

## ORIGINAL RESEARCH

# Comprehensive auditory rehabilitation in adults receiving cochlear implants: A pilot study

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## Abstract

**Objective:** In the United States, most adults who receive cochlear implants (CIs) do not undergo a comprehensive auditory rehabilitation (CAR) approach, which may result in suboptimal outcomes. The objectives of this pilot study were to demonstrate that a CAR approach incorporating auditory training (AT) by a speech-language pathologist (SLP) is feasible in adults receiving CIs and to explore whether this approach results in improved outcomes.

**Methods:** Twenty-four postlingually deaf adult CI candidates were serially assigned to one of three groups: (a) a “CAR group” that received standard of care implantation, programming by an audiologist, an additional preoperative counseling session, and eight one-hour AT sessions; (b) a “passive control” standard-of-care group; and (c) an “active control” group that also received the extra preoperative counseling session. Participants were tested preoperatively and 1, 3, and 6 months after CI using measures of word and sentence recognition in quiet and in babble, as well as measures of quality of life (QOL).

**Results:** The CAR approach was feasible, but this pilot study was underpowered to determine efficacy. Differential time courses of speech recognition improvement were seen for sentence and word recognition. All QOL measurements showed improvement from pre-CI to 1 month post-CI activation. Results revealed issues to consider for a larger-scale study of CAR revolving around participant selection, study measures, and sample size.

**Conclusion:** The CAR approach is feasible in new CI users. A larger trial is needed to investigate whether CAR leads to better outcomes or faster improvement in this clinical population.

**Level of Evidence:** 2.

## KEYWORDS

auditory training, aural rehabilitation, cochlear implants, quality of life, sensorineural hearing loss, speech perception, speech recognition

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## 1 | INTRODUCTION

For adults with moderate-to-profound sensorineural hearing loss, a cochlear implant (CI) restores auditory input. However, broad outcome variability persists on measures of speech recognition,<sup>1-3</sup> some of which can be attributed to patient-related factors (eg, residual hearing)<sup>4</sup> and spectrotemporal resolution.<sup>3,5,6</sup> Additionally, neurocognitive functions, such as verbal learning, working memory, and inhibitory control, relate to outcomes.<sup>3,7,8</sup> Evidence for the efficacy of auditory rehabilitation on both auditory processing and neurocognitive functions continues to grow.<sup>9-11</sup> Moreover, additional factors like patient motivation, device competence, and psychosocial function may be additional targets for intervention.<sup>12-15</sup> We propose that a comprehensive auditory rehabilitation (CAR) approach incorporating sensory management, instruction, counseling, and clinician-guided auditory training (AT) maximizes the opportunity to optimize speech recognition and quality of life (QOL) outcomes for adult CI users.

The concept of a CAR approach for adults is not in itself novel,<sup>16</sup> and addresses four main components, outlined by Boothroyd<sup>17</sup>: (1) Sensory management; (2) Instruction; (3) Counseling; and (4) Perceptual training or AT. This model emphasizes a comprehensive and collaborative approach among surgeons, audiologists, and clinicians who guide AT. In the United States, the third clinician can be an audiologist or a speech-language pathologist (SLP). This clinician is rarely an audiologist in this country: currently the Centers for Medicare and Medicaid Services (CMS) program views audiologists as diagnosticians. As a result, they are technically not able to deliver and bill for therapeutic CAR services. In contrast, SLP rehabilitation services are reimbursable, and their services are typically covered by Medicare, Medicare Advantage, and commercial payors. Equally importantly, SLPs are specifically skilled in training approaches and facilitating learning across a variety of communication impairments.<sup>18,19</sup> Most adult CI centers in the United States do not incorporate clinician-guided AT, likely as a result of poor reimbursement for audiologists for AT services, and a paucity of SLPs with education in AT methods, and even more specifically education in AT for adults with hearing loss. This article reviews a pilot study of CAR with SLP-guided AT in adults receiving CIs.

