NOTTINGHAM CLINICAL TRIALS UNIT
at the University of Nottingham

FAMOUS
Follow-up and monitoring of new USers of NHS hearing aids

# FAMOUS

# Statistical Analysis Plan

## Final version 1.0
## (22 JUN 2023)

Based on Protocol version 3.0 (dated 06 APR 2023)

Trial registration: ISRCTN10589817

The following people have reviewed the Statistical Analysis Plan and are in agreement with the contents

| Name | Job title | Trial Role | Signature | Date |
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## Abbreviations

| Abbreviation | Description |
|---|---|
| AE | Adverse Event |
| CI | Chief Investigator |
| COM-B | Capabilities, Opportunities, and Motivations model of Behaviour change |
| COSI | Client Oriented Scale of Improvement |
| CRCT | Cluster Randomised Controlled Trial |
| DMC | Data Monitoring Committee |
| IOH-HA | International Outcome Inventory for Hearing Aids |
| HHI | Hearing Handicap Inventory |
| HUI-3 | Health Utilities Index-3 |
| NCTU | Nottingham Clinical Trials Unit |
| PROMs | Patient Reported Outcome Measures |
| QoL | Quality of Life |
| RCT | Randomised Controlled Trial |
| SAP | Statistical Analysis Plan |
| SWAT | Study Within a Trial |
| SOS-HEAR | The Significant Other Scale for Hearing Disability |
| TMG | Trial Management Group |
| TSC | Trial Steering Committee |

**Changes from protocol**

The table below details changes to the planned analyses in the SAP compared to the protocol which after discussion with the TMG are not considered to require a protocol amendment.

| Protocol version and section | Protocol text | SAP version and section | SAP text | Justification |
|---|---|---|---|---|
| | | | | |

**Amendments to versions**

| Version | Date | Change/comment | Statistician |
|---|---|---|---|
| | | | |
| | | | |
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| | | | |
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**Additional contributors to the SAP (non-signatory)**

| Name | Trial role | Job Title | Affiliation |
|---|---|---|---|
| | | | |

## 1. INTRODUCTION & PURPOSE

This document details the rules proposed and the presentation that will be followed, as closely as possible, when analysing and reporting the main results from the NIHR-HTA funded FAMOUS trial

The purpose of the plan is to:

1. Ensure that the analysis is appropriate for the aims of the trial, reflects good statistical practice, and that interpretation of a priori and post hoc analyses respectively is appropriate.

2. Explain in detail how the data will be handled and analysed to enable others to perform or replicate these analyses.

Additional exploratory or auxiliary analyses of data not specified in the protocol may be included in this analysis plan.

This analysis plan will be made available if required by journal editors or referees when the main papers are submitted for publication. Additional analyses suggested by reviewers or editors will be performed if considered appropriate. This should be documented in a file note.

Amendments to the statistical analysis plan will be described and justified in the final report of the trial and where appropriate in publications arising from the analysis.

Health economic and qualitative analysis plans are beyond the scope of this document.

