The COACH Trial:
A randomised controlled trial of cochlear implantation versus hearing aids in adults with severe hearing loss

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Short title:	**CO**mp**A**ring **C**ochlear implants with **H**earing aids in adults with severe hearing loss
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SYNOPSIS

Title	A randomised controlled trial of cochlear implantation versus hearing aids in adults with severe hearing loss
Acronym	COACH
Short title	**CO**mp**A**ring **C**ochlear implants with **H**earing aids in adults with severe hearing loss
Chief Investigator	Professor Douglas E.H. Hartley
Objectives	**Primary objective** To evaluate the effect of cochlear implantation on speech understanding in quiet in comparison to the use of acoustic hearing aids (HAs) in adults with severe hearing loss whose audiometric thresholds and/or speech perception scores fall outside current UK candidacy criteria for cochlear implantation (as per NICE guidance TA566). **Secondary objectives** a. To evaluate the effect of cochlear implantation on broader hearing-related outcomes including speech understanding in noise, difficulties with listening in everyday environments, listening-related fatigue, and tinnitus in comparison to those using acoustic HAs. b. To evaluate the effect of cochlear implantation on broader health and well-being outcomes including mood, hearing-related quality of life, and health-related quality of life in comparison to those using acoustic HAs. c. To assess the safety of cochlear implantation and acoustic HAs. d. To characterise the duration and nature of cochlear implant (CI) and HA use.
Trial Configuration	Two-arm, multi-centre, parallel group, randomised controlled trial, with blinded primary outcome assessment.
Setting	This trial will take place in organisations providing cochlear implantation and audiology services for the UK National Health Service.
Sample size estimate	Fifty-five participants per treatment arm are required to detect a difference of 15 percentage points in mean AB word scores at 9 months (primary outcome measure), between treatment groups at a 5% significance level (2-sided) with 90% power, assuming a SD of 24% in both treatment groups. To allow for non-collection of the primary outcome (e.g., due to loss to follow up), from up to 15% of participants, 65 participants in each treatment group should be randomised – a total of 130 participants.
Number of participants	130 participants
Eligibility criteria	**Inclusion criteria:** • Adults, aged 18 years or older • Patients with a severe sensorineural hearing loss in both ears. "Sensorineural" is defined as the absence of a conductive hearing loss, which itself is defined as an air-bone gap of 20 dB or greater averaged over 0.5, 1, and 2 kHz, or as many of these frequencies as an air-bone gap can be calculated for. In the absence of any measurable air-bone gaps at 0.5, 1, or 2 kHz due to the limits of the audiometer, a sensorineural loss may be confirmed by a tympanometry trace within normal limits, as described in the British Society of Audiology Recommended Procedure for Tympanometry

(2013). “Severe” is defined as pure-tone audiometric threshold equal to or greater than 70 dB HL at 2 or more frequencies including 500 Hz, 1,000 Hz, 2,000 Hz, 3,000 Hz and 4,000 Hz bilaterally without acoustic HAs

- Patients with appropriate HA devices and prescriptions, with a minimum of:
  - 6 weeks having elapsed since any significant change to a prescriptive gain of >5 dB in gain averaged across the frequencies 250Hz to 6000Hz, where it is possible to reach prescriptive gain targets generated by standardised target rules such as NAL-NL2, DSL v5. If the prescriptive target at any frequency cannot be met despite the maximum gain of the hearing aid being delivered, this frequency can be ignored as a contributor to the average as insufficient change can be effected.
  - 0 weeks having elapsed since any other changes to hearing aid parameters deemed not clinically significant
- Patients with a phoneme score <60% on the AB Word test when tested in quiet at 70 dBA with acoustic HAs
- Patients in whom history, examination and pre-operative imaging suggests a healthy middle ear in the ear to be implanted, and a structurally normal and fully patent cochlea with no evidence of a widened vestibular aqueduct
- Patients for whom unilateral cochlear implantation is not recommended by NICE either because they do not meet the definition of severe to profound deafness (pure-tone audiometric threshold equal to or greater than 80 dB HL at 2 or more frequencies between 500 Hz, 1,000 Hz, 2,000 Hz, 3,000 Hz and 4,000 Hz), or because they meet the definition of adequate benefit from HAs (a phoneme score ≥50% on the AB Word test when tested in quiet at 70 dBA with acoustic HAs), or both (as per recommendation 1.5, NICE TA566)

		Pure-tone audiometry (any 2 frequencies between 0.5 and 4 kHz)		
	Better ear	≥ 80 dB HL	≥ 70 to < 80 dB HL	≥ 70 to < 80 dB HL
	Worse ear	≥ 80 dB HL	≥ 80 dB HL	≥ 70 to < 80 dB HL
Speech Perception (in quiet at 70 dB(A))	AB Phoneme score ≥ 50 to < 60%	**RCT** (ineligible on NHS due to AB score)	**RCT** (ineligible on NHS due to AB score and HL)	
	AB Phoneme score < 50%	**Eligible on NHS as per NICE TA566**	**RCT** (ineligible on NHS due to HL)	

Figure 1: A summary of the audiometric and speech eligibility criteria to distinguish the categories of patients who are eligible for the COACH trial (yellow areas; RCT: Randomised Controlled Trial) from those who are currently eligible under NICE guidance (grey area).

- Patients who are capable of speaking and understanding the English language
- Patients who are capable and willing to provide written/electronic informed consent

Exclusion criteria:

- Patient characteristics falling outside the indications for use of the trial devices as per their CE marking

	• Inability to undergo speech perception testing and/or inability of audiologist to obtain an accurate measurement of speech perception abilities • Patients who would not be able to adhere to trial procedures or complete the trial questionnaires • Patients whose hearing loss is suspected or confirmed to be wholly or partly unexplained by anatomic or physiologic abnormalities (non-organic hearing loss) • Patients who have a congenital profound hearing loss (no measurable or aidable hearing in both ears from birth) • Any known factor that may restrict full insertion of the electrode array • Patients with any known contraindication for cochlear implantation • Patients whose primary concern is the suppression of tinnitus • Patients in whom cochlear implantation would present an unacceptable risk to balance function • Any serious concerns about medical fitness for surgery or cochlear implantation • Participation in other research related to hearing loss while participating in the trial (i.e., until collection of primary outcome), including research that involves any changes to or use of hearing devices, changes to hearing care/management, or duplication of trial outcome assessments.
Description of interventions	**Cochlear Implantation** Unilateral CI with the option to receive a new hearing aid for the non-implanted ear. Programming and follow-up of the CI to be provided in accordance with the quality standards of the British Cochlear Implant Group (BCIG 2018, or latest version available). A CI system works by converting sound in the environment into electric pulses that stimulate the hearing nerve, allowing the brain to perceive sound. An implanted part of the CI is positioned under the skin behind the ear, which receives electrical signals from an external part of the CI worn behind the ear (sound processor) and delivers these signals to the inner ear (cochlea). The choice of CI system will be restricted to either the CI622 or CI632 CIs manufactured by Cochlear™ Ltd, whichever is routinely used by the CI centre as part of their standard practice, and whichever is the most appropriate CI for the patient as determined by the local clinical team. The choice of sound processor will be restricted to the CP1000, CP1110 or CP1150 devices manufactured by Cochlear™ Ltd, whichever are routinely used by the CI centre as part of their standard practice and deemed the most appropriate for the patient by the local clinical team, with an element of patient choice as appropriate. Participants will be offered an optional danalogic GN HA (or offered to have their existing HA optimised). If this offer is accepted by the participant, it will take place in line with usual clinical practice and no later than 6 months following CI activation. **Hearing Aids** Optional offer of bilateral danalogic GN acoustic HAs, with telephone follow up and ad-hoc face-to-face support as required. A HA optimisation appointment will be conducted with patients that do not elect to take up the offer. Fitting of both CIs and HAs will be in accordance with manufacturer recommendations and in line with UK clinical standards. Trial-specific clinical procedures will be provided in supplement to the trial protocol as Working Practice Documents (WPDs)

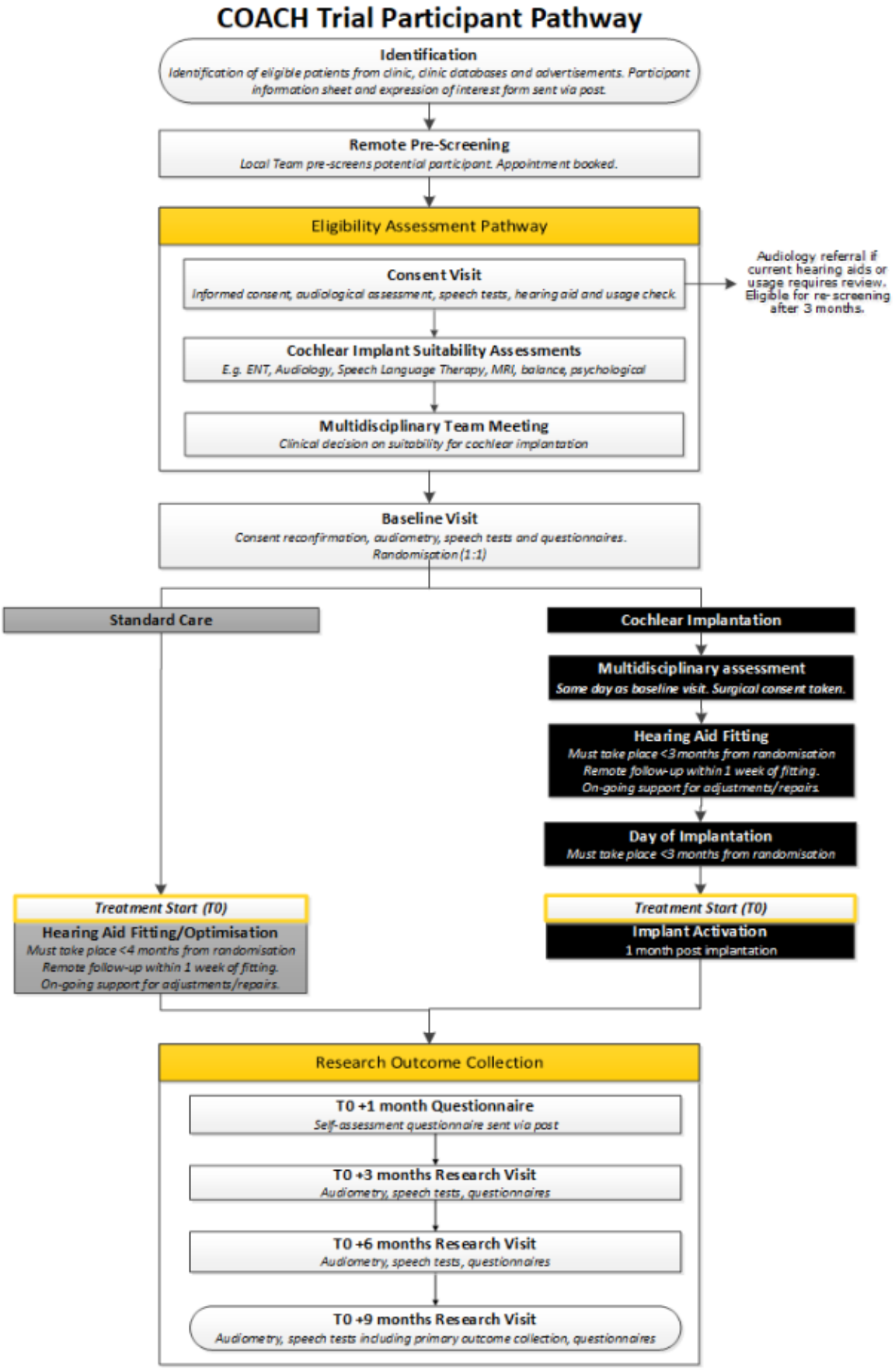
Duration of trial	On average, each participant will participate in the trial for 18 months. The waiting times before treatment will vary for participants due to local factors and logistics, but the time between treatment and follow up is fixed and will not vary.
Randomisation and blinding	Participants will be individually randomised on a 1:1 ratio, minimised by trial site, severity of tinnitus, and AB word test phoneme score. Blinding of participants, the direct clinical care team, or the local trial team will not be possible given the requirement for some participants to undergo a surgical procedure to receive a CI and the obvious visible differences between a CI speech processor and a HA. However, the scoring of the primary outcome will be undertaken by independent, blinded assessors.
Outcome measures	**Primary Outcome:** The primary outcome will be a measure of speech understanding; the perception of phonemes as quantified by the phoneme score on the AB word test presented at 60 dBA, in the best-aided condition (i.e., using the devices that the participant considers will help them hear as well as possible), at 9 months post first treatment activation (intervention arm: first CI activation; comparator arm: first HA fitting/optimisation) measured by independent blinded assessors. **Secondary Outcomes:** *Clinical:* - Phoneme perception (AB Word test) (same test as primary outcome but assessed live by audiologist at 3, 6 and 9 months) - Word perception (AB Word test) - Sentence perception in quiet (BKB sentence test) - Sentence perception in noise (BKB sentence test) - Device usage (device logging) - Audiometric thresholds (aided and unaided) Clinical measures will be administered in the best-aided condition (i.e., using the devices that the participant considers will help them hear as well as possible), except for unaided audiometric thresholds which will be measured without any devices being worn. Clinical measures will be administered at baseline and at 3, 6, and 9 months post first treatment activation. *Patient-Reported:* - Difficulty with listening (SSQ12 scale) - Listening effort and fatigue (EAS, FAS and LEQ-CI*) - Tinnitus severity (TFI) - Tinnitus loudness (VAS-L) - Mood (HADS) - Hearing-specific quality of life (NCIQ, YBHRQL and HHIA) - Health-related quality of life (EQ-5D-5L, HUI3, and ICECAP-A) - Global ratings of change*:* At each follow up appointment following first treatment activation, participants will be asked to indicate on 7-point Likert scale ranging from 'Much Worse' to 'Much Improved' whether hearing and quality of life have improved or worsened relative to two anchor points: (1) immediately prior to first treatment activation; and (2) since the last trial appointment. - Device usage (participant self-report)

	Patient-reported measures will be administered at 1, 3, 6, and 9 months post first treatment activation, except for tinnitus loudness (also measured at first treatment activation) and device usage (participant self-report measured until 9 months). *Data to be collected using LEQ-CI questionnaire once licence is in place **Safety outcome** Participant and investigator reported complications, recorded in the eCRF and participant questionnaires. Information from medical notes may also be consulted, if deemed necessary (i.e. for serious adverse event reporting).
Statistical methods	The evaluation of the primary outcome will be performed using mixed effects regression modelling to compare the mean proportion of phonemes repeated correctly during the AB word test in the intervention and comparator groups at 9 months. This will be called the phoneme score. The regression model will be adjusted for baseline phoneme score and minimisation variables. The comparison will be presented as an absolute difference in mean 9-month phoneme score in the CI group compared with the HA group with the associated 95% confidence interval. Similar analyses will be carried out for the secondary outcomes using appropriate regression models dependent on outcome type, except for the audiometric thresholds and device usage which will be summarised using appropriate descriptive statistics. Repeated measures regression modelling will investigate whether any between group differences change over time by including a term for the interaction between the treatment arm and time in the model. Sensitivity analyses for the primary outcome including investigating the potential impact of any missing data using multiple imputation, will be specified in the SAP. Safety data will be summarised according to the treatment the participant received, irrespective of randomisation.

ABBREVIATIONS

AB	Arthur Boothroyd
AE	Adverse Event
BKB	Bamford-Kowal-Bench
CI	Cochlear Implant
CE	Conformité Européenne
CRF	Case Report Form
DAP	Data Analysis Plan
EOI	Expression of Interest
dB	Decibels
dBA	Decibels (weighted)
DMC	Data Monitoring Committee
EAS	Effort Assessment Scale
EOT	End of Trial
EuroQol (EQ-5D-5L)	Health-related Quality of Life
FAS	Fatigue Assessment Scale
GCP	Good Clinical Practice
HA	Hearing Aid
HADS	Hospital Anxiety and Depression Scale
HHIA	Hearing Handicap Inventory for Adults
HL	Hearing Loss
HUI3	Health Utilities Index mark 3
ICECAP-A	ICEpop CAPability measure for Adults
ICF	Informed Consent Form
ISF	Investigator Site File
LEQ-CI	Listening Effort Questionnaire – Cochlear Implant
MDT	Multi-Disciplinary Team
MHRA	Medicines and Healthcare Products Regulatory Agency
NCIQ	Nijmegen Cochlear Implant Questionnaire
NCTU	Nottingham Clinical Trials Unit
NHS	National Health Service
NICE	National Institute for Healthcare and Excellence
NIHR	National Institute for Health Research
PI	Principal Investigator at a local centre
PIS	Participant Information Sheet
PPI	Patient and Public Involvement
PROM	Patient Reported Outcome Measure
REC	Research Ethics Committee
RCT	Randomised Controlled Trial
R&D	Research and Development Department
SAE	Serious Adverse Event
SSQ12	Speech Spatial and Qualities of listening scale
TFI	Tinnitus Functional Index
TMG	Trial Management Group
TSC	Trial Steering Committee
WPD	Working Practice Document
VAS	Visual Analogue Scale
VASL	Visual Analogue Scale of Loudness
YBHRQL	York Binaural Hearing-Related Quality of Life

Trial Flowchart



TRIAL BACKGROUND INFORMATION AND RATIONALE

In countries around the world, cochlear implantation is indicated for adults with severe to profound deafness who gain insufficient benefit from acoustic hearing aids (HA) for the purpose of improving the ability to recognise sounds and understand speech (Vickers et al., 2016). Candidacy criteria for cochlear implantation have expanded gradually since the 1980s as clinical experience with the procedure, the rehabilitation of implant recipients, and the process of selecting those candidates who are likely to benefit the most has matured (Cohen, 2004; Leigh et al., 2016; Lovett et al. 2015). However, these changes have occurred in the absence of robust evidence from clinical trials (Bond et al., 2010; van Schoonhoven et al., 2013) for a number of reasons:

First, cochlear implantation was historically used in profoundly deaf individuals where any improvement in sound awareness quickly became recognised as clinically meaningful given the lack of treatment alternatives and the rapidity with which implantation was established as a safe intervention (Niparko, 2009).