Adult postlingually deafened CI candidates who had already selected implantation with a Cochlear (Sydney, Australia) device were invited to participate and were serially assigned to one of three groups (1) a "CAR group" that received standard of care implantation, programming by an audiologist, an additional preoperative counseling session, and 81-hour AT sessions; (2) a "passive control" standard-of-care group that received a CI and programming; and (3) an "active control" group that received the extra preoperative counseling session, implantation, and programming. The active control group was included because the additional preoperative counseling might result in benefits from more realistic patient expectations. Participants were tested preoperatively and at 1, 3, and 6 months after CI activation using measures of speech recognition and self-reported QOL. For this pilot study, we hypothesized that (1) the CAR approach would be feasible in new adult CI users, and (2) the CAR group would demonstrate

a trend toward improved speech recognition and self-reported QOL as compared with the active and passive control groups. Results were expected to inform the future design of a larger randomized controlled trial of CAR.

## 2 | MATERIALS AND METHODS

### 2.1 | Participants

Twenty-four adults with postlingual hearing loss between the ages of 49 and 91 years were recruited from a tertiary CI program. CI candidacy required moderate-to-profound sensorineural hearing loss and best-aided sentence recognition scores of <60% on AzBio sentences.<sup>20</sup> In five cases, patients only met traditional criteria when tested at +10 dB SNR in 10-talker babble. Patients were informed that the study aimed to study different forms of auditory rehabilitation. After enrollment but prior to preoperative testing, participants were assigned serially to the CAR, passive control, or active control group.

Participants had varying etiologies of hearing loss. The Mini-Mental State Examination (MMSE) was performed using written instructions to rule out cognitive impairment.<sup>21</sup> All demonstrated better than 20/40 corrected near vision. Because participant demographics (age, socioeconomic status—SES, duration of hearing loss—age at enrollment minus patient-reported age at onset of hearing loss), preoperative residual hearing, and cognitive abilities might be expected to impact speech recognition and QOL outcomes,<sup>1-4,7,8</sup> these were assessed preoperatively and compared among the groups (CAR, passive control, or active control). Details of these measures are provided in the Appendix. Means and standard deviations (SDs) for these measures are shown in Appendix Table A. One-way analyses of variance (ANOVAs) demonstrated no significant differences among the three study groups on any of these measures.

### 2.2 | Equipment and materials

Tests were performed in a soundproof booth or a sound-treated testing room. Participants were tested preoperatively using their hearing aids if worn. During post-CI testing, participants used their typical hearing prostheses, including any contralateral hearing aid or ipsilateral acoustic component. Auditory stimuli were presented in the soundfield by a speaker placed 1 m directly in front of the participant.

#### 2.2.1 | Speech recognition

Speech recognition tasks were presented using recorded material, chosen because they are widely used clinically. Stimuli were presented at 60 dB SPL. Three measures were used: AzBio sentences in quiet, AzBio sentences in 10-talker babble, and Consonant-Nucleus-Consonant (CNC) words in quiet.

## 2.2.2 | Patient self-reported measures

Three hearing-related assessments were completed at home with no time limit, and responses were mailed back. These consisted of the Nijmegen Cochlear Implant Questionnaire (NCIQ<sup>22</sup>), the Hearing Handicap Inventory for Adults/Elderly (HHIA/HHIE<sup>23,24</sup>), and the Speech, Spatial and Qualities of Hearing Scale (SSQ<sup>25</sup>). The NCIQ is a general measure of CI-related QOL, with higher scores representing better function. The HHIA/HHIE looks at the effects of individuals' hearing loss on functioning in particular scenarios, with lower scores representing better function. The SSQ measures hearing disability across speech, spatial hearing, and other qualities, with higher scores representing better function.

## 2.3 | General approach

The study was approved by the local Institutional Review Board, protocol number 2016H0257. All participants provided written consent and were reimbursed \$12.50 per hour of testing. Preoperative testing was completed over a single 2-hr session, with breaks to prevent fatigue. Postoperative testing sessions were completed over 30 minutes each.

## 2.4 | CAR group (clinician-guided AT plus preoperative counseling plus standard-of-care)

In addition to our center's standard-of-care management, participants in the CAR group were treated by the SLP (author C. R.) and audiologist (author J. B.) for 1 hour weekly for 8 weeks. Treatment was individualized based on functional assessments and goals. Device instruction, counseling, and a combination of analytic and synthetic speech-based AT tasks were used; AT tasks were modeled after those described in the Adult Aural Rehabilitation Manual.<sup>26</sup> All CAR participants also received an additional preoperative one-hour counseling session by the Research Audiologist (author K. V.) including discussion of expectations and goals.