## 2. SYNOPSIS OF STUDY DESIGN AND PROCEDURES

| | |
|---|---|
| **Full Title** | Follow-up and structured monitoring for adults offered an NHS hearing aid(s) for the first time (FAMOUS): a cluster randomised controlled trial. |
| **Trial design** | Multi-centre, two-arm parallel group cluster randomised controlled trial with integral internal pilot, economic and process evaluations. |
| **Objectives** | Primary Objective:<br>To determine the effects of the FAMOUS structured care intervention in adults offered hearing aids for first time compared to usual care, on self-reported daily hearing aid use, 12 months after initial hearing aid fitting.<br><br>Secondary Objectives:<br>• To determine the effects of the FAMOUS structured care intervention on self-reported hours of daily hearing aid use<br>• To determine the effects of the FAMOUS structured care intervention on self-reported hours of daily hearing aid non-use<br>• To determine the effects of the FAMOUS structured care intervention on hearing-related quality-of-life (QoL)<br>• To determine the impact on relationships with and QoL of significant others (i.e., partner))<br>• To understand the barriers and facilitators to behaviour change within standard practice e.g., capabilities, opportunities and motivations (mechanisms of impact)<br>• To understand and appreciate experiences and acceptability of the FAMOUS structured care intervention to service users and service providers (process evaluation)<br>• To estimate the cost to the NHS and value to society |
| **Eligibility criteria** | Inclusion criteria:<br>• Adults (≥18 years); using hearing aids for first time<br>Exclusion criteria:<br>• Adults offered an auditory implant of any kind<br>• Adults offered non-conventional hearing aids e.g., that re-route sound between ears. |
| **Description of intervention** | The intervention is 'structured care' that adds structure to current NHS care, comprising of a four-step follow-up and monitoring intervention that includes:<br>(i) encouraging patients to reflect on situations in which hearing is difficult and where hearing aids may help.<br>(ii) an individualised hearing aid user checklist and diary (action plan) to reinforce where and when to use the hearing aids.<br>(iii) monitoring, feedback, and problem-solving support within seven days of receiving hearing aids; and<br>(iv) a follow-up at six weeks after fitting. |
| **Outcome measures** | <u>Objective One: Clinical Outcomes</u><br>• The primary outcome is self-reported daily hours of hearing aid use 12 months post fitting (also a secondary outcome at 12 weeks). Therefore, the question, 'On a typical day over the last week, how many hours did you use your hearing aid?' will be collected via participants' preferred contact method (post, telephone, text). |

| | |
|---|---|
| | • Secondary outcomes collected at 12 weeks and 12 months include:<br>(i) proportion of non-users, defined as ≤ 1 hour/day.<br>(ii) International Outcome Inventory for Hearing Aids (IOI-HA) survey with questions on usage benefit, satisfaction, QoL, impact on others and residual difficulties.<br>(iii) Hearing Handicap Inventory (HHI) survey with questions on hearing related QoL, and Capabilities, Opportunities, Motivations and Behaviour (COM-B) questionnaire that measures capabilities, opportunities, and motivations.<br><u>Objective Two: Impact on Families</u><br>• The Significant Other Scale for Hearing Disability (SOS-HEAR) questionnaire will be completed at 12 months. This questionnaire has been designed to be completed by a partner. <u>Objective Three: Process evaluation</u><br>• We will conduct semi-structured interviews with participants to explore experience and acceptability of usual care and the intervention.<br>• Early, semi-structured interviews with service managers and audiologists will focus on perceptions and attitudes, training, and reflections on initial implementation experiences. Later interviews will focus on the barriers and enablers to integrating the FAMOUS intervention within existing management care pathways.<br><u>Objective Four: Health economic evaluation</u><br>• Effects will be captured at the individual patient level through calculating quality-adjusted life years (QALYs) using Health Utilities Index 3 (HUI-3) at 12 months post-hearing aid fitting. |
| **Sample size** | There are approximately 140 NHS services fitting hearing aids to 355,000 new adult users each year, so approximately 211 per service each month. We assume that 25% of participants will provide individual follow-up research data with 80% of these providing primary outcome data and clinics will each recruit for three months, giving an average cluster size for analysis of approximately 130 participants. The intra-class correlation coefficient (ICC) for the primary outcome is unknown, but based on published ICC data for a broad range of outcomes and settings we assume it to be between 0.02 and 0.05. Our target treatment effect is a difference in mean hours of use per day of 1–1.5 hours. With 90% statistical power, 5% two-sided significance level, ICC = 0.02, standard deviation = 5.5 hours and target mean difference of 1 hour, a total of 36 sites and 4,680 participants are required for the analysis. Based on a 25% consent rate (and 80% of these participants providing primary outcome data) a total of 23,400 patients would need to be recruited, with a total of 5,850 participants consenting to follow-up data collection. |
| **Expected recruitment duration** | Each participating centre will have a 3-month recruitment period, starting from site green light.<br>23,400 patients will be enrolled over the period of 16 months. |
| **Randomisation** | Sites will be randomised with a 1:1 allocation ratio to either structured care or usual care (stratifying by site size determined by the number of new hearing-aid referrals per month). All eligible patients at that site will receive the intervention as per site randomised allocation. |
| **Study Within A Trial (SWAT)** | We will investigate the effects of the timing of telephone contact with potential participants return of 12-week questionnaires. |

## 2.1. Sample size and justification

There are approximately 140 NHS services fitting hearing aids to 355,000 new adults each year, so approximately 211 per service each month. We assume that 25% of patients will provide individual follow up research data with 80% of these providing primary outcome data and clinics will each recruit for three months, giving an average cluster size for analysis of 130 patients. The intra-class correlation coefficient (ICC) for the primary outcome is unknown but based on published ICC data for a broad range of outcomes and settings[28] we assume it to be between 0.02 and 0.05.

