Randomized Trial of Telehealth vs. Conventional Hearing Care Delivery in the ACHIEVE Study (ACHIEVE-HIFU)

Protocol

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ACHIEVE
HEALTHY AGING

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Summary of Changes from Protocol Version 1.2 to 1.3

Minor changes to page numbering and formatting and minor corrections and clarifications were made throughout the document. Substantive changes are highlighted in the below table.

Affected section(s)	Brief description of change	Brief rationale for change
2.1 Synopsis	Updated the Outcomes and the Statistical Methods	Updates were made to correspond with the final HIFU Statistical Analysis Plan
3 Study objectives and end points	Updated the list of secondary and exploratory outcomes	List of outcomes were updated for consistency with the study's final Statistical Analysis Plan
7.1 Schedule of activities, Table 1	Updated the footnotes previously noted as "Procedures that are intermittent based on protocol"	The footnotes have been updated to provide details about when or why the procedures are or are not completed
10.2 Adverse events	Updated information in the SAE section to reflect previously approved changes to the DSMP	These edits were missed during the previous update to reflect the study's revised DSMP and are now being incorporated
11.2 Analytic approach	Updates were made to the list of confounders, and a description was added to account for a non-normal distribution, continuous secondary outcomes, and for adjustments for multiple comparisons	Updates were made to correspond with the final HIFU Statistical Analysis Plan

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1 Statement of Compliance

The trial will be carried out in accordance with International Conference on Harmonisation Good Clinical Practice (ICH GCP) and the United States (US) Code of Federal Regulations (CFR) applicable to clinical studies (45 CFR Part 46, 21 CFR Part 50, 21 CFR Part 56, 21 CFR Part 312, and/or 21 CFR Part 812). All personnel involved in the conduct of this study have completed Human Subjects Protection and ICH GCP Training.

The protocol, informed consent forms, recruitment materials, and all participant materials will be submitted to the Institutional Review Board (IRB) for review and approval. Approval of both the protocol and the consent form must be obtained before any participant is enrolled. Any amendment to the protocol will require review and approval by the IRB before the changes are implemented to the study. In addition, all changes to the consent form will be IRB-approved; a determination will be made regarding whether a new consent needs to be obtained from participants who provided consent, using a previously approved consent form.

2 Protocol summary

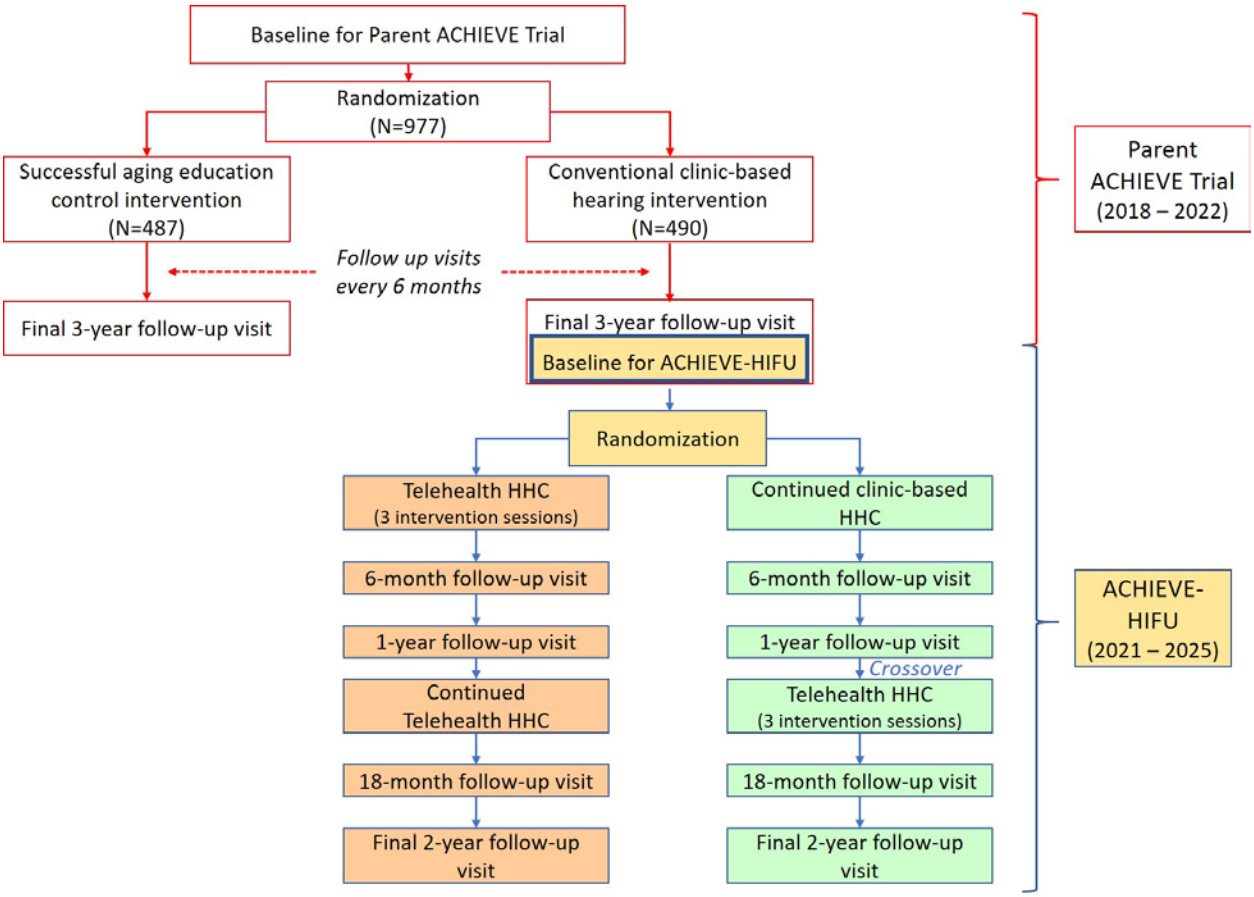
2.1 Synopsis

Title	Randomized Trial of Telehealth vs. Conventional Hearing Care Delivery in the ACHIEVE Study
Short Title	ACHIEVE-HIFU (ACHIEVE Hearing Intervention Follow-Up)
Field Sites	• George Comstock Field Center, Johns Hopkins Bloomberg School of Public Health, Washington County, MD • University of Mississippi Medical Center, Jackson, MS • University of Minnesota, Minneapolis, MN • Wake Forest University, Forsyth County, NC
Other Study Sites	• University of South Florida (hearing intervention unit) • Johns Hopkins University (analysis and study governance unit) • University of North Carolina Chapel Hill (coordinating center)
Design	Multi-site randomized trial comparing conventional in-person hearing health care (HHC) versus in-person HHC plus telehealth audiology sessions among existing hearing aid users.
Sample Size and Population	This study is predicated on an already established cohort of existing hearing aid users with a fixed sample size from the original Aging and Cognitive Health Evaluation in Elders (ACHIEVE) trial (N=490 hearing intervention cohort). We conservatively estimate that N=400 participants currently in the hearing intervention group will be recruited into this follow-up study.

Main Eligibility Criteria	To be eligible for the current study, participants must: 1) have been eligible for and participated in the hearing intervention arm of the ACHIEVE trial (see main original criteria below), 2) agree to be randomized to receive hearing care via continued conventional in-person visits or conventional in-person care with the addition of telehealth audiology sessions. Participants randomized to conventional in-person care only would also receive telehealth sessions after one year, and 3) agree to participate and able and willing to be followed for 2 years in the follow-up study. Original ACHIEVE criteria: Community-dwelling adults aged 70-84 years with mild to moderate audiometric hearing impairment, and free from substantial cognitive impairment at baseline.
Objectives	Primary: 1. To compare the effect of the telehealth hearing health care (HHC) versus conventional HHC delivery models on hours of hearing aid use (primary outcome) at 1-year post-randomization. Secondary: 2. To compare the effect of the telehealth HHC versus the conventional HHC delivery model on patient-centered hearing and communication outcomes, social functioning, and quality of life at 1-year post-randomization. 3. To compare utilization of hearing services required by each HHC delivery model. 4. To evaluate the association of the telehealth HHC intervention with changes in hearing aid use and patient-centered hearing and communication, social functioning, and quality of life measures from baseline to up to two years post-intervention.
Outcomes	Primary: Average daily hours of hearing aid use at 1 year, as measured through objective hearing aid data logging. If a participant wears a hearing aid in both ears, then the ear with the greatest number of hours logged will be selected. Key secondary: • Treatment satisfaction, as assessed by a single item from the International Outcome Inventory – Comprehensive Hearing Intervention (IOI-CHI) • Ability to hear for the primary communication goal, as assessed by a single item from the Client-Oriented Scale of Improvement (COSI) goals achievement questionnaire • Hearing-specific quality of life, as assessed by the Hearing Handicap Inventory for the Elderly Screening Version (HHIE-S) questionnaire

Randomization and stratification	1:1 random block randomization, stratified by degree of hearing loss (mild vs. moderate or greater), cohort (originally recruited to the ACHIEVE study from the Atherosclerosis Risk in Communities Study [ARIC] or de novo from the community), and field center to achieve balance among these factors between treatment arms. Similar to ACHIEVE, spouse pairs will be randomized to the same treatment group.
Study Interventions	Conventional HHC: Participants randomized to continued conventional HHC group will, for the first year of this study, continue to receive the same conventional, clinic-based hearing intervention received in the original ACHIEVE study, with clinic-based visits every 6 months to reinforce self-management strategies and perform hearing aid checks. In year two, participants randomized to continued conventional HHC will crossover to receive telehealth HHC. Telehealth HHC: The telehealth HHC intervention allows for remote access to hearing health care services and continuous support of participants' hearing loss needs via telehealth in addition to conventional clinic-based hearing booster sessions that occur every 6 months. Participants randomized to the telehealth HHC group will receive telehealth HHC for both years of the study.
Participant Duration	2 years, with data collection follow-up visits occurring every 6 months
Study Duration	5 years
Statistical Methodology	Primary: The primary analysis compares hearing aid utilization between groups randomized to telehealth HHC versus conventional HHC delivery model under the intention-to-treat paradigm, analyzing individuals according to their random allocation, irrespective of the treatment received. Consistent with best practices in clinical trials, we will assess the comparability of the randomized groups with respect to known confounders (e.g., recruitment source, site, level of hearing impairment, Quick Speech in Noise score, self-reported acceptance of telehealth at baseline, self-reported and objectively measured baseline hours of hearing aid use, self-reported baseline hours of hearing assistive technologies use, the number of days hearing log data was measured prior to randomization, and the number of visits prior to randomization at which a participant provided hearing logging data). These variables will be considered as covariates in all models. We will use a weighted regression model with an identity link to compare average daily hours of hearing aid use at 1-year post-randomization between participants assigned to the telehealth HHC and conventional HHC. To account for the non-normal distribution of the outcome, confidence intervals and p-values will be obtained using a bias corrected and accelerated bootstrap resampling procedure with 10,000 replicates.