CAR group participants were also given instruction for daily home practice, using live voice activities as well as computer-based training (eg, AngelSound). Each participant was instructed to complete 30 minutes of AT daily. Compliance with homework in this pilot study was followed informally by having patients complete a daily log; however, details of the activities were not tracked closely.

## 2.5 | Passive control group (standard-of-care)

Passive controls underwent the standard-of-care approach, beginning with CI candidacy evaluation and the visit with the surgeon. Patients then had a preoperative CI device selection appointment with one of five CI audiologists. Patients underwent implantation and a

postoperative visit with the surgeon. At 3 to 4 weeks after surgery, initial CI activation was performed. Audiology visits were held at 2, 4, and 8 weeks after CI activation, with additional visits as needed.

## 2.6 | Active control group (preoperative counseling plus standard-of-care)

In addition to the standard-of-care management, participants assigned to the active control group received the preoperative one-hour counseling session by the Research Audiologist (author K. V.). Otherwise, management was equivalent to the passive controls.

### 2.6.1 | Data analyses

Because this was a pilot study, analyses were exploratory. One-way ANOVA models were used to test for differences between treatment groups at the preoperative time point. Linear mixed models with preoperative performance adjustment were used to check for differences between the treatment groups in the postoperative periods. Models without preoperative response as an explanatory variable were used to check for differences between preoperative and 1 month postoperative time points. Because the sample size was small for this pilot study, no covariates (eg, demographic, audiologic, or cognitive factors) were entered during these analyses. Models without the explanatory variable treatment group were used to examine the time course of changes in speech recognition and QOL over time for the entire cohort.

## 3 | RESULTS

### 3.1 | Feasibility

Twenty-four participants agreed to participate. One participant did not show up for preoperative testing, so 23 participants completed preoperative testing. One participant decided not to undergo CI surgery. Three participants withdrew after implantation but before 1 month postactivation testing: one moved out-of-state, and two could not keep up with the time commitment. Nineteen participants had complete preoperative testing: six CAR, seven passive controls, and six active controls. At 1 month postactivation, one passive control did not return the QOL measures. At 3 months post-activation, five participants (two passive control, two CAR, and one active control) did not return the QOL measures. At 6 months, three participants (all passive control) did not return the QOL measures. The 19 participants who had complete preoperative testing all completed their planned treatment courses. All CAR participants completed all eight AT sessions. All CAR participants reported completion of some AT homework between sessions using their daily logs. For both the CAR and active control group, all participants received the one-hour extra

**TABLE 1** Demographics for individual participants in the three study groups of comprehensive auditory rehabilitation (CAR), passive control (PC), and active control (AC)

Subject	Group (CAR, PC, AC)	Gender	Age (years)	Side of implant	Etiology of hearing loss	Age at onset of hearing loss (years)	Preoperative Better ear PTA (dB HL)
1	CAR	M	55	R	Unknown	13	80
2	CAR	M	77	R	Progressive as adult, noise	20	87.5
3	AC	M	74	R	Genetic, noise	30	91.25
4	PC	F	61	R	Noise	20	73.75
5	PC	M	68	R	Physical trauma	40	80
6	PC	F	58	B	Genetic	6	120
7	CAR	M	68	R	Progressive as adult	53	71
8	PC	M	75	R	Progressive as adult, noise	40	76
9	AC	F	54	R	Genetic, sudden	1	106.3
10	CAR	F	75	R	Progressive as adult	57	67
11	PC	M	91	L	Genetic, noise	48	114
12	AC	M	67	R	Genetic	45	78
13	CAR	M	65	L	Menieres	25	65
14	AC	M	65	L	Progressive as adult, noise	50	80
15	PC	F	53	R	Genetic, progressive	12	80
16	AC	M	73	R	Genetic, progressive	40	66
17	PC	F	49	R	Congenital	0	102
18	CAR	M	73	R	Progressive as adult, noise	45	75
19	AC	F	76	R	Progressive as adult	50	88

Abbreviations: B, bilateral; F, female; L, left; M, male; PTA, pure-tone average for 0.5, 1, 2, and 4 kHz; R, right.

preoperative counseling session. Eighteen participants received either a right or left CI; one participant underwent bilateral simultaneous implantation. Seven (36.8%) females and twelve (63.2%) males were included. Demographic and audiologic data for the 19 individual participants who completed the study are shown in Table 1.

