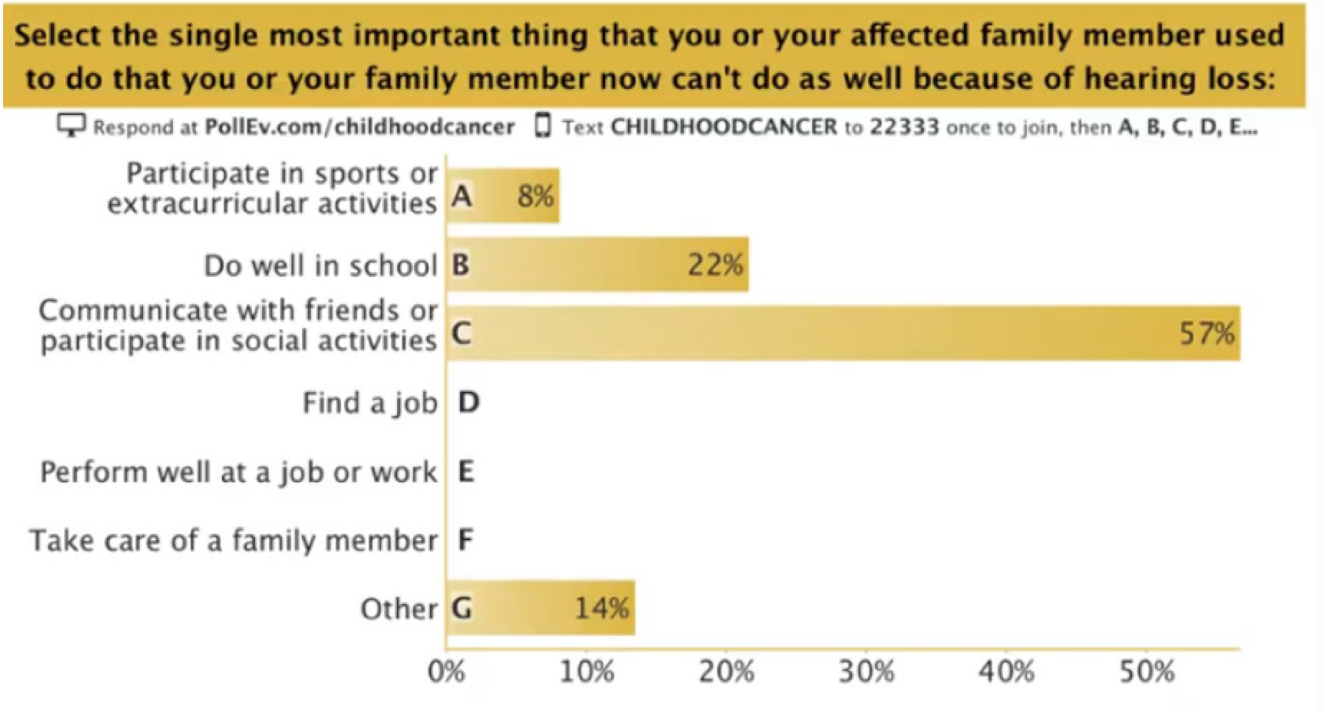
Characteristics of polling participants and their hearing loss

First, meeting participants who were or represented (as caregivers) someone with chemotherapy-induced hearing loss were asked their ages and to characterize their hearing loss. The majority of the respondents were in fact caregivers (about one quarter of the respondents were individuals with hearing loss).

Most individuals with hearing loss represented in the poll received chemotherapy quite early in life, with almost 47% starting when they were between 0-3 years of age. Approximately 26% were between 4-8-years old. About 19% had been between the ages 9-12 years, and the remainder had been adolescents or young adults. At the time of the meeting, however, most of those with hearing loss who were represented in the live polling were adolescents or young adults (~56% were aged 13-25 years); most of the rest were younger but several were older adults. Almost two-thirds had hearing loss for more than 6 years; almost half more than 11 years. One had lived with chemotherapy-induced hearing loss for 26-35 years.

The vast majority (89%) had at least moderate hearing loss, defined as only hearing sounds above 40-55 decibels (dB) at some frequency range. For many (24%), the loss was moderately severe (at 55-70 decibels [dB]), while it was severe (at 70-90 dB) for almost 14%, and profound (at 90-120dB) for almost 30% of the individuals represented in the poll. More than three-fourths of the participants indicated that the impact of hearing loss had become greater over time, or affected additional areas of their lives (home, school, work, friendships, etc.) (Appendix 3, question 10).

“We both suffer from degenerative hearing loss, and it continues to spiral down,” said the panelist with severe hearing loss whose son now suffers the same fate.



Perspectives on hearing loss-related issues that most impact the daily quality of life:

Other polling questions systematically explored how hearing loss had affected patients' lives and served as a launching point for a wider facilitated group discussion.

In the first of these (Appendix 3, question 8), poll participants were asked a multiple choice question about the issues related to hearing loss that had the greatest impact on them and their quality of life. Due to a technical issue, respondents could only select one response, effectively ranking the issues as noted in the Appendix. Of note, however, the answers closely paralleled those to another question (#9), which queried patients on the most important activity they could no longer do as a result of hearing loss.

A. Ability to socialize/social anxiety

> *"He wants to be a normal 14, almost 15-year-old, and he can't be. He can't hear what they're saying. He sees them walking down the halls, laughing and talking to each other and he can't join in."*

More than any other issue, the panelists and meeting participants focused on how hearing loss can make social situations awkward and create social anxiety as indicated in responses to polling question #8. This is consistent with the dominant ranking in question #9 identifying the inability to communicate with friends and participate in social activities as the most significant consequence of hearing loss.

"Socially she will never be like her peers. Hearing loss causes her a lot of anxiety," said one caregiver.

A few participants described how their hearing loss made socializing difficult: "When I begin a conversation with somebody who I have never met, I will either be too loud, or too quiet, and I mumble. Which, when making a first impression, can be very difficult. You sort of come off as obnoxious or shy," said one of the young panelists with hearing loss. He added that when responding to questions from people in a social context, "you say whatever weird response comes and usually when you're not with friends, it will be awkward and very strange."

"During lunch at school, she couldn't hear her friends, so she'd sit, not talk, because she couldn't hear what was going on around her," one caregiver said of her daughter. "She has suffered socially and really doesn't hang out with any of her friends that she used to hang out with."

"In social situations, at the playground and schoolyard, it leads to misunderstandings and missed opportunities both for myself and my children," said the mother with hearing loss who cares for a son with hearing loss.

Other caregivers expressed the same concern: "[His old friends], they're normal teenagers, growing ahead of him. They laugh, they play, they socialize. They're in group activities. This is something that he cannot do. He cannot understand a lot of what's happening," one mother said of her son, during the group discussion.

Large social gatherings can be particularly challenging according to one young woman with hearing loss, who said that while in school:
"I didn't attend parties or large events because I couldn't hear what was going on. The music was really loud, so I went upstairs. Even one floor away, it was still too loud for me. I tried to have conversations with people, but I had to spend so much energy focusing on their face trying to figure out what they were saying, that after three conversations, I went and sat in the corner exhausted from having to focus so hard," she said.

Even today, she said that she doesn't go to events "because I don't want my friends to have to take care of me in crowded situations… I also don't like activities with smaller groups of 5-6 people, because it's hard to follow what everyone is saying."

During the group discussion, another woman with severe hearing loss concurred. "As I got older - in high school and more in college - I had more social anxiety and felt more socially isolated. It's gotten worse as I got older. Now, like going to any events or social gatherings with people - either with groups of people or where there might be background noise or anything else that might make it harder to hear - makes me anxious. I'll plan on going to an event, but when it comes time to leave, I can't get myself to leave. So, I'll just skip it," she said.

Many of the people with hearing loss also spoke about now losing or being unable to make friends. "I don't have the friends that I used to have anymore," said a teenage girl during the group discussion, who only began to lose her hearing after she was diagnosed with neuroblastoma two years ago.

Some are treated poorly by others in society. "He responds slowly when asked questions. Not everyone is kind and patient. He has already been the target of bullying," one caregiver said about her 11-year-old son.

"I have very few friends now that I'm hard-of-hearing, as I've become somewhat anti-social and introverted," said an 18-year-old with hearing loss from panel two, who offered a video testimony. "I avoid people in general now, which makes me feel lonely. I feel like no one understands what I'm dealing with."

He added: "The fact that I need so much help to have a normal conversation makes me feel like more of a problem than a person."

B. Learning/school challenges

> *“Learning in school and now at work has been very difficult. I miss words in conversations and so I have to process and put together the puzzle before I understand what is being said. Now I learn at a slower pace than I did prior to my hearing loss.”*

Hearing loss jeopardizes equal access to an education that is essential for a child's personal growth and to develop the skills they will need to support themselves in adulthood. Notably, concerns about doing well in school scored second highest in both question #8 and question #9 (see Appendix 3). During the testimonies and group discussion, meeting participants described how hearing loss challenges their ability to participate and learn everything they need to do well in school.

"He's not getting everything the teachers are saying," another caregiver said about her son, a ten-year survivor of stage 4 hepatoblastoma with bilateral hearing loss now in 5th grade. Then she added that, "he's not hearing what someone behind him is saying."

Indeed, even children who can lip-read or make use of hearing assistance systems may only be able to focus on one speaker at a time, and thus miss out in interactive learning environments.

An adult woman with severe hearing loss said this problem remained with her even into higher education: "It impacted me throughout high school years, and in my early childhood education program, which I completed post-high school. While other students would either be presenting or speaking in a group setting, I struggled to understand what was being said. It prevented me from hearing my instructors."

Many with chemotherapy-induced hearing loss can only hear lower frequencies, which creates a problem when, as one of the panelists said, "approximately 76% of public schoolteachers are female with higher-pitched voices."

In many cases, children have to deal with teachers who are insensitive to their condition.

"Teachers and therapists would often comment that he was distracted and not focused. He wasn't distracted or lacking focus at all. In fact, he was super focused and constantly trying to figure out what was going on around him," one caregiver said about her son who struggled in school.

"I once had a teacher that refused to repeat a sentence in class when I told her I couldn't hear. She said I could figure it out on my own," said one of the panelists.

"[His] teachers couldn't even understand and didn't sympathize with the ongoing effects. They hear, 'oh, he's over chemo and radiation' [so] boom, he should be back to normal. We talked to the teachers, we've had numerous meetings about his hearing issues. They don't understand the perspective where he's coming from," one caregiver said about her 15-year-old son.

In some cases, some children with hearing loss would even be punished for mistakes.

"I would get in trouble for not paying attention. But it wasn't because I wasn't paying attention, it was because I couldn't hear what they were saying," one of the young panelists said about her experiences in elementary and high school—where she couldn't always be seated as close to the speaker as she needed to be. "I had no idea what was going on. I knew people were talking, but no idea what they were saying," she said.

As a consequence of being treated this way, it isn't surprising that some children grow frustrated with both schooling and their teachers. According to a caregiver who founded one of the organizations sponsoring the meeting: "My boy dislikes school and he's missing out on his education. He's a child who works ten times as hard as his classmates and just can't seem to keep up."

Education is a process, in which an individual must learn some lessons and master some skills before advancing to the next level. Over time, falling behind makes understanding what one is trying to hear all the more difficult.

"Then I am behind in class, I am behind in everything that my peers are way ahead of me. I have to ask everybody else for help. It's really hard," said the teenage girl with neuroblastoma.

A mother on the second panel spoke about this dilemma: "School quickly makes things challenging and it gets harder from year to year. You aren't with your child all day, so you have no idea what they've missed. It makes filling in the gaps that much harder."

Another caregiver echoed this sentiment: "I had to work harder to partner with [his teachers], making up for what he missed in school, at home. As he got older, he needed to learn more and to learn faster and he just couldn't keep up."

Compounding this difficulty, she said was "the auditory processing delay, which can also accompany hearing loss—additional residual issues that combined together actually create even more hearing challenges."

"I have to process and put together the puzzle before I understand what is being said. Now I learn at a slower pace than I did prior to my hearing loss," said the young panelist who gave his testimony by video.

Even when a sound is heard, the brain may not be able to process it in a timely way, and by the time a word or a sentence fragment is understood, the speaker may have moved to the next topic. In most classroom settings a student cannot keep asking a teacher to repeat themselves.

"Sometimes, even though I can't hear what they're saying in class or just whenever I'm having a conversation, I don't tell them to repeat it, because they've already repeated it seven times. And I know they're probably annoyed and just want to have a normal conversation. But that's not possible for me sometimes," said a teenager in the group discussion.

For at least of couple of children, these challenges led them to forego further formal education.

"High school was indescribably hard. And then college was just way too difficult. After a few weeks, it was obvious, it just wasn't the right choice," said one caregiver of her son.

C. Ability to communicate

> *"When around anyone else in the room, he will whisper in my ear what he wants to be communicated or asked. He's too afraid to speak for himself."*

Part of what makes hearing loss so challenging in social situations and in school is the consequence of hearing loss upon the ability to communicate. The first step of the process, stressed by many former chemotherapy recipients and caregivers, is not being able to hear everything that is being said, and not being able to translate what one does hear:

"I can't understand what is being said," said the young man from panel 2 who offered video testimony. "I'm constantly embarrassed if someone will tell me their name and I don't understand or hear what they said. I rarely will ask a second time and pretend that I heard. I can't hear my friends when they talk, and just say 'OK', to be part of the conversation. I miss out on a ton of information as a result. I miss words in conversations and so I have to process and put together the puzzle before I understand what is being said.

"You can't just ask in the middle of somebody crying 'Could you repeat that?' That's not socially acceptable," one young man on the first panel said.

The auditory processing delay was referenced again by a woman with severe hearing loss during the group discussion:

"People think that you either hear something or not when someone says it. When your brain is trying to fill in the holes on the sounds you can't hear, there's also a delay. Someone might say something, I don't understand it right away, then there's a little delay before my brain figures it out," she said.

A number of those who had lost their hearing said that once one becomes lost in a conversation, it is difficult to participate without looking foolish.

"I can't contribute to the group conversation, because I'm not sure I'm hearing things correctly, so what I do say might not be relevant to the conversation and I don't want to embarrass myself. This is especially true if it is a group of people I don't know very well. In those situations, I just sit there quietly," said a young woman on the panel.

For some individuals, hearing loss has also led to speech problems resulting in limited vocabularies that can also make them too self-conscious to engage in the conversation.

Most of the group discussion reflected the importance meeting participants placed upon communication in social contexts. However, a number of older individuals mentioned problems in other contexts as well.

For instance, those who read lips are limited by line-of-sight in personal communication.

"When I'm driving with someone in a car, I can't look at them, and I can't hear them," one woman with severe hearing loss said.

One of the panelists described her problems communicating at work. "During my first job, I soon realized that I was constantly asking my boss to repeat himself, missing important details from conversations and, at times, even avoiding conversations altogether. My hearing loss was affecting my performance," she said, adding: "It was extremely difficult for me to understand conversations over the phone. Because of my hearing loss, I cannot understand what someone is saying if they have their back toward me, if there is a lot of noise around, or if they have a strong accent."

D. Emotional or behavioral problems

> *"Spending an hour in a gymnasium is exhausting for him and results in tears, irritability, raising his voice. I hate having to choose between [him having a] meltdown day or watching my daughter play volleyball."*

The difficulties in communication can be too much to cope with in a healthy way, creating emotional challenges, particularly for some children.

"He has expressed his 'frustration' at school," one caregiver said about her son in grade school. She added that because of his speech impediment that has developed due to his hearing loss, "he tears up when asked to read aloud in class."

Other participants spoke about feelings of embarrassment and irritation upon making mistakes or being corrected for "talking too loud."

"As a young kid, he was very outgoing, social, fearless and funny. But as he got older, his nature changed. He became shy, afraid to make mistakes in school, as well as with peers," one caregiver said.

Others focused more on their anxieties, low self-esteem and compulsive behaviors.

"Feeling different from your peers can be very isolating—and that you always carry that with you," said one woman who also struggled with a hearing loss-related speech impediment.

"I am a lonely and typically anxious person," said the young man who provided a video testimony for the meeting. Some of this anxiety is not due to social issues but to actual physical danger. "I never know if there's an emergency around me. I have severe anxiety about the world around me," he said,

The 34-year-old panelist with hearing loss mentioned she had the same problem. "I cannot hear any high-pitched sounds, such as watch alarms or carbon monoxide alarms," she said.

Another young man with hearing loss discussed his "anxiety and paranoia" with driving.

"When driving a car—it has happened to me before—where you have an ambulance going by, and you're the only person in front of the ambulance, until it is five feet behind you. Everybody else on the highway is looking at you," he said.

"My hearing loss makes me nervous 24/7. It is worse when I'm in situations in which I can't hear what's going on around me," said one of the young panelists. "It might be taking the Metro someplace I've never been before, because I can't understand the [public service] announcements and am afraid of missing my stop."

"Even when I'm at home, I'm always nervous. I have a somewhat irrational fear of crickets. In my house, I scan the room for crickets. We don't even have a cricket problem. It just makes me anxious because I can't hear them," she said.

E. Participation in sports, the performing arts or other extracurricular activities

> *Hearing loss has robbed many of their abilities to participate, or at least enjoy participation, in sports and other extracurricular activities—and was scored third on question #9 in the activities that individuals could no longer do as well.*

"I also don't think that people understand how complex it is to have hearing loss, how many things it impacts, how many daily activities," a woman with severe hearing loss said during the group discussion.

Several meeting participants focused the effect of hearing loss on physical activities.

One caregiver spoke about her son's passion for baseball, which was even expressed energetically while he was in the hospital on chemo: "He learned to slide, head first, up or down the halls of Sloan Kettering so the mediport in his chest… was kept off the ground," she said. But later on, sports became a struggle. "As a Little Leaguer, his love and willingness for the game changed significantly. He was frustrated with hearing aids. He couldn't hear much with a batting helmet on or from the outfield if that's where he was playing. He struggled with coaches and teammates to process what they were saying. Over time, he lost interest. He gave up in the fifth grade."

Another caregiver said that her son, now in sixth grade, had "never been on a team or even wants to try."

The ability to participate in sports and other physical activities can also be impacted by another consequence of hearing loss: a loss of balance.

"[My daughter] also has issues with balance. We make a joke of it in the house, because I'm the same way. We both have hearing loss. Mine is not chemo-induced, though. We both have issues with balance," one caregiver said during the group discussion.