2.2 Schema



3 Study objectives and endpoints

The aims of the *Randomized Trial of Telehealth vs. Conventional Hearing Care Delivery in the ACHIEVE Study* (ACHIEVE Hearing Intervention Follow-Up, or ACHIEVE-HIFU) are:

Primary aims

1. To compare the effect of the telehealth HHC versus the conventional HHC delivery model on hours of hearing aid use (primary outcome) at 1 year post-randomization.

Secondary aims

2. To compare the effect of the telehealth HHC versus the conventional HHC delivery model on secondary outcomes of patient-centered hearing and communication outcomes, social functioning, and quality of life at 1 year post-randomization.
3. To compare utilization of hearing services required by each HHC delivery model.
4. To evaluate the association of the telehealth HHC intervention with changes in hearing aid use and patient-centered hearing and communication, social functioning, and quality of life measures from baseline to up to two years post-intervention.

Primary outcome

The primary outcome is average daily hours of hearing aid use obtained from objective hearing aid data logging at 1 year post-randomization. If a participant wears a hearing aid in both ears, then the ear with the greatest number of hours logged will be selected.

Secondary outcomes

1. Treatment satisfaction, as assessed by a single item from the International Outcome Inventory – Comprehensive Hearing Intervention (IOI-CHI). The IOI-CHI is an interviewer-administered scale that consists of 6 items where participants self-report satisfaction with the hearing intervention using a 5-point Likert scale. A higher score indicates a more favorable outcome.
2. Ability to hear for the primary communication goal, as assessed by a single item from the Client-Oriented Scale of Improvement (COSI) goals achievement questionnaire. COSI goals are rated using a 5-point Likert scale. A higher score indicates the participant is able to hear more of the time.
3. Hearing-specific quality of life, as assessed by the Hearing Handicap Inventory for the Elderly Screening Version (HHIE-S) questionnaire. The HHIE-S is an interviewer-administered questionnaire that consists of 10 items. Participants rate whether hearing loss affects them in different situations (yes, sometimes, or no). The total score is the sum of all responses and ranges from 0 to 20, with higher scores indicating greater hearing issues.

Exploratory outcomes

Exploratory analyses may include, but are not limited to:

1. The 5 remaining items from the IOI-CHI, as well as a composite score created by computing the mean across all 6 items.
2. Ability to hear for the other two communication goals from the COSI goals achievement questionnaire, as well as a composite score created by computing the mean across all 3 goals.
3. Telehealth acceptance, as assessed by an interviewer-administered scale that consists of 5 items in which participants rate the ease of use or utility of telehealth equipment using a 5-point Likert scale. A higher score indicates a more favorable rating. Each item will be examined separately before being analyzed collectively as part of a composite score created by computing the mean across all 5 items.
4. Subgroup analyses of the primary and secondary outcomes including, but not limited to, sex, race, and education. Interactions between treatment assignment and subgroups will be tested relative to $p < 0.10$.
5. The effect of treatment assignment on the total number of contacts between the provider and participant. The total number of provider-participant contacts is quantified by the study audiologists using forms completed at every encounter. In a supplemental analysis, the number of contacts will be examined across specific modalities, including face-to-face contact in a clinic, face-to-face contact outside of a clinic (e.g., home visits), and remote contact (e.g., video calls, phone calls, etc.).
6. The effect of treatment assignment on the total time spent between the provider and participant. The total number of minutes during which the provider and participant

interacted is quantified by the study audiologists using forms completed at every encounter. In a supplemental analysis, the number of minutes will be examined across specific modalities, including face-to-face contact in a clinic, face-to-face contact outside of a clinic, and remote contact.

7. Estimating the linear and potentially nonlinear dose-response relationship between utilization of hearing services and hours of hearing aid use at one-year post-randomization. This will include testing the total number of contacts between the provider and participant, the total amount of time the provider and the participant spend interacting, and differences by modalities such as face-to-face contact in a clinic, face-to-face contact outside of a clinic, and remote contact.
8. Using mixed effects models to examine trends over time from randomization to the two-year follow-up assessment. Time will be defined categorically or continuously with a time spline specified at 12 months. An interaction between treatment assignment and time will be included in the model to estimate the effect of participants in the conventional HHC treatment arm gaining access to telehealth services one-year post-randomization.

4 Background and rationale

4.1 Hearing health care

Age-related hearing loss in older adults fits the World Health Organization's definition of a chronic health condition, with leading professional organizations recommending a comprehensive and multi-dimensional care process.[1–3] In practice, however, hearing health care is predominately delivered via an acute care model that is biomedically focused, clinician-led, and device-centered.[4] Beginning with the initial clinical encounter, the case histories obtained by audiologists often focus on the identification of underlying biomedical issues, with little dialogue focused on the person's psychological or functional difficulties or psychosocial concerns.[5] The application of a biomedical framework to the clinical decision-making process is typically then reaffirmed throughout subsequent clinical activities, rather than the application of a comprehensive, multi-dimensional model of HHC advocated by professional organizations that includes counseling, education, and coaching aimed at improving self-efficacy and locus of control, within a self-management framework.[5,6] Although such non-technological activities are associated with positive outcomes, they are not routinely offered by audiologists.[7]

Perhaps not surprisingly, current rates of hearing aid use among older adults with hearing loss in the U.S. are <20%, and rates of discontinuation of hearing aid use among older adults are high and estimated to be >30%.[8–11] Telehealth delivery of HHC is a form of remote service delivery that makes use of smartphones, tablets, and computers for patients to access health care services away from a clinic, commonly from home. Telehealth can be used to deliver services to adults with hearing loss including ongoing self-management support.[12] While much research has focused on the influence of individual patient characteristics, attitudes, and beliefs on lack of hearing aid uptake and continued hearing aid use,[13–17] there is increasing recognition that the current acute-care, clinic-based HHC model may itself be a leading contributor to low hearing aid uptake and utilization rates.[4,18–20] Technological innovations in telecommunications, particularly with the widespread availability of smartphones, tablets, and broadband internet access, could enhance the accessibility of best practice models of HHC through facilitating ongoing delivery of self-management support services outside the clinical setting.[21,22]

4.2 ACHIEVE background

ACHIEVE (ClinicalTrials.gov identifier: NCT03243422; NIA R01AG055426, R01AG060502; MPIs: Lin/Coresh) is a first-in-kind randomized trial to investigate if hearing loss treatment can reduce cognitive decline in older adults with hearing loss. Recruitment actively began in January 2018 and ran through October 2019, with ACHIEVE enrolling 977 (~10/week) cognitively normal older adults with hearing loss, aged 70-84 years. Participants were randomized 1:1 to a clinic-based, best-practices hearing intervention (hearing needs assessment, fitting of hearing devices, education/counseling; N=490) or a successful aging education intervention (individual sessions with a health educator covering healthy aging topics; N=487). Semi-annual follow-up visits for three years assessed cognitive functioning and secondary outcomes.

The ACHIEVE trial is nested within the Atherosclerosis Risk in Communities Neurocognitive Study (ARIC-NCS). ARIC is a large, biracial prospective cohort study that enrolled 15,792 participants aged 45-64 years from four US communities in 1987-1989: Jackson, MS, Forsyth County, NC, Washington County, MD, and Minneapolis, MN. The Jackson cohort was entirely African-American, and the Forsyth County site was about 15% African-American, with other participants being primarily white. ARIC participants have received multiple assessments of cardiovascular risk factors, measurement of microvascular and macrovascular markers, cognitive testing, PET amyloid, and brain MRI over the last 30 years. The ARIC study is well described with over 1700 papers published in peer-reviewed journals.[23] The ACHIEVE-HIFU study brings together a multidisciplinary consortium of established investigators and leverages the existing research infrastructure, scientific expertise, and well-characterized participant cohort of ARIC-NCS. The 977 participants in ACHIEVE were recruited from the existing ARIC-NCS cohort (N=238) and de novo from the surrounding communities (N=739).

4.3 Preliminary studies of telehealth HHC

Our preliminary studies to assess the feasibility of telehealth HHC delivery were guided by published recommendations for adapting manualized interventions.[24] We began with an online survey of the ACHIEVE study audiologists to determine whether or not components of the conventional hearing intervention could or should be provided via telehealth. Audiologists' responses guided decisions regarding the inclusion of procedures at specific points in time over the course of intervention. The results revealed that after the initial clinic-based sessions, many follow-up procedures and counseling could be delivered remotely. We used the audiologists' responses to help develop our multi-site fidelity monitoring plan for implementation of a manualized telehealth-supported HHC model for ACHIEVE-HIFU. Our team then adapted the parent ACHIEVE manualized hearing intervention to incorporate telehealth to support long-term HHC.

We conducted an initial feasibility study of the adapted telehealth hearing intervention among a convenience sample of 10 first-time hearing aid users, 6 male and 4 female, aged 70-91 years old, who were sampled from a clinical population at the University of South Florida in 2019. Inclusion and exclusion criteria matched that in the parent ACHIEVE trial, with the additional requirement of access to a smartphone. During our pilot study, we identified two major barriers

to successful remote HHC delivery: 1) availability of a compatible smartphone/tablet with adequate internet connection speed, and 2) participant unfamiliarity with telehealth HHC and challenges with how to use a telehealth platform. In order to address these barriers, we incorporated the GrandPad device into our ACHIEVE-HIFU telehealth protocol. The GrandPad is an internet-enabled tablet that was specifically designed for use by older adults, has been effectively implemented at scale for telemedicine, and comes with manufacturer support services to ensure that older adults can effectively use the device.

5 Study population and eligibility

This study is predicated on an already established cohort with a fixed sample size from the original ACHIEVE trial (N=490 for the clinic-based hearing intervention cohort). All participants currently in the ACHIEVE hearing intervention group will be invited to join this follow-up study, and accounting for loss to follow up and refusal to continue participating, we conservatively estimate that N=400 participants will be recruited into this follow-up study.