### 3.2 | Group differences in changes in speech recognition over time

Mean speech recognition scores are shown in Table 2 for each group. Speech recognition scores are plotted in Appendix Figures A through C. Results demonstrate enormous inter-participant variability for AzBio sentences in quiet (Appendix Figure A), AzBio sentences in babble (Appendix Figure B), and CNC words (Appendix Figure C). Preoperative speech recognition scores ranged broadly within and among groups. Using one-way ANOVA, no significant differences existed among the three groups on preoperative speech recognition ( $P \geq .6$  for all scores). Linear mixed modeling analyses demonstrated no significant differences in speech recognition among the groups at 1-, 3-, or 6- post-CI, when adjusting for preoperative performance. However, visual inspection of the figures of the mean performance over time for the three groups suggests the possibility of a more rapid improvement in AzBio sentences in quiet and AzBio sentences in babble for the CAR and active controls as compared with the passive controls.

### 3.3 | Group differences in changes in quality of life over time

Mean QOL scores are shown in Table 3. Self-report measure scores for the participants who returned the questionnaires are plotted in Appendix Figures D through F. Similar sets of analyses were done as above for speech recognition. Again, results generally demonstrate enormous inter-participant variability for NCIQ total score (Appendix Figure D), HHIA/E total score (Appendix Figure E), and SSQ mean score (Appendix Figure F). Preoperative QOL scores ranged broadly. Using one-way ANOVA, no significant differences existed among the three groups on mean preoperative QOL scores ( $P \geq .34$  for all QOL measures). Linear mixed modeling analyses again demonstrated no significant differences in QOL among the groups for any of the self-report measures at 1-, 3-, or 6- post-CI, when adjusting for preoperative QOL.

### 3.4 | Whole-group changes in speech recognition over time

For all 19 participants, box plots of speech recognition scores are shown in Appendix Figure G (AzBio sentences in quiet), Appendix Figure H (AzBio sentences in babble), and Appendix Figure I (CNC words). Mean speech recognition scores are shown in Appendix Table B. As expected, a significant effect of time point was seen for

**TABLE 2** Mean speech recognition scores for 19 new cochlear implant (CI) users at each time point, divided by treatment group

	Preop		1 month post-CI activation		3 months post-CI activation		6 months post-CI activation	
	Mean	(SD)	Mean	(SD)	Mean	(SD)	Mean	(SD)
AzBio sentences in quiet (% words correct)								
Comprehensive auditory rehabilitation	28.7	(20.4)	58.2	(27.9)	70.4	(19.8)	71.5	(24.8)
Passive control	25.6	(40.8)	46.8	(28.7)	63.9	(27.7)	70.5	(19.2)
Active control	31.5	(30.3)	71.1	(8.7)	82.0	(9.3)	80.9	(7.0)
AzBio sentences in 10-talker babble (% words correct)								
Comprehensive auditory rehabilitation	12.6	(10.3)	41.4	(19.4)	47.7	(27.4)	45.0	(27.1)
Passive control	17.4	(28.2)	25.4	(21.1)	41.5	(21.6)	43.8	(20.6)
Active control	19.9	(19.9)	40.3	(13.4)	50.7	(12.8)	52.8	(15.8)
CNC words (% words correct)								
Comprehensive auditory rehabilitation	19.2	(20.4)	40.3	(27.7)	56.0	(16.7)	59.2	(18.7)
Passive control	17.4	(29.7)	39.4	(27.5)	59.5	(23.5)	65.4	(22.9)
Active control	20.0	(19.9)	40.4	(14.5)	66.0	(10.1)	71.7	(12.6)

**TABLE 3** Mean self-report quality of life scores for 19 new cochlear implant (CI) users at each time point, divided by treatment group

