**R33 PHASE STUDY: PROTOCOL**

*Evaluating the clinical effectiveness of a community-based hearing aid fitting service delivery model facilitated by CHWs providing smartphone-based in-situ and pre-set hearing aid fittings in low- and middle-income communities*

**Document Approval**

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**Document Version History**

*This table should be updated with study-specific protocol revisions or amendments following feedback from any Ethics Committee.*

| **Version** | **Date** | **Description** | **Responsible Person** |
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| *1.0* | *2024-06-27* | *First draft development* | *Caitlin Frisby & Karina De Sousa* |
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| 10.0 | 2025-06-17 | Tenth draft development | Caitlin Frisby |

## Table of content

## 1. List of Tables



## 2. List of Figures



## 3. Acronyms and abbreviations

| | |
|---|---|
| ADE | Adverse Device Event |
| AE | Adverse Event |
| AI | Artificial-intelligence |
| ANOVA | Analysis of Variance |
| CAPA | Corrective and Preventive Action |
| CHWs | Community Healthcare Workers |
| CIOMS | Council for International Organizations of Medical Sciences |
| CIP | Clinical Investigation Protocol |
| dB HL | Decibel Hearing Level |
| dB SPL | Decibel Sound Pressure Level |
| DD | Device Deficiency |
| EC | Ethics Committee |
| GCP | Good Clinical Practice |
| HA | Hearing Aids |
| Hz | Hertz |
| IC | Informed Consent |
| IOI-HA | International Outcome Inventory for Hearing Aids |
| LMICs | Low- and middle-income countries |
| mHealth | Mobile Health |

| | |
|---|---|
| NAL-NL2 | National Acoustic Laboratories - Non Linear Version 2 |
| POPIA | Protection of Personal Information Act |
| RCT | Randomized Controlled Trial |
| SAE | Serious Adverse Event |
| SNI | Social Network Index |
| SOP | Standard Operating Procedure |
| TMF | Trial Master File |

## 4. Purpose

The purpose of this study is to advance hearing care in low- and middle-income countries (LMICs) through the rigorous evaluation and optimization of innovative interventions and technologies. This study encompasses the following key aim:

This study aims to establish the effectiveness of community-based hearing aid fittings facilitated by community healthcare workers (CHWs) using mobile health (mHealth) technologies in low- and middle-income communities (LMICs). The primary goal is to determine the efficacy of CHW-facilitated smartphone-based in-situ hearing aid (HA) fittings (a proprietary fitting based on the NAL-NL2 algorithm) and pre-set HAs fittings compared to minimal amplification through a single-blind randomized controlled trial (RCT). By comparing self-reported benefits between the experimental and control groups, this aim seeks to demonstrate the superiority of the CHW-facilitated smartphone-based and pre-set hearing aid fittings compared to minimal amplification.

## 5. Responsibilities

Table 1 describes the roles and responsibilities assigned to clinical research team members.

**Table 1.** Study personnel

| Role | Name | Responsibility |
|---|---|---|
| *Co-Principal Investigator* | De Wet Swanepoel | Study planning, oversight, data analyses, and reporting |
| *Co-Principal Investigator* | David R Moore | Study planning, oversight, data analyses, and reporting |
| *Co-Principal Investigator* | Lisa Hunter | Study planning, oversight, data analyses, and reporting |
| Co-investigator | Herman Myburgh | Study planning, technical oversight, data analyses, and reporting |
| Co-investigator & Statistician | Marien A Graham | Study planning, technical oversight, data analyses, and reporting |

| Role | Name | Responsibility |
|---|---|---|
| Site Coordinator | Tersia de Kock | Study planning, technical oversight, data collection, analysis, and reporting. Site coordinator for Khayelitsha and Drakenstein district |
| Research Coordinator | Karina De Sousa | Study planning, technical oversight, data collection, data analyses, and reporting |
| Research Coordinator & Site Coordinator | Caitlin Frisby | Study planning, technical oversight, data analyses, and reporting. Site coordination for Atteridgeville district |

## 6. Statement of compliance

The clinical investigation has obtained the required approval from the Ethics Committee (EC) of the Faculty of Humanities at the University of Pretoria. Participants will be informed that their participation in the investigation is voluntary. Prior to any data collection, participants will sign a statement of Informed Consent (IC) that meets the requirements of local regulations and the Protection of Personal Information Act (POPIA).

## 7. General

### 7.1. Introduction

Hearing loss is a significant global health issue, particularly in low- and middle-income countries (LMICs) (World Health Organization, 2021). In 2020, over half a billion people globally had a disabling hearing loss, with 1.5 billion experiencing mild-to-complete hearing loss in at least one ear (World Health Organization, 2021). The impact of hearing loss is especially severe in LMICs, where 90% of those with moderate to profound hearing loss reside, yet access to hearing health care is sparse to non-existent (Mulwafu et al., 2017; World Health Organization, 2021). In sub-Saharan Africa, hearing aid penetration is less than 3% among those who could benefit, starkly contrasting with the high prevalence and impact of hearing loss (Bisgaard et al., 2021). Globally, hearing loss ranks as the third leading cause of years lived with disability, underscoring the urgent need to address its impact on communication, cognition, education, employment, and social participation (World Health Organization, 2021).

The World Health Organization (WHO) has outlined several strategies to improve global hearing health, including the use of innovative digital technologies and task-shifting by training community health workers (CHWs) (World Health Organization, 2021). The use of over-the-counter hearing aids, such as pre-set device has also been recommended for LMICs (World Health Organization, 2021, 2024). Our study aligns with these strategies by focusing on scalable and sustainable methodologies in an LMIC context, specifically in South Africa. Our approach integrates CHW-facilitated testing, diagnosis, and intervention into a single holistic process, addressing common barriers such as loss to follow-up and ensuring the provision of

a paper-based hearing aid acclimatization and support programme to aid in hearing aid management and use.

**Study Aims**

This study aims to establish the effectiveness of community-based hearing aid fittings facilitated by community healthcare workers (CHWs) using mobile health (mHealth) technologies in low- and middle-income communities (LMICs). We hypothesize that amplification offered by smartphone-based in-situ hearing aid (HA) fittings and pre-set hearing aid fittings facilitated by CHWs have superior self-reported outcomes compared to minimal amplification.

To test this hypothesis, we will conduct a single-blind randomized controlled trial (RCT) where participants are assigned to either the experimental smartphone-based in-situ hearing aid fitting, pre-set hearing aid fitting, or minimal amplification fitting. A minimal amplification fitting provides only the most basic level of amplification without individualized adjustments. This level of amplification is primarily intended to prevent occlusion effects rather than to offer meaningful hearing benefits. In this study, a flat 10 dB gain will be provided across frequencies regardless of the degree of hearing loss. A placebo-controlled design is essential for assessing the true effectiveness of hearing aid interventions beyond non-specific effects such as participant expectations or the general experience of wearing a device. Comparing experimental conditions to minimal amplification ensures that any observed benefits are attributable to the intervention rather than psychological or external influences.

Outcomes will be measured by self-reported benefits, with control participants offered the smartphone-based in-situ fitting after six weeks. All participants will also receive a paper-based hearing aid acclimatization and support programme on the day of the hearing aid fitting to assist them in hearing aid use and maintenance. The participants will also be provided a contact number for the CHWs to contact if any assistance is needed.

**Rationale**

Given the limited access to hearing care in LMICs due to prohibitive costs and scarcity of trained professionals, this study leverages mHealth solutions and task-shifting to CHWs as a sustainable and scalable approach. Preliminary studies have shown promising results for the components of these interventions, justifying the need for clinical trials to evaluate their effectiveness. By focusing on end-to-end smartphone-based in-situ hearing aid fittings and acclimatization support, this study aims to create an innovative and accessible model of hearing care that could significantly reduce the global burden of hearing loss.

Additionally, understanding the difference in outcomes between meaningful amplification and minimal amplification is crucial for guiding hearing care strategies in LMICs. If substantial benefits are observed in the experimental groups relative to minimal amplification, it strengthens the case for scaling up CHW-facilitated hearing aid provision as a cost-effective solution. Conversely, if minimal amplification yields similar self-reported outcomes, it may suggest that additional interventions (e.g., counseling, expectations management) are necessary for maximizing hearing aid benefits in these settings.