One of the adult panelists, who started chemotherapy after her diagnosis as an infant, but whose hearing loss is progressive, suggested that the loss of balance didn't begin until years later. "My balance didn't go off until about, well, I noticed probably my adolescent years, it started to drop. It continues to deteriorate… hence, the mobility challenges."

"Earlier it was hard for me to stand still without starting to fall over. Sometimes I have to lean back against the wall, so I don't completely topple over," said a teenager who has only had hearing loss for the last couple years. As a dancer, she has been particularly affected by the loss of balance.

"Dancing has been especially hard for me, since I came back from chemotherapy, because it was hard for me to do turns, à la secondes, different types of dance things," she said.

Her mother provided more detail on how hard it has been for her: "It's very frustrating because she went from being in the top of her dance class to being put back with the second and third graders because of balance. She's been penalized because of balance," she said.

Many of the other common activities of life are also limited by hearing loss as well.

"Because I can no longer hear these sounds as well as other sounds, I find I don't enjoy nature like I used to," said the panelist who provided a video testimony. He also said when his family went on a cruise to Mexico, "I wanted so badly to go to the arcade or teen dances, but I was too anxious."

"Watching TV-one of the easiest things to do-is hard because sometimes I don't always hear what's happening. I either have to rewind and watch something again or ask someone to explain what's happening. I also just miss out on things," she said, describing a recurrent sound effect on one of her favorite shows.

F. Speech development

> *"He's losing his vocabulary. He's losing his ability to say words. In kindergarten, he had perfect pronunciation. In grade two, he cannot pronounce letters. He's lost that ability."*

As one caregiver stressed, "kids with hearing loss need speech therapy. [My daughter] was luckier than a lot of neuroblastoma survivors. She was 4 ½ [years-old when she lost her hearing]. She was older and her speech was pretty well-developed," she said.

Another caregiver said that her 11-year-old son who survived his stage 4 congenital glioblastoma, which was diagnosed when he was six weeks old, suffered hearing loss that affected his speech development. "He gets embarrassed because he can't pronounce words like his peers. He has shared with me on numerous occasions that when he is corrected on pronunciation of a word, he feels like an idiot," one caregiver said of her young son.

Another caregiver, whose 2-year-old daughter had just completed chemotherapy spoke about how her daughter "stopped talking during chemotherapy. I didn't know if it was because of the hearing loss or she just felt like crap all the time," she said but she noted that her speech picked up a bit once she had hearing aids. However, her age and her limited ability to communicate her needs causes her mother great emotional distress. "I have to guess them and figure it out until she's old enough to articulate those things and developmentally can help me understand and communicate how it's impacting her," she said

A couple adults with chemotherapy-induced hearing loss spoke about their speech problems. One said that hers was "also from radiation and surgery," but contributed to her social isolation more as she has grown older.

G. Depression

> *"The hearing loss… is the single reason that he says, 'I wish the cancer had killed me.' He thinks that the life we gave him by saving his life isn't worth it right now."*

Depression was commonly mentioned by participants at the meeting but may not have been ranked as highly because it may be seen as a downstream effect, secondary to the primary dilemma. During the testimonies and discussion however, many spoke of feelings of isolation and loneliness.

"I also have depression, which I don't think is completely related to my hearing loss but my hearing loss and everything that comes with that definitely contributes to that," said one young woman.

"It's been really depressing, I guess you could say, because I'm not the person who I used to be," said the teenager girl who loved dancing.

"He's talked about the same feelings of depression," another caregiver said of her son, who feels like his friends are "no longer his friends and surpassing him. The socialization at school has kind of taken him away from everything, and his depression begins, because he's lonely, everyone is isolating him."

"I feel left out and isolated which makes me feel like I'm not part of this world. I'm sad about that," said the panelist who gave his testimony by video. "These same drugs used to save my life in some way also took it away. I'm alive, but I don't feel alive because I feel alone and isolated in this quiet road I live on."

H. Other

During the discussion, some caregivers and former chemotherapy recipients mentioned other symptoms related to otoxicity, as well as other complications to their daily lives that are the result of hearing loss.

One of these was tinnitus, ringing in the ears that can be particularly disturbing when one can hear little else.

- "She complains constantly about tinnitus and I worry because, correct me if I'm wrong, but tinnitus is usually a sign of progressive hearing loss," said one woman.

- "The ringing of the ears—it's going on right now—and it's hard for me to be alone by myself because then all that I'm focusing on is the ringing in my ears. I can't focus on anything else. I want to concentrate without everybody else distracting me, but I also don't want the ringing of the ears to drive me crazy, which it does. I cannot stand it. Ever since I've started hearing it, I've asked my mom and my dad over and over again what we could do to help stop it," she said.

Others mentioned fatigue as a consequence of auditory processing delay—working so hard to understand what was being said:

> - "I have to process and put together the puzzle before I understand what is being said. This is extra time and processing which also causes severe fatigue by the middle of the day at school or work. I find I am extremely exhausted and usually have headaches from concentrating so hard trying to comprehend and process conversations," said the young man who submitted a video testimony.

Some children had trouble getting through a whole day of school without taking a break.

Conversely, another woman with hearing loss (and caregiver) developed insomnia.

> - "When I started having my own children, while I was asleep, I could not hear my babies if my babies woke up crying. The high pitch tone of the monitor made it that much harder to hear. With my husband working late hours, I was afraid to fall asleep in case of an emergency that I could not hear," she said.

The issue that worries former chemotherapy recipients and their loved ones the most about their hearing loss:

The final polling question (Appendix 3, question #11) asked participants to rank which issue out of eight choices worried them the most about their hearing loss. Only one response could be selected, and the overall ranking is described in the following order—with the exception that the top two selections were chosen by an equal number of respondents. During the discussion, the caregivers were the most likely to speak about their concerns.

1. That it will get worse

> *"My son, he's 7 years old, in grade 2, he worries every day, he cries a lot, he's worried his hearing will leave him completely."*

Several meeting participants said that they were quite worried that the hearing loss would grow worse.

One caregiver said that she was worried about her almost 15-year-old daughter's hearing becoming worse. "She has to listen to things at louder volumes to hear them. I worry about that too, because as you talked earlier, because vibrations and those sounds can hurt her hearing for the future," she said.

"As I think about the future, I am often worried if my hearing loss will continue to get worse and what new challenges I may face," said the 34-year-old woman with hearing loss.

The mother with progressive hearing loss spoke about her son—now in first grade—who worries: "He's becoming more self-aware of the diminished hearing and is worried more about how far his hearing loss is going to infringe on his life and what he's going to miss. Jack sees my struggles with hearing loss as it's far worse, and he's worried one day he won't be able to hear at all," she said.

1. Long term mental/emotional health

> *“I worry more each day about how to keep his spirit renewed and to grow his feeling of belonging. He is an intelligent, caring, and kind young man whose spark is fading.”*

Although many participants spoke about their feelings of loneliness, the caregivers are especially worried about long-term outcomes.

The mother to the 15-year-old who no longer felt that his life without hearing is worth living is particularly concerned: "I've got to get him through this part, and I'm worried about that. It doesn't seem like a life or death issue, but it really is to these kids, especially where they are. I cannot watch him every moment of the day. He's going to be 15. This is a severe issue that's affecting him in a way that I would have never imagined."

3. Lack of social interaction

> *“It's hard to pick one thing that worries me the most. One day, it might be missing something other people my age are doing…. Overall, my biggest worry about my hearing is it makes my world so much smaller.”*

4. Academic success

> *“It's the social impact and the academic impact. I hear teenagers and other people talking about how it impacted them in school and bullying is a huge issue in the United States right now. I worry how do I protect her from that?”*

Schools are a difficult environment for children with hearing loss, both socially and academically. Several participants mentioned curtailing their academic aspirations. Caregivers at the meeting were particularly worried about information their children were missing at school, and whether delays in reaching academic milestones put them at risk of not graduating high school or college.

5. Physical safety from not being able to hear adequately

> *“I worry more each day about how to still keep him safe.”*

One caregiver was particularly frank about her worries for her daughter, and her hopes that she would be "able to go out without worrying that there's something behind her she can't hear, whether a friend calling her name, a car speeding through an intersection, or a rapist creeping up behind her."

6. Ability to live independently

> *"I have always wanted my own place, but I'm so worried I won't be able to, because I can't wake up in time for work and school."*

Worries about moving away from home were particularly acute for those at the meeting who are just entering adulthood.

7. Finding a job/career success

> *"He works so hard to try to be independent, but he finds workplace options lacking because of his hearing."*

Although some adults with hearing loss at the meeting described successful careers, they also cited challenges in the workplace. Hearing loss limits options for young adults entering the work environment.

Topic 2: Patient and caregiver perspectives on treatment/management of the chemotherapy-induced hearing loss

The second meeting topic focused on current and future therapeutic approaches, such as: supportive care; medical devices; and accommodations used to help manage chemotherapy-induced hearing loss.

One of the first considerations in management of chemotherapy-induced hearing loss in children with cancer at most risk is whether to continue the offending chemotherapy. Accordingly, the second session began with the presentation from Dr. Greg Aune, focused primarily on cancer treatment options—and how the current cancer drug development model did not adequately assess for the potential of experimental treatments to cause late "off-target effects." He said that he believes "we need more preclinical research focused on how our current therapies damage our normal organs, such as the inner ear and the heart, for example. That's going to lead our ability to potentially prevent these in future patients—and it might even uncover ways to prevent further hearing loss in current patients and just give people a better quality of life."

Following his presentation, testimony from both patients and caregivers provided insight into the inadequacy of the existing options used to compensate for severe hearing loss. There was also some discussion about an approach that could reduce the risks associated with chemotherapy. These comments about the burden of disease are described in the previous section. What follows is primarily focused on treatment, management and accommodations:

- "People judge me and think I do not need additional help or accommodations because of the way I look. This is extremely frustrating and I feel ignored and rejected when I ask for assistance," said an 18-year-old whose testimony was presented as a video, as he had just experienced a post-surgical pneumothorax and was unable to travel to the meeting. He stressed that severe hearing loss puts people trying to advocate for accommodations for themselves at a great disadvantage—when they often miss critical information in such negotiations: "How can I advocate when I don't have the information to do so?"

- "When your child is given a 30% chance of living, you don't really question what the doctors are doing. They tell you that the platinum-based chemotherapies will likely cause hearing loss, but they downplay it, saying, 'oh, the kids get hearing aids, they do just fine,'" said the second panelist, mother to a young woman who spoke on panel one. She and her daughter would discover that hearing aids have definite downsides and that her daughter's hearing loss would profoundly affect her life.

- The next panelist, mother to a young man with hearing loss on the first panel, had similar observations: "There aren't treatments that bring the hearing back. There aren't exercises. There are no specialists that I can send him to, to work with him to restore that hearing," she said. Fighting for the accommodations that he would need to receive an education "turned into another job for me."

- "The current approach to hearing loss is not enough—it does not work in many situations," said the fourth panelist. Despite suffering from severe-to-profound hearing loss after being treated with cisplatin as a child, she had to make the difficult choice two decades later to put her own son on the drug in order to save his life. Now they both have experience with the pros and cons of assistive medical devices, and desperately need a treatment that might stop the ongoing degeneration of both their hearing.

The lack of new treatments for the prevention of chemotherapy-induced hearing loss during those intervening years is a serious deficiency in our medical and research system.

"[My son's] story is very different as a result of having the opportunity to participate in a clinical trial," said the final panelist, the mother of an 11-year-old who ten years ago was diagnosed with hepatoblastoma. He too was treated with cisplatin, but in his case was able to participate in a trial of sodium thiosulfate (STS), which studies suggest may have the "potential to reduce the risk of high-frequency hearing loss." Though his is but one case, it is an encouraging one. "He passed his most recent hearing test, which was five years ago, with flying colors. He hasn't shown any signs of late onset hearing loss and he leads a completely normal life."

Participants at the meeting and online were then asked to respond to polling questions about treatments and other approaches to manage hearing loss and its consequences, as well as preferences on future treatments and participation in clinical trials. They were then asked to expand on their responses in a facilitated group discussion.

Experiences with the current approaches to treat hearing loss and its impacts

In the first polling question (Appendix 3, question #12), participants were asked about which treatments they or their loved one were currently using to either help them hear, or to deal with some of the consequences of hearing loss. This included accommodations and other non-medical interventions. Respondents could choose more than one answer to this question—and the most commonly selected answer was 'none'. Out of the respondents, 13 of 36 (36%) indicated they were not currently using any of the choices suggested in the question (a similar number reported having normal, mild or moderate hearing loss in responses to question #7 [see Appendix 3]). Of the 64% who used some form of treatment or intervention, the most commonly used interventions were hearing aids, followed by educational accommodations/specialized plans (such as individualized education plans [IEP]). However, therapies such as speech/language therapy and treatment to prevent or treat hearing loss and others are also used and described below.

Another question (#14) asked how much these medical devices, equipment, medicines, therapies and other interventions improved the quality of life of the person with chemotherapy induced hearing loss. About 55% responded that they helped at least somewhat in managing the worst symptoms and improving quality of life, but 37% of respondents indicated that they did not help at all.

The views and descriptions of patients and their caregivers of their experiences on these therapies or interventions, from both the panelist testimonies and group discussion, are below.

1. Hearing Aids

"[He] refuses his hearing aids because they hurt, and they make everything sound weird, and they make him different in yet one more way from his peers."

Out of the respondents reporting the use of some form of treatment or intervention, nearly half (48%) were currently using hearing aids. Most of the participants in the meeting indicated that while the devices could be helpful, they have some significant disadvantages.

"I also have a hearing aid in my left ear, and [in] the right ear, a hearing aid would not help," said one 32-year old woman with severe hearing loss in her left ear during the group discussion. She is entirely deaf in her right ear. "The hearing aid helps a lot, but like everyone else has described, it doesn't make up for everything, but only helps in certain situations," she added.

"When I found out my 2-year-old had moderate-to-severe hearing loss I thought, 'well, I'll get the best hearing aids available.' I quickly learned that the aids don't completely replace the loss," one of the caregivers on the panel said during her testimony.

One problem with hearing aids is that they do not work well in noisy environments.

"The hearing aids helped him in being able to hear better in quiet situations, but we quickly found that it actually hindered his ability to hear in a group of people when more than one person is speaking at a time. Large crowds, like at sporting events and the movie theaters, or the mall, the hearing aids actually amplified all the surrounding noises, causing him pain and requiring removal of the device," said the panelist who is both mother to a child with and patient with chemotherapy-induced hearing loss. She herself has had similar experiences with hearing aids while trying to care for children: "I couldn't hear them playing or having a good time, and the noise and laughter would overwhelm my hearing aids. On occasion, I tried removing them."

"Wearing hearing aids was awful for him from the very beginning. His ears hurt. He had headaches all the time and couldn't express how uncomfortable he really was. He was edgy and jumpy. He heard every noise, air conditioner or dog barking down the street when he wore his hearing aids. It was so difficult for him to tune things out. Even with the best hearing aid technology, he still had to work so hard to hear," said the caregiver to a 15-year-old. She added that, "he would often lose or break the hearing aids and was very happy when we couldn't find them and enjoyed, and still does, taking them out to block out life noises."

In fact, several caregivers said their children were eager to remove their hearing aids whenever they had the chance.

One mother described how her 14-year-old son, "will take them off as soon as he leaves home."

Another caregiver, who described hearing aids as "work," said that her son would need to take a break from them on the best of days. "But on the days when he was stressed, when he was tired, if he was sick, if he was struggling with some other side effect that he was struggling with, he might need hours of a break. On those days, the hearing aids were taken out before the shoes were kicked off or that book bag thrown in the corner," she said.

Another issue with hearing aids is the expense.

"Kids with high-frequency hearing loss need digital hearing aids to amplify only the missing ranges. Those cost about $6,000 a pair. As happens in many families, my health insurance wouldn't pay a penny. I appealed the decision and worked with an advocate for childhood cancer survivors, but the insurance company wouldn't budge. They just said: 'hearing aid coverage is just not in your policy,'" said the caregiver whose daughter provided the first panelist testimony.

"I also now have a Bluetooth enabled hearing aid [that] enables me to still have a hearing aid on and connect to a phone call and [doesn't] block out all the sound around me," said the 32-year old woman who has only partial hearing in one ear. "Of course, Bluetooth-enabled hearing aids are expensive. Technically, they're covered by my insurance company, but only one set of hearing aids ever. They don't seem to understand that hearing aids don't last forever. And they cost more than the amount they're willing to pay for them," she said.

The young man with hearing loss on the first panel pointed out some shortcomings in their use: "We have to constantly buy batteries, constantly go to the hearing aid office and have them plugged in to regenerate what will better improve your hearing," he said. He felt that to be more patient-friendly, Bluetooth hearing aids should be developed with settings that users would be able to adjust themselves..

FM systems are another hearing aid technology that children with hearing loss use in the classroom setting. The devices allow a teacher with a microphone (held or worn) to speak and the sounds are sent directly to the hearing aids. The effectiveness of these systems is also limited by "ambient noise"— and by the person wearing the microphone.

"When there were substitute teachers, the FM system was not used," said one caregiver.

"They wouldn't wear it," said the mother of a fifth grader who now has to take the microphone from class to class and hand it to the next teacher. "He doesn't understand that he's got to take it off or it kills his batteries faster [and] there's still so much that he's missing. He's not hearing what someone behind him is saying because they're not wearing the FM system."

The 32-year old woman with hearing loss confirmed that taking the microphone from teacher to teacher was awkward: "I started using an FM system in high school, and I used it in college for a while. I did have to carry it with me to give to my teacher at the beginning of each class. At the beginning, I was self-conscious about walking up to the teacher, giving him this device. Other students didn't know what it was. Then I had to decide if I wanted to explain it or just let them wonder. Then some teachers would forget to turn it on at the beginning of class, so I would have to raise my hand and kind of be like, 'Can you turn the thing on?' They would turn it on, then I'd have to remember to get it back at the end of class. It is hard for the teacher to remember to turn it on and off," she said.

A couple participants also described some unintended consequences of their use.

"I was in a class with a bunch of other hearing-impaired kids. We all use an FM system. Our teacher wouldn't always turn it off when she was in the other room or talking to someone else. So, I was in third grade, and we were at lunch, and we all heard our teacher talking about how annoying we are and how much she hated us," said the young woman who gave the first testimony.

One of the panelist caregivers whose 15-year-old son used the FM system had similar experiences when "many teachers would forget to turn off their microphone and he would hear conversations with other students, teachers, or even the teacher in the bathroom."