Second, like most surgical interventions, the indications for the intervention expanded gradually as familiarity and confidence with the surgical procedure grew (Barkun et al., 2009) given that a wide range of patients did not receive benefits from acoustic HAs (Tyler et al., 2002; UKCISG, 2004).

Third, outcomes have been observed to generally improve over time as technology has improved, as clinical teams have gained experience in selecting appropriate candidates for cochlear implantation, and as scientific knowledge grew around the patient characteristics that were predictive of a favourable outcome (Doran & Jenkinson, 2016; Leigh et al., 2016; Lovett et al., 2015; UKCISG, 2004).

Today, many countries around the world provide access to cochlear implants (CI) to patients with average audiometric hearing thresholds ≥80 dB HL (Vickers et al., 2016). A recent UK consensus exercise involving a wide range of stakeholders in the field of cochlear implantation (including patients, healthcare professionals, industry representatives, and healthcare commissioners) indicated that there is uncertainty around the necessity to expand indications to those adults with severe hearing losses with average audiometric thresholds better than 80 dB HL or with phoneme speech scores from the AB word test better than 50% correct, for two reasons. First, the level of residual hearing in these patients means that they have the potential to derive a clinically meaningful benefit from acoustic HAs. The balance of risks and benefits of cochlear implantation as a comparative treatment to HAs in these patients is as yet unsupported by high-quality clinical evidence, with stakeholders expressing consensus that CI may be appropriate for those with average losses between 70-80 dB HL but not in patients with better hearing than that (Kitterick & Vickers, 2017a). Second, analyses of speech outcomes have demonstrated that the predicted chance of patients with phoneme speech scores ≥50% benefitting from a CI may not be sufficiently high to currently satisfy patients, healthcare professionals, and healthcare payers, but uncertainty around the best treatment option exists for those with scores between 50-60% (Kitterick & Vickers, 2017b).

Based on this evidence, this randomised controlled trial (RCT) will compare cochlear implantation to conventional acoustic HAs in adults who could potentially benefit from CI but who are currently outside current NICE candidacy criteria, either because their average audiometric thresholds fall within the 70-80 dB HL range or because their speech scores fall within the 50-60% range, or both. Conducting such a trial in the current landscape of CI candidacy will have two major anticipated impacts. First, it will provide the level of evidence that would have the capacity to inform any further evaluations of candidacy criteria in

countries like the UK that currently do not provide patients with severe hearing loss (NICE 2019). Second, if the trial finds evidence of superiority for cochlear implantation over acoustic HAs, it will provide evidence to support the ongoing reimbursement of CIs in those countries that already provide access to CIs in this population.

The current context in the UK, which, despite recent changes still has conservative candidacy criteria compared to some other countries, but also has a health service supported by world-class health research infrastructure (https://www.nihr.ac.uk/), provides a unique opportunity to conduct such a randomised trial while access to CIs among adults with severe hearing loss is limited. This is a trial that will gather high-quality evidence of the comparative efficacy of cochlear implantation and acoustic HAs that can be generalised to similar populations in healthcare systems around the world.

DETAILS OF MEDICAL DEVICES

This trial will be using 3 broad categories of devices: Cochlear Implants, Sound Processors and Hearing Aids. All devices used in the trial will be used in line with their CE markings, requiring no letter of no objection from the MHRA for that usage.

The decision for which devices each participant will be offered will be based on trial allocation and individual clinical information. An element of participant choice between available models of sound processors (if applicable) and hearing aids will be offered, where possible. The latest appropriate devices, available as a part of standard NHS care at the time of treatment onset, will be used for the present trial. The below list represents the current devices used as part of standard NHS care at time of protocol writing, and will be updated if newer, appropriate models by Cochlear™ and GN Hearing UKbecome available.

Device Descriptions

Cochlear Implants

There will be a choice of two Cochlear™ CI systems which can be used in the trial:

1. **Cochlear™ Nucleus® CI632 cochlear implant with Slim Modiolar electrode**
2. **Cochlear™ Nucleus® CI622 cochlear implant with Slim Straight electrode**

Cochlear™ Nucleus® CI600 series implants are single use devices intended for long term implantation under the skin in the mastoid region of either side of the head. They are for professional use only. The below information has been taken from their respective instructions for use (Cochlear Limited, 2019a; Cochlear Limited, 2019b).

Indications
A CI provides auditory sensation and sound perception by electrically stimulating the auditory nerve of a hearing-impaired ear. The degree of hearing loss and compromised hearing with HAs must be established and verified clinically using age-appropriate measures before recommending unilateral or bilateral CIs.

Prospective implant recipients and their families should be well motivated, willing to undergo hearing rehabilitation as needed and have appropriate expectations of the potential benefits of unilateral or bilateral implants.

Contraindications
A Cochlear™ Nucleus® CI is not suitable for individuals with the following conditions:
• deafness due to lesions of the acoustic nerve or central auditory pathway
• active middle ear infections
• absence of cochlear development

• tympanic membrane perforation in the presence of active middle ear disease
• ossification of the cochlea that prevents electrode insertion.

Device description
Cochlear™ Nucleus® CI systems are designed to provide useful hearing. The system works by converting sound in the environment into electric pulses that stimulate the auditory nerve, allowing the brain to perceive sound. The Cochlear™ Nucleus® CI systems have implanted and external components.

Implanted component
The CI is surgically implanted under the skin behind the ear. It includes a receiver/stimulator to receive and decode the electrical signals from the sound processor and an electrode to deliver these signals to the cochlea.

External components
The external components include a sound processor, and associated accessories and cables. The system is programmed by a Cochlear™ proprietary programming system.
For information on compatibility between implants and processors, refer to the Custom Sound User Guide.

Sound Processors

The choice for which sound processor to be used will be based on a clinical decision, in line with standard care. There will be a choice of sound processors for the trial as listed below.

1. **Cochlear™ Nucleus® 7 Sound Processor (model number: CP1000)**
2. **Cochlear™ Nucleus® 8 Sound Processor (model number: CP1110)**
3. **Cochlear™ Kanso® 2 Sound Processor (model number: CP1150)**

The below information has been taken from their respective instructions for use (Cochlear Limited, 2020a; Cochlear 2022, Cochlear, 2020b).

Indications
The processor works with the implant (see section above) to transfer sound to the ear and, depending on the model, is made up of a processing unit, earhook, coil and cable, magnet and a battery module.

Contraindications
Patients must be suitable for a CI. Please see contraindications for a CI in section above.

Device Descriptions

Cochlear™ Nucleus® 7 Sound Processor (model number: CP1000) and Cochlear™ Nucleus® 8 Sound Processor (model number: CP1110)

The processor can be powered by disposable or rechargeable batteries.

The processor can be controlled by pressing its button, or by using the Cochlear™ Remote Control or the Nucleus® Smart App.

People with certain types of hearing loss can wear the processor in Hybrid™ mode by adding an acoustic component which sends amplified acoustic sound into the ear canal. The Hybrid mode of use is outside of the scope of this trial.

The batteries provide power to the processor. The coil acts as a transformer coupling that transfers energy and data to the implant.
The processing unit comprises:

Two omni-directional microphones for receiving sound.

- An internal telecoil for receiving magnetic fields radiated by neck loops and room loops.
- Custom analogue and digital integrated circuits with digital signal processing and bidirectional wireless communication capabilities.
- A tri-colour visual indication of processor function or problem.
- Control button allowing user control of key features.
- Custom 4-pin connector for coil cable.
- A range of earhooks and specialised retention options.

Cochlear™ Kanso® 2 Sound Processor (model number: CP1150)
The Kanso® 2 sound processor comprises:

- Two omni-directional microphones for receiving sound.
- Custom analogue and digital integrated circuits with digital signal processing and bi-directional wireless communication capabilities.
- Tri-colour visual indication of processor function or problem.
- Tap interface allowing the user to turn the processor on and off.

The internal battery provides power to the processor, which transfers energy and data to the implant.

Both sound processors are provided with a list of accessories in line with standard care. The full list of included accessories for each processor are outlined in Appendix 2.

Fitting and programming of sound processors will be in accordance with manufacturer's recommendations and clinical best practice.

Hearing Aids

Hearing instruments to be offered in the trial will be any of the Danalogic BTE (behind the ear) or RIE (receiver in ear) hearing aids provided by GN Hearing UK, that are used as a part of standard NHS care. Details of specific devices permitted for use in the trial are provided in a separate audiology protocol, and will be updated if newer, appropriate models by GN Hearing UK become available.

Fitting specifications of each hearing aid will be recorded in the eCRF. Combination devices are not permitted for use in the trial.

Indications
Generic air-conduction HAs are wearable sound-amplifying devices intended to compensate for impaired hearing. The fundamental operating principle of HAs is to receive, amplify, and transfer sound to the eardrum of a hearing-impaired person.

The danalogic hearing aids being used in the trial give access for those with a compatible smartphone to the free Relief app for people suffering from tinnitus. The app includes a combination of sound therapy, relaxing exercises, meditation and guidance. Users can create their own tinnitus-masking soundscapes from a range of sounds. These can be controlled via the app and, if the user has a Nucleus cochlear implant for their other ear, the tinnitus sounds can be wirelessly streamed to both devices simultaneously.

Contraindications
No specific contraindications listed in the manufacturer's user guides.
It is important to note that a HA will not restore normal hearing and will not prevent or improve a hearing impairment resulting from organic conditions. Consistent use of the HA is

recommended as, in most cases, infrequent use does not allow full benefit to be attained from it. The use of a HA is only part of hearing rehabilitation and may need to be supplemented by auditory training and instructions in lip-reading.

Device Description
ReSound's innovative sound technology and design, combined with the customized programming selected by hearing care professionals, aims to make hearing a more enjoyable experience for patients. In order to wholly benefit from the use of the HAs, they should be worn in line with the manufacturers' user guide. A detailed description of all parts of the device is also outlined in the user guides.

Packaging and labelling

As all above devices are used in accordance with their CE marking and supplied in an open allocation, packaging and labelling for implants, sound processors and HAs will follow that of standard clinical practice.

Storage and supply

Cochlear Implants and Sound Processors

Cochlear Implants and Sound Processors will be ordered by sites through their regular procurement processes. Storage and supply to trial participants will also follow in accordance with local standard practice. CI device serial number and personal details of the patient receiving the device will be registered by the trial site with the manufacturer, as per regulatory requirements governing cochlear implantation.

In order to protect the privacy of trial participants and the blinded status of the manufacturer, trial sites will be retrospectively provided, at no cost, with the same number of implants and sound-processors used for trial purposes, to be integrated into their normal stock. This will prevent being able to associate a registered implant to the recipient's status as a trial participant. One CI and one sound processor will be supplied to each participant in the intervention arm.

Hearing Aids

Bulk supply of HAs will be provided free of charge to trial sites, direct from the manufacturer, at the beginning of the trial and throughout, as needed. Trial devices will be securely stored, according to local procedures for hearing aid storage, but sufficiently labelled to indicate their usage for the COACH trial only.

Two HAs will be offered to trial participants in the comparator arm, and one HA will be offered for the contralateral ear of participants in the intervention arm. Participants do not have to take up the offer of a new HA. Trial HAs will be provided to participants, after randomisation, at their HA fitting visit.

Trial sites will also be supplied with spare consumables for any repairs required over the course of the trial.

Accountability, maintenance, and return

For accountability purposes, logs of all trial devices and consumables for spares and repairs will be maintained by site and shared with the Nottingham Clinical Trials Unit (NCTU). Periodic reconciliation will be undertaken to ensure the number of devices used is in line with recruitment numbers and any reported required replacements. These logs will be used to ensure accountability of trial devices as described below in the device accountability section.

Trial devices will be maintained by trial sites until two years post treatment onset, using spares and repairs provided directly by the manufacturers to trial sites.

No trial devices will be returned at the end of trial participation. Participants will keep their devices after the end of their trial participation, and from that point any devices will be maintained or replaced by the NHS in line with current standard practice at the time.

Known Device Effects

All above devices are used routinely in standard care and their safety profiles are well known.

TRIAL OBJECTIVES AND PURPOSE

PURPOSE

To investigate the efficacy of unilateral cochlear implantation compared to acoustic HAs in improving speech understanding in adults with severe hearing loss whose audiometric thresholds and/or speech perception scores fall outside current UK candidacy criteria for cochlear implantation (as per NICE guidance TA566).

Figure 1 below shows patients in the yellow areas for whom cochlear implantation is not recommended by NICE either because they do not meet the definition of severe to profound deafness, or because they meet the definition of adequate benefit from HAs, or both (as per recommendation 1.5, NICE TA566). Patients who are currently eligible for a CI on the NHS under NICE guidance fall into the grey area; whereas patients who fall into the yellow areas are not currently eligible on the NHS because of their hearing test results and/or their speech test scores and so are eligible for the COACH trial.

<table>
<tr><td></td><td></td><td colspan="3">Pure-tone audiometry
(any 2 frequencies between 0.5 and 4 kHz)</td></tr>
<tr><td rowspan="4">Speech Perception
(in quiet at 70 dB(A))</td><td>Better ear</td><td>≥ 80 dB HL</td><td>≥ 70 to < 80 dB HL</td><td>≥ 70 to < 80 dB HL</td></tr>
<tr><td>Worse ear</td><td>≥ 80 dB HL</td><td>≥ 80 dB HL</td><td>≥ 70 to < 80 dB HL</td></tr>
<tr><td>AB Phoneme score
≥ 50 to < 60%</td><td>RCT
(ineligible on NHS due to AB score)</td><td colspan="2">RCT
(ineligible on NHS due to AB score and HL)</td></tr>
<tr><td>AB Phoneme score
< 50%</td><td>Eligible on NHS as per NICE TA566</td><td colspan="2">RCT
(ineligible on NHS due to HL)</td></tr>
</table>

Figure 1: A summary of the audiometric and speech eligibility criteria to distinguish the categories of patients who are eligible for the COACH trial (yellow areas; RCT: Randomised Controlled Trial) from those who are currently eligible under NICE guidance (grey area).

PRIMARY OBJECTIVE

To evaluate the effect of cochlear implantation on speech understanding in quiet in comparison to the use of acoustic HAs in adults with severe hearing loss whose audiometric thresholds and/or speech perception scores fall outside current UK candidacy criteria for cochlear implantation (as per NICE guidance TA566).

SECONDARY OBJECTIVES

a. To evaluate the effect of cochlear implantation on broader hearing-related outcomes including speech understanding in noise, difficulties with listening in everyday environments, listening-related fatigue, and tinnitus in comparison to those using acoustic HAs.
b. To evaluate the effect of cochlear implantation on broader health and well-being outcomes including mood, hearing-related quality of life, and health-related quality of life in comparison to those using acoustic HAs.
c. To assess the safety of cochlear implantation and acoustic HAs.
d. To characterise the duration and nature of CI and HA use.

TRIAL DESIGN

TRIAL CONFIGURATION

The trial will be a two-arm, multi-centre, parallel group, open, randomised controlled trial of CIs versus HAs.

Participants will be randomised to one of two treatment groups:

Intervention: Unilateral cochlear implantation and offer of a new acoustic HA or optimisation of current HA in the contralateral ear.

Comparator: Offer of new bilateral acoustic HAs or optimisation of current HAs.

Participants will be followed up at 1, 3, 6 and 9-months post treatment activation (T0). The primary outcome will be collected at the 9-month timepoint as clinicians report that the identification of words following cochlear implantation stabilises between approximately 3-6 months and therefore assessment at 9 months will ensure performance has reached asymptote.