### 7.2. Sponsor details and investigational site(s)

**Sponsor Name:** National Institute of Deafness and Communication Disorders of the National Institutes of Health (NIH)
**Address:** NIDCD Information Clearinghouse, 1 Communication Avenue
Bethesda, MD 20892-3456, United States of America
**Funding source:** Award Number R21DC019598 awarded to De Wet Swanepoel and David R. Moore; Research Funding

### 8.3 Investigational site(s)

The clinical study will take place at three sites across two Provinces in South Africa. Community centres or homes (if participants do not have access to the community centre) across:

1. Atteridgeville District, Gauteng, South Africa
2. Khayelitsha District, Western Cape, South Africa
3. Drakenstein District, Western Cape, South Africa

### 8.4 Description of the interventions used in experimental design

Two different experimental devices will be used in this study. Namely the Lexie Lumens and the Go Ultras. These two devices each represent a different type of OTC hearing aid, self-fitting in-situ and pre-set devices, respectively. These devices also have differences in terms of price, with the Go Ultras being the more low-cost option. Pre-set devices have also recently been recommended for use LMICs by the WHO (World Health Organization, 2021, 2024). This study will evaluate if one of the experimental devices has superior outcomes. Full details of the devices are reported below:

The Lexie Lumens (Lexie Hearing) are self-fitting wireless air conduction hearing aids consisting of 16 channels, wide-dynamic-range compression technology, feedback reduction, Bluetooth connectivity and programming, digital noise reduction, and a directional microphone array. These hearing aids will be sourced at a cost of $240 USD per pair as this study will be conducted in low-income settings. The hearing aids allow for Bluetooth in-situ hearing aid fitting using the Lexie proprietary fitting algorithm that is based on the NAL/NL2 algorithm from a smartphone application (Lexie Hearing) based on the four hearing thresholds tested.

These digital hearing aids were designed for use by adults over the age of 18 years with known or self-perceived mild-to-moderate hearing loss. The Lexie Lumens are behind-the-ear (BTE) hearing aids powered by replaceable batteries. Individuals can also conduct an in-situ hearing test via the hearing aids to allow for customized amplification. A research version of the application will be used to allow for either a customized in-situ fitting based on the NAL-NL2 algorithm or a minimal gain (10 dB flat across frequencies regardless of degree of HL) fitting facilitated by the CHWs following the in-situ hearing test, also facilitated by the CHWs. A simple push of a button on the smartphone following an in-situ test will program the hearing aids on either the personalized setting or the minimal gain setting. These devices also have 4 different listening environments, namely 1. Everyday use; 2. Noisy indoor; 3. Outdoor, and 4. Music.

Go Ultras (GoHearing) are rechargeable, BTE pre-set hearing aids with advanced audio features, digital sound processing and Bluetooth-streaming capabilities. Designed for adults with mild-to-moderate hearing loss, these hearing aids have four unique programs that the user can manually change to ensure optimal listening comfort. These devices have both program and volume memory functions, as well as noise and wind noise reduction. Go Ultras will be sourced at a cost of less than $130 USD per pair, as this study will be conducted in low-income settings.

### 8.5 Summary of the Clinical Investigation

**Title:** Evaluating the clinical effectiveness of a community-based hearing aid fitting service delivery model facilitated by CHWs providing smartphone-based in-situ and pre-set hearing aid fittings in low- and middle-income communities

**Purpose:** To determine whether a community-based hearing aid fitting service delivery model facilitated by CHWs using mHealth technology to provide smartphone-based in-situ and pre-set hearing aid fittings provide superior benefit for their users.

**Population:** 90 participants over the age of 18 years (No maximum age) with mild-to-severe (20 to < 80 dB PTA in both ears) hearing loss.

**Design:** Single-blind randomized controlled trial

**Initiation date:** March 2025

**Completion date:** October 2026

## 8. Clinical investigation objectives

The main aim of this project is to determine the effectiveness of a community-based hearing aid fitting service delivery model facilitated by CHWs, with the expectation that the interventions will prove superior to minimal gain. This study will investigate the effectiveness of a smartphone-based in-situ (proprietary algorithm based on the NAL-NL2 fitting) hearing aid fitting and pre-set hearing aid fitting in a three-arm, placebo-controlled single-blind randomized clinical trial.

**Primary endpoint hypothesis**

**Primary Endpoint**

The primary endpoint of this study is the self-reported outcome measured using the IOI-HA global score at 6 weeks post-fitting. Outcome measures will also be captured at 12, 26, and 52 weeks post-fitting. The endpoint assesses differences between study groups' overall hearing aid benefit and satisfaction.

**Superiority**

*Null Hypothesis ($H_0$):* There is no difference in the IOI-HA global score between the experimental and control groups (difference <3 points).

*Alternative Hypothesis ($H_1$):* The IOI-HA global score for one or both experimental groups is superior to the control group by a margin of ≥3 points.

**Non-inferiority (comparison of experimental groups)**
*Null Hypotheses ($H_0$):* Self-reported outcomes (IOI-HA) in the pre-set group are non-inferior to those in the smartphone-based in-situ fitting group, with the non-inferiority margin ($\delta_1$) defined as 3.0 for the IOI-HA total score.

*Alternative Hypothesis ($H_1$):* Self-reported outcomes (IOI-HA) in the pre-set group are inferior to those in the smartphone-based in-situ fitting group, exceeding the predefined non-inferiority margin for the IOI-HA total score ($\delta_1 = 3.0$).
**Clinical Relevance**
A difference of ≥3 points in the IOI-HA score is considered clinically significant based on prior research by Apple, representing a meaningful improvement in hearing aid benefit, satisfaction, and quality of life.

## 9. Clinical investigation design

A randomized, three-arm, single-blind placebo trial (full blinding details below) with 90 participants will be used. The estimated timeline for trial completion is approximately 52 weeks post-hearing aid fitting. The clinical trial will be conducted across three sites (Khayelitsha and Drakenstein Districts in the Western Cape Province of South Africa and Atteridgeville District in the Gauteng Province of South Africa). See Figure 1 below for a visual depiction of the trial design.

Randomization (full details provided below) will be conducted before participant enrollment, ensuring that each participant is assigned to one of the three study arms (In-situ fitting, Pre-set fitting, or Minimal Gain fitting) before enrolling in the study (full randomization details below).

After baseline assessments to determine candidacy (T0), participants will be randomly assigned and start with one of the three interventions (T1). There will be one placebo-control group with Lexie Lumen hearing aids fitted to minimal gain (i.e., 10 dB HL across the frequency range regardless of hearing loss levels) with two experimental groups: (i) In-situ hearing aid fitting using a proprietary algorithm on Lexie Lumen hearing aids that are based on the National Acoustics Laboratories Non-Linear Version 2 (NAL-NL2) algorithm (ii) Pre-set hearing aid fitting with Go Ultra hearing aids. Following fitting (T1), there will be a 6-week field trial, with follow-up visits scheduled at 6 weeks (T2). Following that, the minimal gain group (control) will be crossed over to in-situ fitting (CG-T2; Figure 1), and another 6-week field trial will be conducted (follow up at CG-T3; Figure 1). Follow-up visits for the In-situ and Pre-set groups will occur again at 12 weeks (T3), 26 weeks (T4), and 52 weeks (T5).