Our target treatment effect is a difference in mean hours of use per day of 1-1.5 hours (60-90 minutes). With 90% power, a 5% two-sided significance level, ICC = 0.02, SD = 5.5 hours[29] and target difference of 1 hour, a total of 36 sites and 4,680 participants are required for the analysis. Based on 80% providing primary outcome data, a total of 5,850 patients are required to be enrolled.

If the ICC is 0.05, the trial will have 90% power to detect a difference of 1.4 hours (84 minutes), and 80% power for a difference of 1.2 hours (72 minutes). There is an association between daily duration of hearing aid use and reported benefit, such that even a small effect of the intervention in increasing mean hours of hearing aid use could be clinically important. Our PPI contributors indicated that 60-90 minutes is a meaningful increase in usage.

Table 1 shows the detectable differences in mean minutes of hearing aid usage at 80% and 90% power for ICCs ranging from 0.02 to 0.05 and Coefficient of variation from 0.4 to 0.9.

**Table 1:** Detectable differences in mean for minutes of hearing aid usage with varying power, intra-class correlation and coefficient of variation.

| | | **Intra-class correlation coefficient (ICC)** | | | |
|---|---|---|---|---|---|
| | | 0.02 | 0.03 | 0.04 | 0.05 |
| **Coefficient of variation (CoV)** | | 90% power | | | |
| | 0.4 | 60 | 70 | 79 | 86 |
| | 0.5 | 61 | 70 | 79 | 86 |
| | 0.6 | 61 | 71 | 80 | 87 |
| | 0.7 | 62 | 72 | 80 | 88 |
| | 0.8 | 64 | 73 | 81 | 89 |
| | 0.9 | 65 | 74 | 82 | 89 |
| | | 80% power | | | |
| | 0.4 | 52 | 61 | 68 | 74 |
| | 0.5 | 52 | 61 | 68 | 75 |
| | 0.6 | 53 | 61 | 69 | 75 |
| | 0.7 | 54 | 62 | 70 | 76 |
| | 0.8 | 55 | 63 | 70 | 77 |
| | 0.9 | 56 | 64 | 71 | 77 |

## 2.2. Blinding and breaking of blind

Given the nature of the intervention, the trial team, the patients, and site staff as well as the Clinical Investigator and Trial Statistician will be unblinded to the intervention allocation.

## 2.3. Trial committees

A trial management group (TMG), trial steering committee (TSC) and data monitoring committee (DMC) will be assembled to oversee the trial. The general purpose, responsibilities and structure of

the committees are described in the protocol. Further details of the roles and responsibilities of the TSC and DMC can be found in their charters agreed prior to the start of recruitment to the trial.

## 2.4. Outcome measures

Outcomes in the FAMOUS trial will be derived from self-reported questionnaires. The outcomes and their derivations are detailed in Table 1.