The primary outcome will be assessed using the AB word test at 60 dBA. In the UK, a presentation level of 70 dBA is common, whereas lower presentation levels (60 dBA) are frequently used in other countries. The use of a lower presentation level (60 dBA rather than 70 dBA) for the administration of the AB word test for the primary outcome brings the trial in line with speech testing methodologies adopted internationally. The use of a higher presentation level (70 dBA) is included in the secondary outcomes.

Primary outcome

The primary outcome will be an assessment of the perception of phonemes as quantified by the phoneme score on the AB word test (a measure of speech understanding) presented at 60 dBA in the best-aided condition (i.e., using the devices that the participant considers will help them hear as well as possible), at 9 months post first treatment activation (Intervention arm: first CI activation; Comparator arm: first HA fitting/optimisation) measured by independent blinded assessors.

Secondary outcomes

Clinical:

- Phoneme perception (AB Word test at 60 dBA) at 3, 6 and 9 months following first treatment activation, measured by the audiologist
- Word perception (AB Word test at 60 dBA) at 3, 6 and 9 months following first treatment activation
- Phoneme perception (AB Word test at 70 dBA) at 9 months following first treatment activation
- Word perception (AB Word test at 70 dBA) at 9 months following first treatment activation
- Sentence perception in quiet (BKB sentence test at 70 dBA) at 3, 6 and 9 months following first treatment activation
- Sentence perception in noise (Adaptive BKB sentence test) at 3, 6 and 9 months following first treatment activation
- Device usage (device logging) at 3, 6, and 9 months
- Audiometric thresholds (aided and unaided) on the day of treatment activation and at 3, 6 (unaided only) and 9 months following first treatment activation

The AB word tests and BKB sentence tests will be tested in the best-aided condition (i.e., using the devices that the participant considers will help them hear as well as possible) and scored live by the audiologist for the secondary outcomes.

Patient-Reported:
- Difficulty with listening (12-item Speech Spatial and Qualities of listening scale, SSQ12) at 1, 3, 6, and 9 months post first treatment activation
- Listening effort and fatigue (Effort Assessment Scale, EAS; Fatigue Assessment Scale; FAS; Listening Effort Questionnaire-Cochlear Implant, LEQ-CI*) at 1, 3, 6, and 9 months post first treatment activation
- Tinnitus severity (Tinnitus Functional Index, TFI) at 1, 3, 6, and 9 months post first treatment activation
- Tinnitus loudness (Visual Analogue Scale of Loudness, VAS-L) immediately before and after first treatment activation and at 1, 3, 6, and 9 months post first treatment activation
- Mood (Hospital Anxiety and Depression Scale, HADS) at 1, 3, 6, and 9 months post first treatment activation
- Hearing-specific quality of life (Nijmegen Cochlear Implant Questionnaire, NCIQ; York Binaural Hearing-Related Quality of Life, YBHRQL; Hearing Handicap Inventory for Adults, HHIA) at 1, 3, 6, and 9 months post first treatment activation
- Health-related Quality of Life (EuroQol EQ-5D-5L; Health Utilities Index Mark 3, HUI3; ICEpop CAPability measure for Adults, ICECAP-A) at 1, 3, 6, and 9 months post first treatment activation
- Global ratings of change in hearing and quality of life at 1, 3, 6, and 9 months post first treatment activation: At each follow up appointment following first treatment activation, participants will be asked to indicate on 7-point Likert scale ranging from ‘Much Worse’ to ‘Much Improved’ whether hearing and quality of life have improved or worsened relative to two anchor points: (1) immediately prior to first treatment activation; and (2) since the last trial appointment.
- Device usage (participant self-report) at 1, 2, 3, 4, 5, 6, 7, 8 and 9 months

*Data to be collected using LEQ-CI questionnaire once licence is in place

Safety outcomes

From randomisation to 9 months post first treatment activation, safety data, including number of expected AEs and SAEs and unexpected related SAEs will be summarised with descriptive statistics according to the treatment the participant received, irrespective of randomisation. Where a participant did not receive their allocated treatment but had an expected AE, or SAE this will be indicated.

Stopping rules and discontinuation

There is no planned interim analysis of treatment efficacy and no formal stopping rules. The Data Monitoring Committee (DMC) and Trial Steering Committee (TSC) will have ongoing oversight of the safety and feasibility of delivery of the trial. The DMC will also review data to ensure the trial has sufficient power to detect a clinically important difference between the two groups.

Randomisation and Blinding

Before randomisation can take place, a series of eligibility assessments need to take place to ensure the potential participant is suitable for all trial interventions. Consent is received prior to eligibility assessment and reconfirmed prior to randomisation. Randomisation cannot take place until a CI surgeon with delegated responsibility has confirmed the potential participant is eligible, following agreement from the MDT.

Randomisation

After reconfirmation of consent and recording of baseline measures, randomisation will take place at the trial site.

Participants will be assigned to treatment groups in a 1:1 ratio, using a concealed, secure internet-based randomisation system developed and maintained by the NCTU. The system will use a minimisation algorithm including a random component, with the following variables and levels: participating site; severity of tinnitus (Tinnitus Functional Index (TFI) score mild (0-28), moderate - significant problems (29-65), and severe (≥66)); AB word test phoneme score at 70 dBA <50% and ≥50 %. Participants that report no tinnitus will be given a score of 0 which falls under 'mild' tinnitus within the TFI. Access to the randomisation system will be granted to site staff by the NCTU in accordance with the roles delegated by the local Principal Investigator (PI) as documented on the delegation log.

Following randomisation, the participant's GP will also be informed that the participant is taking part in the trial by post.

Blinding

Participants, clinicians and treating staff cannot be blinded to the treatment allocation due to the requirement for some participants to undergo a surgical procedure to receive a CI and the obvious visible differences between a CI speech processor and a HA. However, to minimise bias, the baseline and 9-month measures of the primary outcome will also be video recorded and scored by two independent blinded assessors whose score will be that used in the primary outcome analysis.

The independent assessors will be qualified audiologists with experience of administering and scoring clinical speech perception tests in patients with severe hearing losses. These independent assessors will be blinded both to treatment arm and timepoint of the recordings. Disagreement in scores will be resolved by consensus between the two assessors, failing which a third assessor will adjudicate. The full procedures for the blinded assessment of primary outcomes will be documented in a separate working practice document, finalised prior to any baseline or primary outcome recording of the AB word test. The blinded scoring of the primary outcome at baseline and 9 months will form part of the trial datasets for analysis.

The trial and data management staff at NCTU will have access to all data in the eCRF to undertake central monitoring. Only the trial management team at the NCTU will have access to the raw footage for the blinded assessments to perform quality control checks (i.e., ensuring the device cannot be seen in the video footage for blinded assessment).

The trial statisticians and TSC members will be blinded to participant group allocations until after database lock; aggregate data will be viewed for trial monitoring purposes only. The Chief Investigator will remain blinded to treatment allocation overall however this is not possible for participants recruited at his site since he is responsible for their clinical care. The Chief Investigator may need to be unblinded in instances where this is required for full causality assessment of serious adverse events (SAEs). Any data summaries and analyses which require knowledge of the treatment allocation (e.g., within the closed report for the DMC) will be conducted by a statistician who is independent of the trial. Such summaries and analyses will be held in an area which is accessible only to the statistician(s) who are independent of the trial. The Chief Investigator will also remain blinded to primary outcomes.

Maintenance of randomisation codes and procedures for breaking code

The randomisation algorithm will be held on a secure, access-restricted system, to which only NCTU database programmers have access. The allocation will be concealed using a secure web-based system developed and maintained by the NCTU. As this is an unblinded trial, no emergency unblinding processes are necessary.

TRIAL MANAGEMENT

The TSC will meet at least once a year or as required and will provide independent oversight of the trial on behalf of the trial sponsor.

The DMC will meet at least once a year or as required to assess safety, effectiveness and futility of the trial and will report to the TSC.

The Trial Management Group (TMG) will meet more frequently, at least every two months, and will be responsible for the day-to-day management of the trial.

The Chief Investigator has overall responsibility for the trial and shall oversee all trial management.

The data custodian will be the Chief Investigator.

DURATION OF THE TRIAL AND PARTICIPANT INVOLVEMENT

Trial Duration: The trial will continue recruiting until study end date. Participant follow-up will continue for approximately 18 months following the end of recruitment. Recruitment progress and timelines will be monitored against projected recruitment and overall trial timelines will be adjusted, as necessary.

Participant Duration: Individuals will participate in the trial for up to 18 months from initial consent to final follow-up: The COACH eligibility pathway could take up to 6 months, with a further 3 months from baseline and randomisation to treatment(T0), and primary outcome collection at 9 months post T0.

End of the Trial

The end of the trial will be the final database lock.

SELECTION AND WITHDRAWAL OF PARTICIPANTS

Recruitment

Potentially eligible participants will be identified through patient database searches of audiology clinics at sites and Participant Identification Centres (PICs) for patients who do not have a cochlear implant and who may meet the inclusion criteria for the trial based on their most recent audiometric assessment. Potential participants may also be identified through a

database search at a GP practice working as a PIC. The initial approach will be from the patient's usual care team or cochlear implant service which has previously assessed them for CI suitability and may involve NIHR Clinical Research Network staff to whom recruitment activities have been delegated by the local PI; this may be in person, via text or via a letter, patient information leaflet and expression of interest (EOI) form sent to the potential participant from the audiology department or GP practice where they are registered. Where an information pack is sent in the post, the full-length participant information sheet (PIS) and defined pre-screening questions may also be included, dependent on site preference.

If a patient has just been through the cochlear implant assessment pathway at a site and has been deemed as ineligible for a cochlear implant on the NHS, they may then be approached for the COACH trial. In this case, the potential participant will be given the EOI and leaflet and allowed time to consider joining the trial. Audiometry and speech scores from their recent assessment may then be used as part of their eligibility assessment for the trial, provided that the assessments were conducted by the participating site and meet the requirements of the trial eligibility assessments. These patients would not need to proceed with the full COACH eligibility pathway and some tests need not be repeated if they have been performed within the last 3 months. An audiometric assessment will need to be repeated at the baseline visit for all participants to ensure they are still eligible for the trial before being randomised. The Phoneme score on the AB Word test in quiet at 70 dBA will not be repeated at the baseline visit, in line with standard clinical practice. This test will only be administered once, either at the consent visit or at a previous clinical appointment, as long as any previous assessment was conducted within 3 months of the consent visit.

Potential participants will also be able to self-refer for trial eligibility assessment, using an online EOI form, or by contacting a member of the trial team for a paper form. Opportunistic recruitment will be facilitated through advertisements placed in clinical areas within recruiting audiology services and PICs. The trial will be advertised through charities such as the Royal National Institute for Deaf People, patient organisations such as the National Cochlear Implant Users Association, National Association of Deafened People and through Twitter, Facebook and social media discussion groups related to HAs and CI candidacy. Advertisements in national press and social media may also be used.

All interested potential participants will need to complete the EOI, either paper or online, in order to be pre-screened by a member of the research team. They will be made aware that by returning the EOI, any non-identifiable demographic information collected on the form or during a further pre-screen will be stored on a secure database for administration purposes. Anonymised data will also be used to inform trial screening information for central monitoring and reporting. The NCTU will receive all EOI forms and securely share the information with the preferred site(s) specified by the individual on their form. Any person who submits the EOI will be sent the full-length version of the PIS by a member of NCTU or a local site (if not already sent).

The researcher (delegated member of the trial team at local site) will contact the potential participant for remote pre-screening. To facilitate communication, contact will be made in a medium that the potential participant has stated as accessible for them on the EOI form (e.g., voice or video call, text, email). The researcher will give the potential participant an opportunity to ask questions about the trial and will ask a pre-defined set of trial pre-screening questions to check if the participant fits the inclusion and exclusion criteria that can be checked remotely. Screening information will be collected and recorded by NCTU and sites through all stages of participant identification. It will be made clear to potential participants in the supporting documentation that the data used from EOI forms and remote pre-screening will be used for trial monitoring purposes. They will be informed that the answers to the pre-screening questions will be recorded for the purposes of monitoring of trial screening. By returning the EOI form and undertaking remote pre-screening, the participants will be consenting to their data being used in this way.

If an interested individual is still potentially eligible after the remote pre-screen, they will be invited for a consent visit.

The pre-screening can take place face to face if necessary (e.g., potential participants' difficulties with remote communication, or opportunistic recruitment). However, if the pre-screening takes place in person, the PIS must be given to the participant a minimum of 48 hours before the pre-screening, in order for the consent visit to be offered immediately following a successful pre-screen (to reduce participant burden of travel and to allow sufficient time to fully consider consent).

During the consent visit, the researcher will inform the potential participant of all aspects pertaining to participation in the trial. It will be explained that entry into the trial is entirely voluntary and that their treatment and care will not be affected by their decision. It will also be explained that they can withdraw at any time without giving a reason. In the event of their withdrawal, it will be explained that their data collected so far will be retained and that these data may still be used in the final analyses.

If needed, the usual hospital interpreter and translator services will be available to assist with discussion of the trial, the participant information sheets, consent forms, and training sessions/information. However, consent forms, information sheets, trial information and participant questionnaires will not be available in languages other than English, as participant's ability to read and understand English will be essential for primary outcome collection, and completion of the secondary outcomes collected via questionnaire. To comply with the Welsh Language Act, Welsh translations of the PIS will be made available, however the outcome assessments cannot be translated.

Eligibility criteria

Inclusion criteria

- Adults, aged 18 years or older
- Patients with a severe sensorineural hearing loss in both ears. "Sensorineural" is defined as the absence of a conductive hearing loss, which itself is defined as an air-bone gap of 20 dB or greater averaged over 0.5, 1, and 2 kHz, or as many of these frequencies as an air-bone gap can be calculated for. In the absence of any measurable air-bone gaps at 0.5, 1, or 2 kHz due to the limits of the audiometer, a sensorineural loss may be confirmed by a tympanometry trace within normal limits, as described in the British Society of Audiology Recommended Procedure for Tympanometry (2013). "Severe" is defined as pure-tone audiometric threshold equal to or greater than 70 dB HL at 2 or more frequencies including 500 Hz, 1,000 Hz, 2,000 Hz, 3,000 Hz and 4,000 Hz bilaterally without acoustic HAs
- Patients with appropriate HA devices and prescriptions, with a minimum of:
    - 6 weeks having elapsed since any significant change to a prescriptive gain of >5 dB in gain averaged across the frequencies 250Hz to 6000Hz, where it is possible to reach prescriptive gain targets generated by standardised target rules such as NAL-NL2, DSL v5. If the prescriptive target at any frequency cannot be met despite the maximum gain of the hearing aid being delivered, this frequency can be ignored as a contributor to the average as insufficient change can be effected.
    - 0 weeks having elapsed since any other changes to hearing aid parameters deemed not clinically significant
- Patients with a phoneme score <60% on the AB Word test when tested in quiet at 70 dBA with acoustic HAs
- Patients in whom history, examination and pre-operative imaging suggests a healthy middle ear in the ear to be implanted, and a structurally normal and fully patent cochlea with no evidence of a widened vestibular aqueduct

- Patients for whom unilateral cochlear implantation is not recommended by NICE either because they do not meet the definition of severe to profound deafness (pure-tone audiometric threshold equal to or greater than 80 dB HL at 2 or more frequencies between 500 Hz, 1,000 Hz, 2,000 Hz, 3,000 Hz and 4,000 Hz), or because they meet the definition of adequate benefit from HAs (a phoneme score ≥50% on the AB Word test when tested in quiet at 70 dBA with acoustic HAs), or both (as per recommendation 1.5, NICE TA566)
- Patients who are capable of speaking and understanding the English language
- Patients who are capable and willing to provide written informed consent

Exclusion criteria

- Patient characteristics falling outside the indications for use of the trial devices as per their CE marking
- Inability to undergo speech perception testing and/or inability of audiologist to obtain an accurate measurement of speech perception abilities
- Patients who would not be able to adhere to trial procedures or complete the trial questionnaires
- Patients whose hearing loss is suspected or confirmed to be wholly or partly unexplained by anatomic or physiologic abnormalities (non-organic hearing loss)
- Patients who have a congenital profound hearing loss (no measurable or aidable hearing in both ears from birth)
- Any known factor that may restrict full insertion of the electrode array
- Patients with any known contraindication for cochlear implantation
- Patients whose primary concern is the suppression of tinnitus
- Patients in whom cochlear implantation would present an unacceptable risk to balance function
- Any serious concerns about medical fitness for surgery or cochlear implantation
- Participation in other research related to hearing loss while participating in the trial (i.e., until collection of the primary outcome), including research that involves any changes to or use of hearing devices, changes to hearing care/management, or duplication of trial outcome assessments

It is possible that a participant's hearing loss may progress to the extent that cochlear implantation would be recommended as per NICE Guidance TA566. If this arises before they have been randomised in the trial, the participant would become ineligible for trial participation and would be free to access CI services on the NHS. The participant would not be randomised as they would not meet eligibility criteria at the point of randomisation. If this situation arises after randomisation, the participant would remain in the trial for as long as they had not withdrawn their consent. If it is found that a participant has become eligible for a CI on the NHS at any stage of their participation in the trial, they will be informed of this.