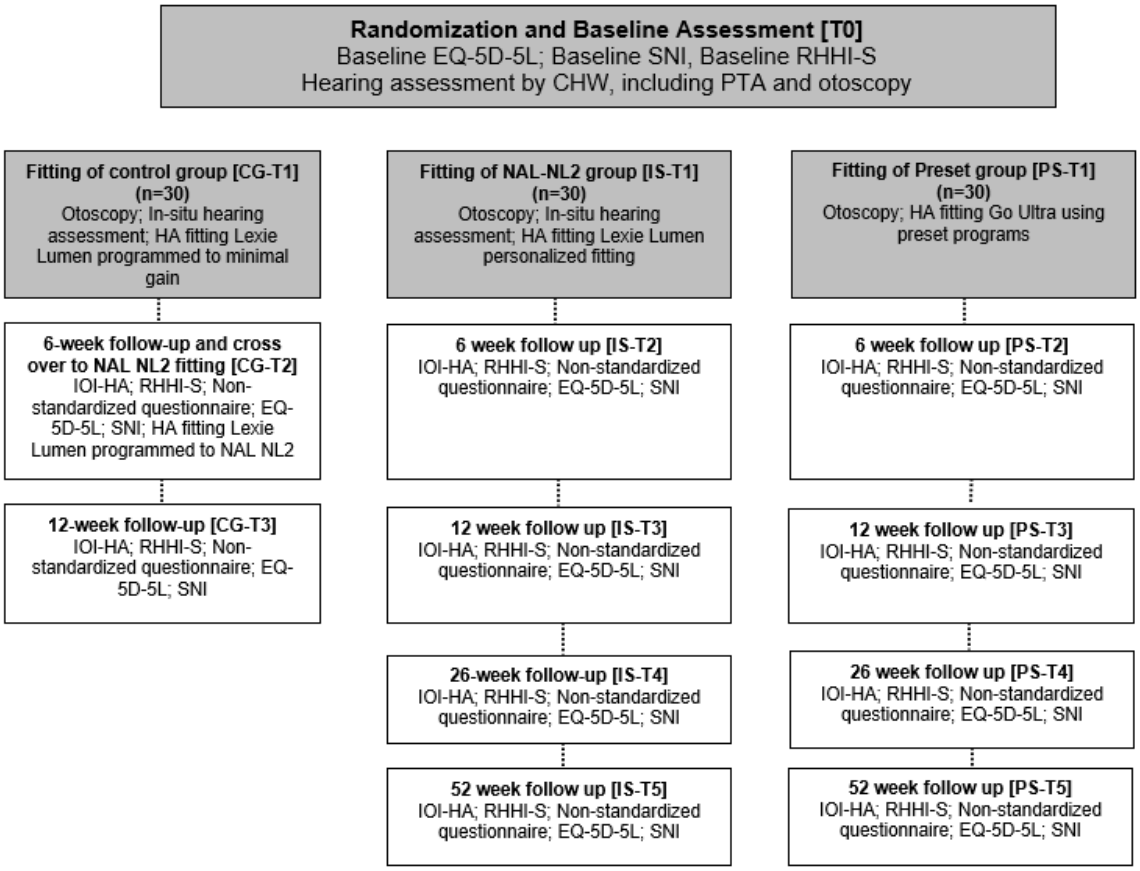


*Figure 1.* Proposed clinical trial design.

The primary endpoint will be at the six-week follow-up. The primary outcome measure will be the IOI-HA. A difference of ≥3 points in the IOI-HA score is considered clinically significant based on prior research by Apple, representing a meaningful improvement in hearing aid benefit, satisfaction, and quality of life.

The secondary measures will be the RHHI-S, EQ-5D-5L, and the Berkman-Syme Social Network Index (SNI). Baseline RHHI-S, EQ-5D-5L, and SNI scores will be compared with scores obtained at subsequent follow-up visits.

Additionally, a questionnaire with Likert scale questions targeting functional use and meaningful life changes will be completed at all follow-up visits.

## 10.1 Blinding

This trial incorporates a single-blind mechanism.

- **Experimental and Control Groups**

For the Experimental and Control groups, the Lexie Lumens hearing aids are programmed via an application after an in-situ hearing assessment. CHWs will use a custom-designed research version of the Lexie Hearing application to program the Lexie Lumens devices. Once the in-situ test has been completed, the app will present two fitting options: A or B. The app will prompt the CHWs to select either option A or B, corresponding to the in-situ fitting or the minimal gain setting (10 dB gain across frequencies). A third party (administrative assistant) observing the session will ask the CHW to select fitting A or B to achieve the respective intervention settings. Only the third party will know if the A or B indicates the in-situ fitting or minimal gain option. This setup ensures that the participants remain unaware of the allocation.

The app interface will not display or provide any information about these settings, ensuring that participants are blind to the intervention applied. The programming process will be identical in appearance and duration for both options, minimizing potential clues.

Participants will be fitted with hearing aids but not informed about the specific programming applied or told that other participants may have different program settings. No visible or functional differences will distinguish the two settings for the participant. Additionally, these hearing aids come with four listening environments, and CHWs will assist participants in selecting the environment they feel most comfortable with.

- **Pre-set Group**

In the Pre-set group, participants will receive Go Ultra hearing aids, which differ from the Lexie Lumens devices used in the other arms. These hearing aids come with four pre-set programs, and CHWs will assist participants in selecting the program they feel most comfortable with. This will be done by allowing the participants to experience listening on all four programs through a conversation with the CHW. The participant will also be taught how to change the program if they later feel another program would be more suitable. CHWs will record the program selected at all subsequent follow-up visits. Participants will remain blinded to the existence of other intervention groups and their respective programming methods.

CHWs will facilitate the selection of one of the four pre-set programs based on participant feedback about comfort and sound quality. Since CHWs directly engage in program selection, they will be aware that this group receives a different intervention than the Experimental and Control groups.

Participants will not know the specifics of the other groups or the nature of their own intervention beyond the hearing aid they receive. Efforts will be made to avoid any communication or behavior from CHWs that might suggest differences in treatment across groups.

A transparent yet neutral approach will be taken in communication with control group participants. They will be informed that the purpose of the study is to evaluate different hearing aid settings to determine which settings work best for them. Specific details about their initial device settings will not be disclosed, but the CHWs will explain that their settings will be changed in six weeks. The CHWs will state that we are not sure which settings will work best for them and emphasize the importance of their honest feedback. Participants will be encouraged to share their experiences openly, including what they liked or did not like about their settings. This approach ensures that they feel involved in the process while maintaining blinding integrity.
These two different experimental devices were selected as they represent two types of over-the-counter (OTC) hearing aids, self-fitting in-situ and pre-set devices, respectively. These devices also have differences in terms of price, with the Go Ultras being the more low-cost option. This study will evaluate if one of the experimental devices has superior outcomes.

**Maintaining Blinding Integrity**
CHWs will undergo thorough training to ensure they follow standardized procedures for programming and assisting participants and avoid making comments that might reveal allocation details to participants.

Participants will receive uniform instructions and explanations about the study to prevent them from realizing that there are different group allocations. They will be informed that all devices are designed to improve hearing, but will not be told about the differences in programming methods or devices.

To maintain blinding integrity, all hearing aid devices will be repackaged into identical, unbranded packaging before distribution to participants. This ensures that differences in original device packaging do not inadvertently reveal group allocation. By standardizing the appearance of all devices, we minimize the risk of participants perceiving any distinctions between intervention groups, thereby preserving the study's single-blind design.

**App Design for Lexie Lumens:**
The app will feature a streamlined interface without visual or contextual cues indicating the programmed settings. CHWs will be instructed to follow app prompts without questioning or deviating from the process.

**Standardization Across Groups:**
All participants will follow the same study schedule, including fitting sessions, follow-ups, and assessments. Any study materials provided to participants will be identical in format and content, irrespective of group allocation. CHWs will be provided with a checklist and script to ensure they do not inadvertently provide information to the participants that could reveal group allocation.

**Challenges and Mitigation Strategies**

**Cross-Group Communication:**

Participants may discuss their experiences with others, risking unintentional unblinding. To mitigate this, participants will be advised not to share details about their devices or experiences until the study concludes.

## 10.2 Randomization:

Randomization will be conducted before participant enrollment to minimize bias and maintain balance across the study arms. A total of 90 participants (30 per arm) will be recruited across three data collection sites. Randomization will be implemented using a pre-generated sequence and managed via a centralized Google Sheet system to streamline and secure the process.

Permuted block randomization with a block size of 3 will be used. This method ensures that each of the three study arms—"In-situ," "Control," and "Pre-set"—receives an equal number of participants throughout the enrollment process while preventing predictability in participant assignments. Within each block, participants will be randomly allocated to one of the three arms, maintaining allocation concealment.

For example, in a block of 3 participants, one will be assigned to each arm. The order of assignments within each block will be randomized, ensuring no predictable patterns. The randomization will be carried out using a secure software tool or random number generation process such as the online tool Sealed Envelope (https://www.sealedenvelope.com/simple-randomiser/v1/lists), with the final sequence stored securely.

The final allocation sequence will be determined before the study commences to ensure blinding, preserving the integrity of the trial. Once a participant is deemed eligible by the community healthcare worker (CHW), the site administrator will enter their details into the predetermined Google Sheet to assign them to their allocated arm.

## 11. Ethical considerations

The proposed clinical trial has obtained ethical approval from the University of Pretoria Humanities Research Ethics Committee. The protocol will also be registered on Clinicaltrials.gov.

### 11.1 Informed consent

Informed consent ensures adherence to the ethical principle of autonomy, ensuring that the individual makes their decisions freely and independently to partake in the study (DoH, 2020). Study personnel will receive training on the Informed Consent Form (ICF) (Appendix X) and the ICF Standard Operating Procedure (ICF-SOP) prior to study initiation. All training will be logged and recorded within the Site Master File (SMF), and if there are any changes to the ICF process, all study personnel will be retrained.

A CHW will discuss and inform the individual about the study to determine their willingness to participate and obtain written informed consent from the participant. The ICF and consent process will be offered to the individuals in English, isiXhosa, or Sepedi. All individuals willing to participate in the clinical study will be informed to the fullest extent possible about the study in terms that they are able to understand. All individuals willing to participate in the clinical

investigation will have an opportunity to ask questions about the study to ensure that they have a complete understanding of what their participation would entail.