2. Educational accommodations and specialized plans

> *"We had a behavior plan and individualized educational plan (IEP) and 504 plan all set up, different time frames, and none of his teachers at that school would follow it."*

About 39% of those patients represented in the poll who were currently using an intervention, were receiving educational accommodations (e.g., according to a '504 plan' to ensure their academic success) and individually specialized educational plans (IEPs). Others had used these services when they were in school.

But many of the caregivers at the meeting described "having to constantly fight the school system" in order to put a plan in place. "We just sat down with the powers that be, because they would not understand, no matter what experts I brought in, what we were dealing with. It's worked fairly well, but we've had to adjust her educational systems. She's now in a blended charter school education," said one mother.

"Eventually, her IEP did include accommodations for hearing loss and reading issues she had," said another caregiver, who pointed out another downside of this intervention: "Whether the IEP was followed depended on the teacher."

As another mother pointed out: "Even well-intended teachers couldn't always focus on the special needs of my son, despite having a very strong 504 plan."

3. Speech or language therapy

> *"He had many services, hearing education teachers, speech therapists and an amazing oral transliterator who takes notes and prompts him in class."*

Among the polling respondents currently using some form of hearing loss treatment, about 17% are currently receiving speech or language therapy, such as the second-grade boy, who-as one father mentioned-lost his vocabulary and ability to pronounce letters. Additionally, several of the adults who developed chemotherapy-induced hearing loss as children also had speech therapy when they were young.

However, for some it was of limited benefit: "In the eighth grade, a physician told me the speech therapy wouldn't help me since I couldn't even pronounce the sounds that I couldn't hear," according to the 34-year old panelist, who had been treated with chemotherapy during the first four years of her life.

She had already lost much of her hearing at the stage when most toddlers would be learning how to make the sounds of speech.

Others were more fortunate, including a patient who gave the first testimony at the meeting. According to her mother: "She was older and her speech was pretty well-developed. She didn't need intensive services." Nevertheless, she did need some assistance and faced some of the same challenges others described fighting for accommodations and special educational plans.

"I requested an evaluation at the school and returned for the results to find myself on one side of the table and five school district personnel on the other side. They told me how her deficits were developmental and she would outgrow them. I knew that they were typical of high-frequency hearing loss and I did manage to convince them that she needed speech therapy. They agreed to 40 minutes a week. Eventually, her IEP did include speech therapy," the caregiver said.

Some caregivers had to become their own child's speech therapist.

"We worked with a hearing therapist and I found it was me, the parent, who was the most important support. It was just me, and I had to do more for him—so, working with sounds, words, playing language games," said the mother of the young man with hearing loss on the first panel.

4. Medicine to prevent or treat hearing loss

> *"I hope soon everyone else has the opportunity to have that drug that I felt helped with his hearing loss."*

Of those in the poll receiving a hearing loss therapy, 17% indicated that they were currently receiving a medication to prevent or treat hearing loss. However, at present, there are no FDA-approved medications for this use.

There are some medications being evaluated in clinical trials, and the only one that was explicitly mentioned during the meeting was STS, a drug on WHO's List of Essential Medications, used to treat cyanide poisoning and pityriasis versicolor. Its use has been explored in the context of chemotherapy for many years. In fact, during the group discussion, one caregiver said that her son had been in an open-label trial of STS to prevent cisplatin-related ototoxicity seventeen years ago. Since he had previously received standard cisplatin, he had already developed hearing loss. However, she believes that the drug prevented further loss, and moreover had fewer side effects than she had expected.

“If we had had that drug from the very, very beginning, would [he] have had his hearing?” she asked.

Another caregiver whose daughter also began sodium thiosulfate after already experiencing hearing loss, believes her daughter's loss has stabilized. "She has mild-to-moderate high-frequency hearing loss and it seems to have stayed at that level for the last three rounds that she was given," she said.

As mentioned above, the son of one of the caregivers on the second panel also participated in a randomized STS trial. Upon administration, his side effects unblinded the randomization. "He immediately started vomiting, his blood pressure rose, and he was inconsolable. Thankfully, he perked up after the drip finished. These side effects happened during each of the six doses," she said. But as he has shown no sign of hearing loss, she is grateful. "We know he is one of the lucky ones. Who knows what would have happened if he were selected into the other group or hadn't even been offered [the chance] to take part in the trial in the first place," she concluded.

It is beyond the scope of this report to come to a determination around the benefits of this or any other experimental medication, or whether further studies are required to better characterize the use and safety of any experimental medication. However, the drug has been administered off-label to protect kidneys during cisplatin treatment.

5. Medicine for anxiety or depression

> *“By the end of treatment, we were having to put him on antidepressants.”*

A number of meeting participants described feeling depressed or having psychological, emotional impacts related to the social isolation or social anxiety as a result of hearing loss. Approximately 13% of the polling participants using some therapy indicated that they were currently taking antidepressants or treatments for anxiety.

6. Cochlear Implants

> *"I have decided I don't want brain surgery and don't want a magnet stuck to the side of my head."*

Only one of the participants reported having had a Cochlear implant to treat their hearing loss. She spoke about having bilateral cochlear implants during the group discussion.

"My experience has been really good with cochlear implants. It gave me really good quality of life back overall," she said. But she did describe a number of downsides.

"I got my first cochlear a week after my 14th birthday in 2004, and it got turned on a month later. I got chronic migraines shortly after that, every day, all day long, and when I woke up in the morning they're right there, right next to me. I have a vibrating alarm clock. In college, a hole started to burn through my scalp from the magnet in the cochlear. There have been different side effects. My ears get sore. I can't sleep with the cochlears on anymore, because of my skin sensitivity in my head, because it burns holes in my scalp," she said. She added that the batteries also die—sometimes at inconvenient times.

The invasiveness of the implants may put off some individuals who have already lived through chemotherapy and surgeries. According to the young man who provided a video testimony: "I feel like I've been a guinea pig for my life, poked, prodded, and now the next step is if a surgery can fix the side effects of the drugs that saved my life?"

Another concern mentioned by a caregiver was the potential destruction of residual hearing: "One of the leading doctors at Johns Hopkins—I consulted him about an implant for [her]. He said she had too much residual hearing and that that hearing would have to be destroyed and the cochlear implant wouldn't compensate for that," she said.

The operative question for some was the risk versus benefits of implants in comparison to less invasive hearing aids.

"I did have hearing aids before I got the cochlear implants, and I just couldn't really figure out what people were still saying," said the one participant with bilateral implants. She also said their settings were adjustable. "I have four different programs in my cochlears that I strategically create, where the first program is everyday life, the second program blocks out background sound, third increases volume, the fourth turns off the back microphones. In different environments or situations, I kind of navigate and figure out 'where am I? In a bar, restaurant, in a crowded place?' It still takes a lot of hard work, though I have been able to re-create this sense of hearing, but it still has given me my life back, in some sense, which is great."

However, it should be noted that uptake of Cochlear implants is likely limited by the expense, which is dramatically greater than that of hearing aids.

Perspectives on clinical trial participation

According to a large majority (81%) of polling respondents, there has been no progress in the development of treatment options for hearing loss since they, or the family member they were representing, first suffered hearing loss (see Appendix 3, question 15). Only a small number (5) believed that there had been some new treatment options, and these are likely to have been those who have participated in clinical trials.

Similarly, in a question asking about their experiences and perspectives on participating in a clinical trial of a new drug, 77% indicated that they had not participated in a trial, because they did not know such an opportunity existed. About 14% (5 individuals) said that they had participated in a trial and would be willing to do so again. One had tried to join a trial, but had not been eligible.

The only participants to mention trial participation at the meeting were in the STS trials mentioned previously.

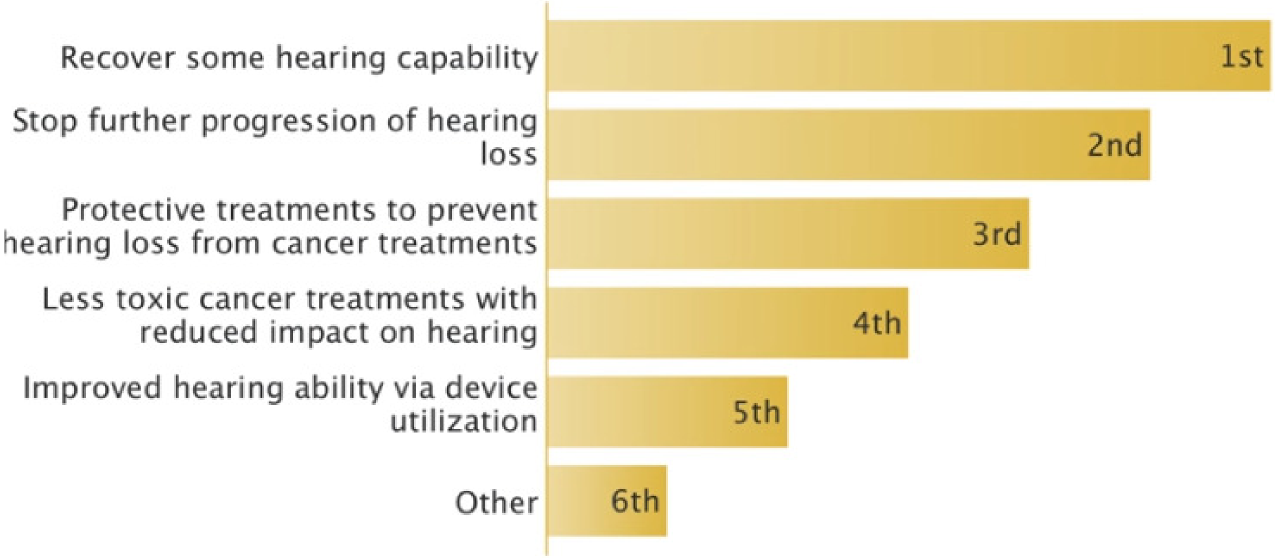
The panelist described a few factors involved in her decision-making process, including preventing hearing loss, trust in the researchers to provide optimal care for their child while in the study, and the contribution to progress in the field that would benefit others.

> *"We both decided that we had to give [him] the best possible chance of survival, but also if there was a chance of minimizing [hearing loss], we had to give it a go. We trusted the doctors and nurses and knew that he would be in the best possible hands. We also knew if the trial had positive results, STS could become part of the treatment plan for children and adults who need cisplatin in the future."*

What people with chemotherapy-induced hearing loss most want from future treatment

> *"We feel strongly that prevention of hearing loss, as well as better treatments after hearing loss has occurred is important to the pediatric cancer patient population."*

One of the primary reasons for these externally-led patient focused drug development meetings was to gather patient perspectives on what sort of benefit they were looking for in new treatment—and what sort of risks they would accept in exchange for that benefit. Consequently, the final polling question (#16) asked participants to rank several treatment outcomes in order of preference.



1. Recover some hearing

> *"We need to find a way to reverse the hearing loss so that [he] and current and future generations of children suffering from cisplatin-induced hearing loss can begin to lead a more normal life, to hear birds chirping, traffic bells and voices of their loved ones."*

The greatest number of polling respondents indicated that 'recovering some hearing capability' would be most important to them.

According to one caregiver, her daughter placed the recovery of some hearing even higher than a treatment addressing another late effect of chemotherapy.

"I asked if she could fix one, what would it be? I was 95% sure she'd say the ovarian failure. I know how much she loves kids and wants to have children. I was really surprised she said it would be her hearing, because her whole life would be so much better if she could just hear," she said.

2. Preventing and stopping further progression of chemotherapy-induced hearing loss

> *"I'd like to stress the importance of finding a way to put a stop to the ongoing degeneration of hearing loss as a result of cisplatin."*

After restoration of hearing, participants next ranked two other goals of therapy, stopping further progression of hearing loss,' and 'preventing chemotherapy-induced hearing loss' as being highly important to them.

Responding to some of the experimental treatments that might be protective of hearing during chemotherapy, one caregiver said that while she was willing to put her child on toxic compounds to save his life, "I at least want to be given the option to maybe protect him in some way."

Other parents emphasized halting the ongoing hearing loss in their children.

"The biggest thing for us is stopping the degradation, the ongoing hearing loss. The platinum is still in their bodies, but why? Why aren't they doing anything to clear that out of their system? He needs the ongoing progression to stop, even if it's not restored, at least stopped, before it can be restored," one father of a 7-year-old with hearing loss said.

3. Better cancer treatments

> *“My hope is that children faced with cancer treatments in the future have better options to avoid long-term effects.”*

Respondents indicated that 'less toxic cancer treatments with reduced impact on hearing' should be prioritized.

One caregiver said that her daughter's treatment was causing her daughter to lose what she most loved in life: dancing. "We need better treatment."

4. Improved hearing ability via device utilization

Finally, a smaller number would seek 'improving hearing ability via device utilization'—such as was mentioned during testimony by the young man with hearing loss on the first panel who wanted more customizable hearing aids. "If I'm the one experiencing all of this, I should be the one to change and better it," he said.

Perspectives on benefit-risk analyses

Another insight provided in this externally-led PFDD was how patients and caregivers would weigh the potential risk or benefit of future treatments.

This was addressed quite passionately by the mother whose son's cancer has been treated but who no longer believes his life is worth living. She placed the emphasis on access and the right of the patient to make their own determination regarding the risks and benefits:

"It's too late for them if we wait another five, ten years - especially for these drugs that have been around that many oncologists, until it becomes something mainstream, are not going to do it. We need to get these options to parents. I would like parents to be given the option to say here's the risks and benefits. You need to be aware, but you also need to have some of the control over the choice," she said.

As emphasized repeatedly over the course of the meeting, parents and individuals with cancer are faced with life and death decisions all the time - and in some cases make choices contrary to the advice of their doctor.

During the discussion, one caregiver spoke about how her son's oncologist advised the family against further cancer treatment in order to preserve her son's quality of life. In her family's case, she was able to get a second opinion, and decided to continue cisplatin.

"Regardless of his hearing, this was his life," she said. "That, in the end, is the most important."

Others, such as the young woman who was losing her balance - and the ability to dance - make a different choice.

"We need to look at what is best for us, quality vs. quantity. For her, treatment didn't come in an IV bag or pill, it came down to dance," her mother said.

However, patients and caregivers were clearly in agreement that it would be better "not to have to make that choice" but rather to readily access treatments that would prevent or treat chemotherapy-induced hearing loss.

Post-meeting questionnaire

After the meeting, a questionnaire was distributed to patients, caregivers and other community members to provide further feedback about their experiences that could not be shared that day.

In responding to the questionnaire, 29 individuals completed the survey, 17 of whom attended the meeting in person. The remainder watched the webcast and thus could not participate in the discussions at the EL-PFDD meeting. Responding to a description of their role, 24 were caregivers to individuals with chemotherapy-induced hearing loss, with the remainder from other sectors of the cancer community (including some other family members). Twenty-seven people responded to a question (#3) about the age of the cancer survivor they were representing. The age of patients represented varied widely—but three-quarters were younger than 26 years of age. Most (69%) of the patients had first received chemotherapy when they were 0-3 years of age, and about 31% had initiated chemotherapy when they were between 4-18 years of age (question #4). The duration of hearing loss of cancer survivors responding to the survey ranged from one to 25 years. One was currently on chemotherapy, but had not yet experienced hearing loss.

Given the relatively small number of responses in comparison to the meeting, and the overlap of some participants, emphasis should not be placed on the multiple choice results of the questionnaire. The responses were similar to the polling responses during the EL-PFDD meeting, though there were some questions on the survey that were not included in the live polling or during the discussions at the meeting. The open-ended answers in particular add nuance and allow this report to more faithfully represent the voice of the patient with chemotherapy-induced hearing loss.

Of note, this narrative reorganizes some of the questions and answers offered based upon a thematic analysis.

Consequences of hearing loss that most impact the lives of cancer survivors

Question #6 of the survey asked participants to list the top one to three symptoms, concerns or issues due to hearing loss that have the most significant impact on the life of a survivor of childhood cancer. Speech development, learning, behavioral symptoms, and quality of life were listed as possible examples. While this question was similar to one asked in the live polling session, technical issues prevented anyone from selecting more than one response, and some of the examples listed had not been included among the multiple choice options. Consequently, speech development, quality of life, and learning/school challenges were mentioned as often-if not more often-than socialization issues. However, some respondents still ranked the social issues as being the most important of a number of concerns.

"Social isolation is the most significant issue. Near impossible to have conversations in classrooms. Missing sounds change meaning of what is heard. Next is speech development," wrote one.

Many of these complications of hearing loss are interwoven, however:

"[She] currently receives speech therapy twice a week in school and twice a week out of school. We worry about learning, if she can't hear all the sounds correctly then it's hard for her to learn correctly. She also gets pulled out of class for speech therapy and so she loses those lessons too. Third grade, the curriculum is getting harder and she is falling behind. We also worry about her socially and behaviorally. She exhibits aggressive behaviors sometimes in social situations and we just realized it could be linked to her not being able to hear what everyone is saying," one participant wrote.

Several other respondents also mentioned emotional/behavioral problems, particularly if this included issues such as depression, anxiety and "lack of confidence"—which is unsurprising when, as one participant wrote, the child has to endure "peers being mean."

Several respondents cited, "Being in crowded or noisy situations makes her anxious because she can never be sure what is going on or if she is missing things being said."

Some of the anxiety experienced could be linked to safety issues mentioned, such as concern about "fire alarms at night." Another wrote "when hearing aids malfunction it's like taking away your glasses on a busy highway."

All of these issues likely detract from the quality of life, including specific physical discomforts, such as "certain loud sounds hurting her ears" and "sleep loss from tinnitus." Others linked quality of life to participation in things that bring joy to life. One stated that the "ability to communicate and participate in 'normal' childhood activities, music and dance have been the most impacted."

Activities that cannot be done as well or fully as one would like, or at all, because of hearing loss

Question #7 explored the issue of activities that could not be done or participated in as well, or at all, due to hearing loss—and suggested activities such as participation in sports, social activities, or academic pursuits. Notably, virtually all the answers related broadly to these types of activities, with most respondents indicating that cancer survivors with chemotherapy-induced hearing loss were not able to participate as fully or well in social functions, sports/recreational activities (including the performing arts) or school.

However, several narrative responses described specific activities in great detail:

- "Participation in music and in dance or gymnastics (the gym is so loud that it would be impossible for her to hear a teacher over the deafening background noise). Being a part of social activities or even 'normal' preschool is not possible because of her severe speech delay due to her hearing loss."

- "She cannot go to typical school parties/dances because she can't hear people, she doesn't go out with groups of more than 3 or 4 people because she can't follow conversation, she quit the swim team because she couldn't understand instructions/coaching at the indoor pool."