	Preop		1 month post-CI activation		3 months post-CI activation		6 months post-CI activation	
	Mean	(SD)	Mean	(SD)	Mean	(SD)	Mean	(SD)
NCIQ total score								
Comprehensive auditory rehabilitation	144.4	(49.9)	179.0	(36.6)	182.6	(46.7)	205.4	(34.8)
Passive control	140.9	(45.9)	170.0	(60.4)	202.6	(18.0)	172.7	(64.8)
Active control	144.8	(33.3)	177.2	(42.5)	207.1	(33.7)	192.1	(41.7)
HHIA/HHIE total score								
Comprehensive auditory rehabilitation	61.3	(16.1)	48.0	(12.7)	50.0	(16.2)	36.0	(21.3)
Passive control	66.6	(21.7)	56.2	(32.2)	35.2	(26.7)	44.3	(30.8)
Active control	69.0	(16.8)	53.0	(23.3)	40.4	(14.8)	40.0	(15.3)
SSQ mean score								
Comprehensive auditory rehabilitation	2.7	(1.5)	4.8	(1.2)	4.7	(0.9)	5.5	(1.5)
Passive control	2.6	(1.3)	4.2	(1.4)	5.2	(1.0)	4.3	(2.1)
Active control	3.5	(1.6)	4.3	(2.1)	5.7	(1.5)	5.9	(1.5)

AzBio sentences in quiet ( $F_{(3,47)} = 23, P < .001$ ). Contrast tests demonstrated significant changes in scores of AzBio sentences in quiet from preoperative testing to 1 month after CI activation ( $P < .001$ ), and from 1 to 3 months after CI activation ( $P = .01$ ), but not from 3 months to 6 months after CI activation ( $P = .542$ ). Similarly, for AzBio sentences in babble, a significant effect of time point was seen ( $F_{(3,48)} = 6.0, P = .001$ ). No significant change in score of AzBio sentences in babble was found from preoperative testing to 1 month after CI activation ( $P = .117$ ), a significant change from 1 to 3 months after CI activation ( $P = .04$ ), but not from 3 months to 6 months after CI activation ( $P = .605$ ). Finally, for CNC words, a significant effect of time point was seen ( $F_{(3,51)} = 44.4, P < .001$ ). Significant changes in CNC word scores were found from preoperatively to 1 month after CI activation ( $P < .001$ ), from 1 to 3 months after CI activation ( $P < .001$ ),

as well as from 3 to 6 months after CI activation ( $P = .04$ ). In summary, significant improvements were seen from 1 to 3 months after CI activation for both AzBio sentences in quiet and in babble. In contrast, CNC words continued to improve up until at least 6 months after CI activation.

### 3.5 | Whole-group changes in self-report quality of life over time

For all 19 participants, box plots of self-report scores are shown in Appendix Figure J (NCIQ total score), Appendix Figure K (HHIA/HHIE total score), and Appendix Figure L (SSQ mean score). Mean whole-group preoperative, 1-, 3-, and 6-months post-CI activation QOL

scores are shown in Appendix Table C. As expected, a significant effect of time point was seen for NCIQ ( $F_{(3,47)} = 9.3, P < .001$ ). Contrast tests demonstrated a significant change in total NCIQ score from preoperative testing to 1 month after CI activation ( $P = .002$ ), but no additional significant sequential changes from 1 to 3 months ( $P = .08$ ), or from 3 to 6 months after CI activation ( $P = .67$ ). Similarly, for HHIA/HHIE total score, a significant effect of time point was seen ( $F_{(3,47)} = 9.4, P < .001$ ). Tests showed significant changes in HHIA/HHIE from preoperative testing to 1 month after CI activation ( $P = .01$ ), but no additional significant sequential changes from 1 to 3 months ( $P = .17$ ), or from 3 to 6 months after CI activation ( $P = .45$ ). Finally, for SSQ mean score, a significant effect of time point was seen ( $F_{(3,47)} = 19.1, P < .001$ ). Tests demonstrated significant changes in SSQ mean score from preoperatively to 1 month after CI activation ( $P < .001$ ), but not from 1 to 3 months after CI activation ( $P = .10$ ), or from 3 to 6 months after CI activation ( $P = .68$ ). In summary, for each of the self-report QOL scores, significant improvements were only seen from preop to 1 month post-CI activation.

#### 4 | DISCUSSION

This study evaluated the feasibility of a comprehensive approach to auditory rehabilitation in an adult CI center and collected pilot data to inform the design of a future larger trial. The CAR approach was generally feasible. Study attrition occurred early after enrollment. Compliance was maintained, and participant retention was 79.2%. Our main difficulty in data collection was in getting participants to mail in QOL assessments, resulting in missing QOL data for 9 time points. Although the intention was to shorten the in-person testing sessions, future studies will obtain QOL measures in person.

