Interventional trial (non-CTIMP, non-device trial)
Protocol Template

Full title of trial	Treating Auditory impairment and CogniTion: a randomised, parallel, pilot trial in older adults with mild cognitive impairment and hearing loss of an intervention to provide and support hearing aid use vs a health education intervention for dementia risk (TACT)
Short title	Treating Auditory impairment and Cognition (TACT) pilot trial
Version and date of protocol	Version 1_6, 27/07/2020
Sponsor:	University College London (UCL)
Sponsor protocol number	18/0079
Chief Investigator:	Dr Sergi Costafreda Gonzalez Mental Health of Older Adults Division of Psychiatry University College London (UCL)
Funder (s):	Alzheimer's Research UK
Intervention:	Hearing intervention v Healthy Ageing Intervention
Single site/multi-site:	Single site
Sponsor Representative:	Suzanne Emerton, semerton@nhs.net Joint Research Office, UCL, 1st Floor Maple House, 149 Tottenham Court Road, London W1T 7NF Postal address:

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Protocol Version History

Version Number	Date	Protocol Update Finalised By (insert name of person):	Reasons for Update
0_1	01_02_2018	Kingsley Powell	Transferred protocol to new (correct) template and made track changes.
0_2	20_02_2018	Sergi Costafreda Gonzalez	Integration of protocol with ACHIEVE operating procedures
0_3	28_03_2018	Sergi Costafreda Gonzalez	Integration of trial interventions and inclusion/exclusion criteria with ACHIEVE interventions
0_4	05_04_2018	Kingsley Powell	Final formatting and consistency checks ready for submission to sponsor
0_5	18_04_2018	Rumana Omar	Statistical edits
1_0	04_05_2018	Kingsley Powell	Submission to sponsor and approval
1_1	17_05_2018	Kingsley Powell	Removal of MoCA, incidental learning, logical memory 1 and 2 and digit symbol substitution to reduce participant load.
1_2	29_05_2018	Kingsley Powell	Addition of COSI to 6 month outcome measure visit and monitoring plan in response to sponsor risk assessment
1_3	06_06_2018	Kingsley Powell	Removal of blinding procedures as it was decided blinding is not possible in this trial. Healthy ageing lesson 2, 'regulate blood glucose, changed to 'eat a healthy diet'. Added as part of the REC review request: If hearing loss detected, audiologist will send referral letter to GP, and participants in healthy ageing arm will be reminded to follow up hearing loss with their GP at the end of session D (last intervention visit)

1_4	06_02_2019	Kingsley Powell	- Addition that reminder texts will be optional and removal of reminder texts for healthy ageing intervention. - Statement added to say Phonak is the hearing aid provider and Way With Words will be used to transcribe the qualitative interviews. - Relax inclusion criteria from 'MCI diagnosed or confirmed in the last 12 months' to 'clinical diagnosis of MCI'. - Change in audiometric hearing impairment criterion to 'Participants must have adult-onset hearing impairment with a four-frequency pure tone average (0.5, 1, 2, 4 kHz) in the better-hearing ear of >= 25 decibels Hearing Level (dB HL) and <70 dB HL or a pure tone audiometric threshold at 4 KHz in the better ear of >= 30 decibels dB HL and <70 dB HL' - Change in exclusion criteria from 'Any self-reported hearing aid use in the past year' to 'potential participants who have already been prescribed hearing aids in the past will be excluded if they report any hearing aid use within the past month. Temporary exclusion: Potential participants will also be excluded if their hearing aids were prescribed in the past three months, irrespective of their use; however, we will contact these potential participants again after 3 months following prescription of their hearing aids and they will be eligible if they have not used their hearing aids in the past month' - Relax exclusion criterion 'Unwillingness or inability, in the opinion of the researchers, to complete trial procedures and/or wear hearing aids on a daily or near daily basis' by removing the additional text that expanded on this criterion. - Correction of incorrect statement in 'Planned recruitment rate' section. 'We conducted a small (n=12) feasibility study with the same inclusion and exclusion criteria as the proposed trial' changed to 'We conducted a small (n=12) feasibility study with similar but less restrictive inclusion and exclusion criteria as the proposed trial.'

1_5	21_10_2019	Kingsley Powell/Sergi Costafreda	- In the Section '2 Summary', we have corrected the title of the trial which had erroneously included "single blind" as this is, in fact, an open label trial. - In the Section '2 Summary', we have corrected the duration from a '12 week' to a '6 week' intervention as the longer duration was introduced in error. - Under section '2 Summary' of the protocol, we have corrected the criteria based on the approved substantial amendment 1 which removed the need for MCI to be diagnosed in the last 12 months, and allowed inclusion of participants with no use of hearing aids in the last month (rather than the last year). - Under section 4 of the protocol, titled 'Objectives', we have moved the objective to 'estimate the difference in adherence to hearing aid between the arms' from a primary objective to a secondary objective. - We updated the inclusion criterion (Section 6.1) for audiometric hearing impairment to remove the upper limit for potential participants included because of a pure tone audiometric threshold at 4 KHz in the better ear of >=30 decibels dB HL. - We updated the eligibility criteria (Section 6.1) to include people who have 'low use' of hearing aids, rather than only those who report no use in the last month. - We have changed the wording for the audiological onwards medical referral criteria. - In point 8 of the exclusion criteria (Section 6.2), we have expanded the ways in which we will advise participants how to get their cerumen removed. - Under section 7 of the protocol, titled 'Informed consent', we have added a paragraph to explain how we will adapt the informed consent process for those who are physically unable to sign the informed consent form. - We have added the 'Questionnaire on need for help for hearing aid use' to the protocol under Session A and Session C of the Healthy Ageing intervention (Section 8.3) as this is missing in error. - We have removed the repeated C2Hear video shown at Visit 3 Session B. - Update to say that either the audiologist or research assistant can conduct Session A and

			Session C of the hearing intervention instead of research assistant only. - Update to say we will replace up to two pairs of hearing aids instead of only replacing once. - Change to the definition of the primary outcome relating to recruitment and randomisation. - Change to wording for the secondary outcome related to timely hearing aid fitting. - Under the section '11. Statistical Considerations' and '11.6 Statistical analysis', we have unified the primary and secondary outcomes regarding hearing aid use. - Change to the outcome measure definition for the comparison of hearing aid use between the two intervention arms. - We added a statement to say we will contact participants via a third party software called 'GreenText'.
1_6	15_07_2020	Kingsley Powell/Sergi Costafreda	Substantial amendment with protocol changes for the Remote Hearing Intervention (RHI) sub-study during COVID-19: - Section 2.Summary: to summarise protocol changes - Section 3.Background: providing rationale for RHI sub-study. - Section 3.1. Assessment of risk: measures to ensure safety and prevent exposure to COVID-19 during RHI sub-study. - Section 4. Objectives: updated with the objectives for the RHI sub-study - Section 5: Design. Updated to include design description for RHI sub-study during COVID-19 - Section 6: Selection of participants: updated with eligibility criteria, recruitment and consent procedures for the RHI sub-study - Section 7: added description of the RHI. - Section 8: description of RHI procedures and data collection - Section 11: added outcomes specific to RHI. - Added Appendix 2. Schedule of assessments for the Remote Hearing Intervention sub-study (during COVID-19) Other minor change to protocol outside of RHI sub-study changes: - Removal of Likert scale measuring acceptability of the interventions during qualitative

			interviews and added to the list of assessments at Session D for the original TACT pilot trial. This was approved to be asked at Session D but the protocol has not been amended to reflect this, we now wish to correct this error.

Contents

List of abbreviations

Commonly used abbreviations – add or delete as applicable:

AE	Adverse Event
CI	Chief Investigator
CRF	Case Report Form
CRO	Contract Research Organisation
DMC	Data Monitoring Committee
GAfREC	Governance Arrangements for NHS Research Ethics
GCP	Good Clinical Practice
HTA	Human Tissue Authority
IB	Investigator's Brochure
ICF	Informed Consent Form
IDMC	Independent Data Monitoring Committee
IMP	Investigational Medicinal Product
ISF	Investigator Site File
ISRCTN	International Standard Randomised Controlled Trial Number
NHS R&D	National Health Service Research & Development
PI	Principal Investigator
PIS	Participant Information Sheet
QA	Quality Assurance
QC	Quality Control
RCT	Randomised Controlled Trial
REC	Research Ethics Committee
SAE	Serious Adverse Event
SDV	Source Document Verification
SOP	Standard Operating Procedure
SPC	Summary of Product Characteristics
TMG	Trial Management Group
TSC	Trial Steering Committee

1 Trial personnel

See protocol cover page for Chief Investigator and Sponsor contact details.

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2 Summary

Objectives:	To establish the feasibility of a future fully powered trial of early hearing aid provision in people with Mild Cognitive Impairment (MCI) and hearing loss in terms of delaying the onset of dementia. The pilot trial will test recruitment, attrition, and acceptability of two interventions: the hearing and healthy ageing interventions. During the COVID-19 pandemic, the trial will instead pilot a remotely delivered version of the active intervention of early hearing aid provision and support to test recruitment, feasibility and acceptability (the Remote Hearing Intervention or RHI sub-study).
Type of trial:	TACT is a pilot randomised, parallel group trial in participants with MCI and hearing loss. During the COVID-19 pandemic, the RHI sub-study will be a single-arm, non-randomised trial in the same participant population.
Trial design and methods:	For TACT, participants with hearing loss and MCI will be randomised to a hearing intervention (home-based provision of hearing aids, and adherence support delivered over a 6 week intervention) or a healthy ageing intervention (home-based educational intervention, to match intensity of social contact). Participants will be assessed on their hearing, quality of life, physical activity, mood, social interactions, and daily function at baseline and 6 months. During the COVID-19 pandemic, the RHI sub-study will be a single-arm, non-randomised trial in patients with MCI and hearing loss, who will receive a remotely delivered hearing intervention over 4 weeks.
Trial duration per participant:	6 months for intervention delivery and follow-up in TACT. The RHI sub-study during COVID-19 pandemic will last 4 weeks per participant.
Estimated total trial duration:	24 months
Planned trial sites:	Single-site
Total number of participants planned:	76 for TACT During the COVID-19 pandemic, we aim to recruit 12 participants to RHI sub-study.
Main inclusion/exclusion criteria:	Participants will be 55 years of age or older, with a diagnosis of MCI, and with mild to moderate adult-onset hearing loss, community-dwelling, without any self-reported hearing aid use in the past month.

	For the single-arm Remote Hearing Intervention sub-study during the COVID-19 pandemic, we will invite those participants that had been consented for the randomised trial prior to the onset of COVID-19 who either (a) completed the healthy ageing intervention and are not using hearing aids; or (b) were included in the trial but could not complete their allocated intervention due to the onset of COVID-19.
Statistical methodology and analysis:	The main feasibility questions that the pilot aims to answer are: (a) is the trial feasible, in the sense of resulting in sufficiently high recruitment and sufficiently low dropout (retention); (b) are the interventions and schedule of assessments deliverable and acceptable to participants; (c) we will estimate the difference in hearing aid use at 6 months between the hearing intervention and healthy ageing intervention arms to inform sample size estimates for the future trial. We are including cognitive outcomes to assess their feasibility and acceptability, and to provide estimates including standard deviation to be used in the sample size calculation for the full trial. Only descriptive analysis will be reported. We will also conduct qualitative assessment of the interventions acceptability. Prior to the onset of COVID-19, we randomised and obtained complete data for n=36 participants, confirming recruitment and retention (primary objective). These data will also allow us to address the questions (b-c) above. During the COVID-19 pandemic, we will test the feasibility and acceptability of a remote version of the hearing aid intervention.

3 Background and Rationale

Hearing loss and cognition

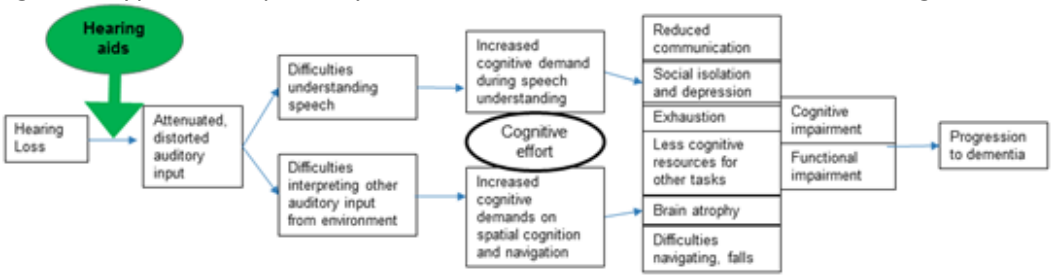
It is a new finding that hearing loss is a risk factor for subsequent dementia. Studies have recruited people aged 50 to 70 years old without dementia, measured their hearing, and followed them for up to 20 years. People with hearing loss developed dementia at nearly double the rate of people with unimpaired hearing [1]. The mechanisms for this elevated risk are unknown, but they are likely to include direct detrimental effects of hearing loss on cognitive load and the amount of cognitive effort required from the brain to meet the challenges of daily life [2]. People with hearing loss are also at increased risk of depression and social isolation, which may be an intermediate step towards dementia [3]. Long term hearing loss is associated with accelerated brain atrophy, which is the biological marker with the strongest association to dementia [4].

Hearing loss affects 2 out of 3 people over 65 in the UK [5], but most of the people who in theory would benefit from a hearing aid never get one. Even when hearing aids are prescribed, up to half of people stop using them after a short time, particularly if they have memory problems [6].

Hearing aids and dementia prevention

Untreated hearing loss may be a missed opportunity to delay and prevent dementia in a substantial number of people. Figure 1 shows the putative mechanisms whereby hearing aid use may reduce dementia risk.

Figure 1. Hypothetical pathway to dementia that could be treated with hearing aid use



Hearing aid provision is the first-line clinical intervention for adults with mild to moderate hearing loss, which constitute the vast majority of people with this condition. Hearing aids are safe, and effective at improving hearing-specific health-related quality of life, general health-related quality of life and listening ability [7]. There is some evidence that hearing aid use may improve cognitive performance immediately after fitting [8], and continuing after 4 months of use [9]. It is unknown whether these benefits of treating hearing loss on cognitive performance persist and if they translate into reduced cognitive and functional decline over time, which is key to achieving reduction in dementia risk. The only way to find out if hearing aids can help to delay dementia is to run a randomised controlled clinical trial to directly compare the effect of using hearing aids, as against usual care, on the risk of developing dementia. Such a trial has not been conducted before.