**Table 2:** Summary of the outcome measures

| Outcome measures | Scale, description and source | Derivation of scores | Time point | Analysis method described in: |
|---|---|---|---|---|
| | | | | |
| **Primary outcome** | | | | |
| Self-reported daily hours of hearing aid use at 12 months post fitting. | Participant reported at 12 months.<br><br>Response to question:<br>"On an average day over the past week, how many hours did you use the hearing aid(s)?" on the participant reported questionnaire at 12 months. | Number of hours of hearing aid use will be used as a continuous scale. | 12 months post fitting | Section 7.1 |
| **Secondary outcomes** | | | | |
| Self-reported daily hours of hearing aid use at 12 weeks post fitting. | Participant reported at 12 weeks.<br><br>Response to question:<br>"On an average day over the past week, how many hours did you use your hearing aid(s)?" on the participant reported questionnaire at 12 weeks. | Number of hours of hearing aid use will be used as a continuous scale. | 12 weeks post fitting | Section 7.4 |
| Proportion of non-users at 12 weeks and 12 months post fitting. | *Participant reported at 12 weeks and 12 months.*<br><br>Non-user defined as ≤1 hour a day | Participants will be categorised as a 'non-user' if they use their hearing aid for ≤1 hour a day and 'users' will be defined as those who use their hearing aid for more than 1 hour a day. | 12 weeks and 12 months post fitting | Section 7.4 |
| Hearing related quality of life measured using the International Inventory for Hearing Aids (IOI-HA) at 12 weeks and 12 months post fitting. | *Participant reported at 12 weeks and 12 months.*<br><br>The IOI-HA is a 7-item questionnaire completed after people are provided with hearing aids. The survey was developed to | The 7 questions on hearing aid use scored from 1-5 each with higher score indicating better outcome.<br><br>Benefit and Residual difficulty subscales are calculated by | 12 weeks and 12 months post fitting | Section 7.4 |

| Outcome measures | Scale, description and source | Derivation of scores | Time point | Analysis method described in: |
|---|---|---|---|---|
| | facilitate comparison across studies with questions on usage benefit, satisfaction, QoL, impact on others and residual difficulties. | summing the scores from questions 2, 4 and 7 and 3, 5 and 6 respectively. Question 1 is not included in either subscale as it pertains to usage.<br><br>Mean score is presented for each subscale and total. | | |
| The Significant Other Scale for Hearing Disability (SOS-HEAR) questionnaire will be completed at 12 months post fitting. | *Reported by participant's partners at 12 months (if the participant has a partner).*<br><br>The SOS-HEAR consists of 6 factors: Communication changes, Communicative burden, Relationship changes, Going out and socializing, Emotional reactions, and Concern for partner.<br><br>Each question is scored from 0-4 with 0= "no problem", 1= "a mild problem", 2= "a moderate problem", 3= "a severe problem" and 4= "a complete problem" | Higher SOS-HEAR scores indicate greater difficulties for the significant other.<br><br>Mean score is presented for each factor and total. | 12 months post fitting. | Section 7.4 |
| Modified hearing related quality of life measured using the Hearing Handicap Inventory (HHI) at 12 weeks and 12 months post fitting. | *Participant reported at 12 weeks and 12 months.*<br><br>A modified version of the most commonly used hearing-related QoL questionnaire.<br><br>The HHI consists of 22 questions scored from 0-6 with 4="yes", 2 ="sometimes" and 0="no". Results reported for total. | Higher HHI scores indicate worse outcome.<br><br>Mean total score compared. | 12 weeks and 12 months post fitting. | Section 7.4 |

| Outcome measures | Scale, description and source | Derivation of scores | Time point | Analysis method described in: |
|---|---|---|---|---|
| 6-item COM-B questionnaire [54] that measures capabilities, opportunities and motivations. | *Participant reported at 12 weeks and 12 months.*<br><br>6 item self-evaluation health psychology questionnaire: physical capability, psychological capability, physical opportunity, social opportunity, reflective motivation, automatic motivation | The 6 questions on hearing aid use scored from 0-10 each with higher score indicating better outcome.<br><br>Mean scores for the 6 items will be compared separately. | 12 weeks and 12 months post fitting. | Section 7.4 |
| Health Utility Index Mark 3 (HUI-3) at 12 months | *Participant reported at 12 months.*<br><br>Details included in Health Economics Analysis Plan | | 12 months post fitting | HEAP |
| Modified Client Service Receipt Inventory (CSRI) at 12 months | Details included in Health Economics Analysis Plan | | 12 months post fitting | HEAP |

## 3. INTERIM ANALYSIS

There is no planned interim analysis of treatment efficacy. However, an assessment of recruitment and retention will be performed following the internal pilot phase to determine the feasibility of recruiting sites and sites adherence with delivering intervention according to agreed progression criteria outlined in section 8.4 of the protocol.