- "My son struggles a great deal in school and has limited social interactions. He also has a lot of difficulty in loud venues so cannot enjoy things like assemblies, concerts or sporting events. The loud and ambient noise at these venues is too overwhelming and all the sounds run together."

- "Just sitting in the school cafeteria or participating in school events. It is too noisy to be able to hear and interact. Sports, as he cannot hear instructions coaches give from a distance. Birthday parties, as they are always either too noisy or held in very noisy locations."

Several noted that participation in sports could be difficult "because of hearing coaches' instructions in noise filled environments."

"Water sports" in particular were singled out. One highlighted "Swimming and other very physical activities where she cannot wear hearing aids;" another wrote: "She is a competitive swimmer and has trouble hearing the starting beep."

Some noted that in older cancer survivors, hearing loss had limited job options, while a couple noted that hearing loss makes it difficult to participate in phone calls and another caregiver noted that their son had chosen to be a farmer—but that "safety is a main concern especially with hearing loss."

How has the impact of your child's hearing loss changed over time?

A question asked during the live polling session queried whether the hearing loss had changed over time. Question #8 explored a similar question, and as in the meeting, a number of respondents to the survey indicated that hearing loss was growing worse: "Hearing loss has been continual and did not plateau," wrote one (*this narrative response was submitted to an earlier question).

Note: there may be some difficulty knowing whether hearing loss is actually changing in children and young people who are maturing. In response to another question (#11), most indicated that there was no significant difference between how their child with hearing loss performs on hearing assessments in the clinic and how their hearing seems to work at home (or at school). Most of those who did see a difference felt that their child performed better in the assessments, while there were more distractions at home or at school: "There is more background noise, noise we cannot control at home and at school" wrote one. Conversely, another indicated: "It may appear he 'hears' better at home, but in reality, he is working very hard to utilize more than just his hearing such as 'environmental cues' to understand others." However, a concern noted by several caregivers was that some of their children were "too young to participate in the hearing tests accurately—she gets bored very fast and doesn't want to do them." Consequently, as they age, children may learn better how to participate in such tests—and how to use other cues in the environment to deal with the effects of hearing loss.

Importantly, question number #8 asked how the impact of hearing loss had changed. Consequently, many respondents focused on the growing consequences of their hearing loss, rather than the degree of hearing loss experienced:

- "The gap between her and her peers becomes wider every day."
- "She has grown more anxious and self-conscious over time. She is less willing to try new things/situations where she anticipates having hearing problems."
- "At first it impacted his speech and language learning and ability, but has now evolved into much greater impact for him socially and academically."
- "He's become more withdrawn and depressed at the isolation it has caused."
- "He is more aware of his deficits, thus causing to withdraw more. Whispers in my ear to avoid embarrassment."
- "His speech quality deteriorated during his teen years because he didn't want to wear the hearing aids."
- "Over time the social isolation has become more apparent. She refuses to wear hearing aids because they cannot make sounds clearer. Only louder. They cause her ears to make lots of wax. She denies she has a disability."
- "As she has aged, she has noticed more how she is different. Also, as school is more difficult each year, she has to put in so much extra effort to hear and process."
- "More self-conscious of her disability as she enters her teen years."

A handful felt that therapy and aids were helping to mitigate the impact of the hearing loss. However, one response suggested that just as children's ability to take hearing tests may change over time, some may actually refine their strategies to cope with hearing loss. This may, in some cases, conceal the severity of their disability and the extent of its impact: "She is getting more and more creative working through it or-I am afraid-faking it, so we are not concerned," one respondent wrote.

What worries one the most about chemotherapy-induced hearing loss?

Notably, nine out of 24 responses to the next question (#9) – what worries caregivers and patients the most about hearing loss – was that its severity will worsen: "We worry that with every ear infection her hearing will worsen so we are constantly going to the doctors," wrote one. "That it will progress to complete loss," wrote another.

Other responses related to long term impact of hearing loss, with many focused on "long-term social isolation" and related "depression and emotional struggles later in life."

"That she will become depressed and retreat from normal life because she can't hear or speak as well as others," wrote one caregiver.

A few expressed concerns about "struggling academically" or people thinking that their child is "slow" because of the time it takes them to respond due to auditory processing delay associated with hearing loss. "That she will have trouble in school socially and academically. That teachers or other caregivers will not help her and accommodate her needs. That other kids will not be understanding," wrote one caregiver.

More expressed concerns about their child 'transitioning into adulthood.' "His world is very small," wrote one parent, who was worried about his son's "ability to work and sustain himself [and] success with life skills." Another expressed a similar concern about their daughter: "that she will misunderstand something important at work. I worry that she may have difficulty finding a job."

Another caregiver was worried hearing loss would rob her daughter of all that she most valued in life, "I worry that she won't be able to sing or enjoy music, which is what she loves more than just about anything."

Others worried about their daughters' safety when alone. One mother wrote that she was most concerned about "Safety. As a young woman, I was once nearly mugged walking out at night, but I heard the person walking faster behind me and ran. She would not hear something like that and in the same situation would likely have been attacked." Then she added that she feared because of her daughter's isolation that she might not be equipped to protect herself emotionally either, "She is lonely and I worry that if the wrong type of person showers her with attention she could end up in a dangerous or abusive situation because she does not have many friends or people to turn to."

How has hearing loss impacted you/your child's social relationships?

The effect that hearing loss could ultimately have on social relationships was the topic of question #10. Consistently, caregivers indicated that hearing loss has severely limited the social relationships of their children, and that they have "very few close friends."

Some of this may partly be the consequence of being a cancer survivor or a patient being treated for the consequences of hearing loss: "Sadly he only knows the medical world," wrote one. "We spend SO much time in various forms of therapy that there isn't time for her to be a part of play groups or other social activities," wrote another.

Others described their children withdrawing or avoiding social situations—particularly large groups—because of the effort involved in trying to hear: "At lunchtime, she would go off by herself so she could turn off her hearing aids and take a break from the strain of hearing;" or the fear that they might look foolish: "He's so scared he has missed something that was said and will sound stupid that he is too scared to approach other teens or try and join a group conversation."

"She has learned to nod or just smile instead of appropriately answering questions because she did not hear them," wrote one caregiver.

Several wrote that their child had become "less confident," "insecure," and "more introverted and cautious of social situations."

A few caregivers indicated that troubling challenges involving how to participate in social relationships are affecting their child's friendships.

"He seems to misunderstand people's intentions, and then he feels like people don't like him. And he feels different," wrote one parent. "He has no social skills," wrote another.

"She only has one real friend, she has gone through friends quickly and we are just starting to figure out that it may be because of her behavior," another caregiver wrote.

Currently used approaches to hearing loss management, how well they work, and their downsides

Caregivers were asked a series of questions about the therapies that were currently being used by their children to manage chemotherapy-induced hearing loss and its consequences (question #12), how well it helps treat symptoms (question #13) or aided the important activities in the child's life (question #14), as well as the downsides of these strategies or treatments (question #15).

The therapies and management strategies used were similar to those mentioned during the EL-PFDD meeting, with hearing aids the most commonly used, followed by: speech therapy; FM systems; other forms of occupational therapy and mentoring; and 504 plans for school (or other adaptations to the academic environment). In addition, one child was learning American Sign Language (ASL) to use "in noise filled environments." Another respondent was using a "zeolite" spray, in an effort "to try to detox the platinum from chemo and hopefully prevent more loss."

Responses regarding how well these interventions work were mixed. Some reported that their approach worked "moderately well" for their child, others only "somewhat," but for many not at all: "I don't see that much improvement," was one response, and another: "I'm not sure it really treats symptoms." There was similar feedback in response to the question about whether these strategies improved the child's ability to engage in activities that were important to them—with one highlighting how the therapist adapts to their child's needs, and another that their management strategy "only addresses the actual hearing loss and not any of the social and educational side effects."

Most of the responses addressed the problems with these management strategies, particularly in reference to hearing aids. Although participants at the EL-PFDD meeting mentioned that hearing aids were taken out or not used, the extent to which this occurs became more evident in several of the responses to the post-meeting questionnaire. "She has hearing aids but has pretty much given up on them," wrote one. "She refuses to wear hearing aids," another responded. Others indicated that their child only wears them sometimes:

- "He currently has hearing aids but he usually doesn't wear them and the hearing aids making everything sound 'electronic' according to my son."
- "Periodically uses hearing aids, though at this time has decided to go without due to feeling 'different'"

Still others described situations where they could not be worn: "Hearing aids aren't meant to be worn where it's dirty, sweaty or dusty—but that is everyday conditions on the farm;" and "Wearing hearing aids isn't possible while swimming."

Some described the other limitations of hearing aids, such as "background noise renders them useless," and "[they] give feedback a lot and aren't truly capable of giving her complete access to sound. They get full of ear wax, are hard to clean, and the ear molds have to be replaced frequently as she grows." A couple mentioned the cost: "The digital aids she needs that can be tuned to only the frequencies where she has loss, are $6000+ per pair"—which is particularly high when children often take them out, breaking or losing them. Others described the dangers of being dependent on a battery-operated technology: and "constantly having to replace batteries for hearing aids." Some emphasized the discomfort, which seemed to go beyond just "hurting the ears" but probably due to social stigma "caused some additional emotional upset" and "has become a trigger for cluster migraines".

"The hearing aids do not replace all the sounds lost, make other sounds sound odd and add another level of emotional distress given that children can be cruel. Being a cancer survivor with multiple late effects - adding one more thing that makes a child different and doesn't provide significant benefit is not ideal," wrote one.

Similarly, FM systems helped some in the educational context, but that was all: "It only helps a little academically. But sometimes the FM system isn't working right, or it bothers her ear, and she only wears it in the classroom." A downside is that the system "singles her out as different and special—she just wants to fit in. "He hated the FM system with the teacher mic as it emphasizes his struggles and draws more attention to himself in an unusual way."

Another issue mentioned generally is that the interventions require work and cause fatigue, stress, frustration, and "discord in our home after he tries to hear all day, exhausted." Several mentioned the time that various therapies and interventions take: "They take time away from him being a kid. We cannot do extracurricular things because he is busy dealing with speech lessons."

Others expressed a desire for something other than what is currently available: "There is no treatment. I am very interested in drug trials to regrow the hairs that allow high frequency hearing."

A treatment not mentioned as being used was Cochlear implants. One response provided by a caregiver earlier in the survey illustrates one reason why some patients do not use it: "I worry that if her hearing loss increases to the point of needing a cochlear implant, that she will lose opportunities for treatments that are currently being developed (such as stem cell treatments to regenerate cilia/hair cells in the ear) which she has no access to."

What would be an ideal treatment for chemotherapy-induced hearing loss?

Question #16 asked participants to describe their perception of an ideal treatment. There were a few types of responses.

A small number wanted better access or use of the available options: "Better insurance coverage for hearing aids and equipment for them," "improved learning environments," and even call for a more positive attitude and acceptance from one caregiver whose son's "hearing loss is managed well with hearing aids." But even this caregiver wrote "Yes, I may be even more grateful if he didn't have hearing loss but I can't play that 'what if' game."

Soliciting patient preference was, in the fact, the objective of the EL-PFDD process: to influence drug development and regulatory approval so that other patients with hearing loss have options and that future cancer survivors do not experience chemotherapy-induced hearing loss.

The vast majority of the participants indicated that they wanted treatments that restore "hearing loss that [are] not hearing aids or implants," or-short of that-could put a "permanent end to loss progression and an end to tinnitus."

A few focused on treatments that would "reverse the hearing loss" by addressing the root cause of the loss and "restore/regrow cilia/hair cells within the ear." Some are looking for "a medication or treatment that would restore the hearing loss without permanent or long term side effects," preferably "an oral medication," though others wrote "something that could restore normal hearing would be worth almost any risk." There was also a call for options or trials for older youth.

The other type of response was a call for treatments that could prevent chemotherapy-induced hearing loss in the first place:

- "Ideal? I wish this could have been avoided! I am hopeful that treatments to help mitigate the damage done by cisplatin will be approved and become part of the protocols for brain cancer so other children will not have to suffer this late effect. For my son - the damage has been done."

- "Something that can be taken during or after chemo/radiation to prevent progression of hearing loss, or pediatric chemos that would not cause hearing loss at all."

- "For future children, getting trial drugs to market so that we can prevent future families from undergoing the same struggles my son is facing."

- "PREVENTION!! My son was able to participate in a trial drug program, sodium thiosulfate, during his relapse where he had no further hearing loss while on the cisplatin drugs and with no side-effects, he had NO additional hearing loss. So sad to think this was 17 years ago and that hearing loss could be prevented for many children."

- "I wish we would have had STS given to her on the first two rounds of chemotherapy. We saw her audiology test drop from before chemo to round two. After round two through round six there was no decrease in loss. Wish we would have been disclosed STS before she started chemotherapy. How do we get rid of the platinum on her ears now that causes further hearing loss from here into the future?"

These responses anticipated the final survey question (#17), soliciting their willingness to add a treatment that might have prevented the hearing loss.

While your child was in active treatment, would you have considered adding a treatment that could help prevent potential hearing loss to their treatment protocol?

The resounding answer, was "YES!" and "absolutely."

Many mentioned sodium thiosulphate (STS). Some had used it:

- "Yes and I did pursue STS. She had a total of 6 rounds of Cisplatin. She was given STS per my request three of the six rounds. At the start of her 3rd round she had her first hearing test since chemo had begun and it showed she had a loss in the higher frequencies. Her baseline hearing test showed perfect hearing."
- "We used STS after round two; it worked wonders. I wish we knew about it before we started."

Indeed, others were angry that they had not known it was an option:

- "Sodium thiosulphate wasn't available when my child started treatment. I would have pursued this if it was."
- "I am angry that my daughter's oncologists didn't even know about clinical trials for STS that had been going on for many years. I spent countless hours researching and trying to figure out how to help stop her hearing loss and to hopefully be able to regain hearing but when I mention any treatment to the oncologist, she responds with 'a deaf baby is better than a dead baby' and greatly underplays the life-altering (and at least somewhat preventable) and life-long consequences that come because of the chemo."
- "Yes. I think it is just as important to offer parent's options as it is to try and eliminate the cancer. All treatments/interventions come with risks, but families should be included in the decision-making process and not have decisions made without their knowledge." And: "Apparently my son's oncologist knew about the trials to prevent his loss but was not impressed enough to consider it until it has been through more trials. I feel that this should have at least have [been] brought to our attention. My son will tell you that he would have rather run the risk than to have ended up with the struggles he is currently dealing with."

Finally, one respondent made a plea to FDA to consider what it had seen about STS at the EL-PFDD meeting:

- "At the meeting our daughter was seated with two other survivors with hearing loss they got 12 to 15 years ago. Directly behind them in the next row was a boy that received the preventative medication for hearing loss 17 years ago. He was with his mom and doctor who gave him the preventative medication. It must have been so frustrating for the doctor to have the knowledge that the three girls seated in front of him could have received the preventative medication and not have hearing loss as they do now. It is my hope that the FDA was able to see that physical picture in front of them at the meeting."

Incorporating patient input into a benefit-risk assessment framework for chemotherapy-induced hearing loss

Over the past several years, FDA has developed an enhanced structured approach to benefit-risk assessment in regulatory decision-making for human drugs and biologics. The Benefit-Risk Assessment Framework involves assessing five key decision factors: Analysis of the Condition, Current Treatment Options, Benefit, Risk, and Risk Management. When completed for a particular product, the Framework provides a succinct summary of each decision factor and explains FDA's rationale for its regulatory decision.

In the Framework, the Analysis of Condition and Current Treatment Options rows summarize and assess the severity of the condition and therapies available to treat the condition. The assessment provides an important context for drug regulatory decision-making, including valuable information for weighing the specific benefits and risks of a particular medical product under review.

The input provided by patients and patient representatives through the Chemotherapy-Induced Hearing Loss EL-PFDD meeting and docket comments may inform the understanding of the Analysis of Condition and Current Treatment (or Prevention) Options for this late effect of cancer chemotherapy.

The information in the top two rows of the sample framework for chemotherapy-induced hearing loss, below, draws from various sources, including what was discussed at the EL-PFDD meeting on September 13, 2018, and the sources cited on page three of this report. This sample framework contains the kind of information that, it is anticipated, could be included in a framework completed for a medication under review to treat or prevent chemotherapy-induced hearing loss. This information is likely to be added to or changed over time based on a further understanding of the condition or changes in the treatment armamentarium.

Decision Factor	Evidence and Uncertainties	Conclusions and Reasons
Analysis of chemo-induced hearing loss	Chemotherapy-induced hearing loss is a serious late effect of childhood cancer treatment, particularly platinum-based chemotherapy which is used in about 60 to 70% of all children with solid tumors. The hearing loss results from permanent damage to the sensory hair cells within the cochlea, caused when platinum-based drugs are taken up by cells within the inner ear. Damage begins at the opening of the cochlea, or base, where high frequency sounds are processed, and then progresses to the apex where low frequency sounds are encoded. In 20-50%, the damage may be progressive. The loss of hearing has consequences for speech development and the ability to communicate. Chemotherapy-induced hearing loss creates barriers to learning, such as delayed auditory processing. This limits academic pursuits and career options for many individuals.	Chemotherapy-induced hearing loss is a major disability—a very serious life-altering toxicity that creates a barrier of silence between the patient and the rest of the world. In addition to the loss of hearing, this disability can cause speech development issues, and creates communication difficulties. Though non-life threatening, the emotional consequences of social isolation, challenges to learning, and decreased employment options that may limit the ability to live independently are very real and serious.

Decision Factor	Evidence and Uncertainties	Conclusions and Reasons
Analysis of chemo-induced hearing loss	Hearing loss also has a profound impact on socialization and relationships and the ability to participate in sports or the performing arts, reducing the quality of life for patients and their families. Many children with chemotherapy-induced hearing loss withdraw from the world. The inability to hear alarms and other sounds may put individuals at risk of bodily danger.	Individuals with chemotherapy-induced hearing loss have complex treatment needs for therapies that address both the cause of the condition, and its consequences.
Current Treatment Options *See the Voice of the Patient report for a more detailed narrative.*	Current management for hearing loss relies on a number of interventions including hearing aids, speech and occupational therapy, and other adaptive strategies. There are, however, many downsides to these approaches. These do not replace lost hearing, may not work well in certain settings, and many children refuse to use them. These treatments only mitigate the symptoms and clinical consequences and not the underlying causes of the hearing loss (damage to cells of the inner ear and the endocochlear potential). Participants expressed a desire for treatments that restore lost hearing, and short of that, stop further progression of hearing loss. There was also an interest in treatments that could prevent hearing loss in other children with cancer.	There IS an unmet need for more effective and tolerable FDA-approved therapies to restore lost hearing and stop progression of hearing loss. There is also a need for alternative chemotherapy options that do not have hearing loss as a side effect, and for other safe and effective medications that may prevent the damage caused by chemotherapy to the ear.