In the United States, our collaborator Dr Frank Lin is conducting the ACHIEVE trial [10], which will be assessing the effect of hearing aid use on cognitive decline in a cognitively healthy population. In our trial, we have chosen people with mild cognitive impairment (MCI) as our trial population, because people with MCI are at much higher risk of dementia (approximately 15% incidence of dementia per year, or 50% risk over 3 years) than the cognitively healthy population of the same age, so that any benefits of hearing aid treatment should be apparent within a relatively short trial period. Recruiting participants with cognitive impairment brings additional challenges, in particular it will be more difficult for our participants than for cognitively healthy subjects to learn to use the hearing aids and remember to use them regularly. Our intervention design, with home-based assessments and integration with daily routine, will address these specific obstacles.

The anticipated fully-sized trial will be powered to identify differences in cognitive decline between those allocated to an interventional arm of supported hearing aid use versus a healthy ageing intervention in the MCI population. The current project will perform preparatory work for this future full-sized trial addressing the difficulties that this future trial faces to be successful. The definitions of pilot and feasibility randomised studies used in this document are as per CONSORT statement [11].

Addressing the challenges raised by COVID-19 Pandemic

COVID-19 is a grave global challenge for public health. It is also a challenge for clinical trials, especially those relying on face-to-face delivery of interventions, such as TACT. This has been recognised by

funders and regulatory agencies. In the following we have followed recent guidance on how to restart trials safely [1],[2].

For TACT, the main challenge is ensuring the safety of participants. Participants are aged 55 and over, so they are at higher risk from COVID-19 complications; some of our participants are in the high-risk category and shielding. The initial home-based hearing aid and support intervention would therefore not be suitable as it could put participants at increased risk of contracting the virus. This is a challenge also faced by NHS audiological cases, which have been paused during the epidemic except for urgent audiological treatment. Hearing aid provision and support is not an urgent treatment. However, given that in the absence of a vaccine social distancing for vulnerable populations may be maintained for months or years, it is important that Remote Hearing Interventions for audiological care are developed and tested, with a view to potential dementia prevention in the MCI population. Effective hearing aid treatment is likely to be particularly important during the pandemic as the measures in place to prevent the spread of the virus, such as social distancing and face coverings or masks, will have a disproportionate detrimental impact in those people with impaired hearing, who often rely on lip reading for communication., We will therefore test the feasibility and acceptability of a Remote Hearing Intervention during the COVID-19 pandemic.

3.1 Assessment and Management of Risk

Adverse effects: Hearing aids are generally considered a safe treatment without clinically significant adverse effects, although safety has been identified as an understudied topic in clinical trials of hearing aid efficacy [12]. The only RCT in people with cognitive impairment and dementia to have reported on adverse effects [13] did not identify any side effects over 6 months in a sample of 48 patients.

Dizziness, nervousness and headaches are considered rare but possible adverse effects, probably linked to poor fitting of the hearing aids. In consumer surveys [14] symptoms of local discomfort have been reported, but no more serious adverse events. Noise-induced hearing loss, due to over-amplification from inappropriate hearing aid fitting is a possible but unverified adverse effect.

These risks will be minimised through strict adherence to best practices recommendations for hearing assessment and hearing aid fitting from the British Society of Audiology. We will also incorporate the upcoming NICE guidelines which are expected to be published in May 2018 [Hearing loss in adults: assessment and management; National Guideline Centre; https://www.nice.org.uk/guidance/indevelopment/gid-cgwave0833]. This is the same guidance followed within NHS audiological services. Therefore, we do not expect increased risk of our intervention for participants relative to normal standard practice, when it is considered to be a low risk intervention.

[1] Guidance On The Management Of Clinical Trials During The Covid-19 (Coronavirus) Pandemic (28/04/2020). European Medical Agency [https://ec.europa.eu/health/sites/health/files/files/eudralex/vol-10/guidanceclinicaltrials_covid19_en.pdf].

[2] A framework for restarting NIHR research activities which have been paused due to COVID-19 (21/05/2020). National Institute for Health Research [https://www.nihr.ac.uk/documents/restart-framework/24886]

In our trial we will proactively ask participants about potential side effects, and, if present, they will be reviewed by the research audiologist to identify whether these issues can be remedied by adjusting the hearing aid fitting, or if they require assessment by GP or secondary services.

This trial is categorised as:

- Type A = No higher than the risk of standard medical care

The table below summarises the risks and mitigations of all tests above standard care that are being performed:

Intervention	Potential risk	Risk Management
Otoscopy	Risk of transferring an infection between the ears Accidental damage or injury (e.g., bruising, bleeding, discomfort) to the ear, if for example, the participant makes a sudden movement during otoscopic examination	Performed by trained audiologist. Follow British Society of Audiology (BSA) Recommended Procedure for Ear Examination (2016).
Audiometric testing	Excessive noise exposure when using high intensity stimuli. Exacerbation or onset of tinnitus when using high intensity stimuli.	Performed by trained audiologist. Follow BSA Recommended Procedure for Pure-tone air-conduction and bone conduction threshold audiometry with and without masking (2011).
Tympanometry	Risk of transferring an infection between the ears Accidental damage or injury to the ear drum if insertion of the probe tip pushes impacted cerumen (ear wax) further into the external auditory canal Accidental damage or injury to the external ear and/or the ear drum due to the presence of a foreign body in the ear canal	Performed by trained audiologist. Follow BSA Recommended Procedure for Tympanometry (2013).

	Heightened pain or discomfort if undertaken with existing otalgia and/or otitis externa Accidental damage or injury to the ear if tympanometry is carried out following recent (</= 2 months) ear surgery	
Phoneme Recognition in Quiet testing	Excessive noise exposure when using high intensity stimuli.	Performed by trained audiologist following Manual of Operating Procedures.
Speech in Noise testing	Excessive noise exposure when using high intensity stimuli.	Performed by trained audiologist following Manual of Operating Procedures.
Aural Impressions	Accidental damage or injury (e.g., bruising, bleeding, discomfort) to the ear, if for example, the participant makes a sudden movement during otostop insertion using an otolight Accidental damage or injury (e.g. bleeding, brusing) to external auditory canal if otostop creates undue pressure on ear canal wall Pain or discomfort and accidental injury (e.g. bleeding, bruising) if otostop inserted too deep Accidental damage or injury to the ear drum if insertion of the otostop pushes impacted cerumen further into the external auditory canal Injection of impression material may cause discomfort or move beyond the otostop Accidental damage or injury to the ear if participant makes sudden	Performed by trained audiologist. Follow BSA Recommended Procedure for Taking an aural impression (2013).

	movement during injection of impression material	
Cerumen (ear wax) Removal	Accidental damage or injury (e.g., bruising, bleeding, discomfort) to the ear, if for example, the participant makes a sudden movement Accidental damage to the eardrum due to the pressure from an irrigation or suction instrument Risk of transferring an infection between the ears Dizzy episode due to the physical sensation of instrument or cerumen plug Excessive noise exposure as suction instruments may reach high intensity levels Exacerbation or onset of tinnitus due to high intensity level of instruments. Skin irritation of external auditory canal due to removal of essential moisture	We will advise participants to access accredited cerumen removal services, following recent NICE guidelines (https://cks.nice.org.uk/earwax, and "Hearing loss in adults: assessment and management"; NICE Guideline, June 2018 [NG98]). OR, cerumen removal will be performed by a trained audiologist who has undergone necessary training for cerumen removal procedures. The audiologist will incorporate any relevant NICE guidelines, which are expected to be published in May 2018 [Hearing loss in adults: assessment and management; National Guideline Centre]
Accelerometer	Local discomfort and skin irritation during use	Fitting performed by trained research assistant following Manual of Operating Procedures
Neurocognitive testing and questionnaires	Distress due to potential failure to perform as expected in some of the testing, or distress in answering sensitive questions about mood or function	Training on testing and questionnaire procedures will be provided by senior members of the trial team with clinical experience in administering these tests and in minimising and managing the potential distress.

Safety of research participants and personnel for the single-arm remote hearing intervention study: As discussed above we will follow the NIHR Restart Framework and EMA Guidance for management of trials during COVID-19. The measures to mitigate risk of exposure to COVID-19 include:

- No face to face study visits: all contact with participants will be conducted through remote means (SMS, phone or video calls), with participants remaining in their homes.
- There will be no visits of participants to the UCL study site.
- All study materials including hearing aids will be exchanged with participants through post. Hearing aids and associated materials will be appropriately cleaned and disinfected with appropriate measures before posting to participants.
- The study team will adhere to government guidance on social distancing, restart of work at UCL, and travel.

4 Objectives

The TACT trial will pilot a randomised controlled trial of a Hearing Intervention v Healthy Ageing Intervention **to establish the feasibility** of a future fully powered trial of early hearing aid provision and adherence support in people with MCI and hearing loss in terms of delaying the onset of dementia. The primary objective is therefore to establish feasibility of recruitment, randomisation, retention, and acceptability of the study interventions.

Secondary objectives include the assessment of trial procedures, including whether the interventions and schedule of assessments are delivered as per randomisation allocation, and whether these are acceptable to participants. The pilot will also estimate the difference in adherence to hearing aids between the arms and it will assess the feasibility and practicalities of use of novel hearing screening procedures for more efficient recruitment in the future fully-powered trial.

Details on how these primary and secondary objectives are operationalised is provided in the sections on Statistical Considerations.

During the COVID-19 pandemic, and in keeping with the overall primary objective, the study will be a single-arm, non-randomised trial piloting a remotely delivered version of the active intervention of early hearing aid provision and support to test recruitment, feasibility and acceptability .

5 Trial design

The trial is a randomised controlled pilot trial. 76 participants with mild cognitive impairment and hearing loss will be randomised on a 1:1 ratio to the TACT Hearing Intervention of home-based hearing assessment, timely hearing aid fitting, and psychological and practical support to sustain adherence to treatment, versus a Healthy Ageing Intervention (HAI), whereby the participant will be given information about their hearing impairment and advised to consult with their GP to obtain NHS audiological treatment, as well as being provided with one-to-one sessions with a researcher (matching the intensity of social contact of the Hearing Intervention) on behavioural changes that can promote healthy ageing and may reduce risk of progression from MCI to dementia.

Participants for the pilot trial will be aged 55 years or above and recruited from memory clinics with a diagnosis of mild cognitive impairment, who have evidence of hearing loss as per audiologist

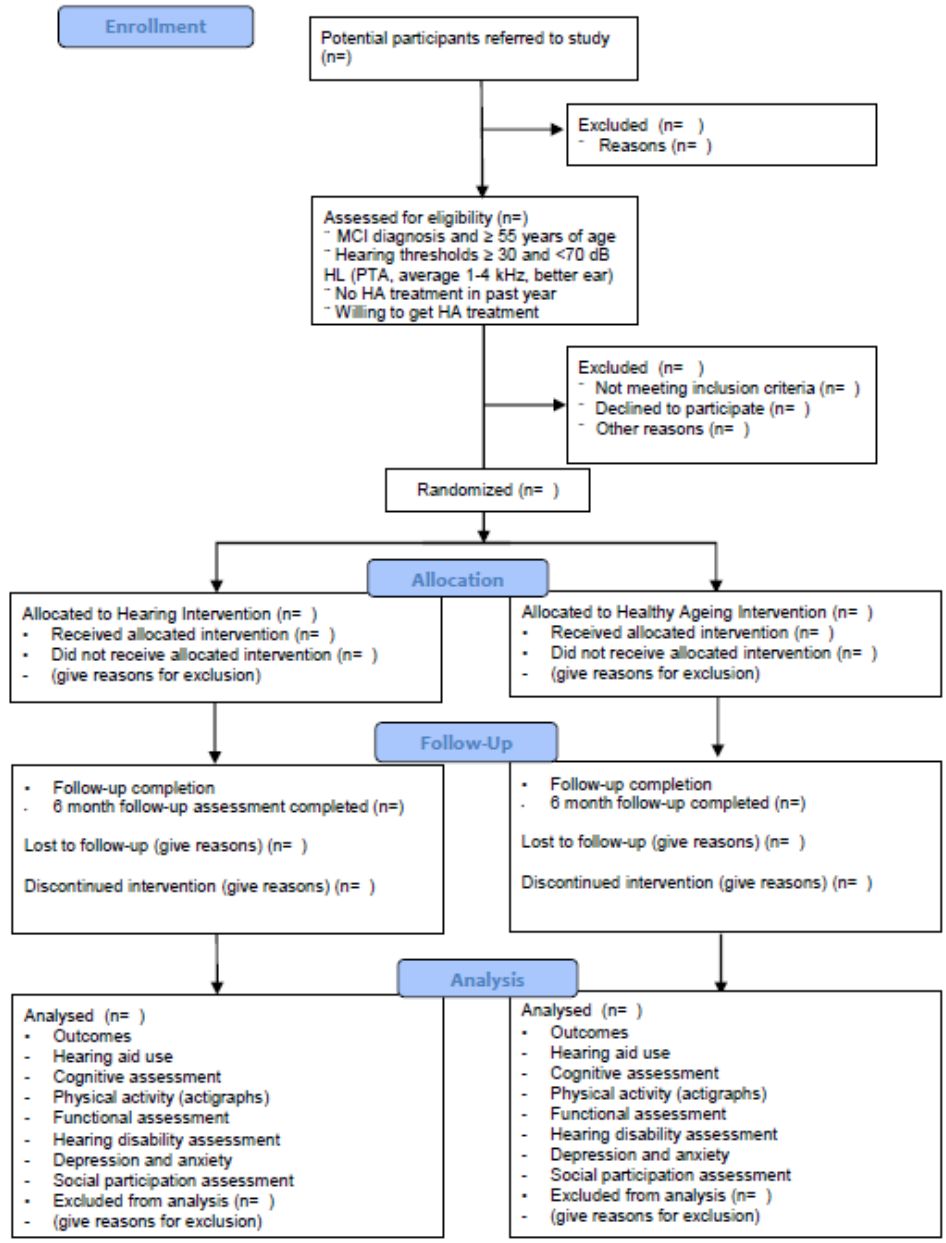
assessment, and who are willing to be treated with hearing aids if appropriate following audiology assessment. Assessments will take place in people's homes. Figure 3 presents the expected flow of participants through the trial.

The duration of follow-up in this pilot trial will be 6 months. People who abandon hearing aid use do so shortly after starting treatment, typically during the first few weeks of being fitted with aids. Conversely, there is evidence that behavioural health change, when sustained for 6 months or more is likely to be permanent [15], and therefore that adherence to hearing aids at trial end is likely to provide a valid estimate of longer term compliance. It is expected that participants allocated to the Hearing Intervention will be able to sustain adherence to hearing aids. The trial objective of 70% adherence to hearing aids treatment in the hearing intervention at 6 months, if met, will be a strong indicator that adherence is solidly established and that a longer duration definitive trial is feasible. We envisage the duration of a fully-powered trial to be 2 to 3 years.