## 4. GENERAL ANALYSIS CONSIDERATIONS

### 4.1. Analysis sets

The primary approach to between-group comparative analyses will be by intention-to-treat (i.e., including all patients according to randomised allocation regardless of site adherence to trial allocation). The primary analysis will include all randomised participants who consent to provide follow-up data at 12 weeks or 12 months.

### 4.2. Timing of final analysis

All outcomes will be analysed collectively at the end of the trial when all data relating to all outcomes have been collected and the database has been locked.

### 4.3. Statistical software

All analysis will be performed using Stata version 17 or above.

### 4.4. Derived variables

Details of how questionnaires are scored are contained within Table 2. For details on how missing items will be dealt with refer to section 4.5.

### 4.5. Procedures for missing data

**Missing baseline data**

Missing data for baseline characteristics (both cluster-level and participant-level) are expected to be very rare as patient-level characteristics will be collected via routine sources from each site. However, where necessary, missing baseline data will be imputed using the mean score at each site for the purposes of including these participants in the analysis. These simple imputation methods are superior to more complicated imputation methods when baseline variables are included in an adjusted analysis to improve the precision of the treatment effect (Sullivan TR, Epub 2016 Dec 19).

**Missing items in questionnaires**

**Table 3:** Rules for imputing missing items within questionnaires.

| Questionnaire | Imputation method |
|---|---|
| IOI-HA | Missing scores are imputed pro-rata if no more than one item is missing across the whole questionnaire. |
| SOS-HEAR | Missing scores are imputed pro-rata for each subscale if no more than one item is missing per subscale. |
| HHI | Missing scores are imputed pro-rata if no more than one item is missing across the whole questionnaire. |
| COM-B | Missing scores are imputed pro-rata if no more than one item is missing across the whole questionnaire. |

# 5. DESCRIPTION OF PARTICIPANT CHARACTERISTICS

## 5.1. Participant flow

The flow of sites and participants through the trial will be summarised in a CONSORT diagram detailing:

- The number of sites who completed an expression of interest form.
- Of those sites who completed an expression of interest, the number of sites who were not randomised and the reason why.
- The total number of sites randomised
- The number of sites randomised to each group
- The number of eligible participants within each group. The mean and standard deviation of the number of eligible participants across sites randomised to each group.
- The number of participants consented in each group. The mean and standard deviation of the number of consented participants across sites randomised to each group.
- The number of sites and participants adhering to the intervention, where adherence is defined as per section 6.2. The mean and standard deviation of the number of participants adhering to the intervention across sites randomised to the intervention group. No details on adherence to standard care will be presented.
- The number of participants providing the primary outcome at 12-weeks within each group. The mean and standard deviation of the number of participants providing the primary outcome at 12-weeks across sites randomised to each group.
- The number of participants providing the primary outcome at 12-months within each group. The mean and standard deviation of the number of participants providing the primary outcome at 12-months across sites randomised to each group.
- The number of sites and participants included in the primary analysis in each group. The mean and standard deviation of the number of participants included in the primary analysis across sites randomised to each group.

## 5.2. Baseline characteristics

**Site-level baseline characteristics**

Sites will also be described by treatment group with respect to the following baseline characteristics:

- Number of new hearing-aid referrals per month: small (<100), medium (≥100-250) and large (≥250) as per stratification factor for randomisation
- The proportion of follow-up appointments currently offered routinely to all new fittings (yes/no) and the proportion offered follow-up, if not routine
- Who typically organises follow-up (staff/patient/both) and proportion split if follow-up organised by both staff and patient
- Proportion of patients typically receiving follow-up
- Proportion of follow-ups which are typically face-to-face, video-call or telephone
- Typical time point when the follow up is conducted (1st month, 2nd month, 3rd month or longer after fitting)
- Level of seniority of who conducts the follow-ups (band 3-4/ band 5 and above/ both)

**Participant-level baseline characteristics**

Participants who have consented to complete questionnaires will also be described by treatment group with respect to the following baseline demographic and clinical characteristics:

- Demographics (age, deprivation score, sex, ethnicity)
- Audiometric data (pure-tone average of better ear)
- Whether hearing aid was fitted following assessment

- Whether the initial fitting was bilateral (yes/no)
- Manufacturer of first hearing aid
- Model of first hearing aid
- Real ear measurement verification completion (yes/no)

Baseline characteristics of participants who did not consent will also be presented alongside those who do consent.