Conclusion

This meeting emphasized the urgent need for increased awareness of hearing loss as a late effect of childhood cancer treatment, particularly platinum-based chemotherapy. Participants described how hearing loss affected their social lives and relationships, academic pursuits, ability to participate in sports or the performing arts and ultimately their career options. Participants emphasized both the need to find less toxic alternative cancer therapies as well as the unmet need for treatments that mitigate and compensate the effects of hearing loss. This EL-PFDD meeting also provided a unique opportunity to hear about the consequences of hearing loss on the daily lives of patients as well as what they most need from potential treatments.

"We've done a fantastic job over the last 40 or 50 years improving the outcome for children with cancer. But it takes us a long time to start dialing down on the intensity of therapy to prevent late effects, to make sure that we can do that safely. So we really have to look at things differently," said Dr. Greg Reaman of the CDER at FDA. Dr. Reaman, who is currently the associate director for pediatric oncology in FDA's Oncology Center of Excellence, noted that even though many parents said they "wouldn't change a thing" and would make the same choice to use these platinum-based chemotherapies to save their child's life despite the risk of hearing loss: "We have to change things. We as clinicians; we as investigators; we as regulators of new drugs."

Dr. Reaman summarized some of the other key messages he heard from cancer patients and survivors, as well as their caregivers during the meeting:

- Some treated with chemotherapy as children feel they "don't have a life" despite surviving cancer, due to their hearing loss.
- Many frequently feel embarrassed by awkward social situations that are a consequence of their hearing loss, socially isolated, and that they need to avoid large groups. Some have even been bullied because of hearing loss.
- Many live the rest of their lives with constant white noise and tinnitus.
- Some feel like they are a burden to others because they require assistance all the time.
- Some are fearful (that they may not hear dangers in their environment).
- Some feel frustrated and that their potential is limited by their hearing loss.
- The impact of hearing loss increases over time in over 80% of people affected.
- Most are unaware that there are potential therapy options in development—including current new drug applications.
- What those with chemotherapy-induced hearing loss want from a potential therapy is the recovery of some normal hearing and -short of that-halting progression of ongoing hearing loss.

Dr. Reaman said that he was not aware of any treatments in development that might restore hearing—making it all the more important to focus on prevention.

"This is a major toxicity of a drug probably used in about 60 to 70% of all children with solid tumors, and there's nothing on the horizon that looks like it's going to replace it in anytime soon. This is real," Dr. Reaman said. "We really need to look at less toxic regimens."

"When we talk about the risk/benefit considerations for pediatric cancer therapies, we are much more focused on immediate risks but here we're looking at long-term risks," said Dr. Reaman. "We don't have 30, 40 years to do something about this. So, we really have to start thinking differently. We need to do things a little bit differently as far as clinical trial design."

He said that doing things differently should also include looking at the preclinical evaluation of new drugs for off-target effects—not only on the major organ systems (heart, kidney, liver, and neurologic system) but issues such as hearing loss.

"Ultimately, there needs to be a replacement for cisplatin, or at least a way that cisplatin can be given with an oto-protectant in all situations so that it's going to prevent hearing loss or prevent the ototoxicity of platinum therapy," Dr. Reaman said.

"This is a very, very serious disability, a very serious—not life-threatening—but life-altering toxicity that can and must be dealt with, that can and must be considered in risk/benefit analysis of new drug therapies," he concluded.

George Dahlman of Children's Cause for Cancer Advocacy, one of the organizations hosting the event drew the meeting to a close. He thanked all the patients, their families and caregivers, and the physicians and scientific experts who participated in the meeting—a

"We all feel the same kinds of frustrations and potential outcomes and hopes that we have for development," said Dahlman. "It inspires us to stay together and to keep the momentum going, both for the FDA and for the companies and for all of us as a community."

The goal of this process is to improve outcomes of children with cancer—and to make certain that the late-effect of hearing loss is not a disability that any will have to endure for the rest of their lives. It is the hope of all the organizations sponsoring the event that the information shared at the meeting, and in this report, will be used to guide approvals of much needed therapies to prevent and ultimately treat chemotherapy-induced hearing loss.

APPENDIX 1

Externally-Led Patient Focused Drug Development (PFDD) Meeting
Childhood Cancer Hearing Loss

September 13, 2018, 1:00-5:00 pm
College Park Marriott Hotel & Conference Center
Hyattsville, MD

1:00-1:10 **Opening Remarks**
Cat Paciente, Momcology

1:10-1:25 **Welcome Remarks**
Rea Blakey
Associate Director, External Outreach and Engagement
Oncology Center of Excellence
Food and Drug Administration

1:25-1:40 **Chemotherapy-Induced Hearing Loss Clinical Overview**
Kristy Knight, MS, CCC-A, FAAA
Associate Professor
Audiology Training Coordinator, Oregon LEND Program
Child Development and Rehabilitation Center, Doernbecher Children's Hospital
Oregon Health and Science University

1:40-1:50 **Introduction and Meeting Overview**
James Valentine, JD, MHS, Meeting Moderator

1:50-2:00 **Audience & Remote Demographic Polling**

2:00-3:10 **Topic 1: Living with Chemotherapy-Induced Hearing Loss**
Panel (25 minutes)

Audience & Remote Polling (10 minutes)

Moderated Audience Discussion (35 minutes)

3:10-3:25 **Break**

Externally-Led Patient Focused Drug Development (PFDD) Meeting
Childhood Cancer Hearing Loss

September 13, 2018, 1:00-5:00 pm
College Park Marriott Hotel & Conference Center
Hyattsville, MD

3:25-3:35 **Challenges in Clinical Trial Design in Chemotherapy-Induced Hearing Loss**
Greg Aune, MD, PhD
Assistant Professor
UT Health San Antonio-Greehey Children's Cancer Research Institute

3:35-4:45 **Topic 2: Current & Future Treatments from the Patient and Caregiver**
Panel (25 minutes)

Audience & Remote Polling (10 minutes)

Moderated Audience Discussion (35 minutes)

4:45-5:00 **Meeting Summary**
Greg Reaman, MD
Associate Director for Pediatric Oncology
Oncology Center of Excellence
Food and Drug Administration

5:00-5:10 **Closing Remarks & Next Steps**
George Dahlman, CEO, Children's Cause for Cancer Advocacy

Adjourn

APPENDIX 2

Patients - Total		**29**
	On Site	**25**
	Remote	**4**
Caregivers - Total		**76**
	On Site	**47**
	Remote	**29**
Industry Professionals		**12**
Researchers		**1**
Non-Profit Org		**14**
Other		**40**
Government		**16**
Hearing Loss Professional		**33**
Health Care Professionals		**13**
On Site Total		**153**
Remote Total		**98**
1st PFDD Meeting Attended?		**252**

As of September 13, **252** individuals had registered for this meeting; this included representation from patients, caregivers, patient advocacy organizations, key FDA staff and industry partners. Of these:

- **153 attended in person**
- **98 attended via webcast**

Of those registered to attend in person, **three (3) were FDA officials** within CBER and CDER, including:

- Opening Remarks: Rea Blakey, Associate Director, External Outreach and Engagement, Oncology Center of Excellence, FDA
- Meeting Summary: Greg Reaman, MD, Associate Director for Pediatric Oncology, Oncology Center of Excellence, FDA

Of those registered to attend in person, **eleven (8) were industry representatives** from the following companies:

- Sensorian
- Otonomy
- Fennec Pharmaceuticals
- Decibel Therapeutics
- Spiral Therapeutics

Of those registered to attend in person, **sixteen (16) were patient advocate representatives** from the following organizations:

- Children's Cause for Cancer Advocacy
- Momcology
- Children's Brain Tumor Foundation
- Mattie Miracle Cancer Foundation
- National Coalition for Cancer Survivorship
- Leukemia and Lymphoma Society
- Hearing Loss Association of America
- Along Comes Hope

Of those registered to attend either in person or online, **medical professionals or hearing loss professionals** were represented from the following hospitals or universities:

- Harvard/Dana Farber Cancer Institute
- National Institutes of Health/NIDCD
- University of Maryland
- Ohio State University
- Medical College of Wisconsin
- Oregon Health and Science University (panelist)
- Children's Hospital Colorado
- Cook Children's
- Mayo Clinic
- UT Health San Antonio-Greeley Children's Cancer Research Institute
- Wesley Healthcare

Of those registered to attend either in person or online, **105** were either: individuals diagnosed with the condition; a parent of a child with the condition; or a primary caregiver of a child with the condition.

Individuals who had registered to attend the meeting in person and via webcast included representation from the following states and countries:

States:
VA, DC, MD, OH, WI, CO, MA, OR, TX, KS, CA, NY, AZ, PA, GA, IL, HI, RI, UT, MN, FL, MO, NJ, CT, NC

Countries: US, UK, Canada, India, France

Externally-Led Patient-Focused Drug Development Meeting: Chemo Induced Hearing Loss

Polling Questions and Results

Total number of respondents: 44 (The number varied by question).

DEMOGRAPHIC POLLING QUESTIONS (asked at beginning of meeting)

1) I am a: (select all that apply)	Number of participants (percentage)
Person living with chemotherapy-induced hearing loss	10 (25%)
Caregiver of someone living with chemo-induced hearing loss	26 (65%)
Not sure	4 (10)

Total number of responses: 40, unique responses: 40

2) Your age or, if you are a *caregiver,* the age of your affected family member (pick *one* to discuss):	Number of participants (percentage)
0-3 years old	1 (2.33%)
4-8 years old	5 (11.63%)
9-12 years old	8 (18.6%)
13-18 years old	14 (32.56%)
18-25 years old	10 (23.26%)
26-35 years old	3 (6.98%)
36-45 years old	0 (0)
46-55 years old	1 (2.33%)
older than 55	1 (2.33%)

Total number of responses: 43, unique responses: 43

3) Where do you currently reside?	Number of participants (percentage)
Eastern Standard Time Zone	21 (47.73%)
Central Standard Time Zone	7 (15.91%)
Mountain Standard Time Zone	2 (4.55%)
Pacific Standard Time Zone	5 (11.36%)
Canada	4 (9.09%)
Mexico	0 (0)
Outside of North America	5 (11.36%)

Total number of responses: 44, unique responses: 44

4) Do you live in:	Number of participants (percentage)
A city	10 (23.26%)
A rural area	10 (23.26%)
A suburban area	23 (53.49%)

Total number of responses: 43, unique responses: 43

5) Age you or your affected family member first received chemotherapy:	Number of participants (percentage)
0-3 years old	20 (46.51%)
4-8 years old	11 (25.58%)
9-12 years old	8 (18.6%)

13-18 years old	3 (6.98%)
18-25 years old	1 (2.33%)
26-35 years old	0 (0%)
36-45 years old	0 (0%)
45-55 years old	0 (0%)
older than 55	0 (0%)

Total number of responses: 43, unique responses: 43

6) Number of years you or your/your loved one has been living with hearing loss:	**Number of participants (percentage)**
I am currently on chemotherapy and have not yet experienced hearing loss	1 (2.5%)
1-5 years	13 (32.5%)
6-10 years	7 (17.5%)
11-15 years	10 (25%)
15-25 years	8 (20%)
26-35 years	1 (2.5%)
More than 35 years living with hearing loss	0(0%)

Total number of responses: 40, unique responses: 40

PANEL 1 POLLING QUESTIONS (asked after Panel 1 presentations): Living with Hearing Loss and Daily Impacts that Matter Most to Patients

7) What is the most severe level of hearing loss you suffer at any frequency range?	**Number of participants (percentage)**
Normal (-10-20 dB)	2 (5.41%)
Mild (20-40 dB)	2 (5.41%)
Moderate (40-55 dB)	8 (21.62%)
Moderately severe (55-70 dB)	9 (24.32%)
Severe (70-90 dB)	5 (13.51%)
Profound (90-120dB)	11 (29.73%)

Total number of responses: 37, unique responses: 37

8) Rank the *issues that are a result of hearing loss that most impact* you or your affected family member's *daily quality of life:*	**Rank [more?]**
Speech development	6
Ability to communicate	3
Learning/school challenges	2
Emotional or behavioral problems	4
Participation in sports or other extracurricular activities	5
Ability to socialize/social anxiety	1
Depression	7
Other	8

Total number of responses: 29, unique responses: 29

9) Select *the most important thing* you or your affected family member *used to do* that you or your family member *now can't do as well because of hearing loss:*	**Number of participants (percentage)**
Participate in sports or extracurricular activities	3 (8.11%)
Do well in school	8 (21.62%)
Communicate with friends or participate in social activities	21 (56.76%)
Find a job	0 (0%)
Perform well at a job or work	0 (0%)
Take care of a family member	0 (0%)
Other	5 (13.51%)

Total number of responses: 37, unique responses: 37

10) How has the impact of you/your loved one's hearing loss changed over time?	**Number of participants (percentage)**
Impact has gotten greater or affects additional areas of life (home, school, work, friendships, etc.)	29 (76.32%)
Impact has stayed the same	6 (15.79%)
Impact has lessened	0 (0%)
Not sure	3 (7.89%)

Total number of responses: 38, unique responses 38

11) Rank this issue that worries you/your loved one the most about the hearing loss:	**Rank [More?]**
Academic success	4
Finding a job/career success	7
Ability to live independently	6
Lack of social interaction	3
Physical safety from not being able to hear adequately	5
Long term mental/emotional health	1
That it will get worse	1
Other	8

Total number of responses: 32, unique responses 32

PANEL 2 POLLING QUESTIONS (asked after Panel 2 presentations): Patients' Perspectives on Current Approaches and Future Treatments

12) What are you/your child currently doing to help treat the condition or its impacts (select all that apply):	**Number of participants (percentage)**
Speech/language therapy	4 (8.7%)
Hearing aids	11 (23.91%)
Cochlear implant	1 (2.17%)
Medicine to prevent/treat hearing loss	4 (8.7%)
Medicine for anxiety or depression	3 (6.52)%
Other medicines	0 (0)
Educational accommodations/specialized plans	9 (19.57%)
Counseling/behavioral intervention	0 (0)

None	13 (28.26%)
Other	1 (2.17%)

Total number of responses: 46, unique responses 36

13) What is your experience in, and perception of, clinical trials for a new hearing loss drug?	**Number of participants (percentage)**
I am currently participating in a trial	0 (0)
I have participated in a trial, and I would do so again	5 (14.29%)
I have participated in a trial, and I would not do so again	0 (0)
I have not participated in a trial, because I didn't know about the opportunity	27 (77.14%)
I have not participated in a trial because I was not eligible	1 (2.86%)
I have not participated in a trial, although I was aware of the opportunity and eligible	0 (0)
I would never enroll in a clinical trial	0 (0)
Not sure	2 (5.71%)

Total number of responses: 35, unique responses 35

14) In general, how much do these medical devices, equipment, medicines, counseling or lifestyle changes improve your or your affected family member's quality of life:	**Number of participants (percentage)**
In general, they have ***really*** *helped manage the most difficult issues* and *improving my or my family member's quality of life*	3 (9.09%)
In general, they *have helped* ***somewhat*** *in managing the worst symptoms* and *improving my or my family member's quality of life*	18 (54.55%)
In general, they *have* ***not helped much at all*** *in managing the worst symptoms* and improving my or my family member's quality of life	12 (36.36%)

Total number of responses: 33, unique responses 33

15) How have treatment options for hearing loss changed since you or your affected family member first suffered hearing loss?	**Number of participants (percentage)**
No new treatment options	25 (80.65%)
Some new treatment options	5 (16.13%)
Do not choose to treat	1 (3.23%)
Other	0 (0%)

Total number of responses: 31, unique responses 31

16) Please rank what would be the most important impacts from a new treatment for you or your affected family member	**Rank [More?]**
Less toxic cancer treatments with reduced impact on hearing	4
Improved hearing ability via device utilization	5
Stop further progression of hearing loss	2

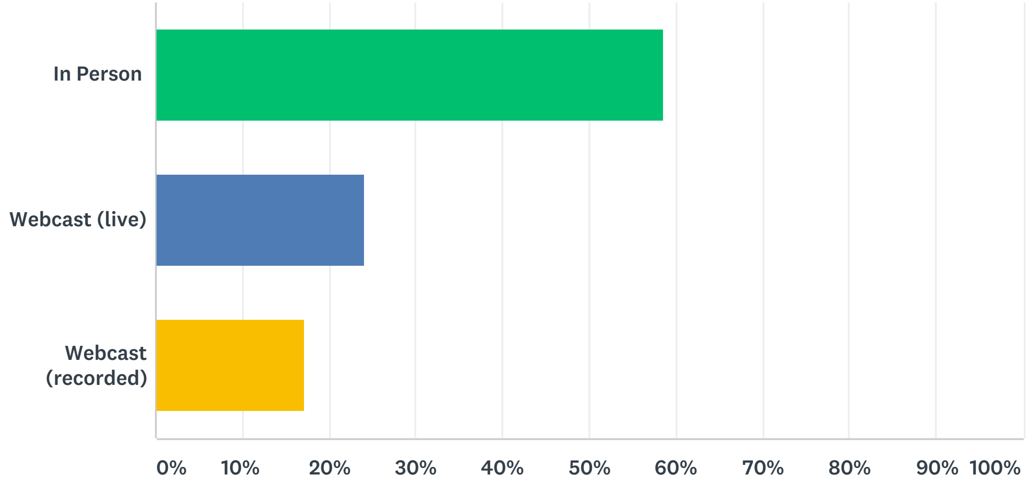
Recover some hearing capability	1
Protective treatments to prevent hearing loss from cancer treatments	2
Other	6

Total number of responses: 30, unique responses 30

-

Q1 Describe how you participated in the September 13th meeting:

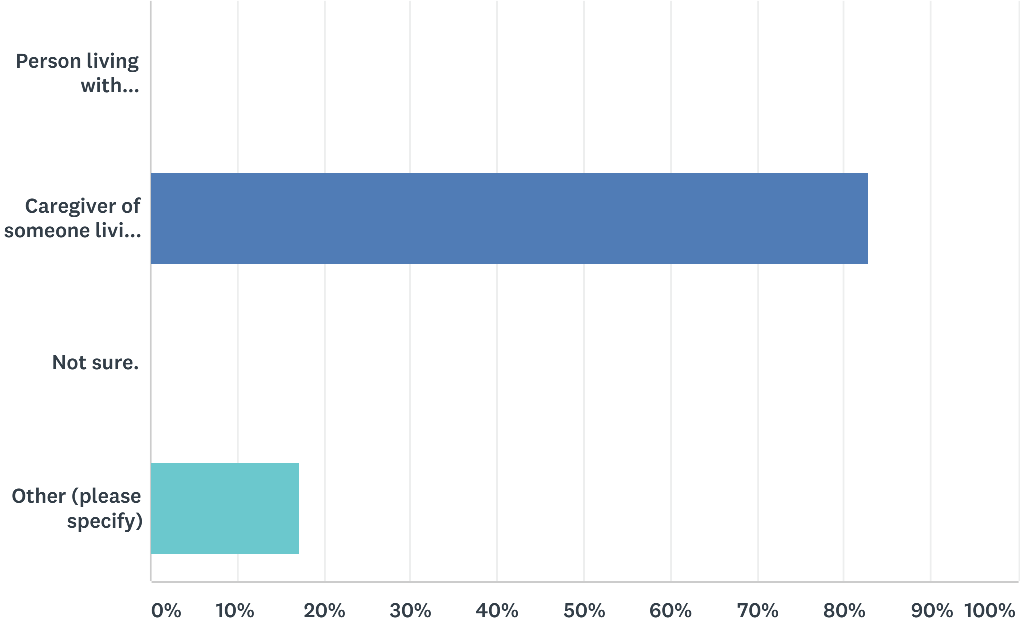
Answered: 29 Skipped: 0



ANSWER CHOICES	RESPONSES	
In Person	58.62%	17
Webcast (live)	24.14%	7
Webcast (recorded)	17.24%	5
Total Respondents: 29		

Q2 I am a:

Answered: 29 Skipped: 0

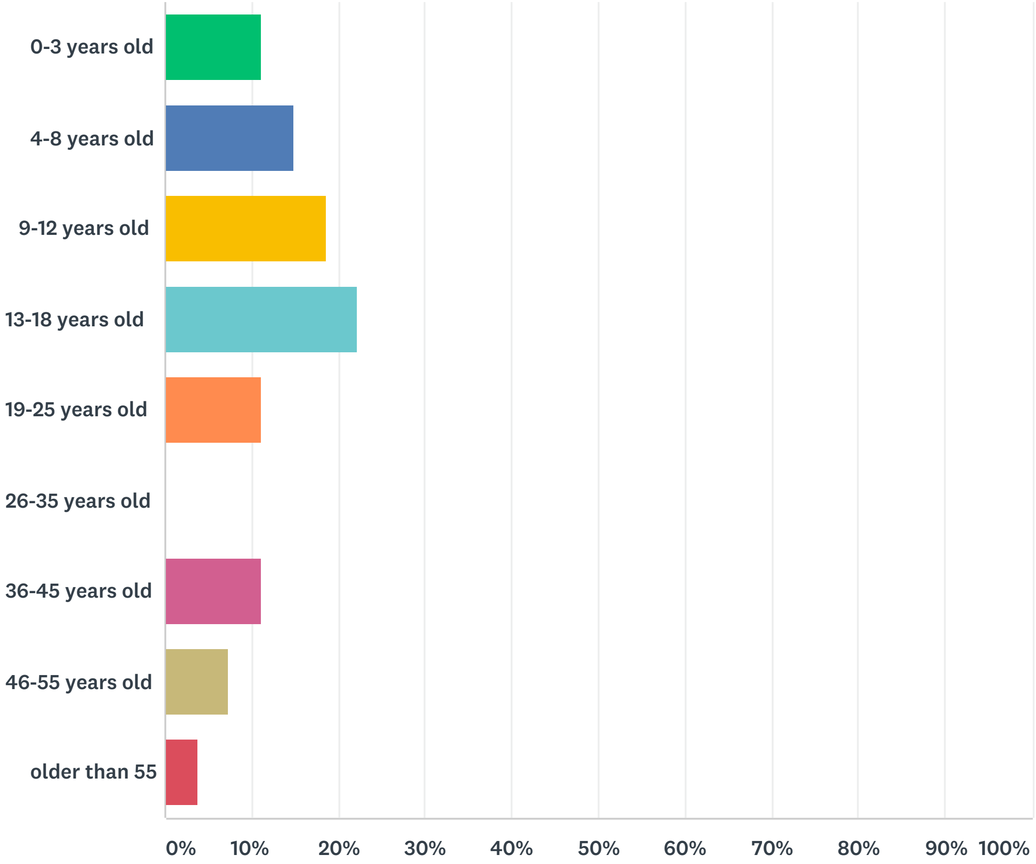


ANSWER CHOICES	RESPONSES	
Person living with chemo-induced hearing loss.	0.00%	0
Caregiver of someone living with chemo-induced hearing loss.	82.76%	24
Not sure.	0.00%	0
Other (please specify)	17.24%	5
Total Respondents: 29		

#	OTHER (PLEASE SPECIFY)	DATE
1	Representing a meeting organizer	10/29/2018 2:19 PM
2	Grandmother of person living with chemo induced hearing loss	10/16/2018 7:43 PM
3	Friend of Fennec	10/16/2018 6:47 PM
4	Caregiver of someone with no chemo-induced hearing loss following clinical trial.	10/4/2018 4:24 AM
5	Researcher	10/2/2018 11:24 AM

Q3 Your age or - if you are a caregiver - the age of the affected family member:

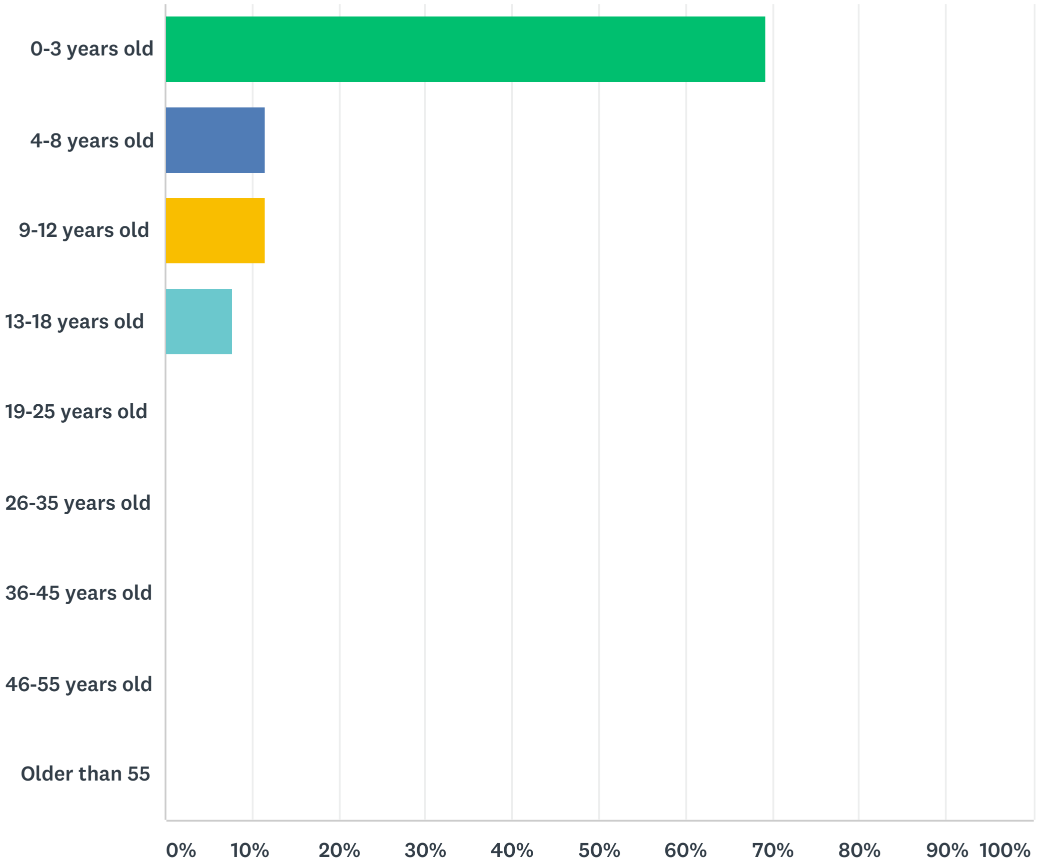
Answered: 27 Skipped: 2



ANSWER CHOICES	RESPONSES	
0-3 years old	11.11%	3
4-8 years old	14.81%	4
9-12 years old	18.52%	5
13-18 years old	22.22%	6
19-25 years old	11.11%	3
26-35 years old	0.00%	0
36-45 years old	11.11%	3
46-55 years old	7.41%	2
older than 55	3.70%	1
TOTAL		27

Q4 Age that you or your affected family member first received chemotherapy:

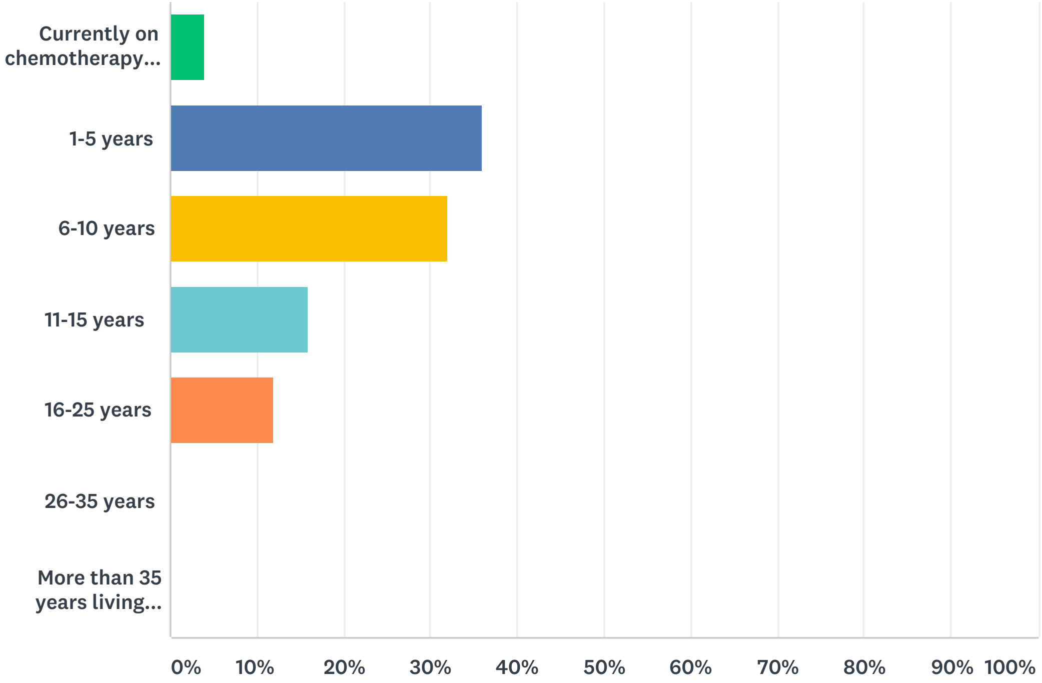
Answered: 26 Skipped: 3



ANSWER CHOICES	RESPONSES	
0-3 years old	69.23%	18
4-8 years old	11.54%	3
9-12 years old	11.54%	3
13-18 years old	7.69%	2
19-25 years old	0.00%	0
26-35 years old	0.00%	0
36-45 years old	0.00%	0
46-55 years old	0.00%	0
Older than 55	0.00%	0
TOTAL		26

Q5 Number of years that you or your loved one has been living with hearing loss.

Answered: 25 Skipped: 4



ANSWER CHOICES	RESPONSES	
Currently on chemotherapy and have not yet experienced hearing loss.	4.00%	1
1-5 years	36.00%	9
6-10 years	32.00%	8
11-15 years	16.00%	4
16-25 years	12.00%	3
26-35 years	0.00%	0
More than 35 years living with hearing loss.	0.00%	0
TOTAL		25

Q6 Of all the symptoms/concerns that your child experiences because of hearing loss, which 1-3 issues have the most significant impact on your/your child's life? (Examples may include speech development, learning, behavioral symptoms, quality of life…)

Answered: 25 Skipped: 4

#	RESPONSES	DATE
1	Speech development, quality of life - ability to communicate and participate in “normal” childhood activities, music and dance have been the most impacted.	10/31/2018 2:17 AM
2	Socialization/quality of life, learning, anxiety	10/30/2018 9:01 PM
3	Quality of life due to hearing loss, and sleep loss from tinnitus.	10/29/2018 2:06 PM
4	Learning struggles and social impact	10/29/2018 1:28 PM
5	Hearing loss processing issues foot drop	10/25/2018 7:43 AM
6	learning, quality of life, social/emotional/mental health	10/20/2018 12:59 PM
7	learning/working, socializing, quality of life	10/17/2018 3:29 AM
8	Quality of life	10/16/2018 7:43 PM
9	Na	10/16/2018 6:57 PM
10	Quality of Life and being unsure if this is Progressive. Speech, Developmental, Learning.	10/16/2018 12:50 PM
11	Speech Social Settings/Isolation (QOL) Safety (fire alarms at night)	10/10/2018 2:47 PM
12	Speech development, Chloe currently receives speech therapy twice a week in school and twice a week out of school. We worry about learning, if she can't hear all the sounds correctly then its hard for her to learn correctly. She also gets pulled out of class for speech therapy and so she loses those lessons too. 3rd grade the curriculum is getting harder and she is falling behind. We also worry about her socially and behaviorally. She exhibits aggressive behaviors sometimes in social situations and we just realized it could be linked to her not being able to hear what everyone is saying.	10/9/2018 10:00 AM
13	Learning through out his life definitely was the leading concern and had the most impact on his life. Learning to read, speech and conflictive development were some of the issues.	10/7/2018 12:51 PM
14	speech development, missing social cues, social struggles	10/4/2018 9:15 AM
15	Speech development Certain Loud sounds hurting her ears Tones and volumes of sounds she cannot hear	10/3/2018 6:58 PM
16	Quality of life, speech development and social life	10/3/2018 10:43 AM
17	Quality of life, speech, lack of confidence	10/2/2018 9:57 PM
18	Speech.. development.. learning.. behavioral	10/2/2018 8:15 PM
19	Social isolation is the most significant issue. Near impossible to have conversations in classrooms. Missing sounds change meaning of what is heard. Next is speech development. When hearing aids malfunction it's like taking away your glasses on a busy highway.	10/2/2018 6:20 PM
20	speech development, learning, & quality of life	10/2/2018 2:49 PM
21	Learning, quality of life, social experiences	10/2/2018 2:47 PM
22	1. quality of life 2. speech (articulation) 3. comprehension	10/2/2018 1:29 PM
23	Quality of life, safety issues when not wearing hearing aids, hearing appropriately at school and in social spaces	10/2/2018 12:51 PM
24	speech, self confidence, peers being mean	10/2/2018 12:22 PM

Q7 Are there specific activities that are important to you/your child but that you/your child cannot do at all or as fully as you would like because of his/her hearing loss? (Examples of activities may include participation in sports or social activities, academic achievement, …)

Answered: 24 Skipped: 5

#	RESPONSES	DATE
1	Participation in music and in dance or gymnastics (the gym is so loud that it would be impossible for her to hear a teacher over the deafening background noise). Being a part of social activities or even “normal” preschool is not possible because of her severe speech delay due to her hearing loss.	10/31/2018 2:17 AM
2	Participation in social and extracurricular activities. For example, she cannot go to typical school parties/dances because she can't hear people, she doesn't go out with groups of more than 3 or 4 people because she can't follow conversation, she quit the swim team because she couldn't understand instructions/coaching at the indoor pool. Being in crowded or noisy situations makes her anxious because she can never be sure what is going on or if she is missing things being said.	10/30/2018 9:01 PM
3	It is difficult at school and at movies. Loud noises trigger tinnitus.	10/29/2018 2:06 PM
4	My son struggles a great deal in school and has limited social interactions. He also has a lot of difficulty in loud venues so cannot enjoy things like assemblies, concerts or sporting events. The loud and ambient noise at these venues is too overwhelming and all the sounds run together.	10/29/2018 1:28 PM
5	Just sitting the the school cafeteria or participating in school events. It is too noisy to be able to hear and interact. Sports, as he cannot here instructions coaches give from a distance. Birthday parties, as they are always either too noisy or held in very noisy locations.	10/25/2018 7:43 AM
6	sports because of hearing coaches instructions in noise filled environments, social not wanting to be in noise filled environments.	10/20/2018 12:59 PM
7	participation in sports, social activities, job options	10/17/2018 3:29 AM
8	Academic achievement,social and sports (PE)	10/16/2018 7:43 PM
9	Na	10/16/2018 6:57 PM
10	Difficulty with some Sports we are so New to the Hearing Loss World and still adjusting. my son is Four Years old and its hard to tell what exactly is being affected.	10/16/2018 12:50 PM
11	Participation in sports Fatigue in "noisy" places; gyms, concerts, any crowd Classroom setting challenging to learn	10/10/2018 2:47 PM
12	Social activities, anywhere there is loud music.	10/9/2018 10:00 AM
13	We have a family farm and our son has chosen this as his occupation. Safety is a main concern especially with hearing loss	10/7/2018 12:51 PM
14	No	10/4/2018 9:15 AM
15	Anything with large crowds involved, loud areas or sounds	10/3/2018 6:58 PM
16	Swimming and other very physical activities where she cannot wear hearing aids.	10/3/2018 10:43 AM
17	Public school	10/2/2018 9:57 PM
18	Social emotional..	10/2/2018 8:15 PM
19	to the child. social activities, & academic achievement	10/2/2018 2:49 PM
20	I wouldn’t say that she cannot participate but her hearing loss makes participating difficult. For example, she is a competitive swimmer and has trouble hearing the starting beep	10/2/2018 2:47 PM
21	academic achievement water sports phone calls listening with headphones	10/2/2018 1:29 PM

22	Social activities with lots of background noise	10/2/2018 12:51 PM
23	school. social functions	10/2/2018 12:22 PM
24	Not yet experienced. He plays sports, sings on tune, and plays a musical instrument -- all with profound hearing loss in mid and high frequencies.	10/2/2018 11:37 AM

Q8 How has the impact of your child's hearing loss changed over time?