All individuals will be informed that their participation is voluntary and they can withdraw from the study at any time without penalty. They will be required to personally sign the ICF, which will include a statement that meets the requirements of local regulations and the Protection of Personal Information Act (POPIA). The ICF will also be signed and dated by the person responsible for obtaining informed consent from the individual. A copy of the ICFs will be provided to the participant, and a signed copy will also be filed with the participant's source documentation. Should the individual be illiterate, an impartial witness will be asked to sign and date the ICF on behalf of the individual after verbal consent has been obtained.
The Ethics Committee of the Faculty of Humanities at the University of Pretoria has reviewed and granted approval. (Appendix X).

Topics covered in the ICF include:

- A description of the clinical investigation
- Information regarding their voluntary participation
- Potential risks and discomforts
- Benefits to participation
- Alternative procedures or treatments
- Confidentiality
- Data collection and sharing of results
- Conditions of termination of participation
- Reimbursement
- Compensation in the event of a trial-related injury
- Contact details

If any updates or revisions are made to the currently approved version of the ICF, the revised version will be re-approved by the EC, and re-consent will take place to ensure the participant is aware of the changes made and agrees to continue to participate in the study. The ICF-SOP (doc number xxx) provides an in-depth overview of the procedure discussed above.

### 11.2 Reimbursement

Study participants will not be reimbursed for participation in the study. All participants will have their hearing assessed free of charge by trained CHWs. All participants who are eligible to receive hearing aids will be able to keep their hearing aids free of charge upon completion of the study. All participants using the Lexie Lumen devices will be provided with batteries for the duration of the study (batteries to be provided until the 52 week follow-up post fitting).

### 11.3 Confidentiality

All participant records and results will be coded alpha-numerically to ensure adherence to the ethical principle of confidentiality. No identifying information or results will be made known in the data analysis or reporting process to allow others to become aware of a specific participant's identity. Information regarding confidentiality will also be contained in the ICF (Appendix XXX). The research team members and CHWs will know the identity of the

participants. However, a participant code will be assigned to each participant so that the data captured, recorded, stored, and reported remains anonymous.

The data will be kept in hard copy in the Trial Master File (TMF) for a period of 10 years and will also be stored electronically in a password-protected Excel spreadsheet that only the research team will have access to. This electronic version will also be stored for a period of 10 years as per the University of Pretoria's data management policy. The results obtained from the research study will be recorded anonymously and reported honestly and as accurately as possible.

### 11.4 Validity and reliability

Validity determines if the measurements are accurate and whether they are measuring what they intend to measure (Portney, 2020). To ensure validity, all baseline measurements will be conducted in the same manner by trained CHWs. The CHWs all have the same training on the equipment. A refresher training session that covers equipment use and study procedures will be done prior to data collection commencement. Training for all participating CHWs will be recorded on the trial training log (Appendix X). Testing will be done using the same standard of equipment at each site, which will be calibrated according to the necessary regulations before any testing is conducted. To enhance validity, each participant will have multiple follow-up visits at set intervals (Figure 1 above) to provide accurate feedback about their experience with each of the devices.

Reliability describes the consistency of measurement or correlation between repeated observations or measurements (Irwin et al., 2018). To ensure reliability, the study protocol will remain the same for each participant where possible. During the baseline and follow-up visits, standardized questionnaires will be used to assess participants' subjective experiences with the hearing aids. Using standardized, validated questionnaires ensures consistency in the measurement of subjective experiences across all participants and visits. Consistency in the questions and response options helps in obtaining reliable and consistent data over time, improving the reliability of the study.

### 11.5 Follow-up

The following follow-ups will be needed where participants will complete self-reported outcome measures:

- 6 weeks (cross-over for Control Group)
- 12 week
- 26 weeks (both Experimental groups; not specifically part of the RCT, but we plan to continue follow-ups for longitudinal data)
- 52 weeks (both experimental groups; not specifically part of the RCT, but we plan to continue follow-ups for longitudinal data)

# 12. Participant population

## 12.1 Recruitment

Participants will be recruited using a self-report or community referral mode of hearing loss detection and snowball sampling within communities (Leedy & Omrod, 2015). Community healthcare workers from the hearX Foundation (also residing in the communities) will contact leaders of various community networks such as community NGOs, elderly groups, and religious groups to explain and create awareness of the study. Interested individuals will be provided with the CHW's contact details, and they will then have the opportunity to contact the CHWs for more information. CHWs will also conduct awareness talks at various community networks such as community NGOs, elderly groups, and religious groups to inform community members of the study. Participants will be selected from such individuals who indicate their availability to be part of this study and grant permission to be included as participants. The participants' contact details will be kept strictly confidential, and only the CHWs will have access to these details.

**Power:** Sample size calculations for this three-arm experimental study, involving four repeated measures (baseline and follow-up assessments at 6, 12, 26, and 52 weeks), were performed using the GLIMMPSE software (GNU General Public License, version 2). GLIMMPSE is specifically designed to compute sample size and statistical power for Generalized Estimating Equations (GEE), which are particularly suited for longitudinal and repeated measures data where observations within participants are correlated. In this study, GEE was deemed appropriate because it accounts for the within-subject correlations across multiple time points, ensuring more accurate and robust estimates for group effects. The calculations focused on the primary outcome, IOI-HA, and were designed to detect a medium effect size ($d = 0.5$; Cohen, 1969) with at least 80% statistical power. It is widely acknowledged that determining sample sizes to detect small effect sizes is often unnecessary, as such effects, while potentially statistically significant ($p \leq 0.05$), may lack practical or real-world relevance (Baicus & Caraiola, 2009; Peeters, 2016). Consequently, this study prioritized the detection of at least a medium effect size. The analysis indicated that a total of 69 participants (23 per arm) would be sufficient to achieve a statistical power of 0.811, assuming a Type I error rate of 0.05. The sample size calculation employed the Hotelling-Lawley Trace test and incorporated a correlation matrix with decreasing correlations over longer time intervals between measurements.

## 12.2 Inclusion criteria

Consenting adults fulfilling the following criteria will be recruited for the clinical trial:

- 18 years and older
- Confirmed mild to severe (20 to < 80 dB PTA in both ears; (World Health Organization, 2021)) hearing loss (determined during baseline assessments)
- Willing/available to commit to at least 6- and 12-week follow-ups

The inclusion and exclusion criteria form will be completed to keep a record of all the individuals who have met the criteria and are included in the clinical investigation. Records will also be kept in the TMF.

### 12.3 Exclusion criteria

- Younger than 18 years
- Hearing loss too severe (≥80 dB HL PTA)
- Normal hearing (<20 dB HL PTA)
- Middle ear pathology such as otitis media; active drainage from the ears.
- Unwilling/unavailable to commit to at least 6- and 12-week follow-ups.
- Unilateral hearing loss

The inclusion and exclusion criteria form will be completed to keep a record of all individuals who meet the criteria and those who were excluded from the study. The investigational devices are designed for a set criteria of individuals, hence the specific exclusion criteria that have been set out to ensure that the results/ feedback from the clinical investigation are able to be generalized to the appropriate population and relevant claims made to be appropriate.

### 12.4 Procedure for withdrawal

Individuals have the right to withdraw from the study at any point in time without any negative or adverse consequences. All participants who are enrolled in the clinical trial will be recorded on the screening and enrollment log form after ensuring that they meet all the inclusion criteria. Participants will be withdrawn from the study when/if it is deemed that there are any risks associated with the use of the devices. These events/risks will be documented on the Adverse Events (AE) or Serious Adverse Events (SAE) form, and actions taken will be logged so that there is a record of the duration of participation in the clinical trial.

All individuals enrolled in the clinical trial will be recorded in the enrollment log. Should there be participants who are lost to follow-up, the researchers will try to contact them. Should they be unreachable, the details will be documented with their case report forms, including the duration of their participation in the study, the reason for exclusion/lost-to-follow-up, and methods used by the researchers to follow up with them.

The clinical study aims to enroll 90 participants. If a large number of participants withdraw from the study, resulting in minimal information being collected to substantiate the clinical results, then recruitment and enrollment of new individuals need to be considered.

### 12.5 Relationship between investigation population and target population

The population that most often requires access to community-based hearing aid fitting services are individuals 18 years of age or older with self-perceived or confirmed mild to moderate hearing loss. Therefore, as mentioned above, the selected adults who meet the outlined inclusion and exclusion criteria are representative.