5.1 Eligibility

To be eligible for the current study, participants must meet the following criteria:

1. Eligible for and participated in the hearing intervention arm of the ACHIEVE trial (see original criteria below)
2. Agree to be randomized to receive hearing care via either a telehealth or conventional delivery model for the first year before being offered telehealth options, and
3. Agree to participate and able and willing to be followed for two years in the follow-up study.

ACHIEVE participants who have developed cognitive impairment are eligible for ACHIEVE-HIFU if they are willing to participate and are consented with a proxy (see section 6.1 below).

Original ACHIEVE inclusion criteria:

- Age 70-84 years
- Community dwelling, fluent English speaker
- Availability of participant in area for study duration
- Adult-onset hearing impairment, defined as four-frequency pure tone average (PTA, 0.5-4kHz, better ear) ≥ 30 dB & < 70 dB
- Speech recognition scores in quiet ≥ 60% in better ear
- MMSE ≥ 23 for high school degree or less; ≥ 25 for some college or more

Original ACHIEVE exclusion criteria:

- Reported disability in ≥ 2 activities of daily living (ADLs)
- Vision impairment (worse than 20/63 on MN Near Vision Card)
- Self-reported use of a hearing aid in the past 1 year
- Medical contraindication to use of hearing aids (e.g., draining ear)
- Unwilling to wear hearing aids on daily basis
- Conductive hearing impairment with air-bone gap > 15 dB in two or more contiguous frequencies in both ears

5.2 Recruitment and retention

The parent ACHIEVE cohort has already been recruited, and all participants assigned to the hearing intervention (N=490) in the parent study presenting for their final 3-year visit and who are willing and able to be followed for an additional two years will be eligible for inclusion in this proposed study. We expect that nearly all participants will choose to enroll in this follow-up study for the following reasons: 1) Continued enrollment in the study ensures that participants will have continued long-term access to free care and management of their hearing aids with their study audiologist, with whom they have an established relationship (in contrast, participants would otherwise be responsible for covering on their own future costs related to replacement/repair of their hearing technologies and follow-up visits with another audiologist); 2) All participants will be provided with a free GrandPad for use for the duration of their participation in this follow-up study; and 3) Participants have been strongly engaged with this study, as evidenced by current rates of study retention, which is likely driven by the immediate and tangible benefits that the study provides to them. We will also continue to use retention strategies for ACHIEVE participants that been highly effective to date. In brief, some of these strategies include: provision of transportation to sessions and home visits as needed, mailed newsletters, birthday and holiday cards, reminder cards and phone calls, small study incentives (e.g., tote bags, mugs, calendars, etc.), and meals/snacks provided at study visits.

The following procedures are also implemented in order to enhance retention:

- When scheduling sessions, participants will be asked about their preferred time and date
- When scheduling in-person clinic visits, participants will be asked about:
    - How participants prefer to get to the clinic visit
    - Need for assistance getting to or moving around the clinic
    - Existence of any medical conditions (e.g., diabetes, dietary restrictions) which might affect the examination and/or type of snack provided
- Reminder calls will be placed and/or reminder packets will be mailed to the participant prior to the scheduled appointment as needed, confirming the study session date and time
- Free parking is provided to all participants for in-person sessions
- Participants will be reimbursed for travel costs, or transportation will be covered for a participant if he/she is not able to drive and/or obtain a ride to attend a study visit
- Participant study incentives will include study-related items (GrandPad device, pens, bags, mailed holiday cards, etc.) and/or modest payments (~$20 to ~$40) for participating in each study visit [individual field sites will determine the participant incentives to provide based on their previous experience and knowledge of their participants and community]
- Participants will be contacted by telephone and/or mail to reschedule the appointment if participants fail to arrive for a scheduled appointment or cancel their appointment to encourage continued participation and to identify and overcome barriers to participation
- Home or telephone-based visits by study staff will be conducted as necessary when participants may be physically unable to come to the field site (e.g., from illness or injury) [these visits will be informed by the experiences of study staff in performing such visits in the parent ACHIEVE and ARIC studies]

Each no-show case will be individually reviewed by study field site staff. Efforts to engage the participant will include a combination of telephone contacts, letters, and the possibility of offering an abbreviated visit. Field site staff, in consultation with the study coordinator and/or field site PI and/or hearing intervention unit/analysis and study governance unit, will determine how long to continue contact efforts. A participant will only be considered "withdrawn" if he/she explicitly requests to withdraw from the study. Participants are free to refuse, or re-enter the study protocol after refusal, at any time.

6 Participant rights and confidentiality

6.1 Informed consent

A signed consent form is obtained from each participant by trained study personnel. The consent form describes the purpose of the study, how randomization works, the procedures to be followed, and the risks and benefits of participation. The consent process informs a volunteer about the study, indicates that participation is voluntary, and that the participant has the right to stop at any time. Risks are enumerated in the informed consent form and described orally during the consent process.

The purpose of the informed consent form is:

- To inform the prospective participant as much and as accurately as possible about:
    - The procedures involved in the study
    - What is expected of participants who consent to enroll
    - What the study can and cannot provide to the participant
    - What are the reasonable risks and benefits
    - What are the alternatives to participation
- To document the participant's consent to participate in all of the respective study procedures
- To provide a prospective participant with a legal document summarizing the study and his or her rights as a study participant
- To provide the participant with ongoing explanations and continuing information that help the participant decide whether to begin or continue in the research study

Re-obtaining consent in the event of consent changes

- If substantive changes to the consent form occur after the participant has signed the consent form at the randomization visit, the participant will be informed of the changes prior to their next study visit or interaction.
- Whenever possible and permitted by the IRB, verbal re-consent will be obtained from the participant and documented by study staff in the participant's chart.
- If written re-consent is required for changes to the consent form, re-consent can occur in person or remotely. Remote consent would be obtained by emailing or mailing two copies of the consent form to the participant, having trained study personnel review the updated consent form, noting the changes, ensuring the participant understands the changes, and asking the participant to sign one copy of the form and mail it back. Upon receipt, the study personnel who obtained consent would sign the form and document the consent process in a note in the participant's chart.

Re-obtaining consent in the event of cognitive impairment

- Although those with dementia were not enrolled at baseline of the parent ACHIEVE trial, given the age of the cohort, some participants may have developed or may in the future develop cognitive impairment over the course of the study. Participants determined to have significantly reduced cognitive capacity and who wish to take part or remain in this follow-up study will be re-consented with consent from a designated proxy.
- If re-consent with a proxy is required during the course of the follow-up study, the re-consent may occur in person or remotely. Remote consent would be obtained by mailing two copies of the consent form to the proxy, having trained study personnel review the consent form with the proxy and participant over the telephone (answering questions and ensuring understanding), and having the proxy and participant sign one copy of the form and mail it back. Upon receipt, the study personnel who obtained consent would sign the form and document the consent process in a note in the participant's chart.
- We will use procedures established by the parent ACHIEVE and ARIC studies to classify decision-making capacity. Given the minimal risk associated with the study procedures, relatively conservative criteria will be used to trigger re-consent with a proxy. These criteria include: (1) a diagnosis of dementia based on cognitive testing at any of the study sessions, or (2) judgment of our trained staff at the time of a study session. These criteria adhere to the published recommendations of the Alzheimer's Association.[25]

6.2 Participant confidentiality

Data from the ACHIEVE-HIFU study are used only in aggregate, and no identifying characteristics of individuals will be published or presented. Per the existing parent study (ACHIEVE and ARIC) protocols, results of select testing (weight, body mass index, and blood pressure) are given to participants, and they can choose to share those data with their health care provider. Study results of depressive symptoms, blood pressure, or cognition, which may indicate the need for referral for medical care, will be provided to participants, who are encouraged to share the results with their private physician. If participants have given permission, the results may also be sent to participants' private physicians. Information, including results of testing to be shared with a participant's primary care physician, is not released without written permission of the participant, except as necessary for monitoring by IRB.

Confidentiality of data is maintained by using research identification numbers that uniquely identify each individual. This study utilizes safeguards established as part of the parent studies (ARIC and ACHIEVE) to ensure the security and privacy of participants' study records. Research records are kept in locked file cabinets within locked rooms at the study site. Only selected study personnel will have access to participants' study records on a need-to-know basis. Data are stored on password-protected computers with regularly updated virus software. Identifying information is only kept in the files where it is necessary for the conduct of the study and linkage to other files. In analysis files, study IDs only are used to identify participants.

In compliance with the Health Insurance Portability and Accountability Act (HIPAA) and the Standards for Privacy of Individually Identifiable Health Information of the Department of Health

and Human Services, study staff access protected health information (PHI) and medical records only after receiving signed informed consent or a HIPAA waiver of authorization. Participants' medical records that are obtained for review and abstraction are kept in a locked cabinet that is separate from other file cabinets. Only selected study personnel have access to these files.

7 Study assessments and procedures

As part of this study, participants will complete interviews, questionnaires, audiometric evaluations, neurocognitive assessments, and measures of physical functioning that mirror those completed as part of the parent ACHIEVE trial. To reduce participant burden, data from the final visit in the parent ACHIEVE trial (year 3 follow-up) will serve as baseline data for this follow-up study. The schedule is shown in 7.1 and descriptions of each of the activities, evaluations, or assessments are provided in the sections that follow the table. Full details on data collection and measurements can be found in the Manual of Procedures.

7.1 Schedule of activities

Table 1 details which data will be gathered and when. Data collection visits may be split across multiple days or multiple settings (clinic visits, home visits, telephone contacts, or video calls) to meet the needs of our participants. Some items related to exploratory outcomes might be dropped based upon participant burden, scientific considerations, or available resources.