All efforts will be made to continue follow up procedures and further treatment details would be collected (for example, if a participant had a CI procedure prior to the end of the 9 month period post treatment activation).

Similarly, as hearing loss is often a progressive condition for this population, it is possible that potential participants initially found to fall outside COACH eligibility due to having either better audiometric thresholds and/or phoneme perception scores when first assessed could progress to being within COACH eligibility during the period of trial recruitment. Based on analyses of clinical data, adults whose hearing was initially too good to meet COACH eligibility criteria can be reassessed for COACH eligibility if 9 or more months have elapsed since their previous COACH eligibility assessment. The appropriateness of being given the offer of COACH eligibility reassessment will be determined on a case by case basis at the clinical discretion of

research staff at sites. Potential participants are free to choose whether or not to accept the offer to COACH eligibility reassessment

Expected duration of participant participation

Trial participants will be participating in the trial for approximately 18 months. When a participant has completed the trial, their healthcare will continue as normal at their local care centre who will decide their ongoing care. For up to 2 years after receiving their new hearing aids and/or cochlear implant, ongoing support will be provided for adjustments and/or repairs by the manufacturer. After that period, their care will continue under the NHS.

Participant Withdrawal

Withdrawal from the trial

Any patients that request to withdraw their consent **prior to randomisation** will be withdrawn completely from the trial; they will not be randomised, and follow-up questionnaires will not be issued.

Participants may discontinue participation in the trial or from the intervention(s) at their own request. If a participant wishes to discontinue use of the trial interventions (or further standard care related to the interventions), they may do so, but follow-up will continue in the normal way unless the participant chooses to discontinue from all aspects of the trial. It will be explained to participants that cochlear implantation surgery is irreversible. Whilst participants will be able to discontinue with any trial related activities at any point, they will not be able to reverse the surgery if they are randomised to the CI group and have the surgery. In exceptional circumstances, it may be appropriate for the local PI to withdraw participants from the trial, e.g., if the participant has lost capacity and their ongoing informed consent can no longer be assumed.

Participants will be made aware that discontinuation from either treatment or follow-up will not affect their future care. Participants will be made aware (via the PIS and ICF) that should they withdraw, the data collected will be retained and may still be used in the final analysis.

Participants who withdraw after randomisation will not be replaced and all data collected up to the point of withdrawal will be used in the analysis.

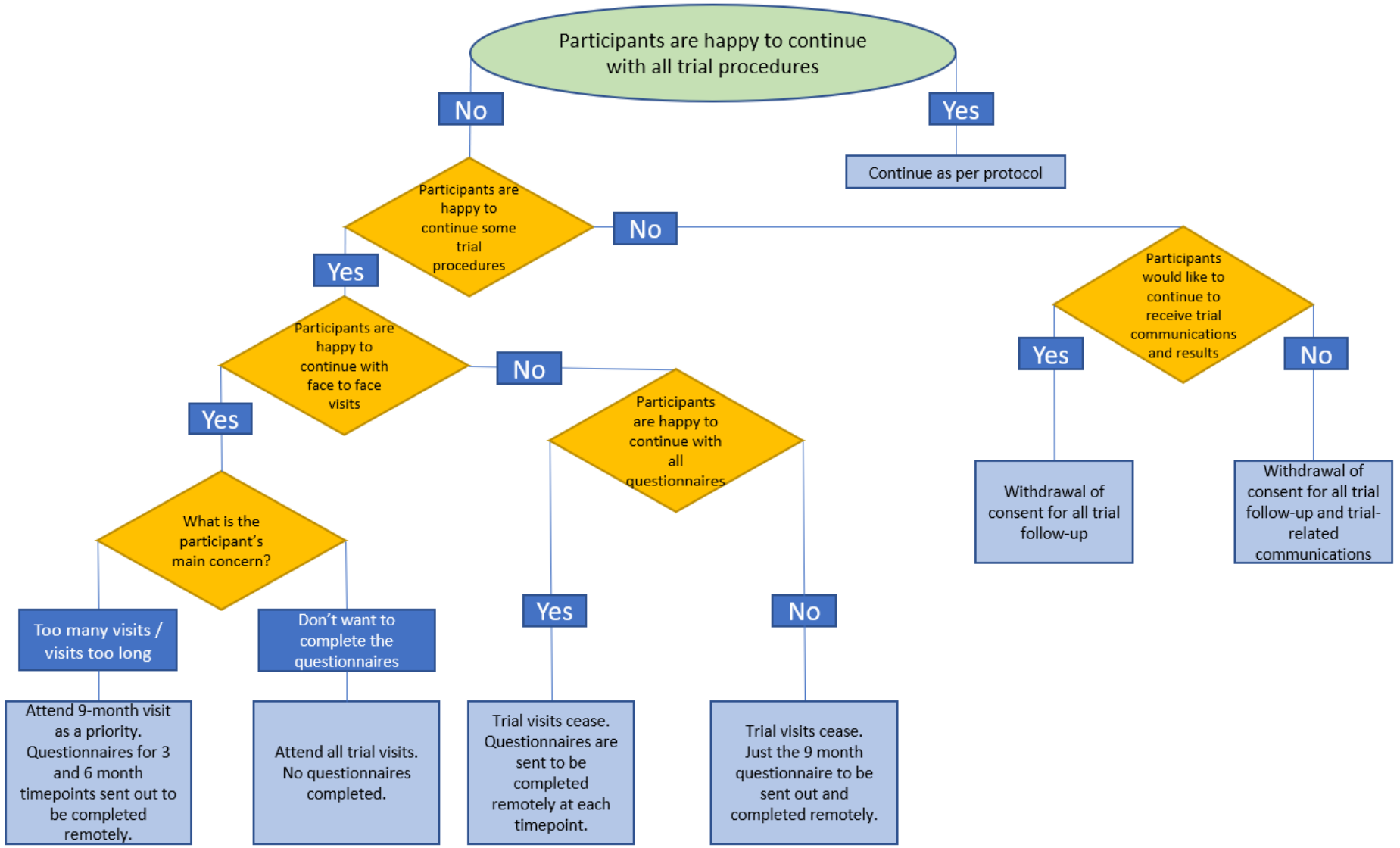
Discontinuation from trial follow-up/other trial-related activities post randomisation

Participants may withdraw their consent for follow-up and/or other trial-related activities or from receiving trial-related communications. The NCTU must be informed of all requests by participants to stop their involvement in the trial; appropriate action will be taken to ensure that the participant's wishes are followed. Data which has already been collected for these participants will be included in trial summaries and analyses.

Participants can request to stop receiving trial communications such as visit reminder texts, phone calls, letters, or emails. Trial results will also be sent to all participants who agreed to receive these at the consent visit, unless a specific request is received to discontinue them from receiving trial results.

Sites will be trained to determine which activities participants may wish to discontinue with by following the flowchart below in Figure 2.

Figure 2: Participant discontinuation flowchart



Informed consent

Following pre-screening, potential participants will be invited to attend an initial face-to-face consent visit and the beginning of the eligibility assessment process will take place. Informed consent must be obtained prior to any trial specific data collection, or commencement of formal trial eligibility assessment.

Throughout this visit the potential participant will be given the opportunity to ask questions. Written informed consent can be obtained by the PI or delegated members of the local research team, from here on referred to as 'the researcher' (as captured on the site delegation log). It remains the responsibility of the PI to ensure informed consent is obtained appropriately.

A PIS will be provided to the potential participant prior to the appointment to facilitate the process of obtaining informed consent. The researcher will ensure that they adequately explain the aim, trial treatment, anticipated benefits and potential hazards of taking part in the trial to the potential participant. They must also stress that there is no evidence for superiority of CI over HAs in this population, and that despite going through the CI assessment process to assess overall trial eligibility (the COACH eligibility pathway), they have an equal chance of being randomised to either treatment arm. The researcher will also emphasise that participation is voluntary and so the potential participant is free to decline participation and may withdraw from the trial at any time.

The potential participant will receive the trial PIS following remote pre-screen (if not prior) and will be given adequate time to read the trial information, ask any questions and discuss their participation with others (i.e., family members, GP, or other healthcare professionals outside of the site research team), before attending the consent visit. Adequate time from pre-screen to consent visit is defined as at least 48 hours from initial pre-screening (unless the pre-screen takes place in person and the PIS was given a minimum of 48 hours prior).

If the potential participant wishes to proceed into the trial, once all their questions have been answered, they will be asked to sign and date the latest version of the ICF. The researcher must talk the participant through each point on the ICF, and the participant much initial each point indicating that they are giving fully informed consent for each element of the ICF. The researcher will then sign and date the form.

One copy of the ICF will be given to the participant, one copy will be filed in the medical notes, one copy will be electronically uploaded to the trial database for central monitoring by NCTU, and the original will be placed in the Investigator Site File (ISF). Once the participant is entered into the trial, the participant's unique trial identification number will be entered on the ICF maintained in the ISF.

Details of the informed consent discussions will be recorded in the participant's medical notes. This will include date of discussion, the name of the trial, version number of ICF signed and the date consent received. Where consent is obtained on the same day that the trial related assessments are due to start, a note will be made in the medical notes as to what time the consent was obtained and what time the procedures started.

The consent visit is expected to take place in person. However, it may be appropriate under certain circumstances for this to take place remotely, for example, where clinical records of recent audiological and speech test measures can be consulted by the researcher to confirm likely eligibility on these grounds, or where a face-to-face visit is not possible at the time (e.g., in a pandemic situation). Certain aspects of eligibility assessment could then proceed to take place remotely, in line with local standard practice at the time, where feasible and clinically appropriate to do so. However, an updated audiogram and speech test measures would have to be taken by the local researcher to confirm full eligibility prior to randomisation into the trial.

E-consent is able to be used for this trial via the trial database. The ICF can be opened directly from the trial database, or a link can be sent to the participant by email. The researcher will

still talk the participant through each point on the ICF, either in person or over the telephone if the participant has been emailed the link, and the participant must tick each statement to indicate that they are giving fully informed consent for each element on the ICF. The participant would then e-sign the form, which is verified by the researcher (countersigned). A copy of the fully signed ICF is then sent automatically to the participant and the trial site by email. A copy will need to be printed for filing in the participant's medical notes and one for the ISF.

For those participants that do not have an email address or access to a computer, telephone consent will instead be received. During the consent call, the potential participants will be asked to give explicit verbal agreement to the same statements as appear on the ICF (which will be sent to the participant via the post). The researcher will talk through every point and answer questions from the participant. The researcher will mark each item on the form as agreed by the participant. The details of the researcher receiving consent will be logged within the online system. The researcher will complete and sign the telephone consent section of the consent form to indicate consent was obtained verbally over the telephone. A copy of this consent form will be uploaded to the trial database, a copy filed at site and another copy posted to the participant.

Full written consent will be received from the participant at the earliest convenience and before randomisation takes place. For participants whom consent was initially received via telephone, the written informed consent section of the original ICF will be signed by both the participant and the person receiving consent at the time of the written informed consent discussion. Following full written consent, the copies of the ICFs will be saved and disseminated as described above.

Consent will be re-confirmed verbally ahead of randomisation. There will be no less than two weeks from the initial eligibility assessment visit to provide adequate time for the participant to consider their participation in the trial. The consent reconfirmation study conversation will be supported by a shortened version of the trial PIS, covering only trial activities that take place after randomisation. The researcher will record re-confirmation of consent in the participant's medical notes and in the eCRF. Following randomisation, a letter will be sent to the participant's GP informing them about trial enrolment. GPs will be asked to contact the research team if they have any questions or to let the research team know if there is any reason why a participant is unsuitable for the trial. The GP may also request a copy of the ICF for their records.

Throughout the trial, the participant will have the opportunity to ask questions about the trial. Any new information that may be relevant to their continued participation will be provided. Where new information becomes available which may affect the participants' decision to continue, participants will be given time to consider and, if happy to continue, will be re-consented. Re-consent will be documented in the medical notes. The participant's right to discontinue from any/all parts of the trial will remain.

Electronic copies of the PIS and ICF will be made available from the NCTU and will be printed or photocopied onto the headed paper of the local participating sites. Details of all participants approached about the trial will be recorded on the trial screening log.

Ensuring Quality in Recruitment / Consent Procedures

Prior work (Donovan et al., 2016) has demonstrated that trial performance can be improved by adopting a systematic approach to monitoring and supporting recruitment and consent procedures. This would seem pertinent for COACH given that many audiology staff and services are likely to be relatively inexperienced in research processes and regulations.

Issues of equipoise might be also pertinent for COACH recruitment and consent. Our patient research partners group has expressed a concern about communicating realistic expectations about the benefit of CI at recruitment. More generally, it has been argued that difficulties of

equipoise are more pronounced where surgical and non-surgical treatments are being compared (McCulloch et al., 2002 and Cook et al., 2008).

In each recruiting site we will:

- Monitor recruitment rates to identify sites that are experiencing difficulties.
- Review local recruitment and consent procedures to identify any procedural issues.

NCTU will provide training on the ideal consent conversation and the importance of equipoise. All site staff who will be receiving consent for the trial will need to complete this training before being delegated to receive consent on the delegation log. Where necessary, the NCTU will provide additional training and support to sites, and trial managers and researchers will visit to support local troubleshooting.

In each recruiting site at an early stage of trial involvement, local recruitment and consenting procedures will be audited and reviewed by a member of the COACH team. An important element of this will be the observation of consent visits. A fidelity checklist will be provided by NCTU to be used at site during each consent conversation. These checklists will be reviewed with individual recruiters as well as with site teams.

On some occasions (following observed good or poor practice) the COACH team may seek to audio record several subsequent interactions to support the generation of training materials. In these cases, permission will be sought, and documented in writing on a recruitment intervention ICF, from both the staff member and the potential participant involved.

Review of fidelity checklists and any recorded interactions will support the generation of training materials to support on-going COACH recruitment. This will also provide insight for other audiology research studies.

TRIAL TREATMENT AND REGIMEN

A participant pathway flowchart illustrates details of trial visits (Trial Flowchart). A summary of research assessments is also provided in Appendix 1: Schedule of Assessments.

COACH Eligibility Pathway

After informed consent is received, the participant will start to be assessed for trial suitability. This is likely to start at the consent visit, and will include assessment of audiometry, AB word test at 70 dBA, medical history, and a HA fitting and HA usage check. These latter checks will be used to determine whether the potential participant has received standard care for severe hearing loss on the UK NHS, i.e., the provision of up-to-date acoustic HAs bilaterally or unilaterally as appropriate. Any potential participant found not to have received current standard care will be referred back to their local audiology department for a HA assessment. Such patients may be rescreened for trial participation a minimum of 6 weeks after a significant change to prescriptive gain amounts of >5dB change in gain averaged across 250Hz to 6000Hz. If any other changes to hearing aid parameters are deemed not clinically significant, then no acclimatisation period is required.

The AB Word test in quiet at 70 dBA will only be administered at the consent visit and will not be repeated at the baseline visit. This choice is to ensure that the use of the AB Word test to assess eligibility aligns with its use in routine clinical care, where meeting the AB word test criterion defined within NICE guidelines at one timepoint is sufficient to proceed to cochlear implantation, if all other criteria are met.

At this point in the eligibility pathway, trial sites may use their own speech testing equipment, or equipment supplied by the COACH co-ordinating centre for use to administer the trial

eligibility and outcome assessments. If the trial sites use their own equipment for eligibility assessments, those assessments must meet the requirements of the trial assessments, including calibration records for the equipment, details of the test materials presented and the responses of the patient. The test must be completed either on the date of the consent visit or within the previous 3 months.

Throughout the trial, should there be a need to minimise face-to-face visits (e.g., due to a pandemic), any aspects of the COACH eligibility pathway that are both clinically appropriate and feasible to take place remotely can be introduced by sites, using any appropriate remote consultation IT systems that are provided by their Trust for use in routine practice.

If on the basis of above initial suitability checks the potential participant is still deemed potentially eligible, the COACH eligibility pathway will proceed according to current local standard procedures for CI suitability at each trial site. The CI suitability process is a multi-disciplinary process which includes a variety of wellbeing and physiological checks, including imaging, and a variety of health care professionals including audiologists, speech and language therapists and ENT surgeons. The COACH eligibility pathway will conclude with a decision of suitability for cochlear implantation made by an MDT.

Participant eligibility, as confirmed by agreement from the MDT, will need final sign off by a CI surgeon delegated the responsibility on the trial delegation log. Participants confirmed eligible will be invited to a baseline visit. All participants must be assessed and confirmed as eligible to receive a CI prior to randomisation to either arm.