### 12.6 Expected number of participants

This study will aim to enroll 90 participants (30 in each arm) using a single-blind, randomized controlled study design. The participants will be divided into three groups and randomized into either the In-situ (smartphone-based proprietary fitting based on NAL-NL2), Control (minimal gain amplification), or Pre-set group. The control group will make use of their treatment option for a period of six weeks. Thereafter, they will cross over and receive the In-situ treatment

option for a period of six weeks. The In-situ and Pre-set groups will make use of their designated treatment option for the entire duration of the study.

## 13. Testing schedule and equipment

Table 2 below details the equipment that will be used during the clinical trial.

**Table 2.** Clinical trial equipment

| Equipment | Description |
|---|---|
| hearScope™ (HearX Group, Pretoria, South Africa) | The trained CHWs will perform otoscopy to inspect the outer ear to identify any possible ear disease (e.g., wax impaction, perforation, or ear infection) and to evaluate the patency of the ear canal to accommodate a hearing aid. These images can be reviewed by an AI imaging classification on the video-otoscopy application. These images are also uploaded onto a secure mHealth cloud-based data management platform where a professional team (audiologists and ENT) can remotely review the images and assist the CHWs in determining participant eligibility. |
| hearTest™ (HearX Group, Pretoria, South Africa) | CHWs will facilitate hearing assessments using the hearTest. Pure tone air conduction thresholds at 500, 1000, 2000 and 4000 Hz will be determined. Participants will be asked to respond (i.e., raising their hand) every time they hear a tone, even when the tones become softer. (Sennheiser HD280 Pro headphones calibrated according to International Organization for Standardization 389-1 [ISO] 2013 and International Organization for Standardization 389-9 [ISO] 2014 standards). These results are also uploaded onto a secure mHealth cloud-based data management platform where a professional team (audiologists and ENT) can remotely review and assist the CHWs in determining participant eligibility. |
| Lexie Lumen Hearing aids (Lexie Hearing) | Lexie Lumen hearing aids (left and right pair) in non-identifying packaging, including the user manual, domes (tulip, open and double of different sizes), cleaning kit and measuring tool. |
| Go Ultra Hearing aids (Go Hearing) | Go Ultra hearing aids (Left and right pair) in non-identifying packaging, including user manual, domes (small, medium, large - open and closed), slim tubes (various sizes), slim tube measuring tool, cleaning kit, and charger. |
| International Inventory for Hearing Aids (IOI-HA) | The IOI-HA is a validated seven-item questionnaire to measure the effectiveness of the hearing aid intervention (Cox and Alexander, 2002). It targets seven domains including, (i) daily use, (ii) benefit, (iii) residual activity limitations, (iii) satisfaction, (iv) residual participation restrictions, (v) impact on others, and (vi) quality of life. Each item has five response choices, from worst to best outcome (Appendix XXX). The IOI-HA has been translated to the languages most commonly used in these communities namley |

| | |
|---|---|
| | isiXhosa and Sepedi. The participants will have the option to complete the IOI-HA in either of these languages or in English. |
| Revised Hearing Handicap Inventory and Screening Tool (RHHI-S) | The RHHI-S is a validated 10-item questionnaire that is a strong unidimensional, clinically informative measure of self-perceived hearing handicap that can be used by adults of all ages (Cassarly, Matthews, Simpson, & Dubno, 2020). Each question has three possible responses, including yes, sometimes, or no. The RHHI-S has been translated into the languages most commonly used in these communities, namely isiXhosa and Sepedi. The participants will have the option to complete the RHHI-S in either of these languages or in English. (Appendix XX) |
| EQ-5D-5L | The EQ-5D-5L is a standardized instrument developed by the EuroQol Group to assess health-related quality of life. It consists of a Descriptive System. This covers five dimensions—mobility, self-care, usual activities, pain/discomfort, and anxiety/depression—each with five levels of severity (from "no problems" to "extreme problems"). The respondent selects one level in each dimension, resulting in a 5-digit health state profile (e.g., 1-2-3-1-1) (Herdman et al., 2011). Each 5-digit health state profile is converted into a single index value (utility score) using a country-specific value set. The utility score reflects the individual's overall health status, where 1 = full health, 0 = dead, <0 = states worse than death. The EQ-5D-5L has been translated into the languages most commonly used in these communities, namely isiXhosa and Northern Sotho (Sepedi). The participants will have the option to complete the EQ-5D-5L in either of these languages or in English. (Appendix XX) |
| Berkman-Syme Social Network Index (SNI) | The Berkman-Syme Social Network Index (SNI) is a well-established tool used to assess the extent of an individual's social connections. The SNI examines the relationship between social networks and health outcomes. The SNI evaluates social integration by assessing four key domains: Marital status – Whether the individual is married or in a committed partnership. Contacts with close friends and relatives – Frequency of social interactions with family and friends. Religious group membership – Whether the individual is part of a church or religious group and attends regularly. Participation in voluntary or community organizations – Involvement in social or civic groups outside of family and work.<br><br>The SNI assigns points based on the individual's responses to the above components. Scores range from 0 to 4, with higher scores indicating greater social integration. |
| Non-standardised Questionnaire | A non-standardized questionnaire will be included to obtain information from the participants on their perceptions of the |

| | |
|---|---|
| | hearing aids. This includes Likert scale and open-ended questions. (Appendix XX) |

**Procedure – All assessment and fitting procedures will be facilitated by the CHWs**

**T0: Baseline assessment**

- Assess participants for candidacy
- Obtain Informed Consent from the participants
- Record demographic information
- Complete the baseline EQ-5D-5L, SNI, and RHHI-S
- Conduct otoscopy
- Conduct audiometric evaluation to ensure that participants meet the pure tone air-conduction thresholds to be included.
- The clinical research audiologists will then establish candidacy by reviewing the otoscopy and PTA results. The eligible participants will be randomly allocated to either the In-situ, Control, or Pre-set group. Randomization will be conducted before participant enrollment, ensuring that each participant is assigned to one of the three study arms (Lexie Lumen with in-situ fitting, Go Ultra with Pre-set fitting, or Minimal Gain) before enrolling in the study. A random number generator will allocate participant numbers to the respective arms. As soon as a participant is enrolled, they will automatically be assigned to one of the three arms based on the predefined randomization process. This approach ensures unbiased group allocation from the outset of the study. This randomization will be done by an additional independent party.

**T1: Hearing-aid fitting**

Once randomized into one of the three groups, participants will be booked for Visit 2 for hearing aid fitting. All participants will undergo otoscopy, and the participants (not the pre-set group) will undergo an in-situ hearing test via the Lumen hearing aids before the hearing aid fitting.

In-situ Group

- The CHW will fit each participant in the in-situ group with the Lumens programmed using the smartphone-based in-situ (proprietary algorithm based on the NAL-NL2) fitting.
- Participants will select the listening environment they feel most comfortable with.

Control Group

- Participants in the control group will be fitted with Lumens programmed using minimal gain (10 dB gain across frequencies regardless of degree of HL). This will be conducted by the CHW.
- Participants will select the listening environment they feel most comfortable with.

Pre-set Group

- The CHW will fit each participant in the pre-set group with Go Ultra hearing aids on one of the four pre-set programs. Participants will select the program they feel most comfortable with.

**T2: Follow-up #1 and cross-over for Control Group**

- After 6 weeks of hearing aid use, participants from all groups will return for a follow-up assessment.
- The International Outcome Inventory for Hearing Aids (IOI-HA), the Revised Hearing Handicap Inventory – Screening (RHHI-S), EQ-5D-5L, SNI, and a non-standardized questionnaire will be completed by the participants.
- The control group will then be offered the in-situ intervention (proprietary in-situ fitting based on NAL-NL2).
- An administrative assistant will collect outcome measures to avoid CHW bias.

**T3: Follow-up #2 (Final follow-up for Control Group)**

- After 12 weeks of hearing aid use, all participants will return for a follow-up assessment.
- The International Outcome Inventory for Hearing Aids (IOI-HA), the Revised Hearing Handicap Inventory – Screening (RHHI-S), EQ-5D-5L, SNI, and a non-standardized questionnaire will be completed by the participants.
- An administrative assistant will collect outcome measures to avoid CHW bias.

**T4: Follow-up #3**

- After 26 weeks of hearing aid use, only participants from the Experimental groups will return for a follow-up assessment.
- The International Outcome Inventory for Hearing Aids (IOI-HA), the Revised Hearing Handicap Inventory – Screening (RHHI-S), EQ-5D-5L, SNI, and a non-standardized questionnaire will be completed by the participants.
- An administrative assistant will collect outcome measures to avoid CHW bias.