Table 1. Schedule of Activities and Evaluations

Follow-up visit	Baseline	Random-ization visit	Telehealth Sessions *Initial Telehealth Randomized HHC arm only*			6-month	Year 1 (12mo)	Telehealth Sessions *Initial Conventional Randomized HHC arm only*			18-month	Year 2 (24mo)
			A[a]	B	C			A[b]	B	C		
Visit relative to parent ACHIEVE Trial (approx.)	Yr 3 (36mo)	--	--			Yr 3.5 (42mo)	Yr 4 (48mo)	--			Yr 4.5 (54mo)	Yr 5 (60mo)
Randomization												
Informed consent		X										
Randomization		X										
GrandPad distribution		X										
Hearing Intervention												
GrandPad instructions for telehealth			X					X				
Intervention check-up	X											
HIFU Intervention check-up		X	X[c]	X	X	X	X	X[c]	X	X	X	X
International Outcome Inventory for Comprehensive Hearing Intervention	X					X	X				X	X
Client-Oriented Scale of Improvement (COSI) goal setting		X										
COSI goals achievement				X	X	X	X		X	X	X	X
Audiometry												
Air conduction audiometry	X						X					X
Bone conduction audiometry	X						X[d]					X[d]
Tympanometry	X						X					X
Word Recognition in Quiet	X						X					X
Quick Speech in Noise (unaided)	X						X					X
Social Functioning and Quality of Life Outcomes												
CES-D Scale	X					X	X					X
Hearing Handicap Inventory for the Elderly - Screening Version	X						X					X
RAND-36 Health Survey	X						X					X
Cohen Social Network Index	X						X					X
UCLA Loneliness Scale	X						X					X
Hospitalizations	X					X	X				X	X
Qualifying (S)AE assessment	X					X	X				X	X

Follow-up visit	Baseline	Random-ization visit	Telehealth Sessions *Initial Telehealth Randomized HHC arm only*			6-month	Year 1 (12mo)	Telehealth Sessions *Initial Conventional Randomized HHC arm only*			18-month	Year 2 (24mo)
			A[a]	B	C			A[b]	B	C		
Covariates												
Health history	X						X					X
Neurologic history	X						X					X
Anthropometry	X						X					X
Seated blood pressure	X						X					X
COVID impact questionnaire	X					X	X				X	X
Telehealth acceptance pre-intervention (TAP)		X					X[e]					
Telehealth acceptance follow-up (TAF)						X[f]	X[f]				X	X
Other Data Collection												
Baecke activity questionnaire	X						X					X
Accelerometry	X						X					X
Falls and mobility questionnaire	X						X					X
Grip strength	X						X					X
Short Physical Performance Battery	X						X					X
Clinical Dementia Rating Scale - Participant (CDP)	X						X					X
Dementia/MCI evaluation if applicable (CDI, CDS, NPI)	X[g]						X[g]					X[g]
Abbreviated neurocognitive battery[g]						X					X	
Full neurocognitive battery[h]	X						X					X

[a]Session A for those randomized to the telehealth HHC delivery arm will occur in-person, often at the end of the randomization visit
[b]Session A for those initially randomized to the conventional HHC delivery arm will occur in-person, often at the end of the Year 1 visit
[c]HIFU Intervention check-up only done during Session A if Session A is not the same day as the Randomization Visit (for those randomized to the telehealth group) or the Year 1 Visit (for those randomized to the conventional group)
[d]Only required if there has been a change in pure tone air conduction
[e]Conventional group only
[f]Telehealth group only, and only if any telehealth sessions have been completed since the last visit
[g]Collected if a participant is selected for informant interview, identified on the Selected to Stage 2 CDART report
[g]Ensuring Speech Understanding (ESU) and MMSE only
[h]ESU, MMSE, Delayed Word Recall Test, Digit Symbol Substitution Test, Incidental Learning, Trail Making Test Part A and Part B, Logical Memory I and II, Digit Span Backward, Boston Naming Test, Word Fluency (FAS), and Animal Naming

7.2 Hearing intervention assessment

7.2.1 Intervention Check-Up

The ACHIEVE-HIFU Intervention Check-Up includes assessments of the following components related to the hearing intervention at the in-person semi-annual and annual visits, and some of the components, as noted below, during both scheduled and unscheduled remote encounters.

- **Hearing aids:** usage of all hearing aids is documented [all contacts]
- **Real-ear aided response:** real-ear measure to verify the gain and output of hearing aids [in-person visits only; as needed]
- **Speech intelligibility index:** a calculated estimate from the real-ear measurements that indicates the amount of the speech signal available to the participants when wearing their hearing aids [in-person visits only; as needed]
- **Hearing aid data logging:** hearing aid use is obtained from the device data log within the hearing aid manufacturer software, including the total hours of use and average hours of use per day [in-person visits only]
- **Hearing assistive technologies (HAT):** usage of HATs is documented [all contacts]
- **Quick speech in noise (QuickSIN; aided):** assesses speech recognition in noise utilizing the hearing aids, where sentences are presented in the presence of background noise, and the participant repeats back what they heard [in-person annual visits only]

7.2.2 Utilization of hearing services

Each provider-participant contact and its duration, along with type/mode of contact, will be documented by the study audiologists. Both scheduled contacts (documented as part of the Intervention Check-Up) and unscheduled contacts will be documented.

7.2.3 International Outcome Inventory for Comprehensive Hearing Intervention

The International Outcome Inventory for Comprehensive Hearing Intervention (IOI-CHI) is a brief, 6-item measure adapted from the International Outcome Inventory for Hearing Aids (IOI-HA)[26] . The IOI-CHI is used to determine benefit from the hearing intervention following a sustained period of regular use.

7.2.4 Client-Oriented Scale of Improvement

The Client-Oriented Scale of Improvement (COSI)[27] is a clinical tool developed by National Acoustic Laboratories (NAL) for outcomes measurement. It is an assessment questionnaire used to document a participant's goals/needs and progress towards achieving those goals.

7.3 Audiometric assessment

The audiometric diagnostic battery will be conducted by a trained audiologist for all participants, regardless of HHC delivery assignment. The diagnostic battery is based on current American Academy of Audiology guidelines.[28] Based on the audiologist's professional discretion, some components of the assessment can be omitted. Cerumen management by the study audiologist will be performed as needed. Participants with more severe cerumen impactions that cannot be easily cleared by the study audiologist will be provided with over-the-counter cerumenolytic ear drops (e.g., Debrox, Murine) and advised to follow-up with their primary care provider or an otolaryngologist.

7.3.1 Air conduction audiometry

Behavioral measurement of minimally perceptible tones tested across the frequencies most important for speech communication delivered through headphones.

7.3.2 Bone conduction audiometry

Behavioral measurement of minimally perceptible tones tested across the frequencies most important for speech communication delivered through a bone oscillator, which allows determination of a sensorineural hearing loss free of middle ear problems. Based on the audiologist's professional discretion, this measurement can be omitted if hearing is stable since last evaluation.

7.3.3 Tympanometry

Objective measurement that determines integrity of the tympanic membrane/ossicles and assists in determination of a sensorineural hearing loss free of middle ear problems.

7.3.4 Word Recognition in Quiet

Confirms that the speech perception abilities are consistent with a hearing loss that can be helped through traditional hearing aid intervention.[29]

7.3.5 Quick Speech in Noise (unaided)

The QuickSIN[30,31] is a speech-in-noise test that measures the signal-to-noise (SNR) necessary for a listener to correctly identify 50% of key words on sentences presented in a babble background noise. A listener's abilities to understand speech in noisy backgrounds cannot be predicted by the audiogram, and this measure provides a tool to counsel the participant on realistic expectations for success with hearing aids and guides intervention decisions regarding hearing assistive technology (e.g., remote FM microphone).

7.4 Social functioning and quality of life

7.4.1 Center for Epidemiological Studies Depression Scale (CES-D)

The CES-D Short Form is a 12-item form to assess depressive symptoms, derived from the original 20-item CES-D.[37] In addition to a reduced administration time and clearer response options (relative to the 20-item version), the Short Form is highly correlated with the original ($r > .94$), has a high internal consistency, retains the same factor structure as the original, and has a similar positive predictive value as a screening tool for identifying clinical depression. The questionnaire is administered by interview, and is scored 0-24.

7.4.2 Hearing Handicap Inventory for the Elderly - Screening Version

This is an interviewer-administered questionnaire to gather data on the perception of the impact of hearing loss.[39] This questionnaire assesses the social and emotional components of perceived hearing impairment such as embarrassment, and limits on personal and social life.

7.4.3 RAND-36 Health Survey

The 36-item RAND Health Survey, assesses health-related quality of life.[40] It is a generic measure, as opposed to one that targets a specific age, disease, or treatment group.

7.4.4 Social Network Index

The Cohen Social Network Index (SNI) is an interviewer-administered questionnaire to gather social network data.[41] The Social Network Index evaluates two outcome variables: 1) Social Network Diversity – number of social roles in which the participant had regular contact with others at least once every 2 weeks, and 2) People in Social Network – total number of people with whom the participant had regular contact (at least once every 2 weeks).

7.4.5 UCLA Loneliness Scale

This interviewer-administered questionnaire[42] measures subjective ratings of social isolation and loneliness (e.g., lacking companionship, feeling left out, and isolated from others, among others).

7.4.6 Hospitalizations

This interviewer-administered questionnaire records recent hospitalizations since the last time of study contact.

7.5 Covariates

7.5.1 Health history questionnaire

This is an interviewer-administered questionnaire that documents a number of chronic diseases or conditions (e.g., hypertension, diabetes, stroke, Parkinson's disease, osteoporosis, among others).

7.5.2 Neurologic history

This questionnaire includes items about past neurologic diagnoses and treatments. This information will be used as possible covariates and by MCI/dementia adjudicators.

7.5.3 Anthropometry

Participant height and weight will be measured using standardized study protocols from the parent studies (ARIC/ACHIEVE). Anthropometric measures include height, weight, waist and hip circumference, and body fat.

7.5.4 Seated blood pressure

Seated systolic and diastolic blood pressure will be measured using standardized study protocols from the parent studies (ARIC/ACHIEVE).

7.5.5 COVID impact questionnaire

This brief questionnaire asks questions about how the coronavirus pandemic, or COVID-19, has affected the participant.

7.5.6 Telehealth acceptance questionnaires

Questions assess the participant's comfort with and acceptance of telehealth HHC both prior to start of the telehealth intervention and after starting the telehealth intervention.

7.6 Physical activity and physical functioning

7.6.1 Baecke Physical Activity Questionnaire

This interviewer-administered questionnaire[38] measures the frequency and duration of self-reported activities. This questionnaire asks about habitual physical activities including sport-related activities during leisure time, non-sport related physical activity during leisure time, and television viewing.

7.6.2 Accelerometry

Physical activity is objectively assessed using the Actigraph Link accelerometer, an FDA approved, triaxial, water-resistant, wrist-worn device that can be worn 24 hours a day, continuously measuring intensity, duration, and frequency of physical activity. Participants will be fitted with the device during their clinic visit and asked to continue wearing the device at all times for the subsequent 7 days[43]. Participants will be asked to wear the accelerometer at baseline and again at follow-up to detect differences in physical activity and sedentary behaviors.