Continuous data will be summarised in terms of the mean, standard deviation, median, lower & upper quartiles, minimum, maximum and number of observations. Categorical data will be summarised in terms of frequency counts and percentages. No formal statistical comparisons will be made.

# 6. ASSESSMENT OF STUDY QUALITY

## 6.1. Randomisation

Randomisation will take place at a cluster level (site) with a 1:1 allocation ratio to usual care or structured care using stratified block randomisation (stratifying by tertile of site size determined by obtaining up-to-date figures on the number of new hearing-aid referrals per month directly from sites before randomisation).

The number of sites randomised to usual care or structured care will be tabulated as well as the number of participants within the recruiting sites randomised to each. The stratification variable of site size will be tabulated as part of the baseline characteristics.

## 6.2. Adherence

Sites' adherence to the structured care intervention will be measured using the patient-level routine data collected from sites via Auditbase. Auditbase is an electronic management system used in NHS audiology clinics. Sites will be considered as adhering to the intervention if 80% of new hearing aid patients receive the below steps in the intervention:

- Step 1: COSI Part 1 completed at hearing aid assessment
    - Defined as completed if the timestamp recorded in Auditbase if the COSI form has been opened is not missing.
- Step 2: FAMOUS Hearing Aid User Checklist and Diary provided to patient, action plan completed, and patient shown how to utilise the checklist and diary
    - Defined as completed if the timestamp recorded for an alert which confirms diary has been given is not missing.
- Step 3: Contact from their audiology clinic 7-days post-fitting by telephone
    - Defined as completed if the timestamp recorded for an alert which confirms at one week if a patient required support (phone call) but did not need a further appointment before 6 weeks is not missing or if a patient's follow-up appointment date, recorded on Auditbase, is one week after fitting date.

The number of sites randomised to the intervention who adhere to each step and overall will be tabulated.

Additionally, adherence will be reported at patient level. The number of patients within sites randomised to the intervention who are provided each step by their site and those who receive all steps will be tabulated.

## 6.3. Follow-up and discontinuations

Participants are followed up by research questionnaires at 12 weeks and 12 months following fitting. The number and percentage of eligible participants who return their 12-week questionnaire and the number and percentage of consented participants who return their 12-month questionnaires will be tabulated in the two groups. The number of weeks to questionnaire completion from fitting will be summarised using the mean, median, lower & upper quartiles, minimum and maximum.

The completeness of individual questionnaires at 12 weeks (Hearing Aid Use, IOI-HA, HHI, COM-B) and 12 months (Hearing Aid Use, IOI-HA, SOS-HEAR, HHI, COM-B, HUI3, modified CSRI) will also be reported.

Completeness will be categorised into the following categories:

- Completed: enough questions have been completed so that the questionnaire can be scored
- Partially completed: some questions have been completed, however not enough to calculated the questionnaire score
- Not done: no questions have been completed

## 6.4. Protocol deviations

A protocol deviation is a divergence or departure from the expected conduct of a study as defined in the protocol. Of particular importance are major deviations which may also be termed violations or non-compliances. These are deviations which may expose participants to increased risk, compromise the integrity of the entire study or affect participant eligibility.

Non-compliance with allocated treatment will be reported as described in Section 6.2.

Non-compliance with the protocol will be reported on a deviation form and assessed by the NCTU to determine if constitutes a violation. The number of participants with protocol violations will be summarised by treatment group along with the type of deviation. Protocol violations will also be listed.

# 7. ANALYSIS OF EFFECTIVENESS

## 7.1. Primary analysis

As hearing aid usage is also reported at 12 weeks, a linear mixed effects model will be utilised with a treatment by time interaction to obtain estimates of the hours of use at 12 months in each group. This longitudinal model permits the inclusion of participants with complete data for at least one timepoint and gives valid inferences when data are assumed missing at random. The model will also include a random effect to adjust for clustering within sites, while site size (categorised by tertile) and participant-level characteristics (age, sex, socio-economic status) will be adjusted for using fixed effects. The model will be fitted using an unstructured variance-covariance. If the model fails to converge, a simpler covariance structure will be used.