Answered: 24 Skipped: 5

#	RESPONSES	DATE
1	She received chemo as an infant, before her speech delay was as noticeable. The gap between her and her peers becomes wider every day.	10/31/2018 2:17 AM
2	She has grown more anxious and self-conscious over time. She is less willing to try new things/situations where she anticipates having hearing problems.	10/30/2018 9:01 PM
3	Definitely getting worse...	10/29/2018 2:06 PM
4	At first it impacted his speech and language learning and ability, but has now evolved into much greater impact for him socially and academically.	10/29/2018 1:28 PM
5	He's become more withdrawn and depressed at the isolation it has caused.	10/25/2018 7:43 AM
6	over time the hearing loss has only gradually decreased	10/20/2018 12:59 PM
7	Progressed to profound loss. Dx/development of co-existing issue of auditory processing delay, compounding the hearing issue.	10/17/2018 3:29 AM
8	Na	10/16/2018 6:57 PM
9	We did Three Stem Cell Transplants and it slowly got worse and worse.	10/16/2018 12:50 PM
10	He is more aware of his deficits, thus causing to withdraw more. Whispers in my ear to avoid embarrassment.	10/10/2018 2:47 PM
11	As she gets older, and more is expected of her, it has gotten extremely difficult. We are terrified she will be left behind academically and socially on school.	10/9/2018 10:00 AM
12	Hearing aids have definitely gotten more advanced but his speech quality deteriorated during his teen years because he didn’t want to wear the hearing aids	10/7/2018 12:51 PM
13	It has grown. We are seeing way more challenges now than we did when he was much younger	10/4/2018 9:15 AM
14	She finished Chemotherapy in June 2018. So far it hasn’t changed or worsened	10/3/2018 6:58 PM
15	It affected her speech development and due to chemo we had to wait until all chemo was done to address the hearing loss and get hearing aids.	10/3/2018 10:43 AM
16	Continuing slowly still	10/2/2018 9:57 PM
17	Alot.. of unanswered questions	10/2/2018 8:15 PM
18	Over time the social isolation has become more apparent. She refuses to wear hearing aids because they can not make sounds clearer. Only louder. They cause her ears to make lots of wax. She denies she has a disability.	10/2/2018 6:20 PM
19	No improvement.	10/2/2018 2:49 PM
20	As she has aged, she has noticed more how she is different. Also, as school is more difficult each year, she has to put in so much extra effort to hear and process.	10/2/2018 2:47 PM
21	Thanks to intensive therapy, the impact is limited, however, reading comprehension is an issue, as well as overall listening comprehension	10/2/2018 1:29 PM
22	More self conscious of her disability as she enters her teen years.	10/2/2018 12:51 PM
23	she is getting more and more creative working through it or I am afraid faking it so we are not concerned and she doesnt bother us (her parents)	10/2/2018 12:22 PM
24	Worsened over time with no plateau so far.	10/2/2018 11:37 AM

Q9 What worries you/your child most about your child's condition?

Answered: 24 Skipped: 5

#	RESPONSES	DATE
1	I worry that she will lose more access to sound and that even if her hearing doesn't get worse, that she won't be able to sing or enjoy music, which is what she loves more than just about anything. I worry that if her hearing loss increases to the point of needing a cochlear implant, that she will lose opportunities for treatments that are currently being developed (such as stem cell treatments to regenerate cilia/hair cells in the ear) which she has no access to.	10/31/2018 2:17 AM
2	Safety. As a young woman I was once nearly mugged walking out at night, but I heard the person walking faster behind me and ran -- she would not hear something like that and in the same situation would likely have been attacked. Isolation -- she is lonely and I worry that if the wrong type of person showers her with attention she could end up in a dangerous or abusive situation because she does not have many friends or people to turn to.	10/30/2018 9:01 PM
3	Tinnitus and progressive loss...	10/29/2018 2:06 PM
4	I worry that the many challenges will result in depression and emotional struggles later in life.	10/29/2018 1:28 PM
5	The isolation his hearing loss has caused.	10/25/2018 7:43 AM
6	Having hearing loss and transitioning into adulthood	10/20/2018 12:59 PM
7	His world is very small, ability to work and sustain himself, success with life skills	10/17/2018 3:29 AM
8	My son is visually impaired which is why we avoid drugs that can cause hearing loss	10/16/2018 6:57 PM
9	That it can be Progressive the Fear of being Deaf is what is most worrisome.	10/16/2018 12:50 PM
10	Losing his sweet spirit, had become more agitated.	10/10/2018 2:47 PM
11	Other than the academic and social things We worry that it will get worse. We worry that with every ear infection her hearing will worsen so we are constantly going to the doctors.	10/9/2018 10:00 AM
12	Quality of life	10/7/2018 12:51 PM
13	The long term social isolation - how he will feel different and the things he will choose not to do or cannot do because of his hearing loss	10/4/2018 9:15 AM
14	Speech and ongoing hearing loss	10/3/2018 6:58 PM
15	That she will have trouble in school socially and academically. That teachers or other caregivers will not help her and accommodate her needs. That other kids will not be understanding of her hearing loss and need for hearing aids. That she will struggle with accepting it.	10/3/2018 10:43 AM
16	People thinking he's slow if he's not responding to them due to hearing issues	10/2/2018 9:57 PM
17	Him being able to take care of his self when he gets older!!!	10/2/2018 8:15 PM
18	I worry that it could worsen. I worry that she will misunderstand something important ant work. I worry that she may have difficulty finding a job.	10/2/2018 6:20 PM
19	hearing loss makes me more worries.	10/2/2018 2:49 PM
20	Struggling academically.	10/2/2018 2:47 PM
21	having to rely on hearing aids and how the technology fails over time	10/2/2018 1:29 PM
22	Her safety when alone, her peer relationships, the sigma of having a disability.	10/2/2018 12:51 PM
23	it might get worse and that she will become depressed and retreat from normal life because she cant hear or speak as well as others.	10/2/2018 12:22 PM
24	That it will progress to complete loss.	10/2/2018 11:37 AM

Q10 How has hearing loss impacted you/your child’s social relationships?

Answered: 24 Skipped: 5

#	RESPONSES	DATE
1	We spend SO much time in various forms of therapy that there isn’t time for her to be a part of play groups or other social activities. Her speech and other developmental delays also make it hard for her to interact with children her age. She usually ends up playing with much younger kids.	10/31/2018 2:17 AM
2	She does not have a lot of friends. In high school she did not have many friends because she couldn't hear in large groups. At lunchtime she would go off by herself so she could turn off her hearing aids and take a break from the strain of hearing.	10/30/2018 9:01 PM
3	She often misses swaths of conversation...	10/29/2018 2:06 PM
4	He has very limited social relationships and few friends.	10/29/2018 1:28 PM
5	He's lost confidence to interact socially unless it in inside our home. Otherwise, he's so scared he has missed something that was said and will sound stupid that he is too scared to approach other teens or try and join a group conversation.	10/25/2018 7:43 AM
6	We tend not to be in noise fill environments.	10/20/2018 12:59 PM
7	He has not learned social norms to the capacity of others, he has accepted that he probably will misread cues and not be clear on topics of conversation, at times he abandons the decision to communicate,	10/17/2018 3:29 AM
8	Na	10/16/2018 6:57 PM
9	Not being able to hear clear, we call them Super Ears and sadly he only know the Medical World we have had an easy time because he is so little but I'm sure this will not be the case in years to come.	10/16/2018 12:50 PM
10	Very few close friends. Adults are not patient for responses.	10/10/2018 2:47 PM
11	She only has one real friend, she has gone through friends quickly and we are just starting to figure out that it may be because of her behavior, and the behavior may be a defense mechanism because she can't hear her friends talking.	10/9/2018 10:00 AM
12	More introverted and cautious of social situations because he cannot participate in group conversations	10/7/2018 12:51 PM
13	It is hard to really know, but he seems to misunderstand people's intentions, and then he feels like people don't like him. And he feels different.	10/4/2018 9:15 AM
14	It has impacted her hearing details for speech and not being able to hear certain sounds and hurt hearing other sounds.	10/3/2018 6:58 PM
15	Since she is only two years old it hasn’t yet impacted it. In social situation other children have tried to grab her hearing aids and ask what they are.	10/3/2018 10:43 AM
16	He doesn't have social relationships due to a big part of hearing loss	10/2/2018 9:57 PM
17	Alot he has no social skills..	10/2/2018 8:15 PM
18	She has few friends. She has learned to nod or just smile instead of appropriately answering questions because she did not hear them.	10/2/2018 6:20 PM
19	It makes me very sad when I see the child isolated.	10/2/2018 2:49 PM
20	Kids aren’t always nice. She has a few solid relationships who stand up for her but it is hard.	10/2/2018 2:47 PM
21	not much	10/2/2018 1:29 PM
22	She has found friends that accept her for who she is and avoids groups that marginalize her	10/2/2018 12:51 PM
23	whenever she wears hearing aids she feels different and insecure. so five years at least	10/2/2018 12:22 PM
24	No impact as of yet.	10/2/2018 11:37 AM

Q11 Is there a difference between how you/your child perform on hearing assessments in the clinic and how you feel your hearing works at home?

Answered: 23 Skipped: 6

#	RESPONSES	DATE
1	Not necessarily.	10/30/2018 9:01 PM
2	I think her results are reflective of her hearing loss...	10/29/2018 2:06 PM
3	Not to my knowledge.	10/29/2018 1:28 PM
4	Not really	10/25/2018 7:43 AM
5	There is no difference.	10/20/2018 12:59 PM
6	no, but assessments with the audiologist do not take into consideration the impact of work to utilize environmental cues for compensation. It may appear he "hears" better at home, but in reality he is working very hard to utilize more than just his hearing to understand others.	10/17/2018 3:29 AM
7	Ma	10/16/2018 6:57 PM
8	Yes that and at School, he seems fine in Clinic and at home and School is an entirely different story.	10/16/2018 12:50 PM
9	No. very typical. Can't hear female voices, needs visual clues.	10/10/2018 2:47 PM
10	No	10/9/2018 10:00 AM
11	One on one during clinic visits but most all social functions are in a group setting	10/7/2018 12:51 PM
12	Yes because there is more background noise, noise we cannot control at home and at school.	10/4/2018 9:15 AM
13	No. My daughter just turning 2 years old, she doesn’t want to keep her hearing aids in so that is a challenge. We believe the hearing aids pickup certain sounds that hurt her ears. Because she can not communicate it makes it extremely difficult as parents to help figure out	10/3/2018 6:58 PM
14	Yes she is too young to participate in the hearingvtests accurately, she gets bored very fast and doesn’t want to do them. She has to have sedated ABR until she is developmentally ready and able to participate in the other hearing tests. She also does not like them and tends to pull out the ear buds making the tests take longer causing her to get frustrated.	10/3/2018 10:43 AM
15	No	10/2/2018 9:57 PM
16	Yes ..	10/2/2018 8:15 PM
17	Not really.	10/2/2018 6:20 PM
18	not a big difference.	10/2/2018 2:49 PM
19	No	10/2/2018 2:47 PM
20	no	10/2/2018 1:29 PM
21	Yes. In clinic she is hyper aware and notice cues more than at home or in social situations. Therefore she “hears” better and doesn’t miss as much.	10/2/2018 12:51 PM
22	don't understand question	10/2/2018 12:22 PM
23	No	10/2/2018 11:37 AM

Q12 What are you/your child currently doing to help treat the condition or its symptoms? (Examples may include prescription medicines, over-the-counter products, and other therapies including non-drug therapies such as behavioral interventions, hearing aids, etc.)

Answered: 25 Skipped: 4

#	RESPONSES	DATE
1	She wears hearing aids and participates in LSL therapy (and will be attending School for the Deaf preschool) with a deaf mentor and speech therapy through early intervention. She has been using Coseva Advanced TRS (a nano zeolite spray) to try to detox the platinum from chemo and hopefully prevent more loss.	10/31/2018 2:17 AM
2	She has hearing aids but has pretty much given up on them (as have other young adult neuroblastoma survivors we have met).	10/30/2018 9:01 PM
3	She doesn’t enjoy the hearing aids, so does not wear them.	10/29/2018 2:06 PM
4	Periodically uses hearing aids, though at this time has decided to go without due to feeling "different" and the hearing aides making everything sound "electronic" according to my son.	10/29/2018 1:28 PM
5	He currently has hearing aids but he usually doesn't wear them. It is difficult to find a balance in a classroom between what is necessary to hear and all the background noise around you. He hated the FM system with the teacher mike as it emphasizes his struggles and draws more attention to himself in an unusual way.	10/25/2018 7:43 AM
6	We control the environment. She refuses to wear hearing aids so we never pursued them. Currently, she is learning ASL and in noise filled environments, we use ASL.	10/20/2018 12:59 PM
7	Josh sparingly uses hearing loss, but nothing recently.	10/17/2018 3:29 AM
8	Hearing aids	10/16/2018 7:43 PM
9	Na	10/16/2018 6:57 PM
10	Hearing aids and Therapy, Speech, OT, Behavioral.	10/16/2018 12:50 PM
11	Hearing aids, visual clues, repetition	10/10/2018 2:47 PM
12	Chloe wears an fm system in school but that's it. It helps a little bit, but not for social interactions.	10/9/2018 10:00 AM
13	Hearing aids	10/7/2018 12:51 PM
14	He wears hearing aids all of the time. He is in speech therapy and we are starting appointments with a counselor.	10/4/2018 9:15 AM
15	Hearing aids Speech therapy	10/3/2018 6:58 PM
16	She wears hearing aids. We also have early intervention involved working with us in speech therapy and they will continue to follow her throughout school.	10/3/2018 10:43 AM
17	Hearing aids	10/2/2018 9:57 PM
18	Prescription medication.. therapy.. social emotional.. speech.. hearing	10/2/2018 8:15 PM
19	Reduce background noises.	10/2/2018 6:20 PM
20	No treatment currently available.	10/2/2018 2:49 PM
21	She used hearing aids. We have a 504plan for school. We also have a few different things we have implemented in the classroom for substitutes and teachers outsid her core class.	10/2/2018 2:47 PM
22	hearing aids fm system	10/2/2018 1:29 PM
23	Hearing aids	10/2/2018 12:51 PM
24	hearing aids. would love to know other options out there	10/2/2018 12:22 PM

25	Hearing aids. And, he is great wearing them. Has no issues (other than wax build up).	10/2/2018 11:37 AM

Q13 How well does your/your child's current treatment regimen treat the most significant symptoms of his/her hearing loss?

Answered: 24 Skipped: 5

#	RESPONSES	DATE
1	Moderately well. She will be starting preschool next month which will give her much more intensive therapy, which hopefully will help her.	10/31/2018 2:17 AM
2	n/a	10/30/2018 9:01 PM
3	We need to schedule an appt with the audiologist, as symptoms have begun to worsen.	10/29/2018 2:06 PM
4	Hearing aides are not ideal. They do not help and have actually caused some additional emotional upset.	10/29/2018 1:28 PM
5	There is no treatment. I am very interested in drug trials to regrow the hairs that allow high frequency hearing.	10/25/2018 7:43 AM
6	Her current treatment works well for her situation.	10/20/2018 12:59 PM
7	n/a	10/17/2018 3:29 AM
8	Na	10/16/2018 6:57 PM
9	Well	10/16/2018 12:50 PM
10	Less than average	10/10/2018 2:47 PM
11	It only helps a little academically. But sometimes the fm system isn't working right, or it bothers her ear, and she only wears it in the classroom.	10/9/2018 10:00 AM
12	He has the best hearing aids money can buy because that is all that is offered to help with his hearing loss symptoms	10/7/2018 12:51 PM
13	Very well. The hearing aids are an absolute must.	10/4/2018 9:15 AM
14	Somewhat	10/3/2018 6:58 PM
15	As good as it can for her age.	10/3/2018 10:43 AM
16	NA	10/2/2018 9:57 PM
17	N/a	10/2/2018 8:15 PM
18	Na	10/2/2018 6:20 PM
19	I don't see that much improvement.	10/2/2018 2:49 PM
20	I’m not sure it really treats symptoms	10/2/2018 2:47 PM
21	Overall ok	10/2/2018 1:29 PM
22	Does a fair job, but it would be great if the hearing aids fully replaced all of missing sounds	10/2/2018 12:51 PM
23	helps when she wears them but she is stuck in the middle. "not deaf" but not deaf enough" at school. so they dont know what to do with her. their statement "she is doing fine" Why should she do fine when they could accomodate her needs and she could excel	10/2/2018 12:22 PM
24	Hearing aids work very well for my son.	10/2/2018 11:37 AM

Q14 How well do your child's therapies address specific activities that are important to your child's daily life?

Answered: 24 Skipped: 5

#	RESPONSES	DATE
1	Moderately well	10/31/2018 2:17 AM
2	n/a	10/30/2018 9:01 PM
3	N/a as of yet.	10/29/2018 2:06 PM
4	Not well.	10/29/2018 1:28 PM
5	His therapist tries to work on how to approach and interact even when he is unsure of all that is going on.	10/25/2018 7:43 AM
6	It works. She is very good at communicating her needs for seating away from loud noises. For her only sport, canoe sailing, she is able to work with her crew to help relay messages to her she cant hear clearly.	10/20/2018 12:59 PM
7	n/a	10/17/2018 3:29 AM
8	Not well	10/16/2018 6:57 PM
9	Speech Therapy and Hearing Aids are a tremendous help.	10/16/2018 12:50 PM
10	Underperforming	10/10/2018 2:47 PM
11	Fm system only addresses her academically.	10/9/2018 10:00 AM
12	They help in one on one situations but with background noise, his hearing aids aren’t effective	10/7/2018 12:51 PM
13	Very well, but he still has great challenges, especially at school.	10/4/2018 9:15 AM
14	Somewhat	10/3/2018 6:58 PM
15	Very well.	10/3/2018 10:43 AM
16	NA	10/2/2018 9:57 PM
17	Very well	10/2/2018 8:15 PM
18	NA	10/2/2018 6:20 PM
19	hearing gain, change of social life.	10/2/2018 2:49 PM
20	I’m not sure what more could be done but would love to hear.	10/2/2018 2:47 PM
21	n/a	10/2/2018 1:29 PM
22	Not really very well. Only addresses the actual hearing loss not any of the social and educational side effects.	10/2/2018 12:51 PM
23	she wears the hearing aids to school and an fm system so that helps but again it singles her out as different and special, she just wants to fit in	10/2/2018 12:22 PM
24	Hearing aids help a great deal with his quality of life.	10/2/2018 11:37 AM

Q15 What are the most significant downsides to your child's current treatments, and how do they affect your daily life? (Examples of downsides may include bothersome side effects, interacts with other medications, time devoted to treatment, etc.)