7.6.3 Falls and mobility

This interviewer-administered questionnaire records living circumstances, self-reported physical ability, fatigue, and falls.

7.6.4 Grip strength

Grip strength will be measured using standardized study protocols from the parent studies (ARIC/ACHIEVE). Grip strength is objectively assessed with a handheld dynamometer. After a practice trial, participants are asked to complete two trials, squeezing as hard as possible, with a 15-20 second rest between trials. Grip strength exclusion is limited to those who have had surgery on both hands or on both wrists in the previous 3 months. If only one side is affected, the unaffected side is tested. The test can be performed if the participant has a current flare-up of pain in their wrist or hand, for example arthritis or tendonitis. This information is recorded on the data collection form.

7.6.5 Short Physical Performance Battery (SPPB)

The Short Physical Performance Battery[44] will be conducted using standardized study protocols from the parent studies (ARIC/ACHIEVE). The SPPB is a series of physical performance tests designed to assess lower extremity function in older adults. The SPPB ranges in score from 0-12; higher scores indicate better function. The total score is the sum of 3 component scores: chair stands, balance, and 4-meter walk gait speed; each component score ranges from 0-4. Exclusion from any performance test is based on examiner assessment or participant concerns that the test would be unsafe. Walking aids are allowed during the 4-meter walk only, if participants feel they are necessary.

7.7 Dementia and MCI assessments

A syndromic diagnosis of MCI and dementia will be determined and used as secondary outcomes. Current criteria for MCI[35] and dementia,[36] which prominently included investigators for this project, are now well-established and have been employed successfully in ARIC-NCS and ACHIEVE. Details of the diagnostic procedures and normative data have been published and are enumerated in the Manual of Procedures. Briefly, MCI and dementia syndromic

diagnoses are determined by a panel of clinicians, taking into account performance on the neuropsychological battery (test scores are compared to age, education, and race-specific norms), cognitive decline across study visits, and subject and informant interviews regarding cognitive functional status. Based on these elements, all examined participants have a computer-algorithmic classification followed by expert-adjudicated review. The computer algorithm, also developed by the expert panel for ARIC-NCS, has been used successfully to enhance uniformity in applying the diagnostic criteria. In ARIC-NCS, the computer algorithm-reviewer agreement was high: 99% for normal, 94% for MCI, and 95% for dementia, suggesting that the algorithm accords well with clinical judgment. The informant interviews noted above are conducted with a knowledgeable informant at every exam where the participants meet a priori criteria for poor cognitive performance and who have significant cognitive decline from prior exams.

7.7.1 Neurological interviews

The neurologic interviews include the Clinical Dementia Rating Scale (CDR) and the Neuropsychiatric Inventory (NPI). In addition, the Functional Activities Questionnaire (FAQ) is used in determining a participant's level of daily functioning, but does not have a dedicated interview or form; rather, all FAQ items are embedded within the CDR interview. Each of the measures are well-validated, standardized instruments that have been widely used in both clinical and epidemiologic studies of dementia.

7.7.2 Clinical Dementia Rating Scale (CDR)

The CDR gives important information about daily functioning, and is a required element in the determination as to whether an individual is demented or has MCI, or is normal. The CDR includes the CDR Participant (CDP), and the CDR Informant (CDI), and the CDR Summary (CDS).

The CDP (the portion of the CDR administered to the participant) is administered by a certified staff member. The CDI is administered by a certified staff member with a knowledgeable informant. After completion of these two components (and not in the presence of the subject or informant), a trained staff member will score the CDR (on the CDS form) based on the responses to the questions on both the CDP and CDI. The CDR scores range from 0 (normal) to 3 (severe impairment) for each of the following 6 areas: memory, orientation, judgment and problem solving, community affairs, home and hobbies, and personal care.

7.7.3 Functional Assessment Questionnaire (FAQ)

The FAQ score is embedded within the CDR. Scores range from 0 (normal function), 1 (has difficulty, but does by self), 2 (requires assistance), to 3 (dependent). There are 9 items from the CDR which are also FAQ questions (there are 10 FAQ questions; one CDR question encompasses two FAQ questions).

7.7.4 Neuropsychiatric Inventory (NPI)

The NPI consists of questions relating to personality and behavioral changes commonly seen in dementia. This scale is completed with a knowledgeable informant after the CDI.

7.8 Neurocognitive battery

This study will utilize the neurocognitive battery (described below) that was previously administered in ARIC-NCS[32] and the parent ACHIEVE trial. Four cognitive domains are derived from factor scores.[33] These domains include:

- Global function
- Memory
- Executive function
- Language

7.8.1 Ensuring speech understanding test

Prior to performing the neurocognitive assessment, a brief test will be conducted to determine whether or not the participant can adequately hear the examiner. In this test, five sentences are read aloud to the participant by the psychometrist, and the participant is asked to repeat back the sentence. Participants are scored on the number of target words repeated back correctly (3 target words/sentence). Steps on how to proceed with neurocognitive testing if audibility is not established are outlined in the Manual of Procedures. The parent ACHIEVE Steering Committee developed this protocol to guard against poor speech understanding from hearing loss directly confounding administration of neurocognitive tests with auditory stimuli.

7.8.2 Mini-Mental State Exam (MMSE)

The MMSE was developed as a brief, standardized instrument for screening a limited number of cognitive functions.[34] The MMSE is administered by interview.

7.8.3 Delayed word recall test (DWRT)

The DWRT is a measure of verbal memory that requires the participant to recall a list of 10 common nouns following a short delay. The participant is presented with a stimulus card for each of 10 words. The examiner reads each word aloud, and asks the participant to repeat the word and use it in a sentence. This procedure is repeated, providing two exposures to the words. Following an approximate 5-minute delay, during which the (non-verbal) digit symbol substitution test (DSST) is given, the participant is asked to recall as many words as possible. Scores range from 0 to 10 words recalled.

7.8.4 Digit Symbol Substitution test (DSST)

The DSST is a measure of psychomotor speed and sustained attention. Besides its own value, the DSST also serves as a nonverbal distracter task, interposed between learning and recall for the DWRT above. The participant is asked to translate numbers (1-9) to symbols using a key provided at the top of the test form. The participant is provided with a pencil (without an eraser). Instructions are provided in a deliberate and slow pace. One point is given for each correctly drawn symbol completed within the 90-second time limit. Scores range from 0-93.

7.8.5 Incidental learning

The Incidental Learning Test was adapted from the WAIS-R NI and provides a non-verbal measure of recent memory. Following the DSST, the participant is presented with the Incidental Learning Template. The participant is asked to write down as many of the DSST symbols as he/she can remember, in any order. Next, the participant is asked to write down the number that was paired with each of the symbols from the DSST. Two scores are yielded: 1) Free

Recall: total number of symbols recalled, regardless of pairing, and 2) Pairing: number of correct symbols correctly paired with corresponding numbers. Scores for each range from 0-9.

7.8.6 Trail Making Test Part A (TMT A)

The TMT A is a timed task in which participants connect numbers in sequence as quickly as possible. TMT measures attention, sequencing, mental flexibility, and visual search and motor function. In TMT A, the participant is asked to draw a line and connect a series of numbers (from 1-25) as quickly as possible. Prior to the test part, the participant is given a sample test to demonstrate the task. The score for TMT A is the number of seconds required to complete the task. A maximum of 240 seconds (4 minutes) and 5 errors is allowed.

7.8.7 Trail Making Test Part B (TMT B)

The TMT Part B is a timed task in which participants connect letters and numbers in sequence as quickly as possible. TMT measures attention, sequencing, mental flexibility, and visual search and motor function. In TMT B, the participant is asked to draw a line and connect a series of numbers and letters, alternating between a given number and letter (e.g., 1 to A, A to 2, 2 to B, B to 3, etc.) as quickly as possible. Prior to the test part, the participant is given a sample test to demonstrate the task. The score for TMT B is the number of seconds required to complete the task. A maximum of 240 seconds (4 minutes) and 5 errors is allowed.

7.8.8 Logical Memory I and II

This test, part of the Wechsler Memory Scale-Revised version, provides a measure of immediate and delayed verbal recall for the number of ideas presented in two stories, which are read to the participant. Two stories are read to the participant, each at a slow and deliberate pace. After each story is presented, the participant is asked to recall as much of the story as possible. The Logical Memory I score provides a measure of immediate recall and is calculated as the average number of ideas recalled from Story A and B. Each story contains 25 scoring units, the maximum score is 25 (25+25/2).

An approximate 20-minute delay follows, during which the remaining (non-memory) tests are administered. Following the delay period, the participant is again asked to recall the stories. The Logical Memory II score provides a measure of delayed recall and is calculated as the average number of story elements recalled from Story A and B. As each story contains 25 scoring units, the maximum score is 25 (25+25/2).

7.8.9 Digit Span Backwards

Digit Span Backwards is part of the Wechsler Memory Scale-Revised and provides a measure of attention and working memory. The participant is read a series of numbers progressively increasing in length from two to eight digits. After the numbers are read, the participant is asked to repeat the numbers in the reverse order. Two trials at each digit length are performed (i.e., 2 trials with 2 digits, 2 trials with 3 digits, etc.). The test is discontinued after two consecutive errors of the same length item. Scores range from 0-12.

7.8.10 Boston Naming test

The Boston Naming Test assesses visual naming ability using black-and-white drawings of common objects. For this study, the 30-item version used by the National Alzheimer's Coordinating Centers Uniform Data Set will be used. The participant is presented with a series of line drawings of objects and asked to name each object. The items become progressively

more difficult based on their frequency of occurrence in the English language. A total score is calculated as the number of spontaneously produced correct responses. Scores may range from 0-30.

7.8.11 Word Fluency

The Word Fluency Test is a measure of verbal functioning. In this task, the participant is asked to produce as many words as possible that begin with the letters ‘F’, ‘A’, and ‘S’ within a time limit of 60 seconds for each letter, avoiding proper nouns, variations, plurals, and repetitions. The score is the total number of admissible words produced across letters.

7.8.12 Animal Naming

Animal Naming is a measure of category fluency (semantic association). Category fluency, and specifically animal naming, is part of the Boston Diagnostic Aphasia Examination, the Stanford-Binet test, and the CERAD. The participant is asked to name as many different animals as possible within a 60-second time limit. The score is given as the sum of all admissible names.