Non-blinding of assessors

It is not feasible, due to the nature of the intervention, to blind the participants, research audiologist or the research assistants delivering the allocated intervention and carrying out the outcome assessments. The TACT trial steering committee considered blinding options for the outcome assessor at the outcome visit which included 'sham' hearing aids for those in the healthy ageing group, all participants wearing no hearing aids, or participants wearing an elasticated headband to cover their ears. After discussion with the research audiologist, trial collaborators and members of the Patient and Public Involvement (PPI) group these blinding options were found to be infeasible because of the potential adverse effects on cognitive testing.

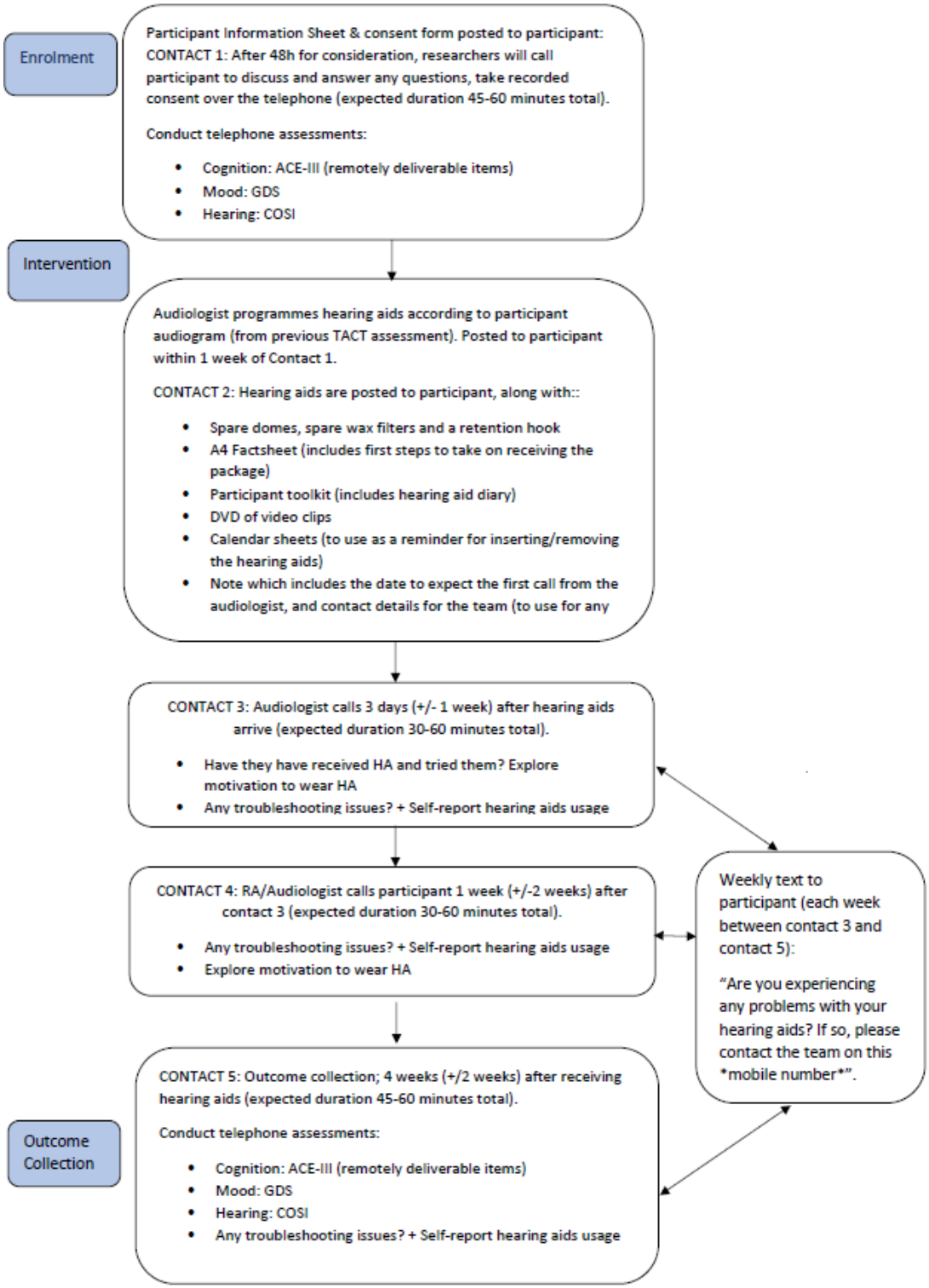
Figure 3. Participant flow diagram of TACT randomised pilot trial



Remote Hearing Intervention study during COVID-19

During the COVID-19 pandemic, the study will be single-arm, non-randomised trial in patients with MCI and hearing loss, who will receive a remotely delivered hearing intervention over 4 weeks. Figure 4 presents the expected flow of participants through the trial.

Figure 4. Participant Flow Diagram for Remote Hearing Intervention study (during COVID-19)



6 Selection of Participants

This pragmatic trial will have broad inclusion criteria to ensure generalisability to a diverse patient population.

6.1 Eligibility criteria

6.1.1 Inclusion criteria for TACT

Inclusion (all to be satisfied)

1. Clinical diagnosis of MCI following internationally recognised clinical criteria (ICD 10), as diagnosed (or confirmed) by an NHS memory Service and not superseded by a diagnosis of dementia**.**
2. **55 years of age or older** (as MCI under 55 is rarely linked to neurodegeneration and future dementia)
3. **Living in the community** (not in hospital or residential care).
4. **Mental capacity to provide informed consent to trial procedures**.
5. **Audiometric hearing impairment.** Participants must have adult-onset hearing impairment with a four-frequency pure tone average (0.5, 1, 2, 4 kHz) in the better-hearing ear of >= 25 decibels Hearing Level (dB HL) and <70 dB HL or a pure tone audiometric threshold at 4 KHz in the better ear of >= 30 decibels dB HL.
6. **Phoneme Recognition in Quiet score ⩾60% in better ear.** A phoneme recognition in quiet score <60% suggests hearing impairment that may be too severe to benefit from conventional amplification devices such as hearing aids.
7. No previous prescription of hearing aids, or, if the potential participant has been prescribed hearing aid in the past, they report no hearing aid use at all in the past month (see temporary exclusion criteria number 8a under temporary exclusion criteria), or low use because of lack of perceived efficacy. Low use is defined as less than 2 hours per day on average over the past 7 days (when at home and in usual health).
8. **Willingness to participate, be randomized and adhere to the protocol.** Participants must be willing and able, in the opinion of the researchers, to consent to participate in the trial, to be randomized, and to adhere to the trial protocol, including willingness to wear hearing aids on a daily or near daily basis if allocated to the intervention arm, and to be followed for the duration of the trial (30 weeks).

6.1.2 Exclusion criteria for TACT

Exclusion (None to be satisfied)

1. **Spoken or written English is not sufficient for trial procedures**, including reading of the trial materials, in the opinion of the research team.
2. **Diagnosis of hearing loss with onset in childhood** (<18 years of age) as reported by the patient during the initial clinical interview.
3. Participant meets **ICD-10 criteria for current substance use disorder** (abuse or dependence) or alcohol-related brain damage.
4. If the audiological assessment shows that the participant meets criteria for onward medical referral (according to British Academy of Audiology criteria), and the issue has not already

been investigated or addressed, we will request their permission to write to their GP with the results of our assessment and recommendation for referral. Where clinically appropriate the participant will continue in the trial, or the participant may be temporarily or permanently excluded based on the audiologist's clinical judgement as to whether the issue identified is a contraindication for hearing aid treatment.'.

5. **Presence of conductive hearing impairment** as determined by standard audiological assessment using the difference between air audiometry and bone audiometry ("air-bone gap") greater than 20 dB over at least 4 frequencies of 0.5,1,2,3,4 KHz on both ears, as well as tympanometry and tuning fork test (British Academy of Audiology, 2017). Because the impact of a conductive (versus a sensorineural) hearing loss on cognitive functioning may potentially differ and programming for hearing aids differs for conductive hearing loss, participants with permanent conductive hearing loss are excluded from the trial.
6. **Unwillingness or inability, in the opinion of the researchers, to complete trial procedures and/or wear hearing aids on a daily or near daily basis.**
7. **Concurrent participation in other interventional research:** participants will be excluded if they are already participating in another trial.
8. **Temporary Exclusion Criteria:**
   (a) Potential participants will be excluded if hearing aids were prescribed in the past three months, irrespective of their use; however, we will contact these potential participants again after 3 months following prescription of their hearing aids and they will be eligible if they report no or low use of hearing aids. Low use is defined as less than 2 hours per day on average over the past 7 days (when at home and in usual health).
   (b) Participants determined to have occluding cerumen as per otoscopy. These participants may be enrolled after cerumen removal. We will advise participants with occluding cerumen to access accredited cerumen removal services, following recent NICE guidelines (https://cks.nice.org.uk/earwax, and "Hearing loss in adults: assessment and management"; NICE Guideline, June 2018 [NG98]). Participants who are identified as needing cerumen removal will be advised to consult their GP to arrange cerumen removal. They will also be offered reimbursement if they choose to have privately arranged cerumen removal by an accredited provider instead. If practicable, and at the discretion of the trial audiologist, participants may also be offered cerumen removal by the trial audiologist, who has undergone necessary training for cerumen removal procedures.

6.1.3 Eligibility criteria for participants for the Remote Hearing Intervention sub-study (COVID-19)

1. For the single-arm Remote Hearing Intervention sub-study during COVID-19 pandemic, we will invite those participants that had been consented for the randomised trial prior to the onset of COVID-19, therefore meeting the inclusion and exclusion criteria at the time they consented to participate in TACT, and who either

(a) completed the healthy ageing intervention and are not using hearing aids; or

(b) were included in the trial but not could not complete their allocated intervention due to the onset of COVID-19.

2. Potential participants will be excluded if in the opinion of the research team, would be unable to complete remote procedures.

3. Potential participants will be excluded if they report any new ear pain or discharge or any audiological symptoms that would require face to face audiological assessment prior to inclusion.

It follows that, as in the pilot trial, participants will be aged 55 years or above and recruited from memory clinics with a diagnosis of mild cognitive impairment, who have evidence of mild to moderate adult-onset hearing loss as per audiologist assessment, and who are willing to be treated with hearing aids if appropriate following audiology assessment.

6.2 Communication partners: criteria for inclusion in the trial

Communication partners (CP) are adults (18+ years) who communicate with the participant on a daily or near-daily basis (4 days a week or more often), and who are able and willing to participate in the trial. Informed consent for communication partners can be obtained at the screening or baseline visit. Communication partners should have sufficient spoken and written English for trial procedures, (e.g. reading trial materials), in the opinion of the research team. Communication partners who consent to be included in the trial will be given questionnaires on communication difficulties with the main participant as well as their own quality of life and mental health, and they will be invited to participate in a qualitative interview to give their views on the acceptability of the intervention. If the main participant can no longer participate or withdraws from the study, data collection for the communication partner will end.

Friends or relatives can also support the main participant through the assessments and intervention in the trial without consenting themselves as a CP research participant. If a friend or relative is supporting the main participant with the intervention, but they are unwilling to be consented as CP research participants themselves, we will record for each trial visit that this support exists, but no other assessments will be administered. Individuals who are enrolled in the trial as a randomized participant are not eligible to also be enrolled/consented as a communication partner in the trial for another randomised participant.

For the Remote Hearing Intervention sub-study, we will collect information about whether the participant has a person who is supporting them in using the hearing aids, but there will be no data collection on CP partners.

6.3 Recruitment

Participant recruitment at a site will only commence when the trial has:

- Been confirmed by the Sponsor (or it's delegated representative), and
- Been issued an 'NHS permission letter'.

Potential participants will be identified from London NHS Memory Services (Patient Identification Centres [PICs]), with a diagnosis of mild cognitive impairment. Potential participants will have been interviewed by a clinician from one of the participant memory services for a cognitive and functional assessment and they will have received, as a result of that assessment, a new or confirmed diagnosis of Mild Cognitive Impairment following ICD-10 internationally recognised criteria [13], which is the classification employed in UK standard clinical practice.

Clinicians from participating memory services will ask potential participants (patients who have had a new diagnosis of MCI or their diagnosis has been confirmed during the period of trial recruitment) about their willingness to be contacted for the trial. Those who agree will be referred to the trial through a secure pathway which adheres to data protection regulations (for example phone and NHS.net contact). Research assistants from the trial will attend memory services' weekly multidisciplinary meetings, which will help us to identify those participants who could potentially be recruited for the trial.

Trial recruitment will also be supported by NIHR CRN funded research nurses if available.

Where available, we will review the list of patients diagnosed with MCI who have indicated their consent to be contacted for research. Patients from Camden and Islington NHS Foundation Trust (CandI, proposed PIC for the trial), are routinely asked about whether they are happy to hear about generic research opportunities (any current or future projects for which they might be suitable) and their answer is recorded in a database. We will conduct database searches of potential participants who have agreed to be contacted for research.

We anticipate that the main recruitment base for the pilot trial will be Camden and Islington Memory services, but we will also apply for permission to recruit from the nearest London Memory Services to facilitate logistics. Camden & Islington Memory Services alone exceed 1200 new patient referrals per year, of which 20% have MCI (240 people per year). We estimate that based on these six PICs, the referral rate will be approximately six potential participants per week; two participants will be suitable and will agree to participate (one per research assistant). We conducted a small (n=12) feasibility study with the same inclusion and exclusion criteria as the proposed trial. This study recruited seven participants in four weeks, of which five were confirmed to have untreated hearing loss and would have met inclusion criteria for the planned trial (1.25 potential participant per week), based on a single memory service, so the projected figures should be achievable.

For the Remote Hearing Intervention sub-study (during COVID-19), we will contact those participants that had previously been consented for the randomised trial prior to the onset of COVID-19, therefore meeting the inclusion and exclusion criteria at the time they consented to participate in TACT, and who either (a) completed the healthy ageing intervention and are not using hearing aids; or (b) were included in the trial but not could not complete their allocated intervention due to the onset of COVID-19. No other new participants will be recruited.

6.4 Informed consent

Potential participants will be told about the trial by their clinicians, or, if they have accepted to hear about research opportunities, we will contact potentially eligible participants by phone, letter or at a memory clinic appointment, to ask whether they would be interested in participating. If the potential participant agrees to hear about the trial, we will send them a participant information sheet. If there is a communication partner involved who would also be happy to participate, we will also send them an information sheet. Following this, we will contact the participant and their communication partner within 48-72 hours to answer any questions they may have about the trial and confirm whether or not they wish to take part.

It is the responsibility of the Investigator, or a person delegated by the Investigator to obtain written informed consent from each participant prior to participation in the trial, following adequate explanation of the aims, methods, anticipated benefits and potential hazards of the trial. Participant consent will be obtained at the screening visit before any procedures. The research assistant will have been GCP trained, and will have received specific training in consent for research purposes provided by the trial team, and they will have been delegated this duty by the CI on the Staff Signature and Delegation of Tasks (delegation log). All researchers will adhere to the respective Trust policies for home visits.