**T5: Final Review**

- After 52 weeks of hearing aid use, only participants from the Experimental groups will return for a follow-up assessment.
- The International Outcome Inventory for Hearing Aids (IOI-HA), the Revised Hearing Handicap Inventory – Screening (RHHI-S), EQ-5D-5L, SNI, and a non-standardized questionnaire will be completed by the participants.
- An administrative assistant will collect outcome measures to avoid CHW bias.

## 14. Statistical design and analysis

Data analysis will be conducted using IBM Statistical Packages of the Social Sciences (SPSS v30.0, Chicago, Illinois). Figures will be completed in R (v 4.3.2; *R* Core Team, 2023).

**Design**: This is a single-blind randomized control trial. This trial will have a control group. Two of the three groups receive the experimental hearing aid algorithm during the trial. The control group receives the in-situ hearing aid fitting immediately after the trial if, as hypothesized, it is effective. The challenges are limitations in the sensitivity of the outcome measures, inability fully to blind the pre-set group.

**Statistical tests**:

Firstly, data cleaning will be done. This process involves fixing or removing incorrect data (which could be due to data capturing errors) and fixing incorrectly formatted data. Following data cleaning, a missing value analysis will be conducted. There are four different types of missing data that are generally categorised, namely, missing completely at random (MCAR), missing at random (MAR), missing not at random (MNAR), and structurally missing data. The type of missing data dictates how it should be handled. Following the missing values analysis, descriptive statistics such as measures of location (mean, median) and measures of spread (standard deviation, interquartile range) and counts (frequencies, percentages) will be extracted. For continuous variables, normality will be tested for using the Shapiro-Wilk test. The Shapiro-Wilk test will be used for this purpose as opposed to the more well-known Kolmogorov-Smirnov test, as the Shapiro-Wilk test is known to have more power in detecting differences from normality (Field, 2024). For correlational analysis, the parametric Pearson correlation (if normal) or the nonparametric Spearman (if non-normal) will be used. To test for differences in biographical data, for differences between two independent groups, say, between male and female, the parametric independent samples t-test (if normal) or the nonparametric Mann-Whitney test (if non-normal) will be used. In the case where there are three or more independent groups, the parametric ANOVA test (if normal) or the nonparametric Kruskal-Wallis (if non-normal) will be used. For all statistical tests, a 5% level of significance will be used.

The IOI-HA, RHHI-S, SNI, and EQ-5D-5L will be outcome measures in these trials. For all these instruments, the respondents will be asked to respond by marking the response which most accurately represents their situation as they perceive it. Descriptive statistics will be computed, and measures of location (mean if normal, median if non-normal) and measures of variability (standard deviation if normal, interquartile range if non-normal) will be reported. Pearson correlations (if normal) or Spearman correlation (if non-normal) will be used to calculate correlations. For example, the number of problems respondents experience with their hearing aids will be correlated with satisfaction and benefit. Comparisons between groups will be made, for example, for differences in satisfaction and benefit between males and females, the independent samples t-test (if normal) or the Mann-Whitney test (if non-normal) will be used. The independent samples t-test and Mann-Whitney tests are used to test for differences between two unrelated/independent groups. For three or more groups, the one-way ANOVA test (if parametric) and the Kruskal-Wallis test (if non-normal) will be used.

The IOI-HA has seven items concerned with the use of hearing aids, covering the benefits perceived, remaining activity limitation, satisfaction, residual participation restriction, effect on significant others, and change in quality of life. The response data will be checked for normality using the Shapiro-Wilk test. If the response data is normally distributed, then parametric tests will be used, and, on the other hand, if the response data differs significantly from normality, nonparametric tests will be used. Descriptive statistics will be computed, and measures of location (mean if normal, median if non-normal) and measures of variability (standard deviation if normal, interquartile range if non-normal) will be reported. Kendall's tau, which is a nonparametric measure of relationships between ranked data, will be used to compute the intercorrelation of the seven questions (Stephens, 2002). The results from the intercorrelations will be supported by a principal component analysis which will be used to identify factors. This is in line with several studies that have applied factor analysis on the IOI-HA, showing that the responses can be described by two main factors (Arlinger et al., 2017). Factor 1 represents use, benefit, satisfaction, and quality of life (i.e., Items 1, 2, 4, and 7), whereas Factor 2 represents residual activity limitations, residual participation restrictions, and impact on others (i.e., Items 3, 5, and 6) (Arlinger et al., 2017). Factor 1 (typically referred to as "me and my hearing aids"), Factor 2 (typically referred to as "me and the rest of the world") and the mean IOI-HA total scores will be related to the demographic questions (age, gender, degree of hearing loss) using correlations and tests for differences. For the latter, these comparisons

between, say, males and females, will be done using the independent samples t-test (if normal) or the Mann-Whitney test (if non-normal). The independent samples t-test and Mann-Whitney tests are used to test for differences between two unrelated/independent groups. For three or more groups, the one-way ANOVA test (if parametric) or the Kruskal-Wallis test (if non-normal) will be used. The mean IOI-HA total score, the mean IOI-HA total score for Factor 1 and the mean IOI-HA total score for Factor 2 will be represented as a function of average hearing thresholds (PTA; 0.5, 1, 2, and 4 kHZ), respectively (Arlinger et al., 2017). Scatterplots with mean IOI-HA total scores (vertical axis) as a function of PTA (horizontal axis) will be created, and second-order polynomial regression lines will be fit to these figures, which will assist with interpreting relationships. Say, for example, the curve has a slightly concave downward shape, then clients with very mild hearing loss reported very high mean scores. Logistic regression models will also be built. For example, the first question of the IOI-HA instrument asks about, on an average day, how many hours a respondent used their hearing aid(s). The options are 'none', 'less than 1 hour a day', '1 to 4 hours a day', '4 to 8 hours a day', 'more than 8 hours a day'. Logistic regression can be utilised to assess predictors (age, gender, degree of hearing loss) associated with the non-regular use of hearing aids (Aazh et al., 2015).

For the RHHI-S, there are ten questions that are scored 0 = “No”, 2 = “Sometimes”, 4 = “Yes”, that assess how an individual perceives the social and emotional effects of hearing loss with questions such as “Does a hearing problem cause you to feel embarrassed when meeting new people?”, and “Do you have difficulty hearing when someone speaks in a whisper?”. The score can range from a minimum of 0 (if a respondent answers “no” to all ten questions) and a maximum of 40 (if a respondent answers “yes” to all ten questions). The values are interpreted as follows: 0-8 (suggest no hearing handicap), 10-24 (suggest mild-moderate hearing handicap), 26-40 (suggest significant hearing handicap) (Mccabe, 2019). The scores will be related to the demographic questions (age, gender, degree of hearing loss) using correlations and tests for differences. As explained above, the tests for differences between two unrelated/independent groups will be conducted using the independent samples t-test (if normal) or the Mann-Whitney test (if non-normal). For three or more groups, the one-way ANOVA test (if parametric) or the Kruskal-Wallis test (if non-normal) will be used. Scatterplots with RHHI-S scores (vertical axis) as a function of PTA (horizontal axis) will be created, and second-order polynomial regression lines will be fit to these figures, which will assist with interpreting relationships. Say, for example, the curve has a slightly concave downward shape, then clients with very mild hearing loss reported very high mean scores. Logistic regression models will also be built. For example, the first question of the RHHI-S instrument asks “Does a hearing problem cause you to feel embarrassed when meeting new people?”. Take the first question of the RHHI-S, for example. Logistic regression can be utilised to assess predictors (age, gender, degree of hearing loss) associated with feeling embarrassed about one’s hearing aid when meeting new people.

The Berman-Syme Social Network Index (SNI) evaluates participants' social connectedness based on four domains: (1) marital status, (2) frequency and quantity of contact with friends and relatives, (3) participation in religious meetings, and (4) involvement in community or organizational groups. Following the approach outlined by Loucks et al. (2006), responses on the Berkman-Syme SNI are converted into binary scores and then summed to create a composite index ranging from 0 to 4. Participants receive a score of 1 if they are married and 0 if they are not. For close social contacts, a score of 0 is assigned if an individual reports having 0–2 close friends and 0–2 close relatives; otherwise, a score of 1 is given. Regarding participation in community organizations, individuals who do not participate receive a score of 0, while those who do are assigned a score of 1. For religious attendance, a score of 0 is given to those attending services less than or equal to every few months, and a score of 1 is assigned to those attending once or twice a month or more frequently. The total score reflects

the degree of social integration, with higher scores indicating greater social connectedness. The scores will be related to the demographic questions (age, gender, degree of hearing loss) using correlations and tests for differences. As explained above, the tests for differences between two unrelated/independent groups will be conducted using the independent samples t-test (if normal) or the Mann-Whitney test (if non-normal). For three or more groups, the one-way ANOVA test (if parametric) or the Kruskal-Wallis test (if non-normal) will be used. Predictors of higher or lower social connectedness scores will be explored using generalized linear models, with age, gender and degree of hearing loss included as covariates.