Baseline Visit

Participants who complete the COACH eligibility pathway and who are determined to be eligible for all trial interventions will be invited to attend a baseline visit. This visit will take place before any interventions are delivered. The visit will take the form of a face-to-face assessment at trial sites. After consent is reconfirmed, a set of baseline assessments will be administered (Appendix 1). The baseline assessments will comprise tests of the participant's ability to hear sounds (a routine hearing test), their ability understand parts of or whole individual words and whole sentences in quiet listening conditions (speech tests in quiet), and their ability to understand whole sentences when a background noise is present (speech test in noise). The participants will also be asked to complete the trial questionnaires at this visit.

There will be separate clinical WPDs for sites to follow that will define the parameters and requirements of the speech tests and will define what constitutes 'noise' and 'quiet'. The trial team will help sites with test set-up and will also perform routine checks to ensure the test conditions and parameters are correct.

Each test will only be performed once at the baseline visit and repeated administrations of the same test within the baseline visit are not permitted. If the results of the baseline assessments indicate that the participant is ineligible to participate in the trial, their eligibility will not be reassessed and they will not be randomised for the trial.

If a participant's hearing changes considerably between consent and baseline visits (>= +/-15dBHL), and hearing aids need to be adjusted, all eligibility checks must be repeated before entry into the trial.

The visit will be carried out by a qualified audiologist and conducted in hearing assessment facilities at trial sites that are used for routine NHS hearing tests and hearing-related assessments. Questionnaires will be self-administered although the audiologist will be on hand to answer any queries about their completion. The participant will be randomised following completion of all the baseline assessments.

Intervention group

Following the baseline visit, participants in the intervention arm will attend a meeting of the multi-disciplinary clinical team at which surgical consent will be obtained by a participating CI surgeon to whom that responsibility has been delegated, and at which the MDT will confirm the choice of ear to be implanted based on clinical judgement. All participants will be offered a danalogic GN HA for the ear that will not be implanted. If taken up, the HA will be fitted in line with standard practice at site for a contralateral HA and no later than 6 months following CI activation. All participants will be encouraged to continue to use their HAs in the period before surgery, and in their non-implanted ear following surgery.

It is our expectation that Cochlear implantation surgery occurs within 3 months following randomisation. Unilateral cochlear implantation will be provided in accordance with the quality standards of the British Cochlear Implant Group (BCIG 2018, or latest available version). Participants will attend for surgery on the designated date. This surgery is routinely undertaken on a day case basis in many hospitals, but the participant will be advised as to whether an overnight stay of 1 or more nights will be required or is anticipated.

The choice of CI system will be restricted to the trial devices, which are those manufactured by Cochlear™ Ltd and the most appropriate device for patients with significant residual hearing in the implanted ear. Sites will need to specify the trial devices that each participating surgeon routinely implants. Routine is defined as at least 5 implantations performed per year. NCTU will keep a log of which sites are implanting which devices. Any changes to the pre-specified choice of device will need to be discussed with the NCTU. A surgical protocol will be defined prior to start of recruitment in consultation with CI surgeons, such as those involved in the trial setup, and departures from the protocol will be permitted only where clinically necessary and will be captured via the trial documentation.

Following the implant surgery, a date for initial implant activation will be arranged, which defines first treatment activation for participants in the intervention arm. Initial implant activation will be conducted by a qualified audiologist and involves fitting the sound processor component of the implant system and switching on the implant for the first time. Recipients will all be issued with the latest model(s) of sound processor provided routinely by the participating sites at the time of their first treatment activation and will have access to device accessories. The number and choice of accessories offered to trial participants will follow current routine practice across the participating sites.

Participants will then be scheduled to attend the trial site on multiple occasions throughout the 9 months following initial activation for follow up visits. The research visits for the intervention group may coincide with routine care appointments, as per the standard care at each CI site (e.g., fitting appointments with audiologists and auditory rehabilitation and communication training). The timing of these visits will be based on the routine post-cochlear implantation care pathway for adults at each trial site. Trial research visits at which outcomes will be assessed have been designed to align with these fitting appointments, all of which are conducted by qualified audiologists. Trial sites may choose for some or part of the post-operative care pathway to be carried out remotely using telehealth systems to reflect routine practice at that time.

Comparator group

Those randomised to the HA group will be offered bilateral danalogic GN acoustic HAs. While the HAs of all participants will have been confirmed as being appropriate for their hearing loss as part of the eligibility assessment, devices available on the NHS may not reflect the very latest available HA technology. Therefore, as with the CI group, patients in the HA group will have access to the most recent HA technology from GN Hearing UK.

If the new HAs are taken up, a fitting appointment will be scheduled within 4 months of the date of randomisation. For those who elect not to take up new HAs, a HA optimisation appointment will be conducted within 4 months of randomisation to ensure their devices are not only appropriate to their hearing loss but also optimally configured to meet their individual needs. Both fitting and optimisation appointments will take place at facilities used routinely for HA fitting and/or assessment at trial sites and will be carried out by a qualified audiologist.

Fitting and optimisation of trial devices

All trial devices (HAs and CIs) will be fitted following standard manufacturer guidance and to the clinical standards established for routine provision within the UK NHS. Trial fitting protocols for HA and CI devices will be agreed across the participating clinical sites. Departures from the trial fitting protocols will only be permitted where clinically necessary and will be captured via the trial documentation. The availability and choice of accessories will follow current standard practice across the participating sites. Data logging will be enabled on all trial devices and the participant informed that the trial devices will record information about the duration of use and the environments in which they use their devices.

For both the intervention and comparator groups, uptake of the new HAs will be suggested but will not be mandatory as clinical experience is that some patients display a strong preference for the sound of certain models of HA and mandating a change of device in these patients could have negative effects on device satisfaction and usage.

All participants in both the intervention and comparator groups will be offered follow-on in-person or remote support within 1 week of HA fitting (for those who take up new HAs) or optimisation (for those who elect to continue using their existing HAs) by a qualified audiologist. Short-term post-fitting follow-up is designed to identify and resolve any initial difficulties promptly. Ad-hoc face-to-face support from an audiologist at the trial site will also be arranged as and when required.

Research outcome collection schedule

The outcomes of participants in both the intervention and comparator arm will be assessed at the same series of timepoints defined relative to the date of first treatment activation (Trial Flowchart): 1 month, 3 months, 6 months, and 9 months (within a window of +/- 2 weeks at each timepoint). The 1-month visit will comprise self-administered questionnaires only and will therefore be carried out in the participant's home. All other outcome collection timepoints will require participants to attend the trial site for assessments that will be conducted at facilities used routinely for hearing assessments and by a qualified audiologist.

Questionnaires will be completed on paper by participants at each timepoint. Data from the completed questionnaires will then be entered into the eCRF by sites, except for the 1-month questionnaire that will be posted directly to NCTU by the participants and subsequently entered into the eCRF by NCTU staff. We will offer and use all methods of delivery of reminders and for the monthly usage checks including postal mail, e-mail, web-based, telephone and SMS text for participant follow-up. Data received from participants will only be received onto password protected devices and accounts. Any SMS texts sent will be done from trial mobile phones held by NCTU and research audiologists at sites, locked with passcodes. At any time during follow-up, trial participants will be able to contact the trial management team at the NCTU for assistance with the questionnaires as well as their trial site (for technical support or clarification). The trial management team will send reminders (via telephone, text message, letter or email) to participants that questionnaires are ready for completion and will follow up (via telephone, text message, letter or email) outstanding questionnaires to achieve maximum completion. We understand participants' life circumstances may change throughout the duration of the trial follow-up. Site staff may contact unresponsive participants by post where necessary, using appropriately sensitive communication developed with PPI colleagues.

Primary outcome

The primary outcome will be a measure of speech understanding, the perception of phonemes as quantified by the phoneme score on the AB word test (Boothroyd, 1968) presented at 60 dBA, in the best-aided condition (i.e., using the devices that the participant considers will help them hear as well as possible), at 9 months post first treatment activation (intervention arm: first CI activation; comparator arm: first HA fitting/optimisation) measured by independent

blinded assessors. Each stimulus will be presented once from a loudspeaker and participants will be instructed to repeat as much of each word as they could hear, even if they only heard part of the word and even if the word does not make sense to them. No time limit will be placed on participants to respond to each stimulus. The test will be administered by a qualified audiologist, who will proceed to present each stimulus only when the participant is facing the loudspeaker and is attentive.

The test will be scored live by the audiologist administering the test at all timepoints with no feedback given to the participant at any point in the testing procedure. Following standard practice, the audiologist may ask the participant to repeat or clarify their response if their initial response is deemed to be inaudible or unintelligible. Audio-visual recordings of the participant performing the test will be made and post-processed to occlude the devices worn by the participant. The resulting occluded recordings will be scored by two independent assessors who will be qualified audiologists with experience of administering and scoring clinical speech perception tests with patients with severe hearing losses. These independent assessors will be blinded to treatment arm and assessment timepoint. Disagreement in scores will be resolved by consensus, failing which a third independent assessor will adjudicate using the video recordings.

Secondary outcomes

- Secondary clinical outcome measures in this trial are:
- *Phoneme perception (AB Word test at 60 dBA) (3, 6 and 9 months following first treatment activation), assessed live by the audiologist*
- *Word perception (AB Word test at 60 dBA) (3, 6 and 9 months following first treatment activation)*
- *Phoneme perception (at 70 dBA) (9 months following first treatment activation)*
- *Word perception (at 70 dBA) (9 months following first treatment activation)*
- These tests will be carried out as described for the primary outcome with the exception that only live scoring by the audiologist administering the test will be used and at 9 months a test at 70 dBA will be performed.
- *Sentence perception in quiet (3, 6 and 9 months following first treatment activation)*
  Sentence perception in quiet will be assessed in the best-aided condition by administering the BKB sentence test (Bench et al., 1979). Sentences will be presented from a loudspeaker and the audiologist will determine the proportion of words repeated correctly by the participant. Different sentence lists will be used at each administration with no list presented more than once to the same participant. The test will be scored live by the audiologist administering the test with no feedback given to the participant at any point in the testing procedure.
- *Sentence perception in noise (3, 6 and 9 months following first treatment activation)*
  Sentence perception in noise will be assessed in the best-aided condition by administering the BKB sentence test while a speech-shaped background noise is presented at the same time and from the same loudspeaker. The relative levels of speech and noise will be varied adaptively based on the accuracy of the participant's responses to estimate a speech reception threshold, defined as the signal-to-noise ratio at which participants can report 50% of sentences correctly. An accurately reported sentence is one in which all key words are repeated correctly by the participant. The test will be scored live by the audiologist administering the test with no feedback given to the participant at any point in the testing procedure.
- *Device usage (device logging)*
  Statistics on device use will be obtained from the data logging features of the trial devices (CIs and HAs). The statistics will include the duration that the devices have been used and information about the nature of the acoustic environments in which the devices have been used. Data will be extracted from the trial devices directly at in-person assessments 3, 6, and 9 months following first treatment activation. Data could also be

downloaded using the standard remote capabilities of the devices, for those using the trial devices and where the participant chooses to use them.

Secondary participant-reported outcome measures in this trial are:

- *Self-reported difficulty with listening*
  Participant-report difficulties with listening in everyday life will be assessed by administering the Speech, spatial, and qualities (SSQ12) scale (Noble et al., 2013).
- *Listening effort and fatigue*
  Self-reported listening effort and fatigue will be measured using the Effort Assessment Scale (EAS) (Alhanbali et al., 2017) and the Fatigue Assessment Scale (FAS) (Michielsen et al., 2003), respectively. The trial will also include the administration of the Listening Effort Questionnaire-Cochlear Implant (LEQ-CI)* (Hughes et al., 2019).
- *Tinnitus*
  The impact of tinnitus on everyday life will be assessed via the Tinnitus Functional Index (TFI) (Meikle et al., 2012), a measure of tinnitus severity that has been validated in a UK audiology population (Fackrell et al., 2018). Tinnitus loudness will be assessed via the visual analogue scale of loudness (VAS-L). Participants mark the loudness of their tinnitus at any point along the numerical scale, with word descriptors utilised as anchor points at 0 for “extremely weak,” 30 for “moderate,” 50 for “strong,” 70 for “very strong,” and 100 for “extremely strong” tinnitus loudness.
- *Mood*
  Depression and anxiety symptoms will be assessed by administering the Hospital Anxiety and Depression Scale (HADS) (Bjelland et al., 2002).
- *Hearing-specific quality of life*
  The impact on aspects of quality of life that are of direct importance and relevance to people with hearing loss will be assessed by administering the Nijmegen Cochlear Implant Questionnaire (NCIQ) (Hinderink et al., 2000). The impact on aspects of quality of life related to access to sound in both ears (bilateral/binaural hearing) will be assessed by administering the York Binaural Hearing-Related Quality of Life (YBHRQL) questionnaire (Goman, 2014). The emotional and social impacts of hearing loss will be assessed using the Hearing Handicap Inventory for Adults (HHIA) (Newman et al., 1990).
- *Health-related quality of life*
  Health status will be assessed by administering generic quality of life questionnaires (EuroQol EQ-5D-5L (Herdman et al. 2011), Health Utilities Index Mark 3 (HUI3) (Horsman et al. 2003). An additional generic measure of QoL – the ICEpop CAPability measure for Adults - (ICECAP-A) (Al-Janabi et al., 2012) that incorporates more social aspects well-being will also be administered.
- *Global ratings of change*
  At each follow up appointment following first treatment activation, participants will be asked to indicate on 7-point Likert scale ranging from ‘Much Worse’ to ‘Much Improved’ whether their hearing and quality of life have improved or worsened (Copay et al., 2007). They will be asked to make these judgements relative to two anchor points: (1) immediately prior to first treatment activation; and (2) since the last trial appointment.
- *Device usage (self-report)*
  Participants will be contacted to self-report the average number of hours of daily use each month up to and including 9 months following first treatment activation.

All patient reported outcomes will be administered at baseline and at 1, 3, 6, and 9 months after first treatment activation. In addition, the visual analogue scale of tinnitus loudness will be assessed on the day of first treatment activation immediately before and after activation.

*Data to be collected using LEQ-CI questionnaire once licence is in place

Other Assessments

To enable both groups to be described on all clinically relevant metrics in the trial reports, the aided and unaided audiometric thresholds of all participants will be measured at first treatment activation and at 3, 6 (unaided only), and 9 months following that time point. Trial-specific clinical procedures for the measurement of audiometric thresholds will be provided in a WPD.

The Hearing Impaired Montreal Cognitive Assessment (HI-MoCA) test (Nasreddine et al., 2005), (Lin et al., 2017) will be administered at baseline to describe cognitive health of trial participants.

Concomitant and Rescue Medications and Treatments

There are no specified concomitant medications/treatments or any rescue medications for this trial.

Compliance

Compliance with the trial interventions will not be assessed. The duration and frequency of use of CIs and HAs varies based on the individual patient's daily requirements for access to sound, and no standard for acceptable compliance can be applied. Use of the trial devices will be recorded as outcomes via both device logging and patient-report. The data logging data will be captured by the fitting software each time participant devices are connected to the fitting software in the clinic at site. CI function, programming parameters and data logging data from fitting software will be exported and captured in order to monitor AEs including device insertion and active electrodes, and to obtain device usage data. Data logging could also be downloaded using the standard remote capabilities of the devices, for those using the trial devices and where the participant chooses to use them. In some instances, data logging may not be possible for those participants who have other devices (e.g., their own HAs).

Compliance with allocation of trial intervention (i.e., whether participants randomised to CIs received them and whether participants randomised to standard care received HAs) will be recorded. Participants in the CI arm will be considered adherent to treatment allocation if they receive a CI during the trial. Participants in the HA arm will be considered adherent to treatment allocation if they do not receive a CI during the trial.

Accountability for devices

The PI, or delegate, will ensure that all devices are stored in a secure area under recommended device storage conditions as per the manufacturer's guidance and following local practice.

To ensure adequate records, all devices will be accounted for in trial records maintained by site and communicated to the NCTU. There is not expected to be any remaining HAs, sound processors or implants left at the end of the trial, as stock of these devices at each site will be in line with the actual number of participants randomised at that site. At the end of the clinical trial all unallocated, unused, or returned consumables used for 'spares and repairs' will be integrated into local stock, destroyed or returned to the funder (or its appropriate agent), as per the funder's wish at the end of the trial.

Criteria for terminating the trial

The trial may be stopped at any time, or one centre terminated if new information becomes available causing major safety concerns, or if there are issues with trial conduct or lack of recruitment. All participants recruited up to this point would still be followed up. This decision will be made from discussions between the TMG, DMC and TSC and the sponsor, and communicated to the funder.

Details of diagnostic or therapeutic ionising radiation

Exposure to ionising radiation with be in line with local standard practice: This will be maximally one exposure during the COACH eligibility pathway for all consented participants, and one exposure after implantation for the intervention arm only. There may be additional imaging as part of routine care.