7.8.13 Telephone neurocognitive assessment

In the event that a participant is unable to be scheduled for an in-person visit (at the field site or at home) to complete the neurocognitive battery, a version of the neurocognitive battery modified for telephone administration may instead be administered. The content of the Ensuring Speech Understanding test, the Digit Span Backwards test, and Animal Naming test remains the same as described above but with some modifications to instructions for telephone administration. The content of the CDP (see section 7.7.2) remains the same, but the order of administration has been modified for use over the telephone. The Word Fluency test has been shortened to collect on 'F' and 'A' words only, with 'S' words dropped.

In lieu of the visual DWRT, an oral 10-item word list memory measure (CERAD, The Consortium to Establish a Registry for Alzheimer's Disease)[45] test is used. A shortened version of the MMSE, with two items modified for phone administration, and 19 original items dropped is used in place of the full MMSE.

Oral versions of Trails A, where the participant is asked to count from 1 to 25 as quickly as they can, and Trails B, where the participant is asked to alternate between letters and numbers as quickly as they can until they reach the number 13, are used. For each of the Oral Trails tasks, up to 5 attempts are allowed, with the maximum time permitted to complete each task being 4 minutes. The total time the participant took to complete the series, the total number correct, and the total number of errors are recorded.

7.9 Characterization of participants who leave the study early

A final interview will be attempted with all participants who are either unable (e.g., due to illness) or unwilling to complete the study. Trained interviewers will collect information by telephone or HIPAA-compliant video call regarding the reason for withdrawal and offer to schedule a home visit/telephone/video call for an abbreviated final study session. In the absence such a session, because dropouts may be more likely to have dementia, we will attempt to ascertain dementia status using a telephone-based/video call-based assessment with the participant or informant interview conducted with a knowledgeable informant.

In the case where the participant is alive and able to communicate by phone/video call, we will administer the Six Item Screener (SIS). The SIS is a short instrument developed to identify cognitive impairment in older adults. In the case where the participant has died or is otherwise unable to communicate by phone/video call, dementia status will be characterized by informant interview via telephone/video call using the AD8--a brief instrument, derived from the Clinical Dementia Rating Scale, developed to discriminate between normal aging and dementia. Notably, these procedures parallel ARIC's ongoing dementia surveillance methods. For ARIC participants, additional sources of information may also be used to complete ascertainment of dementia cases (e.g., discharge codes from hospitalizations, CMS, and ICD codes on death certificates).

8 Randomization

Participants will be randomized in a 1:1 ratio to the telehealth HHC vs. conventional HHC delivery groups. Randomization will be carried out using random blocks of sizes 2, 4, and 8, and will be stratified by degree of hearing loss (mild vs. moderate or greater), cohort (originally recruited from the ARIC Study or de novo from the community), and field center to achieve balance among these factors between HHC arms.

ACHIEVE enrolled some spouses/cohabitating partners who were randomized together. Spouses or cohabitating partners in this follow-up study will also be randomized together. They will be randomized as a unit with, arbitrarily, the first spouse/partner of the pair to be selected according to the random assignment procedure and the second spouse/partner of the pair receiving the same assignment. Spouse/partner pairs will be randomized in spouse/partner-pair specific permuted order blocks of varying sizes within strata defined by participant status (at least one spouse/partner pair in ARIC or both non-ARIC participants) and by field site.

Randomization will be performed after the baseline data for this follow-up study have been collected.

8.1 Measures to minimize bias

Although the ACHIEVE HHC interventions are by nature unmasked, in order to minimize bias based on review of accumulating data by the project team, the ACHIEVE PIs, co-investigators, and key project staff (except one unblinded statistician) will remain blinded to accumulating data. Additionally, study participants will be blinded to study hypotheses.

This study design that incorporates the GrandPad for all participants minimizes potential bias (i.e., all participants receive a GrandPad, reducing the possibility that better outcomes with the telehealth HHC intervention are only due to those participants having access to a GrandPad) and allows for a direct efficacy study of whether telehealth HHC can improve outcomes when barriers to telehealth technology are effectively reduced.

9 Interventions

9.1 All participants

At the ACHIEVE trial year 3 visit, which will serve as the ACHIEVE-HIFU baseline visit, all participants will complete the hearing intervention check-up (see 7.2.1 above), and the audiologist will address any hearing aid maintenance or repairs, as needed.

At the ACHIEVE-HIFU randomization visit, after providing informed consent, participants will be randomized to receive either continued conventional clinic-based HHC or telehealth HHC delivery in addition to clinic-based care. All participants will complete the Telehealth Acceptance Pre-Intervention questionnaire before they will be given a GrandPad tablet with general instructions on how to set it up, an overview of its basic functionality, and how to access manufacturer support services. Prior to being informed of their randomized group, all participants will meet with the audiologist to complete COSI goal setting and complete the hearing intervention check-up (HICF). Participants will then be informed of their randomization assignments.

Participants randomized to the telehealth HHC delivery group will receive their first telehealth session at the end of the randomization visit, and they will continue to receive telehealth HHC for both years of the study, with clinic-based care occurring every 6 months. Participants randomized to the conventional clinic-based HHC delivery group will receive conventional clinic-based HHC for the first year of the study, receive their first telehealth session at the end of the Year 1 visit, and receive telehealth HHC for the second year of the study. The telehealth and conventional HHC delivery models are described next.

9.2 Telehealth hearing health care

We designed a hearing health care (HHC) service delivery model that leverages telehealth in order to provide more accessible long-term support of older adults using hearing aids. The telehealth HHC service delivery model allows for remote access to HHC services and continuous support of participants' hearing loss needs via telehealth to complement clinic-based hearing booster sessions that occur every 6 months. The telehealth HHC intervention includes three telehealth delivery intervention sessions, as well as periodic asynchronous self-management suggestions, and opportunities for ongoing remote support through both synchronous and asynchronous communications as needed.

9.2.1 Telehealth Session A

The first intervention session will occur in person. For participants randomized to the telehealth HHC group, the first intervention session will occur at the end of the randomization visit. The first telehealth session will consist of:

1. Participant instruction in use of the GrandPad for telehealth sessions
2. Re-introduction of the Hearing Loss Toolkit for Self-Management and C2Hear reusable learning objectives (RLOs) within the context of the telehealth platform
3. Individual hearing and communication needs assessment, including review of technical intervention, optimizing the hearing intervention for telehealth sessions, and discussion of how telehealth can be used to achieve COSI goals

9.2.2 Telehealth Sessions B and C

Two follow-up intervention sessions (at approximately 3 weeks and 6 weeks post-randomization) will occur via GrandPad video call (or telephone if the participant does not choose to use the GrandPad). These sessions will primarily be individualized counseling sessions and will consist of:

1. HIFU Intervention Check-Up components that can be collected remotely (i.e., hearing aid use, HAT use)
2. Assessment of COSI goals achievement
3. Discuss participants' comfort with the telehealth platform

9.2.3 Asynchronous provider-to-participant telehealth communications

Clinician-initiated self-management suggestions related to the participant's communication goals will be sent asynchronously via the email/text function on the GrandPad approximately 1-2 times per month or communicated via telephone or other modalities if the participant does not use the GrandPad. These asynchronized contacts could include reminders about:

1. Reviewing the Hearing Loss Toolkit for Self-Management exercises related to their set COSI goals
2. C2Hear RLOs
3. Support of any device cleaning and hearing aid troubleshooting
4. Hearing assistive technology (HAT) use

These asynchronous contacts can lead to synchronous telehealth encounters or even an in-clinic visit if determined to be necessary by the audiologist or requested by the participant. As in the parent ACHIEVE study, participants will be able to reach out to the audiologist to initiate an interim visit/encounter to address any unanticipated needs if they arise, with a shift to telehealth visits as the first option for participants receiving the telehealth HHC delivery model.

9.3 Conventional clinic-based hearing health care

Our research team previously developed the clinic-based, best-practices hearing intervention approach[46] that is currently being implemented in the parent ACHIEVE trial based on the World Health Organization's International Classification of Functioning, Disability and Health (WHO ICF)[47] biopsychosocial framework. In line with the WHO ICF framework, the main goal of intervention is improving a person's quality of life by eliminating or minimizing limitations in activity and social participation. The parent ACHIEVE hearing intervention begins with a comprehensive audiological assessment, followed by goal setting and provision of hearing aids and compatible hearing assistive technologies (HATs). Counseling and education aimed at supporting hearing loss self-management skills are an integral component of the ACHIEVE hearing intervention, and are provided based on individual participant-prioritized goals.

Participants randomized to the conventional, clinic-based hearing health care (HHC) arm will continue to be seen in-clinic semi-annually to reinforce hearing loss self-management strategies and perform hearing aid checks. Following the COSI goal setting and HIFU hearing intervention check-up that all participants will complete during the randomization visit, participants randomized to the conventional, clinic-based HHC arm will be informed of their randomization assignment and reminded about how to continue accessing the conventional HHC supports that they received in the parent ACHIEVE study during the first year of the ACHIEVE-HIFU study

(i.e., participants will be able to reach out to the audiologist to initiate an interim visit/encounter to address any unanticipated needs if they arise).

9.3.1 Crossover to telehealth HHC delivery model

After 12 months, participants assigned to the conventional HHC delivery model will crossover and receive the telehealth HHC delivery model for year 2 of this study. At the end of the 1-year post-randomization visit, participants will receive telehealth session A (see section 9.2.1), followed by telehealth sessions B and C at approximately 3 and 6 weeks later, respectively, as described above.

Full details of the interventions can be found in the Manual of Procedures.

10 Safety monitoring

ACHIEVE-HIFU will follow safety procedures established as part of the parent studies (ACHIEVE and ARIC).

10.1 Data and safety monitoring board

An independent Data and Safety Monitoring Board (DSMB) has been constituted in collaboration with the NIA for the parent ACHIEVE study and provides oversight at convened biannual meetings where interim unblinded and blinded data reports are reviewed. An approved Data and Safety Monitoring Plan (DSMP) and DSMB charter guides data and safety monitoring for the ACHIEVE study. The DSMB members comprise clinicians/investigators with expertise in clinical trials, neuropsychology, dementia, biostatistics, audiology, and otolaryngology. This follow-up study to ACHIEVE will fall under the purview of the existing DSMB, and we will continue to follow all prevailing procedures as detailed in our approved DSMB charter and DSMP during the period of temporal overlap between ACHIEVE-HIFU and the parent ACHIEVE trial. After the completion of the parent trial, we will determine, in consultation with the DSMB, NIA, and NIDCD, whether continued DSMB oversight of this telehealth trial is needed given the minimal risk nature of this study and based on the experience to date with the parent trial. Because the primary outcome of this proposed study is hearing aid use at 1 year and the study interventions are minimal risk, there are no pre-planned interim data analyses to look for efficacy or futility that would lead to early stopping of this proposed trial.