Some potential participants may have physical disabilities that render them unable to initial the consent form. These participants may use ticks instead of initials in the consent form. Potential participants may also be physically unable to sign the consent form. These participants may use a mark or tick instead of

signature. If these alternate forms of consent are used, the researcher taking consent will document the rationale for this in the trial documentation. This procedure is consistent with HRA guidance[3].

The Investigator or designee will explain that participants are under no obligation to enter the trial and that they can withdraw at any time during the trial, without having to give a reason. No trial procedures will be conducted prior to the participant giving consent by signing the consent form. Consent will not denote enrolment into trial. A copy of the signed consent form will be given to the participant. The original signed form will be retained in the trial master file at site and a copy placed in the medical notes. The PIS and consent form will be reviewed and updated if necessary throughout the trial (e.g. where new safety information becomes available) and participants will be re-consented as appropriate.

Potential participants lacking capacity will be excluded. However, as the participants of this trial will have been diagnosed with MCI, we do not expect them to lack capacity. As the trial progresses, we will continue to assess their capacity on an ongoing basis at each visit. All members of the research team with participant contact are GCP-trained and will be trained in the assessment of capacity, including for research participation. Any doubts about capacity will be discussed with the CI.

For the Remote Hearing Intervention sub-study (during COVID-19), we will approach TACT participants as per sections 6.1-6.3 above. Those who agree to consider participation in the RHI sub-study will be posted a Participant Information Sheet & consent form (the consent form is for their reference, but consent will be taken verbally over the telephone). After 48h for consideration, researchers will call these participants to discuss and answer any questions, and take recorded consent over the telephone (expected duration 45-60 minutes total). This consent will be recorded with the participants' permission.

7 Product/Interventions

7.1 Name and description of intervention(s) under investigation

The Hearing Intervention

Motivation for the intervention. A key difficulty in delivering a trial of hearing aids to prevent dementia arises from the expected low adherence to hearing aid use in standard audiological care. Currently less than one in three people with hearing loss in the UK are prescribed hearing aids, and, of those who start using them, up to half of them do not use them consistently or abandon them altogether. Lack of adherence to hearing aids is also more prevalent in those with MCI, as poorer cognition is a risk factor for non-use of hearing aids in those with hearing loss. With optimal fitting and post-fitting support, long-term adherence to hearing aid use can exceed 80% as shown by population-based survey data in Switzerland [17] and as demonstrated in the pilot of the ACHIEVE study [18].

We have conducted preparatory qualitative and feasibility studies, in which we identified several obstacles for hearing aid use in people with MCI and mild dementia. Our qualitative interviews established that people with MCI have additional difficulties to the rest of the population in hearing aid use linked to their cognitive impairment, often forgetting they have them or where they are. We also tested the hearing of 17 people recently diagnosed with MCI, and found that 12 of them (70.5%) had untreated hearing loss. We reported these findings to their GPs, and found that, after three months, only three participants had been assessed by audiology, and of those, only two participants had been prescribed hearing aids, with both of them reporting difficulties using them and declining time of use (less than four hours).

[3] http://www.hra-decisiontools.org.uk/consent/principles-general.html

The conclusion from this preparatory work is that using routine NHS pathways for audiological assessment and hearing aid prescription would not be an effective option for the trial as most participants would remain untreated. Our work has also shown that even if prescribed, many people are likely to abandon hearing aid use if we only provide them with routine, clinic-based NHS care. Low adherence to hearing aids would make a trial unfeasible. We have therefore developed the Hearing Intervention to provide hearing aid treatment and support hearing aid use in people with MCI.

Intervention components. The Hearing Intervention is a manualised intervention which assesses, treats and supports people in their own home so they remain adherent to hearing aid use. The Hearing Intervention adapts the best practices hearing intervention of the ACHIEVE trial (which is clinic-based) to address the additional memory-related obstacles to hearing aid use that we expect in the MCI population. The Hearing Intervention also incorporates the British Society of Audiology best practices guidelines for use in a British context. The intervention consists of hearing aid provision, as well as a series of one-to-one home visits with our researchers to: identify and address the participants' individualised hearing needs; provide training and practical support to use the hearing aids effectively; and provide reminders and cues to hearing aid use that can be integrated into the person's daily routine.

Based on current evidence and our previous work in people with MCI we have modified the ACHIEVE intervention. These modifications have included an added emphasis on training, repetition and simplification of information, simplification of trial procedures as well as adapting these procedures to a home-based intervention. The intervention emphasis will evolve throughout the intervention, with a shifting focus from motivation and planning in hearing aid pre-fitting and fitting meetings, and towards coping, monitoring and support after fitting. A model of the intervention and its components is presented in Figure 2.

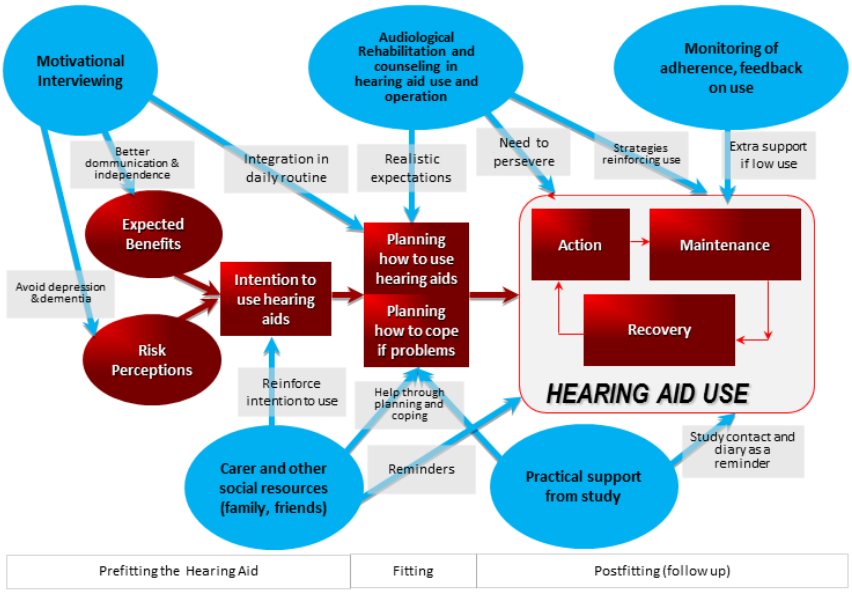


Figure 2. Prototype of the intervention to support hearing aids use. The cognitive processes that lead to the participant deciding to start to use hearing aids and persist with them (in red) are reinforced by the different components of the intervention (blue and light grey). Carers will be included as part of the intervention whenever possible. The Health Action Process Approach framework, HAPA, is adapted from Schwarzer, 2008 [19].

The intervention will be delivered at the participants' homes to facilitate engagement and reduce anxiety, by a research audiologist in combination with a graduate psychologist research assistant. The intervention will be manualised to facilitate standardisation and scalability, but will also be individualised according to the individual's needs and circumstances. If available, a communication partner will participate in the intervention.

Further details on our intervention are provided in section 8.3 of this document (page 34).

The Remote Hearing Intervention (RHI)

The RHI will attempt to replicate the Hearing Intervention during COVID-19, where contact with participants needs to be avoided as it would carry the risk of spreading the virus. Participants will be provided with the hearing aids and an adapted toolkit, factsheet, calendar sheets and DVD of video clips on hearing aids operation and management (Figure 3). This will be remotely supported by the study team, including programmed contact and, if required, troubleshooting by the audiologist. Remote contact will also be used by the researchers to remind participants to wear their hearing aids and promote hearing aid use.

The Healthy Ageing Intervention

From the point of view of hearing care, the Healthy Ageing Intervention will be a control intervention, with audiological treatment as usual provided, whereby participants will be told that the trial assessment has identified a potentially treatable hearing loss, and they will be encouraged to contact their GP and discuss treatment options.

The purpose of this control arm is to judge the acceptability of being randomised after confirmation of hearing impairment, so that we know the feasibility of moving to a full scale trial. Ethical reasons preclude a trial using a non-intervention arm that would deny hearing treatment to people who need it. Therefore, participants in this arm will have the results of their audiological assessment communicated to them with advice to visit their GP should they wish to seek NHS audiological treatment. Based on previous published evidence of poor take-up and low adherence to hearing aids, as well as our own preparatory work, we expect participants in the control arm to obtain and adhere to hearing aids at a very low rate, and sufficiently low to provide a meaningful comparison with participants in the Hearing Intervention, where we expect high hearing aid adherence.

Audiological services in the UK aim to provide treatment (usually a hearing aid) within 18 weeks of GP referral. In London, the median waiting time between referral and treatment is 3.3 weeks, with 97% of patients receiving treatment within 18 weeks, according to recent figures (NHS England, December 2017). Therefore the trial duration (6 months) should allow sufficient time for hearing aid fitting in the Healthy Ageing Intervention arm should the participant wish to pursue this treatment. We will consent participants so we can review GP notes and audiology clinical records as to whether a referral for audiological assessment was made and whether hearing aids were prescribed. NHS-prescribed hearing aids currently have data-logging capabilities, so that objective information on hearing aid use can be obtained from users in the Healthy Ageing Intervention arm as well as in the Hearing Intervention arm. The proportion of people in the Healthy Ageing Intervention arm who will be prescribed hearing aids and the degree to which they will adhere to this treatment when no adherence support is provided are necessary numbers for the planning of the future trial. In the control arm, we expect prescription of hearing aids and compliance to be very low based on previous evidence.

Social contact may be an important element in preventing progression to dementia. The Hearing Intervention as part of the TACT trial is an intensive intervention, involving several one-to-one sessions between the participant and a researcher. The control arm intervention (Healthy Ageing) will therefore be matched to the Hearing Intervention in terms of social contact with researchers. During these matched face-to-face sessions, the researchers will be delivering a Healthy Ageing Intervention of health education on different topics targeting areas of behavioural change acting on several risk factors that have been linked to progression from MCI to dementia. The Healthy Ageing Intervention is based on the ACHIEVE equivalent intervention [18, 20] with modifications for the UK context and

NHS guidance. These topics are delivered as manualised one-to-one sessions with a researcher, focusing on a risk factor at a time. The intervention is manualised, and the researchers delivering the intervention will be certified using existing online training. The topics used in the Healthy Ageing Intervention in this trial will include:

- Lower systolic blood pressure
- Eat a healthy diet
- Be physically active
- Maintain healthy bones, joints and muscles

7.2 Storage and handling of drug at site (if applicable) N/A

7.3 Accountability of drug (if applicable) N/A

7.4 Concomitant medication (if applicable) N/A

7.5 Dosages, modifications and method of administration (if applicable) N/A

8 Trial procedures

8.1 Pre-intervention assessments

Screening visit (Visit 0, day 0)

The screening visit will be conducted by an audiologist (Aud) and research assistant (RA).

The following trial procedures will be conducted at the screening visit (Visit 0):

- Consent of participant, and, if applicable, of communication partner (RA)
- Assessment of non-audiological eligibility criteria: confirm that criteria are met with regards to age, English command, willingness to be randomised and comply with trial procedures (RA)
- If the participant is eligible, then administration of hearing screening: Hearcheck and Shoebox audiometry (RA)
- Measurement of ambient noise (sound level meter), with remedial measures taken if ambient noise greater than 50 A-weighted decibel dB(A) (Aud)
- Interview and assessment by research audiologist, audiological medical history, visual inspection, otoscopy, tympanometry, pure tone audiometry (air conduction (with Audiocups), bone conduction & masking), tuning fork test (if required), phoneme recognition in quiet, speech in noise (QuickSIN); to assess audiological eligibility criteria (Aud)
- if individual meets all the inclusion criteria, inclusive of audiometric eligibility criteria, as per section 6.1 and 6.2: randomisation (Aud)

- if randomised to hearing intervention: evaluation of optimal hearing aid type (based on audiometric test results, physical appearance of outer ear, and manual dexterity); decision on earmold or receiver-in-canal (RIC). If earmold then take impression at end of visit (Aud)
- if hearing loss is detected, the research audiologist will inform the participant's GP of the results of the hearing test

The screening visit can be administered over two sessions on different days if required. The assessment will be timed by the RA, as one of the objectives of the trial is to assess tolerability of the schedule of assessments, with 2 hours considered the maximum tolerable for frail older adults. If the assessment goes beyond two hours, or if the participant requests a break or is showing signs of fatigue in the opinion of the researcher, the researcher will offer scheduling another meeting within 2 weeks to finalise the testing.

Baseline visit (Visit 1)

The baseline visit will be conducted by an RA.

Purpose: to gather baseline measures of primary and secondary outcomes.

When: Day 0 to 2 weeks after screening (V0) and 1-2 weeks before first intervention visit (V2).

The following trial procedures will be conducted at baseline visit (V1) with participant:

- obtain demographic information
- obtain medical history, including history of falls, and current medication
- Procedure to verify that participant can adequately hear instructions from tester and stimuli of the battery
- administer neurocognitive battery
    - Speech audibility procedure (ensuring speech understanding for tests)
    - Delayed word recall test (DWRT): encoding [23]
    - Addenbrooke Cognitive Examination (ACE-III) [22]
    - Trail Making Test (TMT) Part A and B [25]
    - Delayed word recall test (DWRT): recall
- Self-reported hearing disability - Hearing Handicap Inventory for the Elderly – Screening version (HHIE-S) [27]
- Geriatric depression scale (GDS) [28]
- Quality of life questionnaires
    - Short Form 36 [29]
    - EQ-5D [30]
- Items of the Lawton – Brody Instrumental Activities Of Daily Living Scale (I.A.D.L.): rated by RA based on self-report. Items: A. Telephone, F. Transport, G. Medication, H. Finances as those are the most predictive of future progression to dementia [31]
- Social function scale SF-DEM – patient rated version [32]
- UCLA Version 3 Loneliness Scale [33]
- Grip strength
- Fitting of accelerometer

If communication partner is present, the following procedures will be conducted:

- Consent of communication partner (if not done at screening visit – V0)
- Demographic data for communication partner

- Quality of their communication with the participant and HL impact: The Hearing Impairment Impact–Significant Other Profile
- Health-related quality of life of communication partner: SF36 and EQ-5D
- Hospital anxiety and depression HADS34], validated in caregiver population
- Proxy information on participant:
    - Carer-rated version of the SF-DEM [32].
    - Four-items (A,F,G,H) of Lawton – Brody Instrumental Activities Of Daily Living Scale

The assessment will be timed by the RA. If the assessment goes beyond two hours, or if the participant requests an adjournment at any time or are showing signs of tiredness in the opinion of the researcher, the researcher will offer scheduling another meeting within 2 weeks.

All pre-treatment procedures will be carried out as specified in the schedule of assessments (appendix 1). Given that many of the participants will be older adults with poor memory and with some risk of experiencing health difficulties, it may not be possible to complete the visits within the scheduled time then a delay is permitted. There are no cut-off times, rather, every effort should be made for the participant to complete the necessary visits within schedule. Reasons for delays or deviations from the allocated schedule will be recorded.