COACH eligibility assessment: Imaging is done as part of CI suitability assessment. Most NHS CI programmes use 1 MRI scan of the head for pre-operative assessments for CI surgery, which would not include exposure to ionising radiation. However, some sites may alternatively use a CT scan or an Xray for CI suitability assessments as part of their standard care.

Post-operative: X-rays, CT or cone beam CT scans are standard practice in most NHS sites for post-operative assessments for CI surgery. As the participants in this trial would not otherwise be eligible for CI surgery under current criteria, they would not be exposed to the additional radiation from these scans associated with standard care. Participants in the intervention arm will receive 1 post-operative X-Ray, CT or cone beam CT scan of their head if this is normally completed in a trial site following CI surgery.

If a potential participant is pregnant prior to CI surgery, their assessment can be put on hold until post-birth when their eligibility will be reassessed. If a potential participant becomes pregnant following CI surgery, all post-operative scans will be withheld until birth, unless it is deemed medically necessary by clinicians, in which case, special radiation protection measures will be taken.

Maximum Exposures

Radiation exposure will vary across clinical departments, depending on local clinical protocols. The minimum radiation exposure a trial participant will receive will be a plain X-ray of their skull post-operatively. The maximum radiation exposure a CI recipient will receive will be a CT (or Cone beam CT) of their head pre-operatively and a cone beam CT of their head post-operatively.

	COACH eligibility pathway	**Post-Operative**
Comparator Arm	MRI *(no ionising radiation)* **or** Xray *(~0.1 mSv)* **or** CT Scan (~1 mSv)	*N/A*
Intervention Arm	MRI *(no ionising radiation)* **or** Xray *(~0.1 mSv)* **or** CT Scan *(~1 mSv)*	Xray *(~0.1 mSv)* **or** CT Scan (~1 mSv) **or** Cone Beam CT Scan *(~0.05 mSv)*

Although subjects in this trial are exposed to ionising radiation, the amount is low. A head X-ray delivers approximately a 1 mSv dose of ionising radiation. In comparison, the UK average radiation exposure for an individual is about 2.7 mSv (= 2,700 µSv; data obtained from Public Health England [PHE] Ionising Radiation Exposure of the UK Population: 2010 Review) per year. This radiation comes from natural sources, e.g., cosmic radiation, radon gas, and from average medical exposure. How much background radiation individuals are exposed to depends on many factors including geographical location, occupation and home ventilation. It is believed that any amount of radiation that is received carries a risk of later developing serious and possibly fatal conditions.

Ionising radiation has the potential to damage DNA, and cause mutations which have the potential to lead to diseases such as cancer. The risk associated with the maximum possible dose of radiation in this trial is very small and is considered to be acceptable.

Clinical Assessment

The ionising radiation exposures in this trial are all associated with the implantation of a cochlear implant and are additional to standard of care due to the fact that the cochlear implant itself is additional to standard of care for these participants. The exposures are required for the safe implantation of the device and, therefore, are clinically justified. Furthermore, the maximum dose associated with the surgical procedure is approximately 2 mSv [a planning CT and a post-surgical CT] which is less than the average UK annual background radiation dose. The additional risk associated with this maximum dose is approximately 1 in 12,000 of inducing harm from cancer induction which equates to an approximate 0.02% increase in the natural risk of harm from cancer.

Covid-19

In light of the Covid-19 pandemic, the design of the trial has been reviewed to mitigate the impact of Covid-19 and to ensure that Covid-safe measures are implemented as much as possible. Previous engagement with clinical services highlighted the extent to which they have rapidly adapted routine care in response to the pandemic, including the use of remote visits where appropriate and feasible. Any visit which is conducted remotely as part of standard care can be conducted as such as part of the trial, provided it does not interfere with the delivery of the trial interventions or outcome assessments. The implementation of social distancing in the clinic (e.g., waiting in separate room during appointments), considerations for travel expenses for patients who do not wish to take public transport, and patient-facing documents will be developed with PPI input and collaboratively with trial sites to describe Covid-safe measures put into place for the participants.

STATISTICS

Methods

The data will be analysed by the trial statistician using Stata version 17.

The analysis and presentation of the trial results will be in accordance with the CONSORT guidelines. The primary approach to the primary comparative analysis will be to analyse as randomised without imputation of missing data with due emphasis being placed on the confidence intervals for the between arm comparisons. A full Statistical Analysis Plan (SAP) will be finalised prior to database lock and release of treatment allocation codes. The statistician analysing the data will remain blinded to treatment allocation until after database lock.

Continuous variables will be summarised, dependent on distribution, in terms of the mean, standard deviation, median, lower, and upper quartiles, minimum, maximum, and number of observations. Categorical variables will be summarised in terms of frequency counts and percentages.

Baseline characteristics of randomised participants will be compared between the two trial arms, using appropriate descriptive statistics; no formal statistical comparisons will be made.

The primary outcome is the phoneme score on the AB word test presented at 60 dBA at 9 months post first treatment activation. This is calculated as the proportion of phonemes repeated correctly during the AB word test. Evaluation of the primary outcome will be performed using mixed effects regression modelling (with site as a random effect) to compare mean phoneme scores in the intervention and comparator groups. The regression model will be adjusted for baseline and minimisation variables (trial site, severity of tinnitus, and AB word test phoneme score). The comparison will be presented as the difference in mean phoneme score at 9 months in the CI group compared with the HA group with the associated 95% confidence interval.

Appropriate regression models dependent on outcome type (e.g., binary, continuous, count etc), will compare the intervention and comparator groups for each clinical and participant reported secondary outcome, except for the audiometric thresholds and device usage which will be summarised using appropriate descriptive statistics. Pre-randomisation phoneme and word scores on the AB Word test at 70dBA will be recorded at consent rather than baseline; the consent value will be used as covariate where appropriate. The analyses of secondary outcomes will be considered supportive to the primary, and no adjustments will be made for multiple comparisons, therefore all estimates should be interpreted in this light.

Repeated measures regression modelling will investigate whether any between group differences change over time by including a term for the interaction between the treatment arm and time in the model. This modelling will be performed for all clinical and participant reported secondary outcomes with the exception of the AB word test at 70 dBA 9 months post first treatment activation, device usage, and audiometric thresholds.

Safety data will be summarised according to the treatment the participant received, irrespective of randomisation.

No formal interim analyses are planned for this trial. The independent DMC will have access to the data by treatment allocation and will advise if the trial needs to stop or be amended based on the data collected to that timepoint.

Sample size and justification

Sample size for the trial was informed by data from two sources: (1) prospectively collected speech scores from a sample of 15 CI recipients, with words presented at 60 dBA which had a standard deviation of approximately 24%; (2) a consultation with clinicians achieved consensus (52 out of 62 = 85%) that the smallest difference in phoneme scores from the AB word test, that would be considered clinically important was 15%. Fifty-five participants per treatment arm are required to detect a between-group difference of 15% in phoneme scores at 9 months (primary outcome measure), at a 5% significance level (2-sided) with 90% power, assuming a SD of 24% in both treatment groups. To allow for non-collection of the primary outcome (e.g., due to loss to follow up), from up to 15% of participants, 65 participants in each treatment group should be randomised – a total of 130 participants.

Sample size calculations were performed using PASS Version 12.

Assessment of performance

The AB word tests, BKB sentence tests, and audiometric assessments will be administered in the best-aided condition (i.e., using the devices that the participant considers will help them hear as well as possible), except for unaided audiometric thresholds which will be measured without any devices being worn, by a qualified audiologist at baseline (or consent visit stage for AB word test at 70 dBA) and at all scheduled visits.

Device usage data will be collected using device logging and will also be reported by participants, as described above in the ‘compliance’ section.

Questionnaires to collect patient reported outcomes will be administered at baseline and at 1, 3, 6, and 9 months after first treatment activation (see Appendix 1). In addition, tinnitus loudness will be assessed on the day of first treatment activation immediately before and after the activation occurs to identify changes in tinnitus loudness with the acute provision of electrical stimulation. Participants will be contacted by the local researcher to discuss patient-reported device usage at monthly intervals until 9 months after first treatment activation.

Outcome Measure	Derivation
Primary Outcome	
The phoneme score (a measure of phoneme perception) on the AB word test presented at 60 dBA, in the best-aided condition (i.e., using the devices that the participant considers will help them hear as well as possible) at 9 months post first treatment activation measured by independent blinded assessors.	The phoneme score is the proportion of phonemes repeated correctly
Secondary Outcomes	
Phoneme score (phoneme perception using the AB Word test at 60dBA) at 3, 6 and 9 months post first treatment activation assessed live by an audiologist	The proportion of phonemes repeated correctly
Word perception (AB Word test at 60 dBA) at 3, 6 and 9 months post first treatment activation assessed live by an audiologist	The proportion of words repeated correctly
Phoneme perception (AB Word test at 70dBA) at 9 months post first treatment activation assessed live by an audiologist	The proportion of phonemes repeated correctly
Word perception (AB Word test at 70dBA) at 9 months post first treatment activation assessed live by an audiologist	The proportion of words repeated correctly
Sentence perception in quiet (BKB sentence test at 70 dBA) at 3, 6 and 9 months post first treatment activation assessed live by an audiologist	The proportion of key words repeated correctly
Sentence perception in noise (BKB sentence test) at 3, 6, and 9 months post first treatment activation assessed live by an audiologist	The signal-to-noise ratio at which 50% of key words are repeated correctly (speech reception threshold)
Device usage (device logging)	The average hours of daily use and cumulative hours of use for the following periods: • First treatment activation to 3 months • 3 to 6 months • 6 to 9 months Average and cumulative usage will also be reported for the same periods for each characteristic of the acoustic environments captured by the trial devices
Device usage (participant self-report)	The estimated average hours of daily use as reported by patients each month from first treatment activation to 9 months. Cumulative hours of use from the patient-reported daily use estimates, for the following periods: • First treatment activation to 3 months

Outcome Measure	Derivation
	• 3 to 6 months • 6 to 9 months
Difficulty with listening	The mean SSQ12 score at 1, 3, 6, and 9 months.
Listening effort and fatigue	FAS total score, EAS total score, LEQ-CI* total score at 1, 3, 6, and 9 months. Scores will be calculated using the algorithms in the questionnaire manuals.
Tinnitus severity	Global 25-item TFI score Global 19-item TFI score (excluding sleep and auditory subscales) TFI scores for 8 subscales All at 1, 3, 6, and 9 months.
Tinnitus loudness	• VAS-L rating. Participants mark the loudness of their tinnitus at any point along the numerical scale, with word descriptors utilised as anchor points at 0 for “extremely weak,” 30 for “moderate,” 50 for “strong,” 70 for “very strong,” and 100 for “extremely strong” tinnitus loudness. Immediately before and after first treatment activation, and at 1, 3, 6, and 9 months.
Mood	HADS anxiety and depression subscale scores at 1, 3, 6, and 9 months.
Hearing-specific quality of life	NCIQ total and six subdomain scores YBHRQL binaural utility value HHIA total score and two subscale (emotional and social/situational) scores All at 1 month, 3 months, 6 months, and 9 months.
Health-related quality of life	HUI3 multi-attribute utility value, EQ-5D-5L health utility value using EQ-5D-3L UK value set ICECAP-A tariff value All at 1 month, 3 months, 6 months, and 9 months.
Global ratings of change	Likert scale ratings of change (7 points from much worse to much improved) in hearing and quality of life relative to two anchor points (immediately prior to first treatment activation; since the last trial appointment) at 1, 3, 6, and 9 months.
Audiometric thresholds	Unaided audiometric thresholds at first treatment activation and at 3, 6 and 9 months.

Outcome Measure	Derivation
	Aided audiometric thresholds at first treatment activation and at 3 and 9 months.

*Data only to be collected using LEQ-CI questionnaire once licence is in place

Assessment of safety

Safety data, including number of expected AEs and SAEs and unexpected related SAEs will be summarised with descriptive statistics according to the treatment the participant received, irrespective of randomisation; where anyone received more than one treatment (e.g., HA then CI) these will be summarised separately. Where a participant did not receive their allocated treatment but had an expected AE, or SAE this will be indicated.

The number of participants experiencing at least one AE or SAE will be summarised using descriptive statistics. The total number and type of AEs and SAEs will also be summarised, overall and by event.

Procedures for missing, unused and spurious data

It is planned that several strategies to investigate the effect of missing primary outcome data will be undertaken as sensitivity analyses, including the use of multiple imputation with chained equations and minimisation variables as covariates. More information on methods will be included within the SAP.

Definition of populations analysed

Full analysis set, including safety: All randomised participants for whom at least one post-baseline assessment is available.

There will not be a per-protocol dataset.

ADVERSE EVENTS

Reporting requirements

The collection and reporting of Adverse Events (AEs) will be in accordance with the UK Policy Framework for Health and Social Care Research 2017 and the requirements of the Research Ethics Committee (REC). Definitions of different types of AEs are listed in the table of abbreviations and definitions.

Reporting Period

Trial related AEs will be collected from time of randomisation (baseline visit) until the collection of the primary outcome (9 months post-treatment onset).

Definitions

Adverse Events

An **adverse event** is any unfavourable and unintended sign, symptom, syndrome or illness that develops or worsens during the period of observation in the trial.

An AE does include a / an:

1. exacerbation of a pre-existing illness.

2. increase in frequency or intensity of a pre-existing episodic event or condition.

3. condition detected or diagnosed after medicinal product/device administration even though it may have been present prior to the start of the trial.

4. continuous persistent disease or symptoms present at baseline that worsen following the start of the trial.

An AE does not include a / an:

1. medical or surgical procedure (e.g., surgery, endoscopy, tooth extraction, transfusion); but the condition that led to the procedure is an AE.

2. pre-existing disease or conditions present or detected at the start of the trial that did not worsen.

3. situations where an untoward medical occurrence has not occurred (e.g., hospitalisations for cosmetic elective surgery, social and / or convenience admissions).

4. disease or disorder being studied, or sign or symptom associated with the disease or disorder unless more severe than expected for the participant's condition.

5. overdose of concurrent medication without any signs or symptoms.

6. expected AE as listed below.

Expected adverse events

The treatments provided to both intervention arms are widely available within the NHS, used in standard care and considered to be safe. Known adverse events (listed in the table below) are related to their respective trial interventions. These events are secondary outcomes and will be collected as part of the eCRF. The number of occurrences of expected AEs and SAEs will be regularly reviewed throughout the trial by the TMG and the DMC.

Expected AE	Expected SAE
Related to Cochlear Implantation (intervention arm only)	
Facial nerve stimulation (temporary)	Facial nerve stimulation (chronic)
Patient reported decreased hearing ability or loss of residual acoustic hearing (temporary or permanent)	The inability to use the implant or a hearing aid in that ear
Vestibular dysfunction (temporary)	Vestibular dysfunction (chronic)
Perception of non-auditory sensations (temporary or permanent)	Infection requiring hospitalisation (e.g., meningitis and the need for vaccination)
New onset or exacerbation of pre-existing tinnitus	Any surgical complication that requires hospitalisation
Altered taste	Need for revision surgery, reimplantation or explantation
Facial weakness	Subdural injury
Acute otitis media or any other infection treated by oral antibiotics	Chronic pain in or around the implant site or hearing aid
Perilymph fistula	

Expected AE	Expected SAE
Concurrent cerebrospinal fluid (CSF) leakage	
Subcutaneous haematoma	
Unsatisfactory device insertion (e.g., misplacement of electrode array, incomplete electrode insertion, tip fold-over)	
Failure of component parts	
Related to Hearing Aids (intervention and comparator arms)	
Ear infection	None
Exacerbation of eczema	

Serious Adverse Events

A Serious Adverse Event (SAE) is any adverse event occurring following trial mandated procedures that results in any of the following outcomes:

1. Death

2. A life-threatening adverse event

3. Inpatient hospitalisation or prolongation of existing hospitalisation

4. A disability / incapacity

5. A congenital anomaly in the offspring of a participant

A distinction is drawn between serious and severe AEs. Severity is a measure of intensity whereas seriousness is defined using the criteria above. Hence, a severe AE need not necessarily be serious.

Important medical events that may not result in death, be life-threatening, or require hospitalisation may be considered a SAE when, based upon appropriate medical judgment, they may jeopardize the patient or participant and may require medical or surgical intervention to prevent one of the outcomes listed in this definition.

Events deemed by the investigator to be related to COVID-19 infection will not be reportable.

If an adverse event, *not listed as expected AEs above*, meets, or potentially meets, the SAE criteria it will be assessed for seriousness, and causality.

Causality

Not related or improbable: a clinical event including laboratory test abnormality with temporal relationship to trial device which makes a causal relationship incompatible or for which other treatment, drugs, chemicals or disease provide a plausible explanation**.** This will be counted as “unrelated” for notification purposes.

Possible: a clinical event, including laboratory test abnormality, with temporal relationship to trial device which makes a causal relationship a reasonable possibility, but which could also be explained by other treatments, devices, drugs, chemicals or concurrent disease. This will be counted as “related” for notification purposes.