10.2 Adverse events

This follow-up study to ACHIEVE will use the procedures established in the parent ACHIEVE study for adverse events.

Study participation and exposure to the HHC interventions is expected to have a low risk of adverse events for the participant. At the same time, the age of the participants may naturally lead to numerous deleterious health outcomes. In order to efficiently collect safety information that is relevant to study participation, interventions, and procedures, detailed information

concerning a **pre-specified set** of adverse events and serious adverse events will be collected and evaluated throughout the conduct of the trial.

An ***adverse event (AE***) is an untoward medical occurrence, whether or not considered study-related, which occurs during the conduct of a clinical trial.

A ***serious AE*** **(SAE)** is any AE that results in any of the following outcomes:

- Death
- Life-threatening
- Inpatient hospitalization or prolongation of existing hospitalization
- Results in persistent or significant disability or incapacity
- A *major* congenital anomaly or birth defect
- Important medical event that may not result in one of the above outcomes, but may jeopardize the health of the study participant or require medical or surgical intervention to prevent one of the outcomes listed above.

For this study, ***only the following adverse events and serious adverse events will be recorded and reported***:

Adverse Events	**Serious Adverse Events**
• Otitis externa	• Death from any cause
• Cerumen impaction or ear foreign body requiring removal by a physician	

An adverse event of otitis externa is defined as inflammation or infection of the ear canal resulting in pain, swelling, irritation, itching, or other related symptoms as diagnosed by the study audiologist or a physician. Adverse event severity is defined as:

- **Mild** if the symptoms are self-limited and resolve with interventions such as transiently limiting hearing aid use and/or the use of over-the-counter pharmacological therapies such as hydrocortisone cream or swimmer's ear drops.
- **Moderate** if the symptoms require evaluation and management by a physician *and* the use of topical prescription pharmacological therapies such as antibiotic ear drops.
- **Severe** if the symptoms require evaluation and management by a physician and the use of oral or parenteral antibiotics.

An adverse event of a cerumen impaction or ear foreign body requiring removal by a physician is defined as a cerumen impaction and/or ear foreign body that cannot be routinely managed by the study audiologist and requires evaluation and management by a physician (typically an otolaryngologist). Adverse event severity is defined as:

- **Mild** if the cerumen impaction or foreign body is resolved without further need for therapy besides over-the-counter pharmacological therapies such as cerumenlytic drops.
- **Moderate** if there is an associated otitis externa requiring the use of topical prescription pharmacological therapies such as antibiotic ear drops.

- **Severe** if the cerumen impaction or ear foreign body results in a perforation of the tympanic membrane or an associated otitis externa requiring the use of oral or parenteral antibiotics.

AEs or SAEs will be defined as **unexpected** or **expected** based on the judgement of the field site PI in consultation with the field site audiologist and/or study PIs Lin (who is a board-certified otolaryngologist) and Sanchez (who is a licensed audiologist) based on the following definitions:

- **Unexpected:** nature, severity, or frequency of the event is not consistent with information about the condition under study or intervention in the protocol and consent form
- **Expected:** event is known to be associated with the intervention or condition under study.

Study-relatedness of AEs or SAEs will be based on the judgement of the field site PI in consultation with the field study audiologist and/or study PIs Lin/Sanchez based on the following guidelines:

- **Definitely Related:** The adverse event is clearly related to the investigational intervention – i.e., an event that follows a reasonable temporal sequence from administration of the study intervention, follows a known or expected response pattern to the suspected intervention, that is confirmed by improvement on stopping and reappearance of the event on repeated exposure and that could not be reasonably explained by the known characteristics of the subject's clinical state.
- **Possibly Related:** An adverse event that follows a reasonable temporal sequence from administration of the study intervention follows a known or expected response pattern to the suspected intervention, but that could readily have been produced by a number of other factors.
- **Not Related:** The adverse event is clearly not related to the investigational agent/procedure - i.e., another cause of the event is most plausible; and/or a clinically plausible temporal sequence is inconsistent with the onset of the event and the study intervention and/or a causal relationship is considered biologically implausible.

Unanticipated Problems

An unanticipated problem is defined as an incident, experience, or outcome that meets all of the following criteria:

- Unexpected – in terms of nature, severity, or frequency given the procedures and interventions used in the study as described in the protocol and informed consent given the characteristics of the study population
- Possibly or definitely related to participation in the study
- Suggests that the research placed the participant or others at a greater risk of harm (including physical, psychological, economic, or social harm) than was previously known or recognized

Some but not all adverse events may qualify as unanticipated problems.

The Coordinating Center will review all recorded treatment-emergent adverse events and all serious adverse events (SAEs) from this pre-specified list and will provide a report to the

Steering Committee and for submission to the IRB. An SAE that is ***unexpected and possibly or definitely related to study participation or study intervention*** will be reported within 48 hours by the sites to the PI and study project manager who will be responsible for reporting to the sIRB and the NIDCD.

Adverse events and serious adverse events will be recorded on the electronic Adverse Events Form per study instructions. Additionally, for ***unexpected and possibly or definitely related serious adverse events only***, sites will record a narrative description of the serious adverse event, including any relevant test results and dates.

All completed AE forms will be forwarded promptly to the Coordinating Center where they will be reviewed for completeness by the Coordinating Center staff and MPI Lin (who is a board-certified otolaryngologist) and/or MPI Sanchez (who is a licensed audiologist). In particular, the Principal Investigators will assure that documentation of each event is adequate to permit accurate inferences regarding causation (e.g., temporal associations, onset, course, response to patient or physician intervention, alternative etiologies) and severity. Full details of procedures for reporting adverse events can be found in the Manual of Procedures.

11 Statistical considerations

11.1 Sample size

This study is predicated on an already established cohort with a fixed sample size from the original ACHIEVE trial (N=490 for the clinic-based hearing intervention cohort). In order to estimate the minimal difference in hours of continued hearing aid use that could be detected between the telehealth and conventional HHC groups after 12 months, we've made conservative assumptions based on expected loss to follow-up over time that would diminish the sample size and any observable outcomes. The initial cohort receiving the hearing intervention was N=490. Assuming conservatively that 5% of participants per year in this cohort are lost to follow-up or death, we would have a potential cohort of N=420 participants who would be eligible to participate after 3 years of follow-up from 2021-2022. If we further assume that up to 5% of these participants may then decline additional follow-up, we conservatively estimate that N=400 participants currently in the hearing intervention group will be recruited into this follow-up study (ACHIEVE-HIFU). Further conservatively assuming: 1) 10-20% loss to follow-up in the 12-month follow-up data collection; 2) 80% power and a 5% Type 1 error rate; and 3) that patterns of hearing aid utilization will be similar to those observed in the ACHIEVE pilot study, we would have the ability to detect an average treatment effect of 0.8 to 0.9 hours of hearing aid use between the telehealth HHC and conventional HHC arms.

11.2 Analytic approach

The final statistical analysis plan was finalized in discussions between the study investigators and coordinating center.

The comparison for all primary analyses is randomization to the telehealth HHC vs. conventional clinic-based HHC delivery model under the intention-to-treat paradigm, analyzing individuals according to their random allocation, irrespective of the treatment received.

Consistent with best practices in clinical trials, we will assess the comparability of the randomized groups with respect to known confounders, such as recruitment source, site, level of hearing impairment, Quick Speech in Noise score, self-reported acceptance of telehealth at baseline, self-reported and objectively measured baseline hours of hearing aid use, self-reported baseline hours of hearing assistive technologies use, the number of days hearing log data was measured prior to randomization, and the number of visits prior to randomization at which a participant provided hearing logging data.[48] These variables will be considered as covariates in all models. If there is an imbalance between randomized treatment assignment, we may adjust for relevant confounders as well as explore the use of a prespecified inverse probability of treatment weight or a precise, locally efficient, augmented, simple estimator.[49,50] A logistic regression model will be used to model the probability of attrition according to the confounders described above plus age, sex, and applicable interactions. Inverse probability of attrition weights will be calculated and either included in the model for the primary outcome directly or cross-multiplied with inverse probability of treatment weights.

We will use a weighted regression model with an identity link to compare average daily hours of hearing aid use at 1-year post-randomization between participants assigned to the telehealth HHC or conventional HHC. To account for the non-normal distribution of the outcome, confidence intervals and p-values will be obtained using the bias corrected and accelerated bootstrap resampling procedure with 10,000 replicates.

For continuous secondary outcomes, groups will be compared for differences at the 1-year follow-up using the same analytic approach specified for the primary outcome. For binary secondary outcomes, either logistic regression or Poisson regression with robust error variance will be employed, depending on whether the outcome is rare or common. For categorical outcomes, either ordinal or multinomial logistic regression models will be utilized, depending on the nature of the measure and empirical tests of the proportional odds assumption.

Statistical significance for the primary outcome will be defined as $p < 0.05$. Secondary outcomes will be evaluated for statistical significance with a Hochberg modification to the Bonferroni adjustment, in which the p-values of the five outcomes will be ordered. The largest p-value will be compared relative to $p < 0.05$, and if met, all parameters will be considered significant. If not, then the second largest p-value will be assessed relative to $p < 0.05/2 = 0.025$, and if met, then it and all other parameters will be considered significant, and so on for the third p-value at $p < 0.05/3 = 0.017$.

12 Data management

Trained data management and study management staff at the UNC CSCC will be responsible for coordinating data management. The Coordinating Center (CC) uses a customized state-of-the-art web-based data management system using Carolina Data Acquisition and Reporting Tool (CDART) which is also used for the parent ACHIEVE study and ARIC-NCS. A complete description of all data management procedures has previously been developed for the parent ACHIEVE trial and has been approved by the ACHIEVE DSMB. CDART uses a flexible, secure authentication system requiring a username and password. In accordance with HIPAA, all individually identifiable information is encrypted and decrypted for local on-screen display at field sites. The GrandPad tablet is HIPAA-compliant with respect to any telehealth sessions that occur using this platform.