The EQ-5D-5L is a standardized instrument developed by the EuroQol Group to assess health-related quality of life and will serve as one of the secondary outcome measures in this trial. It consists of two components: the Descriptive System and the Visual Analogue Scale (VAS). The Descriptive System captures participant self-assessment across five domains — mobility, self-care, usual activities, pain/discomfort, and anxiety/depression — each rated on a five-level scale from "no problems" to "extreme problems." The VAS records the participant's overall health on the day of assessment on a scale from 0 (worst imaginable health) to 100 (best imaginable health). A utility score will be derived from the five-digit health profile generated from the Descriptive System using the most applicable value set. Since no South African value set currently exists, this study will use the validated Ugandan value set, which has been applied successfully in South African research, including a recent study assessing Health-Related Quality of Life among people living with HIV in KwaZulu-Natal (Moyo et al., 2023). The EQ-5D-5L utility index and VAS scores will be analyzed using both descriptive and inferential statistics. Differences between baseline and follow-up scores (at 6, 12, 26, and 52 weeks) will be assessed using appropriate statistical tests based on data distribution (e.g., paired t-tests or Wilcoxon signed-rank tests). Between-group comparisons (in-situ, pre-set, and control) will be analyzed using one-way ANOVA (if parametric) or Kruskal-Wallis (if nonparametric) tests. Predictors of higher or lower health-related quality of life scores will be explored using generalized linear models, with age, gender and degree of hearing loss included as covariates. A VAS cut-off score of ≥73 will be used to categorize participants as having a good perceived health state, following the threshold used by Moyo et al. (2023). Logistic regression models will also be employed to identify factors associated with achieving a good health state. These analyses will allow us to assess whether the hearing aid interventions lead not only to hearing-specific benefits but also to broader improvements in participants' overall health-related quality of life.

## 15.1 Data management

### 15.1.1 Data entry and collection

Data collection will primarily take place in a paper format, which includes the ICF, patient file data, as well as the Case Report Form (CRF). Data from the CRF will be electronically transcribed for further data analysis.

After obtaining necessary study approvals, the study will employ a comprehensive Subject Eligibility Checklist (Appendix XXX) encompassing all inclusion and exclusion criteria. This checklist will ascertain an individual's eligibility for study enrollment. Each interested individual will undergo this assessment, and the completed form will be securely filed within their respective study file.

Each individual who undergoes the screening evaluation, whether eventually enrolled or not, will be meticulously documented on the Subject Eligibility Checklist (Appendix XXX) specific to

the site. These records will be maintained within the Site Master File (SMF). It is essential to emphasize that no procedures to evaluate eligibility will commence without obtaining informed consent. Likewise, these records will be securely stored within each individual's study file.

Personal and demographic data collected for the study will be meticulously recorded on the Baseline Data Collection form (Appendix XXX) and kept within the respective participant study file. Data from study activities will be accurately documented on the results form (Appendix XXX). All study forms will be securely stored in the participant study files.

Each participant will have a dedicated CRF that comprehensively captures and reflects all their data. This information will subsequently be transferred to an electronic data system for further analysis and management.

### 15.1.2 Data quality control and validation

The PI or responsible research team member will maintain all study documents and source documentation in their original format in compliance with South African Good Clinical Practice (GCP) guidelines.
To ensure data quality all clinical research audiologists will be trained on the study procedure and measures for data collection, prior to participants being assessed. A training log will be kept as proof of training and retraining activities. There will be clear data normalization protocols, i.e., methods of recording data will be consistently captured on the set data collection sheets, and there will be clearly defined protocols for each clinical measure conducted throughout the clinical trial. Clinical evaluations will conform to consistent formats to ensure consistency in the data. Source data will be captured on fillable forms, and captured electronically afterward for statistical analysis.

Internal monitoring activities will take place to ensure data integrity and completeness. A weekly scheduled data validation check will be conducted by the research personnel, where data will be reviewed for completeness and accuracy prior to eCRF capturing. Electronically transcribed data will also be reviewed for completeness and correctness in relation to the source documentation. In addition, the data will be audited for accuracy at each site monitoring visit by an independent monitor.

### 15.1.3 Data privacy and retention policy

Following the ICF completion, where identifying information will be visible, an alphanumeric code will be assigned to each participant. All data to be collected post-ICF will have the specific alphanumeric code to ensure participant anonymity. Only the research personnel working directly with the participant will have access to the identifiable information. Data from the CRF will be transferred/transcribed to a cloud based electronic data platform (Google Suite) with 2-factor authentication access in place.

Participant study data will be kept for a minimum of 10 years as set out by the Health Sciences Research Ethics Committee of Pretoria.

### 15.1.4 Data ownership and data sharing

Data ownership primarily resides with the University of Pretoria and the hearX Foundation who oversees the study and retains ultimate ownership of the collected data. However, all parties involved, including investigators, institutions, and participants, hold a vested interest and responsibility in ensuring data accuracy and integrity. Access to study data, both identifiable and unidentifiable, will be strictly limited to authorized personnel. Any sharing or utilization of the data (unidentifiable) will necessitate prior approval from the University of Pretoria and the hearX Foundation. Distribution, submission, and publication rights shall be vested in HearX (Pty) Ltd.

### 15.1.5 Audit trail

The study will maintain a comprehensive audit trail to document all entries, changes, additions, or deletions made to the study data throughout its lifecycle, whether in paper format or electronically transcribed. This audit trail will include, but not be limited to, a record of all data entry, modifications, and access logs. Any modifications made to the data will undergo rigorous scrutiny. Each alteration will be methodically recorded, and a clear linkage to the responsible party for each change will be established. This meticulous audit trail will serve as a safeguard against unauthorized data handling and provide transparency in data management processes. The maintenance of an audit trail aligns with regulatory requirements, ensuring data integrity, traceability, and compliance with GCP guidelines.

Documents need to be retained for at least 15 years since the discontinuation of the clinical investigation. Documents may be retained for longer periods of time upon agreement with the sponsor or in accordance with regulatory requirements. Records are not allowed to be destroyed without written permission from the Sponsor.

## 16. Adverse events and device defects/deficiencies

### 16.1 Adverse events

Adverse events (AEs) are any untoward medical occurrence, unintended injury or disease in participants related to the investigational device.

For the current clinical investigation, possible AEs could include:

- Risk of an ear infection due to contamination or cross contamination of disease between participants through equipment and/or surface contaminants.
- Possible allergic reaction from use of the hearing aids, due to device material (e.g. itchy ears, or otitis externa).
- Possible increase in wax build-up due to occlusion of ear canals, which may cause itchiness and irritation.
- Possible headaches from prolonged device use, especially during the first few days of use.

### 16.2 Serious Adverse Events (SAE)

Any AE that leads to a death or to a serious deterioration in the health of the participant or that resulted in a life-threatening injury, permanent impairment of a body structure/function, hospitalization or medical intervention is considered an SAE. For the current clinical investigation no SAEs are anticipated.

### 16.3 Adverse Device Effect (ADE)

AE related to the use of an medical device. For the current clinical investigation, possible ADEs could include:

- Device material causing an allergic reaction in a participant's ear
- A device deficiency of unintended loud sound output that may result in a temporary threshold shift.

### 16.4 Device Deficiencies (DD)

Any device defect related to the identity, quality, durability, reliability, safety or performance of the devices. Device deficiencies include malfunctions, use errors, and inadequacy in the information supplied by the manufacturer including labeling. For the current clinical investigation, a possible DD could include:

- Any device defect related to the performance or safety of the devices e.g. audio output, faulty components that would deviate from the standard performance set out by the manufacturer.

### 16.5 Adverse event reporting

All AEs will be recorded on the AE/SAE form and will be added to the participant file.
The research team will discuss any AE within 48-72 hours of the event occurring and decide if any external parities such as the device developers. All AEs will be characterized by the following criteria as set out in Table 3.

**Table 3.** Adverse Event criteria

| Criteria | Grading |
|---|---|
| **Severity** | Mild |
| | Moderate |
| | Marked |
| | Severe |
| **Relationship** | Not related |

| | |
|---|---|
| | Definitely related |
| **Action taken** | None |
| | Study intervention modified |
| | Study intervention discontinued |
| | Subject withdrawal from study |
| | Hospitalisation |
| | Other |
| **Outcome** | Resolved |
| | Ongoing |
| | Worsening |
| | Death |
| | Unknown |
| **Expected** | Yes |
| | No |

## 17. Amendments and deviations to the protocol

A protocol deviation is described as an event where the investigator, research team member or the site personnel did not conduct the study in accordance with the investigational protocol or agreement.