Pre-intervention procedures for RHI sub-study (during COVID-19)

After consent, participants' baseline outcome measures will be obtained through remote interview. These will include a simplified version of the above battery to include:

- Collection of medical or audiological history, or update on any changes in medical or audiological history since TACT baseline visit if applicable (when this information was initially collected)
- Mood: Geriatric depression scale (GDS) [28]
- Cognition: Addenbrooke Cognitive Examination (ACE-III) [22]; these will include only those items that can be obtained by remote assessment
- Hearing: Personalised goal-setting for the Remote Hearing Intervention, using the Client Oriented Scale of Improvement (COSI; developed by the National Acoustic Laboratories of Australia)

8.2 Randomisation Procedures

Following participant consent, and confirmation of eligibility at the screening visit (see section 8.1 for pre-treatment assessments), the participant will be allocated a participant trial number and the randomisation procedure described below will be carried out. An independent statistician will generate the randomisation list which will be uploaded to REDCap (an online randomisation database) for online concealed allocation. Participant randomisation will then be undertaken centrally by the coordinating team using REDCap. Participants will be randomised to either the Hearing Intervention or Healthy Ageing Intervention by computer programme on a 1:1 ratio. The randomisation list and the Trial Subject Log will be kept by the trial manager. The audiologist will receive by secure communication the participant's allocation to the Hearing or Healthy Ageing Intervention.

Participants are considered to be enrolled into the trial following: consent, pre-treatment assessments (see section 8.1), confirmation of eligibility, completion of the randomisation process, allocation of

the participant trial number and intervention by the central coordinating team.

The RHI sub-study (during COVID-19) will not be randomised. All participants will be allocated to the RHI.

8.3 Intervention procedures

Rationale for intervention delivered in home visits

The Hearing Intervention is a home-based intervention. The intervention will be delivered at participants' homes, unless the participant prefers otherwise (in which case it will be delivered at UCL premises), by a research audiologist in combination with a graduate psychologist research assistant. The intervention will be manualised to facilitate standardisation and scalability, but will also be individualised according to the individual's needs and circumstances. If available, a communication partner will also participate in the intervention. Our previous research has shown that the standard audiological pathway that relies on patients proactively attending appointments in NHS clinics is likely to result in many participants not receiving hearing aids or not using them. Attending clinic appointments is a challenge and barrier for care in this population, as people often forget their medical appointment and misplace reminders. This is consistent with the experience of the researchers in the trial who are also clinicians working with people with cognitive impairment and dementia (Dr Costafreda, Prof Livingston), where our Islington Memory service, which, unusually, is almost entirely based on home visits, has achieved near-complete detection of dementia, whilst in many areas dementia diagnosis only reaches 50% of people with the condition. Home visits will also facilitate engagement and reduce anxiety in participants, as well as helping our researchers understand the patient environment and routine, which will be essential to personalise the audiological objectives to each individual participant and lifestyle, as well as helping to integrate hearing aid use into the participant's daily routine.

Overview of the Hearing Intervention and timing of intervention visits

Bilateral, behind the ear (BTE) or receiver in the canal (RIC) hearing aids will be fitted, depending on the participants' characteristics as determined by audiological assessment at the screening visit. The hearing aids will have wireless data logging capabilities, allowing objective recording of adherence, independent of the participant recall. Hearing aids with rechargeable batteries will be used, whenever possible, to minimise and facilitate maintenance. For participants in the Healthy Ageing arm that obtain hearing aids through the NHS or the private sector, we will request permission to download usage data from their devices. We anticipate that in most cases, and particularly for NHS provided hearing aids, we will be able to obtain usage data through data logging. We will collect any failures to obtain data logging from hearing aids as secondary outcomes for the trial.

These hearing aid devices will have fitting and verification procedures that can be conducted at the participant's home. The setting up of the hearing aids will be personalised to maximise audibility and incorporate appropriate noise reduction. Participants will complete a calendar to record their daily use, which will act as a reminder for use. Hearing aids placement, operation and maintenance will be explained, with advice adapted to the person's routine.

We will work with the participant and any family carers to understand the participant's routine and identify practical ways to integrate hearing aid use into their habits by finding specific times of putting on and taking out the hearing aids. A specific spot in the home will be identified at this visit for hearing

aids to be stored when unused in a specific box provided by the trial, which will also contain the usage calendar, literature on how to troubleshoot any practical difficulties, and a hotline (phone and email) to the researchers if that fails. Personalised information on how the hearing aid fits into the participant's routine, in the form of a written schedule of activities for a typical day, will be left with the participant on the cover of the box containing the hearing aids, so that it acts as a reminder of use.

A personalised report on hearing aid use based on data logging will be provided using a traffic light system with red for low use, and additional support will be provided at the visit if needed.

The intervention sessions are anticipated to occur according to the following schedule:

- Session A: Week 3-4 after screening
- Session B: Week 5-6
- Session C: Week 7-8
- Session D: Week 9-10

During treatment phase, visits should occur +/- 14 days of the scheduled date. Efforts will be made to complete the intervention sessions in the timeframe specified. However, if it is not possible for any reason to complete the visit within the scheduled time then a delay is permitted. There are no cut-off times, rather, every effort should be made for the participant to complete the necessary sessions when possible.

Hearing Intervention –Session A (V2)

- Visit will be delivered by RA or research audiologist and will include the communication partner, if applicable. The visit will focus on
    - Overview of the Hearing Intervention and orientation
    - Provide and introduce the trial materials for self-management of hearing loss: binder, box, written reminders for hearing aid use
    - Exploring the participant's routine, daily life activities and communication needs
        - Personalised goal-setting for the Hearing Intervention, using the Client Oriented Scale of Improvement (COSI; developed by the National Acoustic Laboratories of Australia)
        - Assessment of routine activities (scripted questions)
        - Questionnaire on need for help for hearing aid use
    - Discuss and decide on where is best to put reminders for hearing aid use based on routine activities; Placement of reminders for hearing aid use
    - Video C2Hear on "what to expect when wearing hearing aids"
    - Downloading data from accelerometer
    - Adverse events questionnaire

Healthy Ageing Intervention – Session A (V2)

- Visit will be delivered by RA. The visit will focus on
    - Overview of the Healthy Ageing Intervention and orientation
    - Presenting the trial materials for the Healthy Ageing Intervention
    - Lesson: lowering systolic blood pressure
    - Downloading data from accelerometer
    - Questionnaire on need for help for hearing aid use
    - Adverse events questionnaire

Hearing Intervention – Session B (V3)

- Visit will be delivered by the research audiologist and will include the communication partner, if applicable. It will focus on
    - Outcome tools:
        - Review of goal-setting (COSI)
    - Electroacoustic analysis of hearing aid performance (can be conducted prior to Session B without the participant present if time permits)
    - Hearing aid fitting
        - Real Ear Measures (verifying the gain and output of hearing aids) and verifying loudness comfort
    - Hearing Aid Orientation:
        - Demonstration and training on using hearing aids
        - Videos on "adapting to wearing hearing aids"
        - Discussion on realistic expectations: expected benefits and typical initial difficulties (own voice quality, whistling, loud noises); adaptation to hearing aids as a learning process
        - Review of integration in daily routine and use of reminders
    - Provide calendar to record hearing aid use
    - Adverse events questionnaire

Healthy Ageing Intervention – Session B (V3)

- Visit will be delivered by RA. The visit will focus on
    - Lesson: Eat a healthy diet
    - If applicable: self-report on hearing aid use & data logging (with support from the Audiologist if required)
    - Adverse events questionnaire

Hearing Intervention – Session C (V4)

- Visit will be delivered by RA or research audiologist and will include the communication partner, if applicable. It will focus on
    - HA usage estimate
        - Data logging
        - Calendar check & self-report
    - Reviewing integration of hearing aid use in routine
        - Hearing aids benefits (against COSI objectives)
        - Hearing aids problems: placement and typical initial difficulties
        - Practical aspects: batteries, cleaning, maintenance
        - Questionnaire on need for help for hearing aid use
    - Review and reinforce hearing aid orientation and training as needed
        - Videos on "adapting to wearing hearing aids"
        - Realistic expectations
        - Communication strategies that complement hearing aid use and strategies for communication in noisy environment
    - Task 1: as selected by participant from their personalised COSI goals. Feedback on HA use and communication strategies.
    - Adverse events questionnaire

Healthy Ageing Intervention – Session C (V4)

- Visit will be delivered by RA. The visit will focus on
    - Lesson: Be physically active
    - If applicable: self-report on hearing aid use & data logging (with support from the Audiologist if required) and questionnaire on need for help for hearing aid use.
    - Adverse events questionnaire

Hearing Intervention – Session D (V5)

- Visit will be delivered by the research audiologist and will include the communication partner, if applicable. It will focus on
    - HA usage estimate
        - Data logging
        - Calendar check & self-report
    - Reviewing integration of hearing aid use in routine
    - Fine tuning and optimisation of HA fitting including programming adjustments (if required)
        - Review of any ongoing specific difficulties
        - Electroacoustic analysis (if required)
        - Real Ear Measurements
        - Questionnaire on need for help for hearing aid use
    - Review of goal-setting (COSI), any progress made, and barriers to progress
        - Reinforcing and review of communication strategies introduced in Session C
    - Review and reinforce hearing aid orientation and training as needed
    - Adverse events questionnaire
    - Participant rating of the acceptability of the Hearing Intervention using a 5-point Likert scale.

Healthy Ageing Intervention – Session D (V5)

- Visit will be delivered by RA. The visit will focus on
    - Lesson: Maintain healthy bones, joints and muscles
    - If applicable: self-report on hearing aid use & data logging (with support from the Audiologist if required) and questionnaire on need for help for hearing aid use.
    - Adverse events questionnaire
    - For those participants who have not received/sought medical advice for their hearing loss: At the end of session D the RA will remind the participant (and their communication partner where applicable) that their hearing test suggested they have hearing loss and the participant will be advised to follow this up with their GP.
    - Participant rating of the acceptability of the Healthy Ageing Intervention using a 5-point Likert scale.

Additional contact and irregular visits

In addition to the above visits, participants will be contacted through optional SMS to remind them to use the hearing aids and reinforce calendar completion (in the Hearing Intervention Arm). Within the first week after hearing aid fitting, and between visits afterwards, participants will be contacted via

telephone if feasible, or through alternatives (family, the post or visits) to make sure that the hearing aids are working. After the intervention visits are finished we will also proactively contact the participant monthly afterwards through telephone if feasible, or through alternatives.

Additional contact (email, telephone or visits) with the RA or the research audiologist may be scheduled to provide troubleshooting of practical problems or additional training, with the agreement of the trial manager or CI. This can be motivated by participant or by the investigator. The number, modality, goal and duration of contact will be logged and used as a secondary trial outcome to see if the intervention is sufficient as planned.

Intervention in the RHI sub-study (during COVID-19)

The RHI will replicate the Hearing Intervention during COVID-19. The hearing aids will have been programmed by the research audiologist based on the audiogram obtained at the TACT screening visit.

Participants will be provided with these hearing aids and an adapted toolkit, factsheet, calendar sheets and DVD of video clips on hearing aids operation and management (Figure 3). Hearing aid use will be remotely supported by the study team, including programmed contact and, if required, troubleshooting by the audiologist. The following will be planned contacts of the RHI:

Contact 1: Pre-intervention – consent and baseline assessments

Contact 2: Hearing aids are posted to participant, along with:

- Spare domes, spare wax filters and a retention hook
- A4 Factsheet (includes first steps to take on receiving the package)
- Participant toolkit (includes hearing aid diary)
- DVD of video clips
- Calendar sheets (to use as a reminder for inserting/removing the hearing aids)
- Note which includes the date to expect the first call from the audiologist, and contact details for the team (to use for any troubleshooting issues)

Contact 3: Audiologist calls 3 days (+/- 2 days) after hearing aids arrive (expected duration 30-60 minutes total).

- Have they have received HA and tried them?
- Explore motivation to wear HA
- Communication strategies
- Troubleshooting of any issues
- Self-report hearing aids use
- Adverse events questionnaire

Contact 4: RA/Audiologist calls participant 1 week (+/- 1 week) after contact 3 (expected duration 30-60 minutes total).

- Troubleshooting of any issues
- Self-report hearing aids use

- Explore motivation to wear HA
- Adverse events questionnaire

At the end of the RHI there will be an outcome collection contact (contact 5) described in the next section.

Remote contact will also be used by the researchers to remind participants to wear their hearing aids and promote hearing aid use, and to troubleshoot any emerging difficulties. Between contact 3 and contact 5, participants will receive weekly texts with the following: "Are you experiencing any problems with your hearing aids? If so, please contact the team on this *mobile number". Ad-hoc remote contact and postage of hearing aids (for adjustment/repair, with postage paid by the study) between the participant and the audiologist can also be scheduled if required at the request of the participant and at the discretion of the audiologist.

Any of the study contacts can be split over two or several telephone calls, if requested by the participant or at the researcher's discretion.

8.4 Subsequent assessments and procedures

Assessment of adherence

Adherence includes adherence to both hearing aids and protocol trial procedures. Adherence to hearing aid use will be monitored by data-logging and participant self-report and calendar. However, adherence to hearing aids is an outcome of the trial and it would therefore be inappropriate to set a minimal compliance target to remain in the trial. Noncompliance to the protocol procedures will be documented by the investigator and reported to the Sponsor as agreed. Participants who do not fully adhere to the intervention will still be followed and assessed as per trial procedures.

Outcome assessment: Follow-up visit at 6 months (V6)

Purpose: to gather outcome measures of primary and secondary outcomes.

When: 6 months post-randomisation (with a tolerance or +/- 4 weeks)

This visit will be conducted by the RA who will first collect information about hearing aid usage:

- HA usage estimate
  - Data logging
  - Calendar check & self-report

The RA will also try to collect data logging information for Healthy Ageing participants who received treatment as usual for audiological care and were provided with hearing aids through either the NHS or the private sector.