Data collection

The CC has previously led the translation of the protocol data collection specifications into a consolidated set of clear, unambiguous electronic case report forms (eCRFs) for the parent ACHIEVE trial. Each eCRF has a corresponding paper form to be used by sites in cases where data cannot be entered at the time of collection.

Randomization and blinding

Randomization will be implemented within CDART. Although the ACHIEVE hearing interventions are by nature unmasked, in order to minimize bias based on review of accumulating data by the project team, the ACHIEVE PIs, co-investigators, and key project staff (except one unblinded statistician) will remain blinded to accumulating data. In all cases, hours of hearing aid use (primary outcome), a completely objective data point, will be gathered directly from hearing aid data logging software, and source data will be verified as part of the quality assurance procedures. All other non-audiological secondary outcomes will be collected by trained technicians, rather than the site audiologist.

Data quality control and monitoring

Quality and completeness of recorded data will be assured on an ongoing basis by range and logic checks upon entry, queries for missing or inconsistent data, and periodic monitoring. Consistent with the parent ACHIEVE trial a Quality Control Subcommittee chaired by MPI Lin meets monthly to review all data collection procedures and summary data tables to ensure the integrity of data collection and to troubleshoot as needed.

Records retention

MPIs and field center PIs will retain study essential documents and specimens for up to 10 years following study completion.

Ethical considerations

This study is to be conducted according to US and international standards of Good Clinical Practice (FDA Title 21 part 312 and International Conference on Harmonization guidelines), applicable government regulations and institutional research policies and procedures.

This protocol and any amendments will be submitted to a properly constituted single Institutional Review Board (sIRB), in agreement with local legal prescriptions, for formal approval of the study conduct. The decision of the sIRB concerning the conduct of the study will be made in writing to the investigator and a copy of this decision will be provided to the sponsor before commencement of this study.

All subjects for this study will be provided a consent form describing this study and providing sufficient information for subjects to make an informed decision about their participation in this study. This consent form will be submitted with the protocol for review and approval by the sIRB for the study. The formal consent of a subject, using the IRB-approved consent form, will be obtained before that subject undergoes any study procedure. The subject will sign the consent form, as will the investigator-designated research professional obtaining the consents.

13 Study sites and structure of the study team

13.1 Field centers

The field centers where the research will be conducted are the same as the parent ACHIEVE study. The field centers will be responsible for recruiting participants into the new study, administering the HHC intervention, and collecting follow-up outcome data.

- Washington County, Maryland (Johns Hopkins center located in Hagerstown, MD)
- Jackson, Mississippi (University of Mississippi Medical Center)
- Forsyth County, North Carolina (Wake Forest University Health Sciences)
- Minneapolis, Minnesota (University of Minnesota)

13.2 Coordinating Center (CC)

The CC is located at the University of North Carolina (UNC). UNC currently serves as the CC for the ACHIEVE trial and ACHIEVE-MRI study and has served as the CC for numerous other studies, including ARIC. The CC will be responsible for programming data entry screens into the data management system, providing reports on study progress and data quality, creating datasets for sharing with investigators, and participating on study committees. See section 12 Data management for details on the data management system and data monitoring. See section 10.2 Adverse events for details on reporting of adverse events and unanticipated problems.

In addition to data management, the CC manages a centralized study-specific website, where study staff can login with their assigned individual user ID and password to access the latest version of the protocol, manuals of procedures, paper case report forms, current and prior IRB approval letters for each participating site, memos, and other relevant study documents. The website also has a directory feature that maintains contact information for all investigators and study team members at each participating site. The CC is responsible for distributing memos to the site PIs and/or study coordinators when there are changes to the protocol or clarifications to study procedures.

13.3 Hearing intervention unit

The University of South Florida (USF) will be responsible for training and oversight of the fidelity of the hearing intervention. USF will participate on study committees and lead the hearing intervention subcommittee.

13.4 Analysis and study governance site

Johns Hopkins University (JHU) is the analysis and study governance site. JHU will be responsible for overall trial coordination, leading several of the committees (described in the next section). JHU will be responsible for preparing and maintaining the study protocol, consent, and other study documentation, and will work with the CC to have these study documents distributed and/or posted to the study website as needed. JHU will also be responsible for preparing NIH progress reports.

13.5 Single IRB

Johns Hopkins Medicine is serving as the single IRB for this study. It is the preference of Johns Hopkins Medicine IRB to use the SMART IRB reliance agreement as the basis of reliance. The

SMART IRB master reliance agreement was created in 2016 to harmonize and streamline the IRB review process for multisite studies. It enables reliance on a study-by-study basis, clearly defines roles and responsibilities of relying institutions and reviewing IRBs, and eliminates the need to sign reliance agreements for each study [e.g., a non-SMART IRB agreement]. 900+ institutions have already signed onto this agreement and are actively using it as the basis of reliance for multisite projects. Sites that will rely on JHM IRB are still responsible for conducting a local context review prior to the start of research at their site and for following any local and institutionally required policies as it applies to research at their site [e.g., reporting of unanticipated problems].

13.6 Study organization

Study organization will be based directly on the existing organizational framework used in the ongoing ACHIEVE trial consisting of an overarching Steering Committee that interfaces with the ARIC study, NIH, and DSMB (when applicable). Under the Steering Committee, several additional committees (Operations, Quality Control, Neurocognitive Adjudication, Intervention Fidelity and Quality, and Publications) oversee day-to-day execution of the study.

14 History of protocol amendments

Minor changes to page numbering and formatting and minor corrections and clarifications were made throughout the document. Substantive changes are highlighted in the below table.

Protocol version	**Affected section(s)**	**Brief description of change**	**Brief rationale for change**
v1.0 (29-Jun-2021)	Original version of the protocol approved by the sIRB.		
v1.1 (20-Sep-2021)	Version of the protocol approved at the time the first participant was randomized.		
	5.1 Eligibility	Vision impairment exclusion criteria changed from 20/40 to 20/63	This is a correction to match the criteria used in ACHIEVE
	7.1 Schedule of activities (Table 1); 9.2 Telehealth hearing health care; 9.3.1 Crossover to telehealth HHC delivery model	Telehealth Sessions renamed from Session 1, 2, 3 to Session A, B, C	Sessions named with letters, rather than numbers, is consistent with how intervention sessions have been named previously in ACHIEVE
	7.1 Schedule of activities (Table 1)	Visits renamed as follows: Yr 0.5→ 6-month Yr 1→ Year 1 Yr 1.5→ 18-month Yr 2 → Year 2	Consistency with visit names used in the database

Protocol version	Affected section(s)	Brief description of change	Brief rationale for change
	7.1 Schedule of activities (Table 1); 9.1 Interventions – all participants; 9.3 Conventional clinic-based hearing health care	HIFU Intervention check-up added to Randomization Visit and noted as only required at Session A if not the same day as the visit	HIFU Intervention check-up should be done on all participants at the start of HIFU; HIFU Intervention check-up should be repeated during Session A if Session A occurs on a separate day from Randomization/Year 1 Visit; otherwise, it should not be repeated
	7.1 Schedule of activities (Table 1); 7.5.5 COVID impact questionnaire	Added COVID impact questionnaire to semi-annual and annual visits	This questionnaire, which was added during the ACHIEVE parent trial, and which we had planned to continue administering it in ACHIEVE-HIFU, had been inadvertently omitted from the protocol
	7.1 Schedule of activities (Table 1); 7.5.6 Telehealth acceptance questionnaires	"Telehealth acceptability" changed to "Telehealth acceptance"	Correction
	7.1 Schedule of activities (Table 1); 9.1 Interventions – all participants; 9.2.1 Telehealth session A	Telehealth acceptance questionnaires moved out of Session A to the Randomization/Year 1 Visit	TAP should be collected on all participants at Randomization, and ideally, should be collected by a non-audiologist. At the Year 1 Visit, a non-audiologist should administer the TAP or TAF, depending on whether the participant has received the telehealth intervention yet.
	7.1 Schedule of activities (Table 1);	CDP, CDI, CDS, and NPI removed from semi-annual visits.	This is a correction for consistency with what is currently being done in ACHIEVE.
v1.2 (20-Jan-2022)	Cover page	Clinicaltrials.gov identifier added.	The Clinicaltrials.gov registration was completed prior to enrollment of participants, and the protocol is being updated to reflect the identifier.
	3 Study objectives and end points	Details on how outcomes are assessed and scored, and interpretation of scores have been added.	Descriptions of the outcomes were expanded to clarify the outcomes and make them consistent with the outcomes listed in the study's clinicaltrials.gov record.
	6.1 Informed consent	Added sub-section on re-obtaining consent in the event of consent changes.	The protocol did not previously address the process for re-consent due to consent changes. Because the study involves telehealth (remote) visits, and not all contacts occur in person, flexibility has been added to allow re-consent to be provided verbally or via mail.

Protocol version	Affected section(s)	Brief description of change	Brief rationale for change
	6.2 Participant confidentiality	Details on the results provided to participants and their private physicians were updated.	These changes reflect corrections to the planned sharing of results to correspond with sharing of results in the parent ACHIEVE trial.
	7 Study assessments and procedures	Removed the stipulation that the parent ACHIEVE trial Year 3 visit will serve as the baseline *if completed within the 6 months preceding randomization in ACHIEVE-HIFU*.	Decision by the ACHIEVE investigators to allow the Year 3 ACHIEVE visit to serve as the baseline for ACHIEVE-HIFU, even if more than 6 months have passed, and to not conduct a repeat baseline visit. This change allows additional scheduling flexibility and reduces potential participant burden.
	7.1 Schedule of activities (Table 1)	COSI goals achievement removed from the Initial Conventional Randomized HHC arm's Telehealth Session A.	This removal is a correction – goals achievement will be assessed at the Year 1 visit, which will often occur the same day or within the week prior to Session A for the group randomized to conventional HHC, so goals achievement will not be repeated at Session A.
	12 Data management	Removed text indicating that technicians will be blinded to randomization status.	The primary outcome for ACHIEVE-HIFU is objectively measured hours of hearing aid use, so technicians collecting other outcomes are not required to be blinded.
	14 History of protocol amendments	New section added.	The relevant summary of changes for the current protocol version will be outlined in the table at the beginning of the protocol, but the full history of protocol changes will be maintained within this newly added section in the protocol.

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