The clinical trial will be conducted in compliance with the SA GCP guidelines along with the applicable regulatory requirements. The sponsor should notify the regulatory authority and EC of any changes in the study protocol/documentation. If the sponsor intends to make changes after approval has been obtained, a re-application should be submitted to the relevant authority and EC, indicating the contents and grounds for change. Essential changes are such changes that can have an effect on the safety of the participants, influence interpretation of results or influence requirements assessed by the ECs.

Investigators, research team members or site personnel need to obtain approval from the clinical study management team before deviating from the investigational protocol, except in an instance where it is necessary to protect the life or physical well-being of a participant in an emergency. All approvals need to be documented in writing and maintained in the study files. Prior approval is not expected in situations where there are unforeseen circumstances which are beyond the control of the investigator, research team, or site personnel.

### 17.1 Protocol deviations & study violations

**Protocol Deviation:** An accidental or unintentional change to, or non-compliance with the research protocol that does not increase risk or decrease benefit or does not have a significant effect on the participants, safety or well-being; and/or the reliability of the study data.

Examples of possible protocol deviations may include:

- Inadequate record keeping: Incorrect and missing data captured during study assessments/evaluations.
- Incorrect participant enrollment: Enrolling a participant who did not meet the stipulated inclusion/exclusion criteria.

**Study Violation:** A change, divergence from the study design or procedures defined in the protocol that might significantly affect participants' safety, and well-being and/or the reliability of the study data.

Examples of possible study violations may include:

- Incorrect or missing study procedures: Conducting/ performing new procedures/ assessments/ evaluations not in line with the original approved clinical investigational protocol.
- Unreported AE/SAEs: Not reporting or documenting AE/SAEs that occur during the clinical investigational study, that can affect the safety of the study participants.

**Reporting Requirements:**

PIs/site coordinators and their teams must report (Appendix XXX) to the study sponsor and any protocol deviations. This should in turn be documented and submitted to the EC for review.

Study violations should be reported within 24 hours of the event.

**Documentation and Storage:**

All deviation reports and related documents will be kept in the SMF and digital copies of it will be stored electronically on a cloud-based Google server with 2-factor authentication and strict access control.

**Reporting:**

Protocol deviations will also be documented in the final study report upon study conclusion.

**Personnel Training:**

Study personnel will receive pre-study communication training regarding deviation definitions and reporting timeframes to ensure accurate reporting. Training records will be kept for all personnel.

## 18. Dissemination Plan

The study team is committed to disseminating results to contribute to the body of evidence in hearing healthcare delivery in low- and middle-income communities. All dissemination will comply with NIH Policy on the Dissemination of Clinical Trial Information. The trial will be registered on ClinicalTrials.gov no later than 21 calendar days after the study start date. Once registered, the study team will:

- Verify the accuracy of record content and resolve any discrepancies.
- Maintain and update records at least annually, or more frequently as required by NIH and ClinicalTrials.gov regulations.
- Submit aggregate adverse event data at the conclusion of the trial.
- Submit the primary results to ClinicalTrials.gov within 12 months of the study completion date (see study timeline).

The University of Pretoria and hearX Foundation have established internal procedures to ensure compliance with NIH and ClinicalTrials.gov requirements for registration and results reporting.

### Dissemination of Results to Community Partners

The hearX Foundation and collaborating CHWs have established community engagement protocols to ensure that study findings are shared back with participating communities in a culturally and linguistically appropriate manner. This will include:

- Co-developing a one-page lay summary of results (in English, isiXhosa, and Sepedi) and an accompanying PowerPoint presentation with input from CHWs and community advisory boards.
- Sharing findings at community meetings, with local leadership bodies, elderly clubs, and NGOs.

### Dissemination to the Scientific and Professional Community

Results will be presented at national and international conferences in audiology, rehabilitation, and public health. The team will also seek opportunities to present at interdisciplinary conferences focused on digital health, community health worker programs, and LMIC health innovation.

**Peer-Reviewed Publications**

Study findings will be submitted to high-impact, peer-reviewed journals in audiology, rehabilitation, and global health.

## 19. References


1. Aazh, H., Deepak, P., Kiran, N., & and Moore, B. C. J. (2015). Hearing-aid use and its determinants in the UK National Health Service: A cross-sectional study at the Royal Surrey County Hospital. International Journal of Audiology, 54(3), 152-161. https://doi.org/10.3109/14992027.2014.967367
2. American National Standard- Specifications for Audiometers (ANSI/ASA S3.6-2018).
3. ANSI S3.6-2010 : Specifications for Audiometers.
4. Arlinger, S., Nordqvist, P., & Öberg, M. (2017). International Outcome Inventory for Hearing Aids: Data From a Large Swedish Quality Register Database. Am J Audiol, 26(3s), 443-450. https://doi.org/10.1044/2017_aja-16-0123
5. Baicus, C., & Caraiola, S. (2009). Effect measure for quantitative endpoints: Statistical versus clinical significance, or “how large the scale is?”. European Journal of Internal Medicine, 20(5), e124-e125. https://doi.org/10.1016/j.ejim.2008.10.002
6. Bisgaard, N., Zimmer, S., Laureyns, M., & Groth, J. (2021). A model for estimating hearing aid coverage world-wide using historical data on hearing aid sales. International Journal of Audiology, 1-9. https://doi.org/10.1080/14992027.2021.1962551
7. Cohen, J. (1969). Statistical power analysis for the behavioral sciences. Academic Press.
8. Cox RM, Rivera I. Predictability and reliability of hearing aid benefit measured using the PHAB. J Am Acad Audiol. 1992;3(4):242-54.
9. Cox RM, Alexander GC. The International Outcome Inventory for Hearing Aids (IOI-HA): psychometric properties of the English version: El Inventario International de Resultados para Auxiliares Auditivos (IOI-HA): propiedades psicometricas de la version en ingles. International journal of audiology. 2002;41(1):30-5.
10. Department of Health, 2020. South African Good Clinical Practice: Clinical Trial Guidelines Pretoria, South Africa (third edition). https://www.sahpra.org.za/wp-content/uploads/2021/06/SA-GCP-2020_Final.pdf
11. Field, A. P. (2024). Discovering statistics using IBM SPSS statistics (6th edition ed.). SAGE.
12. Herdman, M., Gudex, C., Lloyd, A., Janssen, M. F., Kind, P., Parkin, D., Bonsel, G., & Badia, X. (2011). Development and preliminary testing of the new five-level version of

EQ-5D (EQ-5D-5L). Quality of Life Research, 20(10), 1727-1736. https://doi.org/10.1007/s11136-011-9903-x
13. ISO 8253-1:2010(en) Acoustics — Audiometric test methods — Part 1: Pure-tone air and bone conduction audiometry.
14. Keidser G, Dillon H, Flax M, Ching T, Brewer S. The NAL-NL2 prescription procedure. Audiology research. 2011;1(1):88-90.
15. Loucks, E. B., Sullivan, L. M., D'Agostino, R. B., Sr., Larson, M. G., Berkman, L. F., & Benjamin, E. J. (2006). Social networks and inflammatory markers in the Framingham Heart Study. J Biosoc Sci, 38(6), 835-842. https://doi.org/10.1017/s0021932005001203
16. Mccabe, D. (2019). Hearing Screening in Older Adults. Best Practices in Nursing Care to Older Adults(12). https://hign.org/sites/default/files/2020-06/Try_This_General_Assessment_12.pdf
17. Mulwafu, W., Ensink, R., Kuper, H., & Fagan, J. (2017). Survey of ENT services in Sub Saharan Africa: Little Progress Between 2009 and 2015. Global Health Action, 10(1), 1289736–1289736. https://doi.org/1289710.1281080/16549716.16542017.11289736.
18. Peeters, M. J. (2016). Practical significance: Moving beyond statistical significance. Currents in
19. Stephens, D. (2002). The International Outcome Inventory for Hearing Aids (IOI-HA) and its relationship to the Client-oriented Scale of Improvement (COSI). Int J Audiol, 41(1), 42-47. https://doi.org/10.3109/14992020209101311
20. World Health Organization. (2021). World Report on Hearing. Available from: https://www.who.int/publications/i/item/world-report-on-hearing
21. World Health Organization. (2024). Hearing aid service delivery approaches for low- and middle-income settings. World Health Organization.