Probable: a clinical event, including laboratory test abnormality, with temporal relationship to trial device which makes a causal relationship a reasonable possibility, and is unlikely to be due to other treatments, devices, drugs, chemicals or concurrent disease. This will be counted as "related" for notification purposes.

Definite: a clinical event, including laboratory test abnormality, with temporal relationship to trial device which makes a causal relationship a reasonable possibility, and which can definitely not be attributed to other causes. This will be counted as "related" for notification purposes.

Recording and Reporting of Adverse Events

The below section **does not pertain to** expected AEs and SAEs (included in table of expected events above) which do not require expedited reporting with a trial SAE form. These events are secondary outcomes recorded in medical notes and collected as part of the eCRF, that will be routinely centrally monitored and reported.

All adverse events (AEs) will be recorded as they are reported whether spontaneously volunteered or in response to questioning about wellbeing at trial visits. The questioning about AEs will cover the current visit as well as the period of time between the previous and the current visit. A note of any concomitant medication will also be made, where available, so that a full assessment of the AE can be made.

Abnormal test results that are deemed clinically significant by the investigator and that lead to a change or temporary or permanent discontinuation in the use of the device or require intervention or diagnostic evaluation to assess the risk to the subject will be recorded as adverse events and instigate further investigation and follow up as appropriate.

All AEs and SAEs will be documented in the subject's medical records. As both trial interventions are well established and have extensive safety profiles already available, only related, or suspected to be related, SAEs will be documented on the eCRF.

For related, or suspected to be related, events, participants should be followed up until resolution or stabilisation of the event. Follow-up information should ideally be provided on a new SAE form.

Participants will be asked to contact the trial site immediately in the event of any SAEs. The Chief Investigator or nominated deputy shall be informed immediately of any related, or suspected to be related, serious events and shall determine seriousness and relationship in conjunction with any treating medical practitioners.

SAEs will be recorded and reported to the REC and Sponsor as part of the annual progress reports.

SAEs will be reported within the statutory timeframes to the REC as stated below. The Chief Investigator will be responsible for all adverse event reporting.

The NCTU will also notify the trial funder by email from the Chief Investigator to Dr Mary Beth Brinson, Global Head of Clinical Affairs, Cochlear™ Ltd, MbBrinson@cochlear.com and Chris Warren, Clinical Portfolio Manager, Cochlear™ Ltd, cwarren@cochlear.com of any serious adverse events at the time of regulatory reporting.

The funder will notify the University by email to douglas.hartley@nottingham.ac.uk (cc to sponsor@nottingham.ac.uk) of any reportable events involving devices (Cochlear™ or GN Hearing UK) at the time of reporting to the MHRA, or any other relevant regulatory authorities of any new information which becomes available to them as device manufacturers which could affect the safety of trial participants.

SAE Reporting Procedure for Unexpected SAEs – At Site
On becoming aware that a participant has experienced an SAE, the Investigator (or delegate) must complete, date and sign an SAE Form. The form should arrive at the NCTU as soon as possible and no later than **24 hours** after first becoming aware of the event:

To report an SAE, email the SAE Form to: nctu-sae@nottingham.ac.uk

On receipt, NCTU will allocate each SAE a unique reference number which will be forwarded to the site as proof of receipt. If confirmation of receipt is not received within 1 working day, the site will contact the NCTU. The SAE reference number should be quoted on all correspondence and follow-up reports regarding the SAE and filed with the actual SAE in the ISF.

For SAE forms completed by someone other than the local PI, the Investigator will be required to countersign the original SAE Form to confirm agreement with the causality and severity assessments. For sites where the PI is an audiologist, the responsibility for causality assessment and sign off of SAEs will be delegated to the lead surgeon at site. The form should be returned to NCTU and a copy kept in the ISF.

Investigators should also report SAEs to their own Trust in accordance with local practice.

SAE Reporting Procedure for Unexpected SAE – NCTU
On receipt, NCTU will allocate each SAE a unique reference number which will be forwarded to the site as proof of receipt within 1 working day. The SAE reference number will be quoted on all correspondence and follow-up reports regarding the SAE and filed with the SAE form in the TMF.

On receipt of an SAE Form, seriousness and causality will be determined independently by the Chief Investigator, or their delegate, responsible for determining causality assessments. The Chief Investigator's delegate will review all SAEs reported by the Chief Investigator's host site. An SAE judged by the Investigator, Chief Investigator or their delegate to have a reasonable causal relationship with the trial treatment will be regarded as a related SAE. The Chief Investigator (or their delegate) will also assess all related SAEs for expectedness. If the serious event is unexpected (i.e., is not defined in the protocol as an expected event) it will be classified as an unexpected and related SAE.

SAEs

. Unexpected serious adverse events related to the trial intervention will be reported within the timeframes to the REC as stated below. The Chief Investigator shall be responsible for all adverse event reporting.

A serious adverse event that is unexpected in its severity and seriousness *and* deemed directly related to or suspected to be related to the trial treatment shall be reported to the ethics committee that gave a favourable opinion as stated below.

The event shall be reported immediately of knowledge of its occurrence to the Chief Investigator or their delegate.

The Chief Investigator (or their delegate) will:

- Assess the event for seriousness, expectedness and relatedness to the trial intervention.
- Take appropriate medical action, which may include halting the trial and inform the Sponsor of such action.

- If the event is deemed related to the trial treatment shall inform the REC within 7 days of knowledge of the event.
- Shall, within a further 8 days send any follow-up information and reports to the REC.
- Make any amendments as required to the trial protocol and inform the REC as required.

Reporting to the Research Ethics Committee

Unexpected and Related Serious Adverse Events
NCTU will support the Chief Investigator to ensure that the reporting for all events categorised as unexpected and related SAEs to the REC will be completed within 15 days.

Adverse Events
The REC will be notified immediately if a significant safety issue is identified during the trial. However, reporting of adverse events that are not deemed serious is not required for this trial.

Investigators
Details of all unexpected and related SAEs and any other safety issues which arises during the trial will be reported to PIs. A copy of any such correspondence should be filed in the ISF.

Data Monitoring Committee
The independent DMC will review outcome data at regular intervals throughout the trial, in addition to reported SAEs.

ETHICAL AND REGULATORY ASPECTS

ETHICS COMMITTEE AND REGULATORY APPROVALS

The trial will not be initiated before the protocol, ICF, PIS and GP letters have received approval / favourable opinion from the REC, the respective NHS or other healthcare provider's R&D department, and the HRA if required. Should a protocol amendment be made that requires REC approval, the changes in the protocol will not be instituted until the amendment and revised ICFs and PIS (if appropriate) have been reviewed and received approval / favourable opinion from the REC and R&D departments. A protocol amendment intended to eliminate an apparent immediate hazard to participants may be implemented immediately providing that the R&D and REC are notified as soon as possible, and an approval is requested. Minor protocol amendments only for logistical or administrative changes may be implemented immediately; and the REC will be informed.

The trial will be conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki, 1996; the principles of Good Clinical Practice and the UK Department of Health Policy Framework for Health and Social Care, 2017

INFORMED CONSENT AND PARTICIPANT INFORMATION

The process for obtaining participant informed consent will be in accordance with the REC guidance, the UK Department of Health Policy Framework for Health and Social Care, 2017 and any other regulatory requirements that might be introduced. The investigator or their nominee and the participant shall both sign and date the ICF before the person can participate in the trial. Where consent is initially received via e-consent (following the procedures outlined in the 'Informed Consent' section), full written consent will be received at earliest convenience as always prior to randomisation. Consent needs to be reconfirmed at the time of the baseline visit. This reconfirmation needs recording in the medical notes and eCRF.

The participant will receive a copy of the signed and dated forms and the original will be retained in the ISF. An electronic copy of the ICF will be shared with the NCTU for central monitoring purposes. A further copy will be filed in the participant's medical notes and a signed and dated note made in the medical notes that informed consent was obtained for the trial.

The decision regarding participation in the trial is entirely voluntary. The investigator or their nominee shall emphasize to them that consent regarding trial participation may be withdrawn at any time without penalty or affecting the quality or quantity of their future medical care, or loss of benefits to which the participant is otherwise entitled. No trial-specific interventions will be done before informed consent has been obtained.

The investigator will inform the participant of any relevant information that becomes available during the trial, and will discuss with them, whether they wish to continue with the trial. If applicable they will be asked to sign revised consent forms.

If the ICF is amended during the trial, the investigator shall follow all applicable regulatory requirements pertaining to approval of the amended ICF by the REC and use of the amended form (including for ongoing participants).

RECORDS

Device accountability

Device supplies will be kept in a secure, limited access storage area under the storage conditions specified by manufacturer, and in accordance with local trial site policy and procedures.

The investigator and the local site staff shall maintain records of the HAs received, and spares and repairs consumables for both CIs and HAs. Accountability logs should be kept from the time of delivery to the site, with records taken of what was distributed to each participant. These records will include dates, quantities received, batch / serial numbers, expiration dates, and the unique code numbers (patient trial number) assigned to the trial participant. These records will be part of each participant's eCRF. All trial devices received by the site shall be accounted for. Accountability logs will be shared with the NCTU for oversight and reconciliation.

In order to maintain the blind regarding the manufacturer/funder, records of CIs, sound processors and CI accessories received for trial-purposes, linking them to participants, will not be kept (the devices received will become part of the local stock for general use, and may or may not be used for trial participants). The only accountability that will be undertaken will be that by the NCTU, ensuring that the number of CIs, sound processors and CI accessories requested by the site matches the number of participants randomised into the intervention arm at that particular site. If replacements are needed then trial sites would use the spares and repairs box to provide these to participants, or if the appropriate item is not available in the box, sites will cover the repairs using their usual process as they will have been reimbursed by receiving the equal value in stock within the trial stock box.

Case Report Forms

Each participant will be assigned a trial identity code number, allocated following expression of interest, for use on eCRFs and other trial documents. The documents and database will also use their initials (of first and last names separated by a hyphen or a middle name initial when available) and date of birth (dd/MMM/yyyy).

Participant contact details will be logged separately to the clinical eCRF data, to ensure participant identifiable data is separate to data used for analysis. Participant contact details may also be used by the trial team to send out trial related questionnaires, correspondence and follow-ups, limited to the duration of the participant's participation in the trial. Participants may also optionally consent to their contact details being retained beyond the duration of their participation in the trial, in order to be updated about the outcomes of the research or informed of future research.

The database will have in-built validation to ensure that the identifiers used all match with the allocated participant ID number. CRFs will be treated as confidential documents and held securely in accordance with regulations. eCRFs will be restricted to those personnel approved by the Chief or local PI and recorded on the trial delegation log. Errors will be corrected and recorded on the eCRFs on the audit log. The Chief or local PI (or their designee) will sign a declaration ensuring accuracy of data recorded in the eCRF.

The eCRF will only collect the minimum required information for the purposes of the trial. Access to the information will be limited to the trial staff and investigators and relevant regulatory authorities (see above). Electronic data including the trial database will be held securely and password protected.

eCRFs will be treated as confidential documents and held securely in accordance with regulations. The investigator will make a separate confidential record of the participant's name, date of birth, local hospital number or NHS number, and participant trial number (the trial recruitment log), to permit identification of all participants enrolled in the trial, in accordance with regulatory requirements and for follow-up as required.

All paper forms shall be requested to be filled in using black ballpoint pen. Errors shall be struck through with a line, and not obliterated by using correction fluid. The correction should be inserted, initialled and dated as per GCP correction process. The Chief or local PI shall sign a declaration ensuring accuracy of data recorded in the CRF.

Source documents

Source documents shall be filed at the investigator's site and may include but are not limited to, ICFs, completed questionnaires, current medical records, laboratory results and pharmacy records. A CRF may also completely serve as its own source data. Only trial staff as listed on the delegation log shall have access to trial documentation other than the regulatory requirements listed below.

Direct access to source data / documents

The eCRF and all source documents, including progress notes and copies of laboratory and medical test results shall always be made available for review by the Chief Investigator, Sponsor's designee, and inspection by relevant regulatory authorities (e.g., Department of Health).

DATA PROTECTION

All trial staff and investigators will endeavour to protect the rights of the trial's participants to privacy and informed consent, and will adhere to the Data Protection Act, 2018.

The eCRF will only collect the minimum required information for the purposes of the trial. All trial related paper-based data will be held securely, in a locked room, or locked cupboard or cabinet. Access to the information will be limited to the trial staff and investigators and relevant regulatory authorities (see above). Computer held data including the trial database will be held securely and password protected. All data will be stored on a secure dedicated web server. Access will be restricted by user identifiers and passwords (encrypted using a one-way encryption method). We anticipate that anonymised trial data may be shared with other researchers to enable further research.

Information about the trial in the participant's medical records/hospital notes will be treated confidentially in the same way as all other confidential medical information. Electronic data will be backed up every 24 hours to both local and remote media in encrypted format.

Participant data will be kept securely, and access will be restricted to member of the trial team.

QUALITY ASSURANCE & AUDIT

INSURANCE AND INDEMNITY

Insurance and indemnity for trial participants and trial staff is covered within the NHS Indemnity Arrangements for clinical negligence claims in the NHS, issued under cover of HSG (96)48. There are no special compensation arrangements, but trial participants may have recourse through the NHS complaints procedures.

The University of Nottingham as research Sponsor indemnifies its staff with both public liability insurance and clinical trials insurance in respect of claims made by research subjects.

The University of Nottingham as research Sponsor indemnifies its staff, research participants and research protocols with both public liability insurance and clinical trials insurance. These policies include provision for indemnity in the event of a successful litigious claim for proven non negligent harm.

TRIAL CONDUCT

Trial conduct will be subject to both trial and systems audits of the TMF for inclusion of essential documents; permissions to conduct the trial; trial delegation Log; CVs of trial staff and training received; local document control procedures; consent procedures and recruitment logs; adherence to procedures defined in the protocol (e.g. inclusion / exclusion criteria, correct randomisation, timeliness of visits); adverse event recording and reporting; device accountability, device records and equipment calibration logs.

TRIAL DATA

Monitoring of trial data shall include confirmation of informed consent; source data verification; data storage and data transfer procedures; local quality control checks and procedures, back-up and disaster recovery of any local databases and validation of data manipulation. The NCTU, or where required, a nominated designee of the Sponsor, shall carry out monitoring of trial data as an ongoing activity.
Monitoring of trial data and conduct will also be in accordance with the trial specific monitoring plan, to be finalised prior to the commencement of recruitment.

Trial data and evidence of monitoring and systems audits will be made available for inspection by the regulatory authority as required.

RECORD RETENTION AND ARCHIVING

In compliance with the ICH/GCP guidelines, regulations and in accordance with the University of Nottingham Research Code of Conduct and Research Ethics, the Chief or local Principal Investigator will maintain all records and documents regarding the conduct of the trial. These will be retained for at least 7 years or for longer if required. If the responsible investigator is no longer able to maintain the trial records, a second person will be nominated to take over this responsibility.

The TMF and trial documents held by the Chief Investigator and the NCTU on behalf of the Sponsor shall be finally archived at secure archive facilities at the University of Nottingham. This archive shall include all trial databases and associated meta-data encryption codes.

DISCONTINUATION OF THE TRIAL BY THE SPONSOR

The Sponsor reserves the right to discontinue this trial at any time for failure to meet expected enrolment goals, for safety or any other administrative reasons. The Sponsor shall take advice from the TSC and DMC as appropriate in making this decision.

STATEMENT OF CONFIDENTIALITY

Individual participant medical information obtained as a result of this trial are considered confidential and disclosure to third parties is prohibited with the exceptions noted above.
Participant confidentiality will be further ensured by utilising identification code numbers to correspond to treatment data in the computer files.

Such medical information may be given to the participant's medical team and all appropriate medical personnel responsible for the participant's welfare. If information is disclosed during the trial that could pose a risk of harm to the participant or others, the researcher will discuss this with the CI and where appropriate report accordingly.

Data generated as a result of this trial will be available for inspection on request by the Chief Investigator, the University of Nottingham representatives, the REC, local R&D Departments and the regulatory authorities.

Anonymised participant data may be shared with researchers external to the trial research team in accordance with the NCTU's data sharing procedure. All requests for data should be sent to the NCTU.

PUBLICATION AND DISSEMINATION POLICY

During trial-conduct the protocol will be published in a relevant journal and the trial team will have presence at national and international conferences to raise awareness of the trial and its progress.

Methodology papers will be published for both the main trial and the process evaluation, and trial results papers in high-impact, peer-reviewed journals. Responsibility for and control over the publication of trial results rests solely with the research investigators. The COACH trial will be presented at national and international conferences, such as the British Cochlear Implant Group annual conference and the biannual Conference on Implantable Auditory Prostheses.