Answered: 22 Skipped: 7

#	RESPONSES	DATE
1	Therapy takes up SO much time. Hearing aids are uncomfortable and give feedback a lot and aren’t truly capable of giving her complete access to sound. They get full of ear wax, are hard to clean, and the ear molds have to be replaced frequently as she grows. Wearing hearing aids isn’t possible while swimming.	10/31/2018 2:17 AM
2	The only real treatment for her hearing loss is hearing aids and the digital aids she needs that can be tuned to only the frequencies where she has loss, are $6000+ per pair.This cost gets better when over age 18 as hearing aids can be purchased at Costco/etc. but for young children there are no alternative sources for hearing aids.	10/30/2018 9:01 PM
3	N/a as of yet.	10/29/2018 2:06 PM
4	The hearing aides do not replace all the sounds lost, make other sounds sound odd and add another level of emotional distress given that children can be cruel. Being a cancer survivor with multiple late effects - adding one more thing that makes a child different and doesn't provide significant benefit is not idea.	10/29/2018 1:28 PM
5	There is no assistance other than emotional support.	10/25/2018 7:43 AM
6	Currently she is ok in managing.	10/20/2018 12:59 PM
7	use of hearing aids in puberty has become a trigger for cluster migraines	10/17/2018 3:29 AM
8	Upset stomach and fatigue	10/16/2018 6:57 PM
9	A Little bothersome sometimes he likes his super ears and other days he does not understand why he has to have them.	10/16/2018 12:50 PM
10	Stress Frustration Discord in our home after he tries to "hear" all day, exhausted	10/10/2018 2:47 PM
11	The fm system sometimes hurts her ears, and they sometimes they don't work.	10/9/2018 10:00 AM
12	Hearing aids aren’t meant to be worn were it’s dirty, sweaty or dusty but that is everyday conditions on the farm	10/7/2018 12:51 PM
13	They take time away from him being a kid. We cannot do extra curricular things because he is busy dealing with speech lessons.	10/4/2018 9:15 AM
14	Hearing aids are very bothersome Falling behind in speech No patients with hearing tests	10/3/2018 6:58 PM
15	A lot of time is devoted to appointment to check hearing aids, check hearing and for speech therapy. She also does not like wearing her hearing aids some of the time, takes them out and apart. This is concerning that she will break and lose them. She is not old enough to articulate why she is removing them.	10/3/2018 10:43 AM
16	Constantly having to replace batteries for hearing aids, costs going into that, aids hurts his ears	10/2/2018 9:57 PM
17	Time devoted to treatments	10/2/2018 8:15 PM
18	time devoted to treatment.	10/2/2018 2:49 PM
19	She is not currently in active treatment for her disease.	10/2/2018 2:47 PM
20	n/arepair of cells	10/2/2018 1:29 PM
21	Social sigma, limited hearing of sounds, swimming is an issue without her hearing aids,	10/2/2018 12:51 PM
22	they hurt her ears . sometimes too loud, sometimes background noise renders them useless. never simple and helpful and she just gets more frustrated.	10/2/2018 12:22 PM

Q16 What specific things would you look for in an ideal treatment for your child's condition?

Answered: 24 Skipped: 5

#	RESPONSES	DATE
1	Something that could restore normal hearing would be worth almost any risk. I look for treatments where the side effects aren't worse than the current condition.	10/31/2018 2:17 AM
2	Treatment that would re-grow the cilia	10/30/2018 9:01 PM
3	Permanent end to her loss progression...and an end to tinnitus.	10/29/2018 2:06 PM
4	Ideal? I wish this could have been avoided! I am hopeful that treatments to help mitigate the damage done by cisplatin will be approved and become part of the protocols for brain cancer so other children will not have to suffer this late effect. For my son - the damage has been done. Ideally, I suppose I would love to see therapies and can regenerate hearing for him.	10/29/2018 1:28 PM
5	For my child, getting these trial drugs open to older youth. For future children, getting trial drugs to market so that we can prevent future families from undergoing the same struggles my son is facing.	10/25/2018 7:43 AM
6	A treatment to restore her hearing loss that is not hearing aids or implants.	10/20/2018 12:59 PM
7	the ideal treatment is returning the hearing capacity	10/17/2018 3:29 AM
8	Works quickly, ends quickly, no rebound, oral	10/16/2018 6:57 PM
9	Still Learning these things.	10/16/2018 12:50 PM
10	Restoring his hearing	10/10/2018 2:47 PM
11	A medication or treatment that would restore the hearing loss without permanent or long term side effects.	10/9/2018 10:00 AM
12	PREVENTION!! My son was able to participate in a trail drug program sodium thiosulfate during his relapse were he had no further hearing loss while on the cisplatin drugS and with no side affects, he had NO additional hearing loss. So sad to think this was 17 years ago and that hearing loss could be prevented for some many children	10/7/2018 12:51 PM
13	A way to correct the hearing loss, of course. But also a learning environment that has less background noise.	10/4/2018 9:15 AM
14	I wish we would have had STS given to her on the first two rounds of chemotherapy. We saw her audiology test drop from before chemo to round two. After round two through round six there was no decrease in loss. Wish we would have been disclosed STS before she started chemotherapy How do we get rid of the platinum on her ears now that cause further hearing loss from here into the future?	10/3/2018 6:58 PM
15	Better insurance coverage for hearings aids and equipment for them.	10/3/2018 10:43 AM
16	Something that can be taken during or after chemo/radiation to prevent progression of hearing loss, or pediatric chemos that would not cause hearing loss at all.	10/2/2018 9:57 PM
17	One time drug	10/2/2018 8:15 PM
18	Recovery	10/2/2018 6:20 PM
19	hearing gain, learning development, social life.	10/2/2018 2:49 PM
20	Unsure	10/2/2018 2:47 PM
21	repair of hair cells	10/2/2018 1:29 PM
22	A way to reverse the hearing loss and restore hair cells within the ear	10/2/2018 12:51 PM
23	some place where she could be with kids like her and feel comfortable. and people that understand what she is going through so they can eas her fears and frustrations	10/2/2018 12:22 PM

24	There wasn't a space for any additional comments so I will add this here -- I appreciated the meeting and this topic a great deal; however, from the parts that I was able to attend remotely, I found the stories told to be uniformly negative. I understand that; however, I would like to tell a positive one -- one about my son who went through treatment for high-risk neuroblastoma and relapsed neuroblastoma but who is now 11 years old, keeping up with his peers, happy and active -- all with hearing loss. Yes, hearing loss was an "acceptable side-effect" of treatment but his hearing loss is managed well with hearing aids. He is alive because of his treatment and for that I am truly grateful. Yes, I may be even more grateful if he didn't have hearing loss but I can't play that "what if" game. As much as I appreciated the discussions, I also found it difficult to listen to the stories of the participants and be able to connect with them. I understand that was not the goal of the session; however, I think that it is important to have more balance in the approach to the topic.	10/2/2018 11:37 AM

Q17 If a drug was available while your child was in active treatment that could help prevent potential hearing loss, would you have pursued it to be added to your child's treatment protocol?

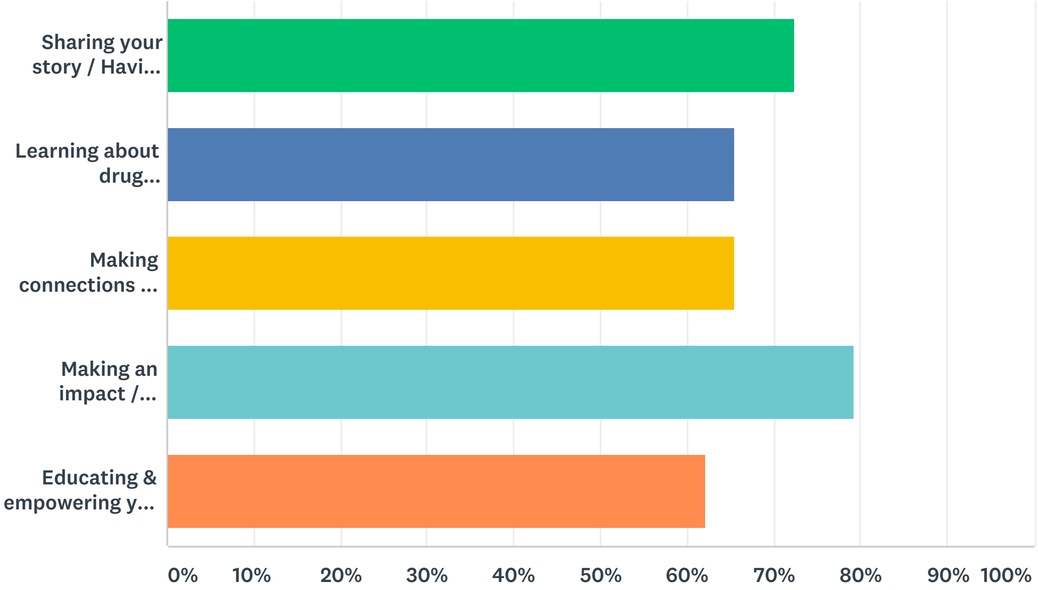
Answered: 25 Skipped: 4

#	RESPONSES	DATE
1	100% yes. I am angry that my daughter's oncologists didn't even know about clinical trials for STS that had been going on for many years. I spent countless hours researching and trying to figure out how to help stop her hearing loss and to hopefully be able to regain hearing but when I mention any treatment to the oncologist, she responds with "a deaf baby is better than a dead baby" and greatly underplays the life-altering (and at least somewhat preventable) and life-long consequences that come because of the chemo. If I had known about either STS or Coseva Advanced TRS when she was in active treatment, come hell or high water, she would've received it.	10/31/2018 2:17 AM
2	In hindsight, yes but at the time she was receiving treatment I did not understand the impact of hearing loss nor was it clearly explained. I was told she might need hearing aids, but kids "get them and do just fine." In contrast to dying of neuroblastoma, it is a small price to pay but I did not understand the impact it would have on her quality of life/survivorship.	10/30/2018 9:01 PM
3	Yes!	10/29/2018 2:06 PM
4	YES!	10/29/2018 1:28 PM
5	Yes. I think it is just as important to offer parent's options as it is to try and eliminate the cancer. All treatments/interventions come with risks, but families should be included in the decision-making process and not have decisions made without their knowledge. Apparently my son's oncologist knew about the trials to prevent his loss but was not impressed enough to consider it until it has been through more trials. I feel that this should have at least have brought to our attention for you consideration as we know our son and what would be most important to him. The idea of saving life at any cost doesn't take quality of life into consideration. My son will tell you that he would have rather run the risk than to have ended up with the struggles he is currently dealing with.	10/25/2018 7:43 AM
6	We would have ablsolutely pursued a prevention drug for hearing loss during treatment. At the meeting our daughter was seated with two other survivors with hearing loss they got 12 to 15 years ago. Directly behind them in the next row was a boy that received the preventative medication for hearing loss 17 years ago. He was with his mom and doctor who gave him the preventative medication. It must have been so frustrating for the doctor to have the knowledge that the three girls seated in front of him could have received the preventative medication and not have hearing loss as they do now. It is my hope that the FDA was able to see that physical picture in front of them at the meeting. For now, the options left for the three girls are to pursue the restorative hearing loss options, hopefully at Frequency.	10/20/2018 12:59 PM
7	most definitely	10/17/2018 3:29 AM
8	Yes	10/16/2018 6:57 PM
9	Yes 100%	10/16/2018 12:50 PM
10	Absolutely	10/10/2018 2:47 PM
11	YES!	10/9/2018 10:00 AM
12	Absolutely! Especially knowing that it works and has virtually no side affects	10/7/2018 12:51 PM
13	ABSOLUTELY.	10/4/2018 9:15 AM
14	Yes	10/4/2018 4:24 AM
15	We used STS after round two it worked wonders. I wish we knew about it before we started	10/3/2018 6:58 PM

16	Yes and I did pursue STS. She had a total of 6 rounds of Cisplatin. She was given STS per my request 3 of the 6 rounds. At the start of her 3rd round she had her first hearing test since chemo had begun and it showed she had a loss in the higher frequencies. Her baseline hearing test showed perfect hearing. I asked for STS and had an audiologist at her hospital who had study information give it to her oncologist at Stanford (surgery resection and oversaw care) and OHSU Doerenbecher (treating hospital) who approved her to have it for the remaining chemo rounds.	10/3/2018 10:43 AM
17	YES	10/2/2018 9:57 PM
18	Yes.. but I just wanted to save his life	10/2/2018 8:15 PM
19	Yes yes yes yes.	10/2/2018 6:20 PM
20	Yes, I would like.	10/2/2018 2:49 PM
21	Absolutely	10/2/2018 2:47 PM
22	YES	10/2/2018 1:29 PM
23	Yes.	10/2/2018 12:51 PM
24	yes	10/2/2018 12:22 PM
25	Sodium thiosulphate wasn't available when my child started treatment. I would have pursued this if it was.	10/2/2018 11:37 AM

Q18 An EL-PFDD meeting is very different than a typical oncology conference, since it reverses the usual format of researchers talking and patients listening. Keeping that unique purpose in mind – of informing the FDA about the patient perspective – please check the boxes by each of the objectives that you feel were met in this meeting: (You may select more than one.)

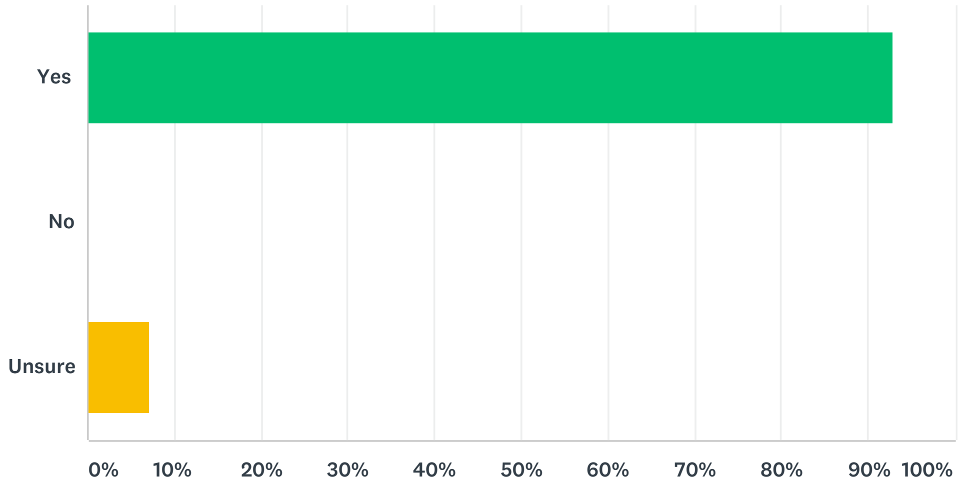
Answered: 29   Skipped: 0



ANSWER CHOICES	RESPONSES	
Sharing your story / Having your voice heard	72.41%	21
Learning about drug development, clinical trials & research	65.52%	19
Making connections / Networking with other families	65.52%	19
Making an impact / Helping to create change	79.31%	23
Educating & empowering your family about possible new treatments or options	62.07%	18
Total Respondents: 29		

Q19 Would you participate in a future Externally-Led Patient Focused Drug Development workshop around another relevant pediatric oncology issue?

Answered: 28 Skipped: 1



ANSWER CHOICES	RESPONSES	
Yes	92.86%	26
No	0.00%	0
Unsure	7.14%	2
Total Respondents: 28		

Q20 Do you have a topic suggestion for a future EL-PFDD conference?

Answered: 14 Skipped: 15

#	RESPONSES	DATE
1	Alternative treatments that could be used in conjunction with traditional medical protocols.	10/31/2018 2:17 AM
2	This is off-topic but since there is no other place for it, I want to say that this was hands-down the most empowering oncology-related event I have ever participated in, and that includes events I have organized. My daughter felt heard, appreciated and validated in a way that she, as a survivor struggling with serious late effects, has not felt at other events. A lot of attention is given to pediatric cancer survivors who excel in some field, be it medicine, the arts, academia, etc., but these kids who overcome hurdles every day just to live a life as close to normal as possible are never recognized or heard. After being told they "survived for a reason" or "God has big plans for you" they often struggle with feelings of failure and self-doubt because getting through the day is just so darn hard. After this conference, my daughter and I were so encouraged to know that not only does somebody "get it," but people in positions to do something to improve the situation now "get it." Thank you for all of the work put into organizing this meeting!	10/30/2018 9:01 PM
3	There are so many late effects of cancer treatment. Each of them could be a topic to address either better, safer cancer treatments with fewer side effects or additional protective therapies to help prevent the side effects. Every organ needs protection, fertility needs to be preserved, endocrine effects, cognition...the list goes on and all need attention. These kids need to have a voice and hopefully people with the ability to affect change will actually listen. We have come a long way in oncology, but we have a long way to go. While it is true that more children are actually surviving their cancers, we now need to look at our measure of success and measure it not only on survival itself, but on the quality of that survival.	10/29/2018 1:28 PM
4	Fertility preservation and Infertility issues of childhood cancer survivors	10/20/2018 12:59 PM
5	if approaching reproduction capacity for survivors, to make sure to include men in the conversation. chemo-induced Cardiomyopathy. Capacity to cope for children survivors maturing through puberty into young adulthood.	10/17/2018 3:29 AM
6	Classifying brain tumors as a cronic disease and having them quaify for medicade. The financial stress of living in a family with pediatric brain tumor	10/16/2018 6:57 PM
7	Cognitive delay Fatigue	10/10/2018 2:47 PM
8	Please have STS approved to all future cases in chemotherapy Please help those of us find a way to get rid of progressive hearing loss after chemo	10/3/2018 6:58 PM
9	No	10/3/2018 10:43 AM
10	Pediatric oncology chemos that cause ongoingissues with muscle function, joints, cramping healing. More FDA approved pediatric only chemo therapies	10/2/2018 9:57 PM
11	Travel funds for parents..	10/2/2018 8:15 PM
12	N/A	10/2/2018 2:49 PM
13	No	10/2/2018 2:47 PM
14	navigating life after cancer. I feel that in our experience we are kind of left alone and people feel "your kid is alive why are you bothering us and complaining" We are grateful our daughter survived, but really think there needs to be more resources for survivors.	10/2/2018 12:22 PM