In this study, patient scores on speech recognition and QOL were generally comparable to those reported by other groups,<sup>27-29</sup> or slightly worse, though sometimes scores were computed differently among studies. Our lower speech recognition scores may be a result of our study sample being slightly older (our mean age across groups was 67 years). More likely it is a result of only testing our new CI users out to 6 months of device use, when mean CNC score for the group was 66%, compared with a mean of 76% CNC score reported by Holden et al., tested at a mean duration of CI use of 4.8 years. This discrepancy suggests that measuring outcomes only out to 6 months of CI use may have limited our ability to find longer-term benefits of the CAR approach.

A number of important findings should be considered in future studies of rehabilitation. First, enormous variability in speech recognition and self-report QOL was evident throughout the entire study. Although we intentionally enrolled participants with variable degrees of preoperative speech recognition abilities, inclusion of participants with relatively good baseline scores likely complicated findings. This broad variability in preoperative performance may have led to ceiling effects for some participants. Three potential future solutions would be (1) to choose more challenging measures of speech recognition;

(2) to develop stricter inclusion criteria, such as relatively poor preoperative speech recognition; or (3) to recruit participants after CI activation with relatively poor speech recognition (eg, <40% words in sentences in quiet) 1 month after activation.

A second interesting finding is that the time course of changes after CI is different for speech recognition measures compared with self-report QOL measures. Improvements in sentence recognition occurred from preoperatively to 1 month (in quiet), as well as from 1 to 3 months after CI activation (in quiet and in babble), but not from 3 to 6 months after activation. In contrast, significant improvements in word recognition continued through 6 months after activation. On the other hand, improvements in self-report QOL were seen across all three QOL assessments only from preoperatively to 1 month post-CI activation. This differing time course among outcomes provides further support for a lack of strong relationships among these outcome measure modalities.<sup>28,30</sup>

Moreover, graphs of our data suggested there may have been a difference in the rate of improvement in speech recognition among our CAR and active control groups as compared with the passive control group. Thus, the trajectory of improvement may have been more rapid for the CAR and active control groups. Perhaps CAR (and/or counseling) does not lead to better overall speech recognition outcomes, but rather more rapid recovery of speech recognition function.

This study has several limitations. First, as a pilot study, the sample was small, and all statistical testing was exploratory. Although demographic, audiologic, and cognitive abilities were not significantly different among our groups at baseline, there were broad ranges in each of these factors; a much larger sample size would be required to reasonably include these factors as covariates in main analyses comparing group outcomes. Second, surgeons, audiologists, and researchers were not blinded to study group, which will be important in future studies.<sup>7</sup> Third, we chose to examine the feasibility and application of the CAR approach as a whole to new CI users; however, this meant that the treatment approach was individualized for each patient. As a result, determining the efficacy of any particular facet of the intervention, even in larger studies of this nature, would be very challenging unless test manipulations of the CAR approach were more specific. Fourth, for this pilot study, datalogging information on device use was not collected, but future rehabilitation studies should capitalize on this technology. For example, there is growing evidence of an association between average hours of CI use per day and both word and sentence recognition outcomes.<sup>31,32</sup> Finally, the lack of clearly identifiable benefits of the CAR approach to either speech recognition or QOL suggests value in expanding our assessments even more broadly, by including measures of performance on self-reported goals,<sup>33</sup> device knowledge and capability,<sup>13</sup> listening comprehension,<sup>34</sup> more valid measures of QOL,<sup>30</sup> and even neurocognitive functioning.<sup>35</sup> It is likely that this expanded battery of assessment tools will better reveal the benefits of CAR over standard-of-care in adult CI users.

## 5 | CONCLUSIONS

This pilot study demonstrated that a CAR approach and study are generally feasible in postlingual adults who are receiving CIs. Study compliance and retention were high, but participant variability posed barriers to understanding the effects of the CAR approach in new CI users. A larger-scale trial will be required to demonstrate the efficacy of the CAR approach as compared to standard-of-care or additional preoperative counseling.

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### CONFLICT OF INTEREST

Aaron C. Moberly serves as a paid consultant for Cochlear Americas and Advanced Bionics, and owns stock and serves as CMO for Otolologic Technologies. Kara Vasil and Christin Ray serve as paid consultants for Advanced Bionics.

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#### SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of this article.

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