Dissemination activities, such as short bulletins, articles in charity and support group newsletters, blogs, our own trial newsletters, audio-visual and social media will be agreed and developed with the patient research partners group to keep participants, people with hearing loss and the general public engaged and informed throughout the trial and in sharing outcomes.

Our public involvement activities and learning will be shared, as the opportunity arises, at a relevant conference and in relevant journals, e.g., the Research Involvement and Engagement, Health Expectations and BMJ Open Journal.

QUALITATIVE STUDY: Process Evaluation

Nested within this trial we will deliver a process evaluation to generate complementary insight that will support interpretation of trial findings and inform future implementation (should trial outcomes indicate accordingly).

This evaluation is built upon the premise that this new CI population may have a different relationship with implantation which needs to be better understood to shape future services.

Aim and objectives:

The aim of this evaluation is to generate detailed insight about individual experiences of the implantation pathway and the impact that implantation has upon everyday life.

It will include a concern for the way in which cochlear implantation is considered by this new population: *are risks perceived differently where residual hearing is greater? Do hopes and expectations differ where residual hearing is greater? What emotional impact does CI have upon notions of identity in this population?*

It will also include a concern for more practical elements of the CI pathway: *does broader/quicker access to CI service impact upon how individuals acclimatise to the potential for CI? What post-implantation support does this new population require?*

Sample & Selection

Participants will be purposively selected from those randomised to the intervention arm (CI) [n=30] and from those randomised to the comparator arm (HA) [n=15] to build a study population which reflects a range of potential experiences of CI and its impact. If a participant ticks the optional box on the COACH ICF to indicate they are happy to take part in the additional

interviews, they may later be approached by researchers at the University of Nottingham to conduct these interviews and provided with the Interview PIS. Participants will be consented separately into this nested study. To accommodate interviews completed by telephone or video call, remote consent may be used for this aspect of the trial. For verbal consent, participants will receive a telephone call or email from a member of the research team. The researcher will ask participants to provide or confirm their email address, and they will provide the participant with the Interview Participant Information Sheet and a copy of the Interview consent form via email. The participant will be given an opportunity to consider their participation and the interview arranged for a later time if they are interested in participating. If a participant is happy to take part remotely they will be consented over the telephone or in the video call; this process will be recorded and recordings stored securely as a record of consent. The researcher will read out each consent statement and ask the participant to confirm their agreement. If a participant is not happy for the interview to be recorded, but wishes to complete the interview remotely, they will be asked to consent electronically using an MS forms version of the COACH interview ICF.

Intervention arm

Baseline clinical data will be used to ensure that the process evaluation includes individuals with different clinical contexts:

- Differing levels of tinnitus severity.
- Differing AB word test phoneme scores.

Baseline demographic data will be used to ensure that the process evaluation includes individuals with different social/economic contexts:

- Younger and older individuals.
- Working and not working individuals, including different occupations.
- Different familial circumstances – living alone, living with caring responsibilities.
- Recruited from different centres.

Comparator arm

In addition to the purposive sampling frame described above it will be ensured that those recruited from the HA group includes both those who accept and those that decline a new HA.

Healthcare Professionals

To generate insight about delivering CI to this new population, healthcare professionals will be interviewed who are participating in the RCT [n=20].

Again, participants will be selected purposively to capture a range of perspectives upon CI services, including:

- Different professional groups.
- Individuals from audiology services.
- Individuals from cochlear implantation services.
- Services where provision is integrated.

Those who declined to participate in the trial.

To ensure that our process evaluation is not skewed by those whose positive attitudes about CI encouraged their participation in COACH a small number of individuals who declined when invited to participate in COACH [n=6] will be selected.

Summary.

Selecting participants in the way described will ensure that findings are reflective of, and responsive to, a broad range of perspectives and experiences.

Our overall sample [n=71] and sub-groups [n=30, n=15 n=20 & n=6] should ensure that data saturation is achieved for those engaged with the trial, i.e., a point is reached where additional data collection offers no new insight.

Data Collection

Intervention arm
Those in the CI group will be interviewed at two time points:

1) post randomisation but before cochlear implantation
2) at the 9-month follow up appointment following first treatment activation.

Comparator arm and those who declined.
These will be interviewed once, within 6 weeks of randomisation or recruitment approach.

Healthcare professionals.
These will be interviewed in the final months of the trial to capture their reflections on CI pathway and research processes.

Topic guides.
All interviews will be semi-structured with open questions to guide a discussion of experiences and opinions. An open and responsive approach will be always taken to allow participants the opportunity to introduce new topics and to focus in areas which they feel are important.

Topic guides will be finalised in consultation with our patient research partners group in line with the following criteria:

A. Initial interviews with participants in the intervention arm will focus upon their expectations of CI.
B. Later interviews with participants in the intervention arm will focus upon their experience of CI and the clinical care pathway.
C. Interviews with those in the comparator arm will focus upon their views upon CI and upon enhanced HA.
D. Interviews with healthcare professionals will focus upon CI provision to this population.
E. Interviews with those outside of COACH will reflect upon their views on CI and upon participating in CI research.

It is expected that most interviews to be undertaken face-to-face.

All interview data will be audio or video-recorded, transcribed in full and handled using the NVivo 12 software package. Due to the trial population, speech may not be completely clear on audio recordings. For some participants with speech difficulties, video recordings will make transcription easier and more accurate. Interviews will be video recorded on a video call platform approved for use by the University of Nottingham.

Data Analysis

In data analysis previous qualitative work will be built upon which has considered both pre- and post-CI expectations and experience – q-COACH, the Foundation study and others.

Interview transcripts will be reviewed and coded thematically – identifying key insight, experiences, or opinions. Coded interviews will be reviewed and compared to characterise recurrent and/or prioritise ideas and themes.

Data analysis will be performed concurrently with data collection. This will allow adaptation of interview topic guides to capture emergent issues and insight. This process will cease when insight is considered to be stable and no longer growing or evolving.

At regular intervals public and patient partners will be consulted to ensure that the characterisation of patient benefit and service delivery is meaningful to them.

Summaries may be generated for each distinct population in this evaluation - i.e., reporting the experiences of healthcare professionals, those that received CI, those that did not. An

overarching synthesis of the different perspectives will construct a detailed and contextualised model(s) of CI patient benefit and models of CI service delivery.

USER AND PUBLIC INVOLVEMENT

Previous research (q-COACH (Auton et al., 2019) and the FOUNDATION study) highlighted patient concerns about participating in clinical trials of cochlear implantation, particularly relating to remaining residual hearing, the permanent nature of implantation and concerns around randomisation. These insights have been incorporated into the protocol, including insights from lay reviewers of the trial proposal.

Public involvement shall continue through:

- Ongoing involvement of patient representative Diane Matthews who joins the TMG.
- Patient representation on the TSC.
- Establishing a patient research partners group to advise and assist at points prior to and throughout the trial.

Purpose

Governance

- Up to two public members will be invited to join the TSC. Ideally, this shall include a member who uses hearing aids and a member who has also recently had a CI to include different perspectives.

Assist in trial set-up

- Involving patients as partners in the setup and conduct of this specific trial will guide the pre-empting and addressing any questions or concerns that potential participants may have. The patient research partners group shall guide the team's planning by sharing viewpoints from their own lived experience, informing aspects such as what is understood about CIs, how the prospect of randomisation would be perceived, how it can be ensured participants are in equipoise, when to approach patients to take part and how to minimise the burden of participation. They shall also assist in drafting and distributing a national survey (below) and patient-facing materials (PIS, ICF and any other media)
- A national survey shall be held, targeted at adults who can help build a fuller understanding of the concerns and priorities of potential participants, so the recruitment strategy and participant information can be defined. Responses shall be gathered from recent cochlear implantation patients and those awaiting implantation; adults who would consider implantation and those who have declined an implant.

Optimise recruitment and retention

- The patient research partners group shall review recruitment plans and what shall be asked of participants. They shall suggest ways to help retain participants' interest and ongoing participation. Members will also help us identify appropriate channels for advertising the trial to potential participants, assist in drafting promotional material and trial newsletters for interested public and potential participants.

Include patient perspective in data analysis

- Collaborative working with patient research partners group and team colleagues will take place, to agree how group members shall contribute to analysing qualitative data, in a way which best draws upon group members' strengths and interests.

Disseminate trial progress and results to patients and public

- Together with the patient research partners group, it shall be agreed and implement a manageable dissemination strategy to help keep participants, people with hearing loss

and the general public engaged and informed throughout the trial and in sharing outcomes.

Conduct

These activities will be supported by Dr Adele Horobin who can also draw upon the advice of the patient and public involvement steering group of the Nottingham Biomedical Research Centre hearing theme, an experienced panel of patients with extensive knowledge of public involvement methodology and practice.

All public and patients involved can opt to attend training, as available, related to patient involvement in research through the regional network of PPI training, Sharebank, which is also co-ordinated by Dr Horobin.

A code of conduct will be established for all groups and committees that include patient involvement and develop lay role profiles to ensure the scope and nature of patient roles in the conduct and oversight of the trial are clear and accessible.

Public members involved will be offered honorary payments, in line with PPI payment policies of the NIHR National Centre for Engagement and Dissemination and the NIHR Nottingham Biomedical Research Centre hearing theme. Reasonable expenses will also be offered.

TRIAL FINANCES

Funding source

The trial is funded by a research grant from Cochlear™ Ltd, a company who make the cochlear implant devices which will be used in the trial. The trial is Sponsored by the University of Nottingham and is being conducted independently of the company.
Researchers from the University of Nottingham and NHS clinicians developed the proposal for the research, in consultation with the Company. A contract was put into place between funder and the research team stipulating that from grant activation date the company will not be involved in the running, oversight or data analysis of the trial. The researchers will provide update reports to the funder, as per the agreed schedule laid out in the contract between the two parties.

Participant stipends and payments

Participants will not be paid to participate in the trial, though participant travel expenses will be reimbursed. As a token of appreciation for participating in a trial of such long duration, trial-branded gifts with a low monetary value (e.g., pens) and/or vouchers for high-street or online shopping will be given to participants periodically throughout the trial, up to a maximum value of £50 per participant over 18 months of participation.

Appendices

Appendix 1: Schedule of Assessments

Measure	Consent	Baseline	Treatment activation (T0)[c]	Time post T0				
				1 month	3 months	6 months	9 months	2,4,5,7,8 months
Primary outcome								
Phoneme perception measured by blinded independent assessors ***(AB word test @ 60 dBA)***		X					X	
Secondary clinical outcomes								
Phoneme perception assessed live by an audiologist ***(AB word test @ 60 dBA)***		X			X	X	X	
Word perception ***(AB word test @ 60 dBA)***		X			X	X	X	
Phoneme perception ***(AB word test @ 70 dBA)***	X						X	
Word perception ***(AB word test @ 70 dBA)***	X						X	
Sentence perception in quiet & noise ***(BKB sentence test @ 70 dBA)***		X			X	X	X	
Device usage (device logging)		X			X	X	X	
Audiometric thresholds ***(Aided, Unaided)***		X	X		X	X	X	
Secondary patient-reported outcomes								
Listening difficulty ***(SSQ12)***		X		X	X	X	X	
Listening effort & fatigue ***(FAS, EAS, LEQ-CI)***		[a]X		[a]X	[a]X	[a]X	[a]X	
Tinnitus severity ***(TFI)***		X		X	X	X	X	
Tinnitus loudness ***(VAS-L)***		X	[b]X	X	X	X	X	
Mood ***(HADS)***		X		X	X	X	X	
Hearing-specific QoL ***(NCIQ, YBHRQL, HHIA)***		X		X	X	X	X	
Health-related QoL ***(HUI3, EQ5D, ICECAP-A)***		X		X	X	X	X	
Global ratings of change				X	X	X	X	
Device usage (self-report)				X	X	X	X	X
Safety outcomes								
Adverse effects			X	X	X	X	X	
Other assessments								
Cognitive health ***(HI-MoCA)***		X						

[a] Data for the LEQ-CI to be collected using the LEQ-CI questionnaire once licence is in place.[b]The VAS-L will be done twice at this timepoint, once immediately before treatment activation and a second time after treatment activation. [c] T0 for HA arm – Either recorded date of HA fitting/optimisation appointment or recorded date of decision that the participant will not attend or 4 months post-randomisation date (whichever occurs first). T0 for CI arm – Either the date of CI activation or the date a decision was made that surgery would not take place.

Appendix 2: Accessories included as part of standard care for processor options

Cochlear™ Nucleus® 7 Kit Unilateral Adult for the Nucleus Profile™ Plus Series Implant (CI600)

- 1x Processing Unit
- 1x Earhook M
- 2x Slimline™ Coils (6 cm/ 8 cm, each 1)
- 2x Magnets (2(I)/ 3(I), each 1)
- 2x Microphone Covers (1 pack of 2)
- 1x Battery Cover
- 1x Battery Holder
- 6x power one IMPLANT plus p675 Batteries (1 pack of 6)
- 1x Battery Cover Locking Tool
- 1x CR310 Remote Control
- 1x Microfibre Cloth
- 1x Storage Case
- 4x Drying Capsules
- 1x Breeze by Dry & Store®
- 3x Dry-Brik® by Dry & Store® (1 pack of 3)
- 1x Recipient Backpack
- 2x Standard Rechargeable Battery Modules
- 1x Compact Rechargeable Battery Module
- 1x Y Battery Charger
- 1x Charger Plug Pack
- 3x Earhooks L (1 pack of 3)
- 4x Safety Cords (Single/ Double, each 1 pack of 2)
- 2x Koala Clips
- 3x Snugfit (S/ M/ L, each 1)
- 3x Earmould Adaptors (1 pack of 3)
- 1x Bilateral Identification Adhesive Labels
- 1x Monitor Earphone Adaptor with Earphones

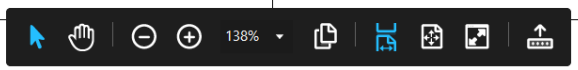
- 2x Aqua+ Sleeves (1 pack of 2)
- 1x Aqua+ Coil (8 cm)
- 1x Activity Kit Case
- 2x Aqua+ Safety Lines (1 pack of 2)
- 4x Microphone Lock Strirrups (1 pack of 4)
- 1x Magnet, Black 3(I)

- 1x True Wireless™ Device Flyer
  (to choose 1 of the following: Mini Microphone 2+/ Phone Clip/ TV Streamer)

Cochlear Nucleus 8 – Unilateral Adult New System Kit

1x Processing Unit	2x Power Extend Rechargeable Batteries
1x Earhook M	1x Compact Rechargeable Battery
2x Slimline Coils (either 6cm or 8cm)	1x Y Charger
2x Microphone Covers (1 pack of 2)	1x Charger Plug Pack
1x Battery Cover	1x Safety cord (single)
1x Battery Holder	2x Snugfits (1 each M & L)
6x power one IMPLANT plus p675 Batteries	1x Breeze by Dry & Store
1x Battery Locking tool	3x Dry Brik (1 pack of 3)
1x Microfibre Cloth	1x Recipient Backpack
1x Storage Case	1x Mini Mic 2+
4x Drying Capsules	

2x Aqua + Sleeves (1 pack of 2)	2x Aqua+ Safety Lines (1 pack of 2)
1x Aqua + Coil	4x Mic Lock stirrups (1 pack of 4)
1x Activity Case	



Cochlear™ Nucleus® Kanso® Kit Unilateral for the Nucleus Profile™ Plus Series Implant (CI600)

- 1x **Sound Processor**
- 1x **Magnet 3(I)**
- 1x **CR210 Remote Control**
- 6x **power one IMPLANT plus p675 Batteries** (1 pack of 6)
- 5x **Softwear Pads** (1 pack of 5)
- 1x **Screwdriver and Brush**
- 1x **Microfibre Cloth**
- 2x **Nucleus Safety Lines - Short Double Loop** (1 pack of 2)
- 15x **Safety Line Hair Clips** (Black/ White/ Brown, each 1 pack of 5)
- 1x **Storage Case**
- 4x **Drying Capsules**
- 1x **Breeze by Dry & Store®**
- 3x **Dry-Brik® by Dry & Store®** (1 pack of 3)
- 1x **Recipient Backpack**
- 1x **Microphone Protector Kit 2-Pack**
- 1x **Bilateral Identification Adhesive Labels**
- 1x **Magnetic Battery Removal Tool**

- 2x **Aqua+ Sleeves** (1 pack of 2)
- 2x **LR44 Aqua Batteries** (1 pack of 2)
- 1x **Activity Kit Case**
- 2x **Nucleus Safety Lines - Long** (1 pack of 2)
- 2x **Headbands** (M Black/L Black, each 1)

- 1x **True Wireless™ Device Flyer**
  (to choose 1 of the following: Mini Microphone 2+/ Phone Clip/ TV Streamer)

SIGNATURE PAGES

Signatories to Protocol:

Chief Investigator: Professor Douglas E.H. Hartley

Signature:

Date:

Trial Statistician:

Signature:

Date:

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