The following trial procedures will be conducted at this visit by the RA, with participant:

- administer neurocognitive battery
  - Speech audibility procedure (ensuring speech understanding for tests)
  - Delayed word recall test (DWRT): encoding [23]
  - Addenbrooke Cognitive Examination (ACE-III) [22]
  - Trail Making Test (TMT) Part A and B [25]
  - Delayed word recall test (DWRT): recall

- Self-reported hearing disability - Hearing Handicap Inventory for the Elderly – Screening version (HHIE-S)
- Quality of life questionnaires
    - Short Form 36
    - EQ-5D
- Four-items (A,F,G,H) of Lawton – Brody Instrumental Activities Of Daily Living Scale
- Question: any falls over the past 6 months.
- Social function scale SF-DEM – patient rated version
- UCLA Loneliness Scale
- Grip strength
- Downloading data from accelerometer
- Adverse events questionnaire
- Client Oriented Scale of Improvement (COSI)
- Questionnaire on need for help for hearing aid use

If a communication partner is present, the following procedures will be conducted with the communication partner:

- Quality of their communication with the participant and HL impact: The Hearing Impairment Impact–Significant Other Profile
- Health-related quality of life of communication partner: SF36 and EQ-5D
- Hospital anxiety and depression HADS, validated in caregiver population
- Proxy information on participant:
    - Carer-rated version of the SF-DEM .
    - Lawton – Brody Instrumental Activities Of Daily Living Scale (I.A.D.L.)

The accelerometer will be recovered by a research assistant one week after outcome assessment visit.

At the end of the trial the participants will be able to keep the hearing aids, which will be covered by the standard guarantees of the manufacturer. If, after the trial, the participants require further audiological advice or care they will be advised to consult their GP to seek a referral to NHS audiological services.

Outcome assessment: Early Discontinuation Visit

In case of Early Discontinuation, we will attempt to conduct a visit with the same procedures as the Follow-up visit at 6 months as far as possible.

Outcome assessment for the RHI sub-study: Contact 5

At the end of the RHI there will be an outcome collection contact (contact 5). Outcome collection will be done at 4 weeks (+/2 weeks) after receiving the hearing aids (expected duration 45-60 minutes total). These will include the same assessment tools administered at the RHI sub-study baseline assessment (a simplified version of the TACT assessment battery), namely:

- Mood: Geriatric depression scale (GDS) [28]
- Cognition: Addenbrooke Cognitive Examination (ACE-III) [22]; these will include only those items that can be obtained by remote assessment

- Hearing: Review of personalised goal-setting for the RHI, using the Client Oriented Scale of Improvement (COSI; developed by the National Acoustic Laboratories of Australia); discussion of any progress made, and barriers to progress.

We will also collect at this contact:

- Participant rating of the acceptability of the RHI using a 5-point Likert scale.
- Adverse events questionnaire
- Collection of information about hearing aid use by self-report & calendar check.

8.5 Samples (if applicable) N/A

8.5.1 Laboratory assessments N/A

8.5.2 Translational research samples (if applicable) N/A

8.5.3 Sample storage and transfer N/A

8.6 Discontinuation/withdrawal of participants

Given that hearing aids are generally considered to be a safe treatment, we do not envisage safety reasons that might result in premature termination from the trial, or that put a complete stop to the trial. Subjects will be withdrawn from the trial if they request it for any reason. Subjects who misplace their hearing aids will not be withdrawn from the trial, instead they will be offered a replacement (up to two times only at the discretion of the audiologist). If they misplace them a third time then they will be offered to remain in the trial until end of their follow-up, but they will not receive any further hearing aids.

The decision to withdraw a participant from treatment will be recorded in the CRF and medical notes. If a participant explicitly states they do not wish to contribute further data to the trial their decision must be respected and recorded in the CRF and medical notes.

8.7 Definition of End of Trial

The expected duration of the trial is 24 months from recruitment of the first participant.
The end of the trial is the date of the last visit of the last participant.

9 Recording and reporting of adverse events

9.1 Definitions

Term	Definition

Adverse Event (AE)	Any untoward medical occurrence in a patient or trial participant, which does not necessarily have a causal relationship with the intervention involved.
Serious Adverse Event (SAE).	Any adverse event that: • results in death, • is life-threatening*, • requires hospitalisation or prolongation of existing hospitalisation**, • results in persistent or significant disability or incapacity, or • consists of a congenital anomaly or birth defect.
* A life- threatening event, this refers to an event in which the participant was at risk of death at the time of the event; it does not refer to an event which hypothetically might have caused death if it were more severe. ** Hospitalisation is defined as an in-patient admission, regardless of length of stay. Hospitalisation for pre-existing conditions, including elective procedures do not constitute an SAE.	

9.2 Assessments of Adverse Events

Each adverse event will be assessed for severity, causality, seriousness and expectedness as described below.

9.2.1 Severity

The generic categories below are given for use as a guide. You may have a more specific scale that you want to use related to the disease (e.g. CTCAE criteria), amend as required.

Category	**Definition**
Mild	The adverse event does not interfere with the participant's daily routine, and does not require further intervention; it causes slight discomfort
Moderate	The adverse event interferes with some aspects of the participant's routine, or requires further intervention, but is not damaging to health; it causes moderate discomfort

Severe	The adverse event results in alteration, discomfort or disability which is clearly damaging to health

9.2.2 Causality

The assessment of relationship of adverse events to the intervention is a clinical decision based on all available information at the time of the completion of the Case Report Form (CRF).

If a differentiated causality assessment which includes other factors in the trial is deemed appropriate, please add/amend the following wording to specify:

It is of particular importance in this trial to capture events related to the procedure (specify e.g. surgery) / product failure / mandatory concomitant medications / device(s) (refer to section 9.17 for reporting requirements). The assessment of relationship of an adverse event to this/these additional safety issue(s) will also be carried out as part of the trial.

The differentiated causality assessments will be captured in the trial specific CRF/AE Log and/or SAE form (amend as required).

The following categories will be used to define the causality of the adverse event:

Category	**Definition**
Definitely:	There is clear evidence to suggest a causal relationship, and other possible contributing factors can be ruled out.
Probably:	There is evidence to suggest a causal relationship, and the influence of other factors is unlikely
Possibly	There is some evidence to suggest a causal relationship (e.g. the event occurred within a reasonable time after administration of the trial intervention). However, the influence of other factors may have contributed to the event (e.g. the participant's clinical condition, other concomitant events).
Unlikely	There is little evidence to suggest there is a causal relationship (e.g. the event did not occur within a reasonable time after administration of the trial

	intervention). There is another reasonable explanation for the event (e.g. the participant's clinical condition, other concomitant treatments).
Not related	There is no evidence of any causal relationship.
Not Assessable	Unable to assess on information available.

9.2.3 Expectedness

Category	Definition
Expected	An adverse event which is consistent with the information about the intervention listed in the SPC, manual of Operation (amend as appropriate) **or clearly defined in this protocol.**
Unexpected	An adverse event which is not consistent with the information about the intervention listed in the SPC, manual of Operation (amend as appropriate)* **or clearly defined in this protocol.**

* This includes listed events that are more frequently reported or more severe than previously reported.

The following events listed below describe expected procedural/disease related AEs: Otitis externa, cerumen impaction or ear foreign body requiring removal by a physician.

9.3 Recording adverse events

Hearing aids are generally considered to have low risk of adverse events. Trial participation and exposure to the hearing aid intervention is therefore expected to have a low risk of adverse events for the participant. At the same time, the age of the participants may naturally lead to numerous deleterious health outcomes unrelated to the trial. We will therefore collect safety information that is relevant to trial participation, interventions, and procedures, as well as any serious AE. A pre-specified set of adverse events and serious adverse events will be collected and evaluated throughout

the conduct of the trial: Otitis externa, cerumen impaction or ear foreign body requiring removal by a physician. This set of AEs, as well as all serious adverse events, will be recorded in the CRF.

9.4 Procedures for recording and reporting Serious Adverse Events

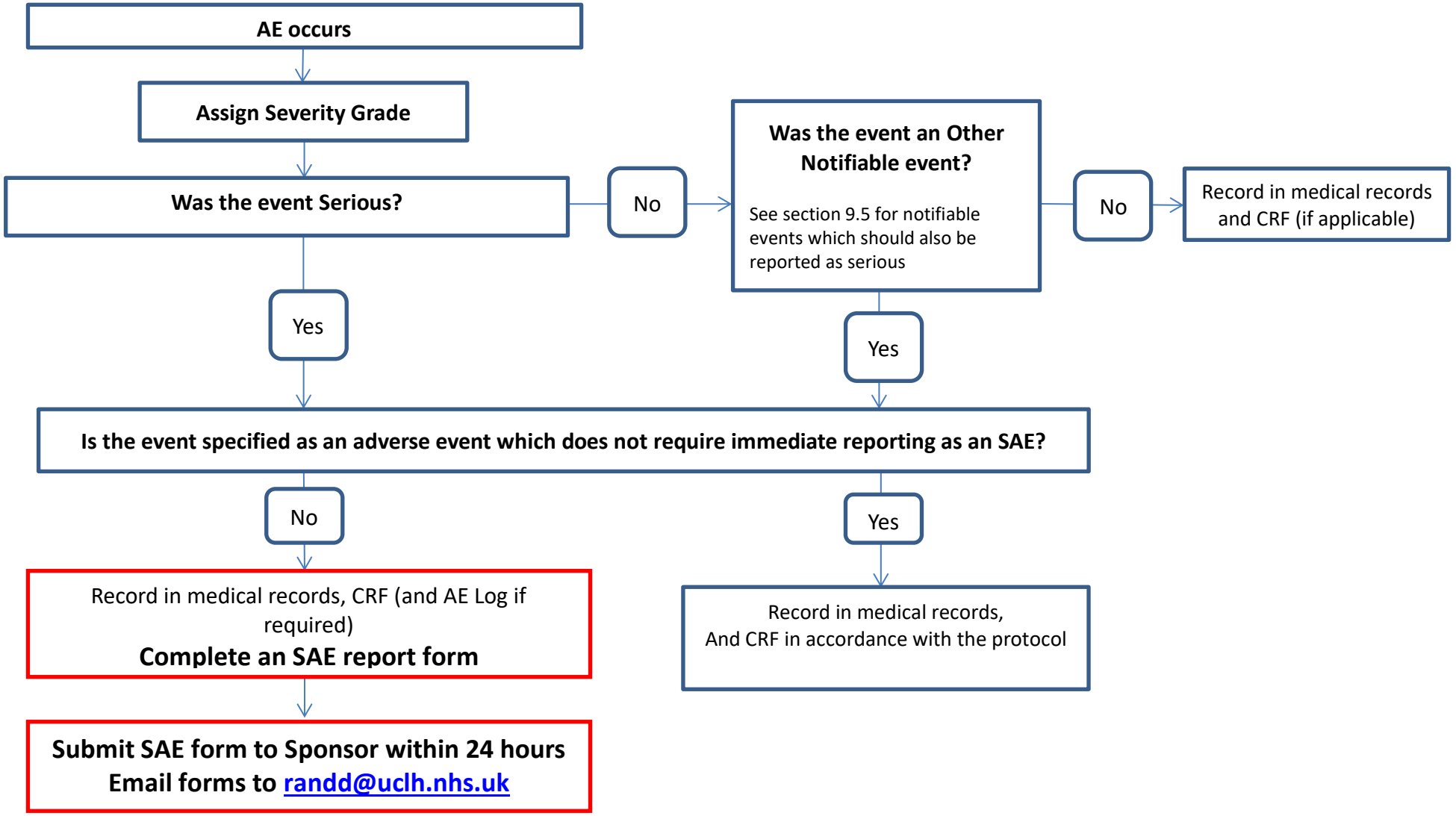
All serious adverse events will be recorded in the medical records and the CRF as well as in the trial database, from which a line listing of SAEs can be extracted for review. The line-listing of SAEs will be reported to the Sponsor once per year.

All SAEs (except those specified in section 9.5 as not requiring reporting to the Sponsor) must be recorded on a serious adverse event (SAE) form. The CI/PI or designated individual will complete the Sponsor's SAE form and the form will be preferably emailed to the Sponsor within 5 working days of becoming aware of the event. The Chief or Principal Investigator will respond to any SAE queries raised by the Sponsor as soon as possible.

Where the event is unexpected and thought to be related to the intervention, this must be reported by the Investigator to the Health Research Authority within 15 days.

Completed SAE forms must be sent within 5 working days of becoming aware of the event to the Sponsor
Email forms to randd@uclh.nhs.uk

Flow Chart for SAE reporting (this simple flow chart is for single site trial, please amend in line with trial specific requirements)



9.5 Serious Adverse Events that do not require reporting (if applicable)

All SAEs will be reported to the Sponsor.

9.6 Unblinding (if applicable)

The allocation will be known to the participant, the trial manager, the research audiologist, and the research assistants delivering the intervention and carrying out the outcome assessments. As such we do not expect there to be any need for unblinding.

9.7 Reporting Urgent Safety Measures

If any urgent safety measures are taken the CI shall immediately and in any event no later than 3 days from the date the measures are taken, give written notice to the relevant REC and Sponsor of the measures taken and the circumstances giving rise to those measures.

9.8 Notification of reportable protocol violations

A reportable protocol violation is a breach which is likely to effect to a significant degree:

(a) the safety or physical or mental integrity of the participants of the trial; or

(b) the scientific value of the trial.

The Sponsor will be notified immediately of any case where the above definition applies during the trial conduct phase.

9.9 Reporting incidents involving a medical device(s) (if applicable)

Any adverse incident involving a medical device will be reported to the manufacturer of the device, in this case the hearing aid manufacturer. This is especially important where the incident has led to or, was it to occur again could lead to an event classified as serious (see section 9.1 for definition of SAE); these will be reported within 24h. Other minor safety or quality problems should be reported along with incidents that appear to be caused by human error.

Adverse incidents related to a medical device can be reported directly to the MHRA via the online system (www.mhra.gov.uk). Alternative contact details: Medicines & Healthcare products Regulatory Agency Adverse Incident Centre (Tel: 020 7084 3080; Fax 020 7084 3109).

9.10 Trust Incidents and Near Misses

An incident or near miss is any unintended or unexpected event that could have or did lead to harm, loss or damage that contains one or more of the following components:

a. It is an accident or other incident which results in injury or ill health.

b. It is contrary to specified or expected standard of patient care or service.
c. It places patients, staff members, visitors, contractors or members of the public at unnecessary risk.
d. It puts the Trust in an adverse position with potential loss of reputation.
e. It puts Trust property or assets in an adverse position or at risk.

Incidents and near misses must be reported to the Trust through DATIX as soon as the individual becomes aware of them.
A reportable incident is any unintended or unexpected event that could have or did lead to harm, loss or damage that contains one or more of the following components:

a) It is an accident or other incident which results in injury or ill health.
b) It is contrary to specified or expected standard of patient care or service.
c) It places patients, staff members, visitors, contractors or members of the public at unnecessary risk.
d) It puts the Trust in an adverse position with potential loss of reputation.
e) It puts Trust property or assets in an adverse position or at risk of loss or damage.

10 Data management

10.1 Confidentiality

All data will be handled in accordance with the UK Data Protection Act 1998. The CRFs will not bear the participant's name or other personal identifiable data. Research identification numbers (Participant IDs) will be used to uniquely identify each participant.

10.2 Data collection tools and source document identification

Data will be collected on trial specific CRFs or data collection tools such as electronic CRFs.

Source data contained in source documents will be accurately transcribed on to the CRF. Examples of source documents are medical records which include audiometric reports and other clinical reports etc.

A source document list will be implemented prior to the start of the trial to identify:

- which data is to be recorded directly onto the CRF;
- which data is recorded firstly into source documents, such as medical notes, and then transcribed into the CRF; and
- which data is not to be recorded in the CRF but only recorded in source documents, e.g. participant questionnaires.

It is the responsibility of the investigator to ensure the accuracy of all data entered in the CRFs. The delegation log will identify all those personnel with responsibilities for patient identification, data collection and handling, including those who have access to the trial database.

10.3 Completing Case Report Forms

All CRFs must be completed and signed by staff that are listed on the site staff delegation log and authorised by the CI to perform this duty. The CI is responsible for the accuracy of all data reported in the CRF. Once completed the CRFs will be kept in secure and locked UCL premises.

10.4 Data handling

In the trial, participant data obtained as described in the Trial Procedures will be collected from patients in accordance with the patient consent form, patient information sheet and sections 8.1 to 8.3 of this protocol. The data will be collected in paper form and electronic format.

All data will be kept in strict adherence to Good clinical practice (GCP) guidance, which includes storing data in a locked cabinet in a locked room controlled by the Chief Investigator (or person designated by the CI according to trial delegation log) and destroying recordings after transcription. Data will be stored in a secure environment to industry standards and accreditation (SLMS Data Safe Haven - IDHS). Backups are made every night of all files created or modified since the preceding night's backup and kept on a backup server that is kept in a secure and fireproof location, separate from the main unit computers. UCL, as the trial Sponsor, is the data controller for this trial. There is a UCL disaster recovery protocol in place to restore lost data from a separate, secure archive.

Qualitative interview data will be collected and stored using digital audio recording (eg MP3) where interviewees permit. Physical data (e.g., digital audio-recordings, hand written field notes) will be kept until data is transcribed and checked to allow traceability and stored in a locked cabinet in a locked room. All data will be anonymised. All documents will be assigned version numbers which will be presented in headers and electronic filenames. We anticipate this to be in the format N.n, where N represents a new, approved or finalised version of a document and n represents draft versions prior to finalisation.

All documentary and transcribed data will be anonymised and imported into the latest version of the qualitative analysis software, currently NVivo 9, which allows the storing, coding and organisation of qualitative datasets. All data files will be kept as .txt or .rtf non-proprietary formats or as .pdf files. Electronic files will be password-protected. We will ensure that data is collected in accordance with the trial protocol and procedures through regular meetings between the CI and researchers. The CI will review the quality of interviews and field notes at regular points across the period of data collection to ensure they are of a high standard. Metadata will be consistent and transparent.

Data analysis will be undertaken by the TACT research team (as per trial delegation log), and as directed by the trial statistician and CI. The TACT research team will process, store and dispose of patient data in accordance with all applicable legal and regulatory requirements, including the Data Protection Act 1998 and any amendments thereto. The participant data will not be transferred to any party not identified in this protocol and are not to be processed and/or transferred other than in accordance with the patients' consent.

The electronic CRF and databases for the trial will be developed by the trial team using standard tools within a secure electronic environment. Once the trial and qualitative interviews finished and the databases locked, all trial documentation will be archived within UCL records office, to ensure documents are not mislaid, damaged or destroyed. This will be the responsibility of the Chief

Investigator and is part of Sponsorship by UCL. The content of each box will be listed and a unique reference number allocated to each file. Access will be restricted to the trial personnel.

The research data arising from this research will be made available to the scientific community in a timely and responsible manner. We are committed to long-term preservation, high quality data management and strengthening the provision for secondary data analysis. All data will be managed within UCL data protection policy and publications policy: www.ucl.ac.uk/platforms/informatics/data_sharing

11 Statistical Considerations

11.1 Primary Outcome

This pilot trial aims at establishing the feasibility of a full-size trial of the hearing aid intervention versus healthy ageing intervention in people with MCI. This future trial will be a scaled-up version of the present pilot, modified with any lessons learnt in the current trial. The pilot's primary objective is therefore to establish feasibility of recruitment, randomisation, retention, and the acceptability of the trial interventions as follows:

1. Recruitment and randomisation: Proportion of eligible participants who are randomised into the trial – expected value ≥50%.
2. Retention: proportion of participants who are followed for the 6 months of trial duration, and endpoint measures are obtained – expected value ≥80%.
3. Acceptability of the Hearing Intervention: proportion of participants allocated to the Hearing Intervention completing ≥2 intervention sessions – expected value ≥80% of intervention group.

The Primary Outcome of the Remote Hearing Intervention sub-study (during COVID-19), in keeping with the overall TACT primary objective, will be the feasibility of the RHI, in terms of:

1. Recruitment: achieving n=12 participants
2. Acceptability of the RHI proportion of participants allocated to the Hearing Intervention completing ≥2/3 intervention sessions – expected value ≥80%.
3. Retention: proportion of participants completing outcome collection – expected value ≥80%.

11.2 Secondary outcome(s)

The pilot will also establish other aspects of feasibility as secondary outcomes. The pilot will assess trial procedures, including whether the interventions and schedule of assessments are delivered as per randomisation allocation, and whether these are acceptable to participants, and whether the allocation to hearing aid intervention or healthy ageing intervention results in a difference in use of

hearing aids between arms at the end of trial follow-up, as well as the use of novel hearing screening procedures for more efficient recruitment in the future trial.

These secondary outcomes will be operationalised as follows:

a) Evaluation of the deliverability and acceptability of the Hearing intervention, Healthy Ageing Intervention and the schedule of assessment for participants.
   i. We will monitor completion rates of the interventions by recording the proportion of participants who completed each visit of the intervention, any refused or discontinued visits for the Hearing and Healthy Ageing Intervention, and any refused or discontinued tests and instruments from the schedule of assessments.
   ii. For the Hearing Intervention, we will record the number of participants with hearing aid fitted within **3 months** (target: 80%) and reported side effects.
   iii. Qualitative assessment of interventions and schedule of assessments: Researchers will also evaluate the experience of the hearing and healthy ageing interventions and of the schedule of assessments through qualitative assessments of trial participants and their communication partners. We will interview up to 24 participants and relatives about each intervention (involvement, practicality, acceptability) and about their opinion of the assessment until theoretical saturation is achieved. We will include both participants who have benefited from the intervention and those for whom it was not useful, to find out what helped and what could be better.

b) Evaluation of the adherence to the intervention in terms of hearing aid use in the Hearing Intervention group and whether the control arm provides a meaningful comparison (i.e. where hearing aid use is in a much lower proportion). This will be assessed by hearing aid adherence based on data usage download from the hearing aids and self-report in the Hearing Intervention and Healthy Ageing Intervention arm (as participants in this arm may obtain hearing aids outside of the trial, through the NHS system or privately). We expect >= 70% adherence in the Hearing Intervention arm and <=20% adherence in the Healthy Ageing Intervention arm. Hearing aid use will be defined as a minimum of 4 hours a day on average since last trial assessment (when at home and in usual health) as defined by data logging at 6 months (end of trial), based on the hearing aid with the highest average use (as each participant has two hearing aids). Self-reported hearing aid use may be employed if needed, for instance if no data-logging is available for a participant. The Statistical Analysis Plan will further specify the use of these measures. We will estimate and report the difference in hearing aid use at 6 months between the Hearing and Healthy Ageing arms to inform sample size estimates for the future trial. The expected value of the difference in daily hearing aid adherence between arms is expected to be ≥50% difference between the Hearing Intervention and Healthy Ageing Intervention arms in the proportions of participants maintaining hearing aid use at 6 months (end of trial). Other data on adherence will also be recorded, to include the number of hearing aids lost by participants in the intervention arm.

c) We will also pilot the use of improved technology for the assessment of hearing which, if valid and acceptable in our MCI population, could then be employed in the future trial for improved trial screening and recruitment. This technology includes hearing screening tools (Hearcheck screener and Shoebox audiometry, an iPad-based audiometric test that can provide a basic

audiogram with minimal supervision by a trained professional that does not need to be an audiologist) which we expect would be sufficient for accurate detection of participants for the main trial, relative to the current screening procedure of full assessment by trial audiologist in all participants, which is very time-consuming and resource intensive. This will be assessed through ROC analysis of HearCheck and Shoebox audiometry relative to gold standard full audiometric testing conducted by the trial audiologist.

The Secondary Outcomes of the Remote Hearing Intervention sub-study (during COVID-19), in keeping with the overall TACT primary objective, will include:

1. Evaluation of the deliverability and acceptability of the Remote Hearing intervention.
    a. We will monitor completion rates of the RHI by recording the proportion of participants who completed each contact visit of the intervention, any refused or discontinued visits, and any refused or discontinued tests and instruments from the remote schedule of assessments.
    b. Qualitative assessment of the remote intervention: Researchers will also evaluate the experience of the RHI and of the schedule of assessments through qualitative assessments of trial participants. We will interview up to 12 participants about the RHI (involvement, practicality, acceptability) and about their opinion of the assessment.

11.3 Sample size calculation

This pilot trial will assess the feasibility of proceeding to the future definitive RCT of sufficient duration to detect differences in cognitive changes between arms. The main feasibility questions that the pilot aims to answer are: (a) is the trial feasible, in the sense of resulting in sufficiently high recruitment, randomisation and sufficiently low dropout at 6 months; (b) is the Hearing Intervention deliverable and acceptable to participants; (c) estimate the difference in hearing aid use at 6 months between the Hearing Intervention and Healthy Ageing Intervention arms to inform sample size estimates for the future trial. We are including cognitive outcomes to assess their feasibility and acceptability, and to provide estimates including standard deviation to be used in the sample size calculation for the full trial. As a feasibility study, the current trial is not powered to detect differences in the cognitive outcomes between the arms. Therefore, only descriptive analyses will be performed using the data collected. No formal power calculation is necessary, and instead the sample size has been determined as to provide sufficient precision (sufficiently narrow confidence intervals) for trial estimates of recruitment and randomisation, dropout, acceptability of the intervention, and difference in hearing aid usage between arms, as detailed below.

With 76 randomised participants, we will achieve the following 95% confidence intervals (CI) for our expected estimates of recruitment, randomisation, dropout, acceptability of the intervention, and difference in hearing aid adherence between the Hearing Intervention and Healthy Ageing Intervention at the end of trial [88]:

1. Recruitment and randomisation of eligible participants with a MCI diagnosis from NHS community memory clinics. Target: 50% of eligible participants will be randomised; with n=76 recruited subjects the 95% CI would be [39-61].
2. Follow-up: target of 80% randomised participants with complete follow-up at 6 months,

95%CI with n=76 would be [71-89].

3. Acceptability of the Hearing Intervention: proportion of participants allocated to the Hearing Intervention completing ≥2 intervention sessions – expected value ≥80% of intervention group, 95% CI with n=76 would be [71-89].
4. Difference in daily hearing aid adherence between arms: target of 50% difference between the Hearing Intervention and Healthy Ageing Intervention arms in the proportions of participants maintaining hearing aid use at 6 months (end of follow-up), 95% CI with n=76 would be [31-69].

Mean, proportions, differences in means and proportions with corresponding 95% confidence intervals will be calculated as appropriate for the cognitive scales and other trial outcomes, to inform the sample size calculation for a full scale trial.

Criteria for the decision of progression to the main trial

We judge that these confidence intervals provide acceptable ranges to inform continuation to the main trial. The final decision to "go" or "stop", that is, whether to proceed or not to the main trial, will be taken by the Trial Steering Committee after the end of trial and with consideration of whether the trial has met its primary and secondary outcomes, as well as any lessons learnt during the pilot.

As a **guidance to this decision**, we anticipate that if the 4 endpoint estimates above in this section, as measured in the pilot trial, fall within their respective expected confidence intervals as detailed above, this will be a "go" signal for a full scale trial. If the endpoint estimates fall up to 10% below the lower limit of their target confidence interval (as detailed above in this section) we will consider whether modifications to the trial design to improve these endpoints would be sufficient to remediate these issues when proceeding to the main trail. If any of these endpoints fall below these minimal rates this will be a "do not progress to RCT" signal.

The Remote Hearing Intervention sub-study (COVID-19) will contribute to this decision by providing initial descriptive data and a qualitative assessment on the feasibility and acceptability of a remote version of the Hearing Intervention.

11.4 Planned recruitment rate

To reach the target sample size of 76 randomised participants, and assuming recruitment rate of 50%, 152 potential participants will need to be approached during the 78 weeks of recruitment, or just under 2 potential participants per week.

The recruitment base will be five NHS London memory services, with 600 MCI patients per year (four times the screening target). Camden & Islington Memory Services alone exceed 1200 new patient referrals per year, of which 20% have MCI (or 240 people per year). We estimate that based on these five patient identification centres, the referral rate will be approximately six potential participants per week; two participants will be suitable and will agree to participate (one per research assistant). We conducted a small (n=12) feasibility study with similar but less restrictive inclusion and exclusion criteria as the proposed trial. This study recruited seven participants in four weeks, of which five had been confirmed to have untreated hearing loss and would have met inclusion criteria for the planned trial (1.25 potential participant per week), based on a single memory service, so the projected figures should be achievable.

11.5 Randomisation methods

Individual-level randomisation with randomly varying block sizes to ensure equal number of participants allocated to each intervention arm.

11.6 Statistical analysis

11.6.1 Summary of baseline data and flow of participants

List of variables to be used to assess baseline comparability of the randomised groups using means (SD) and counts (proportions) as appropriate:

- Age
- Sex
- Cognition scale: Addenbrooke Cognitive Examination (ACE-III) score
- Quality of life: SF36,EQ-5D
- Function: 4-item Lawton-Brody IADL
- Social activities: SFDEM, UCLA loneliness
- Frailty: grip strength
- Physical activity: as measured by accelerometry at baseline
- Geriatric Depression Score
- Self-reported hearing disability - Hearing Handicap Inventory for the Elderly – Screening version (HHIE-S)
- Phoneme Recognition in Quiet score (baseline)
- Hearing Threshold PTA average (0.5-4 KHz)

We will produce a consort flow diagram (http://www.consort-statement.org/) to illustrate the flow of participants in the trial, based on draft (presented as Fig 3).

11.6.2 Primary outcome analysis

We will produce estimates and 95% Confidence Intervals for:

- Recruitment: Number of participants who will be randomised into the trial, divided by the total number of screened participants, expressed as percentage
- Retention: Number of participants that do not drop out before 6 month endpoint assessment, divided by the total number of randomised participants, expressed as percentage
- Acceptability of the Hearing Intervention: proportion of participants allocated to the Hearing Intervention completing ≥2 intervention sessions, divided by the total number of participants randomised to the Hearing Intervention.

11.6.3 Secondary outcome analysis

We will report the number of participants consented, screened, randomised and completing the trial as per trial workflow (Fig. 3).

We will estimate:

- Difference between the Hearing Intervention and the Healthy Intervention arms, in the proportion of participants maintaining hearing aid use, defined as a minimum of 4h a day on average since last trial assessment (when at home and in usual health) as established by data-logging at 6 months (end of trial), based on the hearing aid with the highest average use (as each participant has two hearing aids). Self-reported hearing aid use may also be employed if needed, for instance if no data-logging is available for a participant, as further specified in the Statistical Analysis Plan.
- Percentage of participants rating the interventions (Hearing Intervention and Healthy Ageing Intervention) as acceptable (ratings 3-5 on a 5-point Likert scale) based on Likert scale scores.
- Mean, proportions, differences in means and proportions across treatment arms with corresponding 95% confidence intervals will be calculated as appropriate for the cognitive scales and other trial outcomes, to inform the sample size calculation for a full scale trial.

We will produce appropriate summary estimates and report the following:

- Number of potential participants referred to the study researchers, screening visits scheduled and completed.
- Feasibility of the schedule of assessments, which will include proportion of completed interviews and completion rates of instruments and questionnaires, as well as relevant biometric data.
- Completion rates of the interventions by recording the proportion of participants who completed the intervention, any refused or discontinued visits for the Hearing Intervention and Healthy Ageing Intervention, and any refused or discontinued tests and instruments from the schedule of assessments.
- For the Hearing Intervention, we will record the number of participants with hearing aid fitted within 3 months (target: 80%) and reported side effects.
- Average hearing aid daily use measured as number of hours of use on average over 7 days (when at home and in usual health) as established by data-logging at 6 months (end of trial) for the Hearing Intervention and Healthy Ageing Arms. Self-reported hearing aid use may also be employed if needed, for instance if no data-logging is available for a participant, as further specified in the Statistical Analysis Plan.
- Number of unscheduled contact with participants, including type of contact (face to face or other) and whether this was with RA or research audiologist.
- Number of hearing aids lost by participants in the intervention and control arm.
- ROC analysis of HearCheck and Shoebox audiometry relative to gold standard full audiometric testing conducted by the trial audiologist, on the detection of hearing loss as defined for this trial (four-frequency pure tone average (0.5, 1, 2, 4 kHz) in the better-hearing ear of >= 25 decibels Hearing Level (dB HL) and <70 dB HL or a pure tone audiometric threshold at 4 KHz in the better ear of >= 30 decibels dB HL).

We will also report

- Reported side effects.

A detailed statistical analysis plan will be written prior to database lock.

11.6.4 Sensitivity and other planned analyses

Qualitative analysis

- Qualitative assessment of interventions: We will interview participants and relatives about each intervention (involvement, practicality, acceptability) and about their opinion of the assessment until theoretical saturation is achieved (which we anticipate will be reached with 12-16 participants per intervention arm). We will include both participants who have benefited from the intervention and those for whom it was not useful, to find out what helped and what could be better.

12 Record keeping and archiving

At the end of the trial, all essential documentation will be archived securely by the CI for a minimum of 20 years from the declaration of end of trial.

Essential documents are those which enable both the conduct of the trial and the quality of the data produced to be evaluated and show whether the site complied with all applicable regulatory requirements.

The Sponsor will notify sites when trial documentation can be archived. All archived documents must continue to be available for inspection by appropriate authorities upon request.

13 Oversight Committees

13.1 Trial Management Group (TMG)

The TMG will include the Chief Investigator, trial statistician and trial staff, as well as co-investigators as required. The TMG will be responsible for overseeing the day to day function trial. The group will meet every 3 months at a minimum. The CI can call for additional TMG meetings if required. The TMG will review recruitment figures, SAEs and substantial amendments to the protocol prior to submission to the REC.

13.1 Trial Steering Committee (TSC)

The Trial Steering Committee (TSC) will provide the overall supervision of the trial and will include the trial CI, TMG members and study co-investigators, as well as members who are independent of the trial team, including an independent scientific advisor and a lay person representative.

The TSC will meet immediately before the start of the trial (kick off meeting), 6 months into recruitment and 3 months after last participant visit, when the trial results should be ready for analysis. The TSC will monitor trial progress, and conduct and advise on scientific credibility, adherence to protocol and trial safety. The TSC will also decide whether or not to proceed to the main trial, based on the results of the pilot.

14 Ethical requirements and patient and public involvement

Ethics

The Sponsor will ensure that the trial protocol, participant information sheet, consent form, GP letter and submitted supporting documents have been approved by the appropriate research ethics committee, prior to any participant recruitment. The protocol, all other supporting documents and agreed amendments, will be documented and submitted for ethical and regulatory approval as required. Amendments will not be implemented prior to receipt of the required approval(s).

Before any NHS site may be opened to recruit participants, the Chief Investigator/Principal Investigator or designee must receive NHS permission in writing from the Trust Research & Development (R&D). It is the responsibility of the CI/ PI or designee at each site to ensure that all subsequent amendments gain the necessary approvals, including NHS Permission (where required) at the site. This does not affect the individual clinician's responsibility to take immediate action if thought necessary to protect the health and interest of individual participants (see section 9.6 for reporting urgent safety measures).

An annual progress report (APR) will be submitted to the REC within 30 days of the anniversary date on which the favourable opinion was given, and annually until the trial is declared ended. The chief investigator will prepare the APR.

Within 90 days after the end of the trial, the CI/Sponsor will ensure that the main REC is notified that the trial has finished. If the trial is terminated prematurely, those reports will be made within 15 days after the end of the trial.

The CI will supply the Sponsor with a summary report of the trial, which will then be submitted to the REC within 1 year after the end of the trial.

Patient and public involvement (PPI)

A lay summary of the proposed research was reviewed by patient experts and the comments integrated in the present protocol. Action on Hearing Loss (AoHL), a leading UK charity, is a collaborator in the trial. The application to Alzheimer's Research UK (ARUK) was also reviewed by their PPI volunteers who made comments that have been used to improve this research.

We have conducted PPI meetings with patient and carer experts with lived experience of hearing loss and mild cognitive impairment, who advised us on all patient materials and blinding options. We will continue to ensure public and patient involvement (PPI) throughout the research and implementation in continued partnership with AoHL and ARUK. We will work with these organisations to run workshops (including beneficiaries and users) and meetings to disseminate findings and encourage two-way engagement to maximise the likelihood that the knowledge gained will be taken up by patients and families.

15 Monitoring

The Sponsor will determine the appropriate level and nature of monitoring required for the trial. Risk will be assessed on an ongoing basis and adjustments made accordingly.

The degree of monitoring will be proportionate to the risks associated with the trial.

A trial specific oversight and monitoring plan will be established for studies. The trial will be monitored in accordance with the agreed plan.

The sponsor has deemed the trial to be low risk. The monitoring plan is as follows:
Low risk: Central monitoring
Each site to email to the sponsor annually:

1. Delegation log
2. Adverse Event log
3. Deviation log
4. Minutes of Trial Steering Committee (or equivalent).
5. Annual progress report (Lead site only) when sent to Ethics Committee.

16 Finance

The trial is funded by a grant from Alzheimer's Research UK: Alzheimer's Research UK Prevention and Risk Reduction Fund: ARUK-PRRF2017-001. The hearing aids will be purchased from a hearing aid manufacturer using the grant awarded by Alzheimer's Research UK. We will be using Phonak Audeo hearing aids, which are rechargeable. These will be provided through a donation agreement by Sonova (Phonak's parent company). We will use the company "Way With Words" to transcribe interviews and PPI meetings. We will use a third party software called "GreenText" for SMS contact with participants, including text reminders to wear their hearing aids (hearing intervention group only) and reminders about scheduled trial visits. We will compensate participants for reasonable travel and other expenses incurred as a direct consequences of participation in the trial. At the discretion of the trial team, we will compensate participants for privately arranged wax removal incurred by participants up to a maximum expense of £200.

17 Insurance

University College London holds insurance against claims from participants for injury caused by their participation in the trial. Participants may be able to claim compensation if they can prove that UCL has been negligent. However, as this trial is being carried out in a hospital, the hospital continues to have a duty of care to the participant of the trial. University College London does not accept liability for any breach in the hospital's duty of care, or any negligence on the part of hospital employees. This applies whether the hospital is an NHS Trust or otherwise.

Participants may also be able to claim compensation for injury caused by participation in this trial without the need to prove negligence on the part of University College London or another party. Participants who sustain injury and wish to make a claim for compensation should do so in writing in the first instance to the Chief Investigator, who will pass the claim to the Sponsor's Insurers, via the Sponsor's office.

Hospitals selected to participate in this trial shall provide negligence insurance cover for harm caused by their employees and a copy of the relevant insurance policy or summary shall be provided to University College London, upon request.

18 Publication policy

All proposed publications will be discussed with Sponsor prior to publishing other than those presented at scientific forums/meetings as per standard UCL publication policy.

19 Intellectual property

All background intellectual property rights (including licences) and know-how used in connection with the trial shall remain the property of the party introducing the same and the exercise of such rights for purposes of the trial shall not infringe any third party's rights.

All intellectual property rights and know-how in the protocol and in the results arising directly from the trial, but excluding all improvements thereto or clinical procedures developed or used by each participating site, shall belong to UCLH. Each participating site agrees that by giving approval to conduct the trial at its respective site, it is also agreeing to effectively assign all such intellectual property rights ("IPR") to UCL and to disclose all such know-how to UCL.

Each participating site agrees to, at the request and expense of UCL execute all such documents and do all acts necessary to fully vest the IPR in UCL.

Nothing in this section shall be construed so as to prevent or hinder the participating site from using know-how gained during the performance of the trial in the furtherance of its normal activities of providing or commissioning clinical services, teaching and research to the extent that such use does not result in the disclosure or misuse of confidential information or the infringement of an intellectual property right of UCL. This does not permit the disclosure of any of the results of the trial, all of which remain confidential.

20 Appendices

Appendix 1. Schedule of assessments for TACT

Assessment	Screening	Baseline	Intervention Phase				Follow Up	Early Discontinuation visit
visit #	0	1	2	3	4	5	6	ED
	Day 0	Day 0-14	Week 3-4	Week 5-6	Week -7-8	Week 9-10	F-UP: 6 months	
			A	B	C	D		
	Inclusion Criteria and Covariates							
Informed Consent	X							
Sociodemographic and Medical History	X	X						
Eligibility determination	X							
Randomisation	X							
	Audiometric Baseline							
Audiological History	X							
Otoscopy	X			(X)		(X)		
Cerumen Removal	(X)			(X)		(X)		
Measurement of ambient noise	X							
HearCheck & Shoebox screen	X							
Air conduction audiometry (not masked & masked)	X							
Bone conduction audiometry (not masked & masked)	X							
Tympanometry	X							

Tuning Fork Test	(X)							
Phoneme recognition in quiet	X							
Quick Speech in Noise (unaided)	X							
	Neurocognitive Assessment							
Speech audibility procedure		X					X	(X)
Addenbrooke Cognitive Examination (ACE-III)		X					X	(X)
Delayed Word Recall Test (DWRT): encoding		X					X	(X)
Delayed Word Recall Test (DWRT): recall		X					X	(X)
Trail Making Test (TMT): Part A and B		X					X	(X)
	Outcome Assessments							
The Short Form 36 (SF-36) Health Survey		X					X	(X)
EQ-5D		X					X	(X)
Hearing Handicap Inventory for the Elderly – Screening (HHIE-S)		X					X	(X)
Lawton-Brody Instrumental Activities of Daily Living (IADL)		X					X	(X)
Social Functioning in Dementia Scale (SF-DEM) (Person with dementia questionnaire)		X					X	(X)
UCLA Loneliness Scale		X					X	(X)
Grip strength		X					X	(X)
Accelerometer		X					X	(X)
Adherence Review through data-logging and calendar review					X	X	X	(X)
	Healthy Ageing Intervention Participants Only							
Healthy Ageing			X					

Intervention Visit: Lowering Systolic Blood Pressure								
Healthy Ageing Intervention Visit: Eat a Healthy Diet				X				
Healthy Ageing Intervention Visit: Be Physically Active					X			
Healthy Ageing Intervention Visit: Maintain Healthy Bones, Joints and Muscles						X		
	Hearing Intervention Participants Only							
Hearing aid prescribed/impressions for earmoulds	X							
Client Oriented Scale of Improvement (COSI)			X	X	X	X	X	(X)
Hearing Aid (HA) Review & Orientation			X	X	X	X		
Integration of HA in Daily Routine			X	X	X	X		
C2Hear Video			X	X	X			
Electroacoustic Analysis				X		(X)		
HA fitted				X				
Real ear measurements (HA verification)				X		(X)		
HA fine tuning & optimisation						X		
Communication Strategies					X	X		
	Communication Partners if applicable)							
Informed Consent	X	(X)						
Demographics		X						
The Hearing Impairment Impact – Significant Other Profile (HII-SOP)		X					X	
The Short Form 36 (SF-36) Health Survey		X					X	
Hospital Anxiety and Depression (HADS)		X					X	

EQ-5D		X					X	
Social Functioning in Dementia Scale (SF-DEM) (Carer questionnaire)		X					X	
Lawton – Brody Instrumental Activities of Daily Living (IADL)		X					X	
	Miscellaneous							
Adverse Events review			X	X	X	X	X	(X)
	( ) Parentheticals denote procedures that are optional based on protocol							

Appendix 2. Schedule of assessments for the Remote Hearing Intervention sub-study (during COVID-19)

Assessment	**Consent and Baseline**	**Intervention Phase**				**Follow Up Early Discontinuation visit**
Contact #	1	2	3	4		5
	Day 0	Day 1 (+/- 1 week)	Day 3 (+/- 1 week)	Week 1(+/- 2 weeks)		Week 4 (+/- 2 weeks)
	Inclusion Criteria and Covariates					
Informed Consent	X					
Medical History (update)	X X					
Eligibility determination	X					
	Audiometric Baseline					
Audiological History (update)	X					
	Neurocognitive Assessment					
Addenbrooke Cognitive Examination (ACE-III)	X					X
	Outcome Assessments					
Geriatric Depression Scale	X					X

(GDS)						
Client Oriented Scale of Improvement (COSI)	X					X
Self-reported Adherence			X	X	X	X
	Remote Hearing Intervention					
Hearing aids posted to participant, along with spare equipment for maintenance		X				
A4 Factsheet (includes first steps to take on receiving the package)		X				
Participant toolkit (includes hearing aid diary)		X				
DVD of video clips		X				
Calendar sheets (to use as a reminder for inserting/removing the hearing aids)		X				
Note which includes the date to expect the first call from the audiologist, and contact details for the team (to use for any troubleshooting issues)		X				
Communication strategies			X	X	X	
HA Troubleshooting			X	X	X	
	Miscellaneous					
Adverse Events review			X	X	X	X

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