The treatment effect will be presented as a difference in means, along with 95% confidence intervals and a p-value.

The estimand for the primary outcome is the difference in means of daily hearing aid use 12 months post-fitting between participants at sites randomised to deliver structured monitoring and follow-up versus participants at sites randomised to deliver usual practice, regardless of site or participant adherence, among adults using hearing aids for first time and who consent to provide follow-up data.

| **Domain** | |
|---|---|
| Population | Adults using hearing aids for first time |
| Outcome | Self-reported daily hearing aid use 12 months post-fitting |
| Treatment | Usual monitoring and follow-up<br>Structured monitoring and follow-up |
| Intercurrent events | Intervention discontinuation (at site level) – participants included irrespective of discontinuation – treatment policy<br><br>Non-adherence to the intervention (at participant level) – included irrespective – treatment policy<br><br>Non-consent – excluded from the analysis (principal stratum) |
| Summary measures | Difference in means |

## 7.2. Sensitivity analysis of primary outcome

We will repeat the primary analysis additionally adjusting for any variables with marked imbalance at baseline to check that this does not influence the findings.

The primary analysis will also be repeated using the following assumptions regarding missing data from 12 months:

- Those who do not respond at 12 months are using their hearing aids the same amount as at 12 weeks (12-week observation carried forward).
- Those who do not respond at 12 months have stopped using their hearing aid completely (impute missing data with 0 at 12 months for those who consent only).
- Multiple imputation using baseline characteristics (for those who consent only).

## 7.3. Subgroup analysis of primary outcome

Appropriate interaction terms will be included in the primary regression analyses in order to conduct subgroup analyses according to the following subgroups.

| **Subgroup** | **Levels** |
|---|---|
| Severity of hearing loss in better ear | Mild (20-40 dB HL)<br>Moderate (41-60 dB HL)<br>Severe (61-75 dB HL)<br>Profound (>75 dB HL) |
| Sex | Male<br>Female |
| Deprivation | 1st quintile<br>2nd quintile<br>3rd quintile |

| | |
|---|---|
| | 4th quintile<br>5th quintile |
| Number of hearing aids fitted | Unilateral (hearing aid for one ear)<br>Bilateral (hearing aids for both ears) |

Between-group treatment effects will be provided for each subgroup, but interpretation of any subgroup effects will be based on the treatment-subgroup interaction and 95% confidence interval, estimated by fitting an appropriate interaction term in the regression models. Since the trial is powered to detect overall differences between the groups rather than interactions of this kind, these subgroup analyses will be regarded as exploratory.

## 7.4. Secondary outcomes

The following secondary outcomes will be analysed using appropriate mixed effects models dependant on data type (e.g., binary, continuous, time-to-event), adjusting for factors balanced at randomisation and participant-level characteristics (age, sex, socio-economic status) using fixed effects. The model will include a random effect to adjust for clustering within sites. The between group effect will be reported using an appropriate adjusted effect estimate along with a corresponding 95% confidence interval and a p-value. Where an outcome is also measured at multiple time points a mixed model will be fitted with a treatment by time interaction to obtain estimates of treatment effect at each follow-up time point.

**Binary outcomes**

The following binary outcomes:

- Non-usage of hearing aids

will be analysed using a mixed effects logistic regression model, adjusting for the stratification variable. The model will include a random effect for recruiting site, while participant-level characteristics (age, sex, socio-economic status) will be adjusted for using fixed effects. The between group effect will be reported using an adjusted risk difference and adjusted risk ratio along with corresponding 95% confidence intervals for each. Point estimates and confidence intervals will be obtained using Stata's Margins command with standard errors computed using the delta method [2]. A p-value will be presented for the adjusted risk-ratio only.

**Continuous outcomes**

For the following outcomes derived from participant questionnaires:

- Hearing related quality of like (IOI-HA)
- Hearing related quality of life (HHI)
- Mechanisms of impact (i.e., COM-B)

which are measured at multiple time points, a linear mixed effects model will be utilised with a treatment-by-time interaction to obtain estimates of treatment effect at each follow-up time. This longitudinal model permits the inclusion of participants with complete data for at least one timepoint and gives valid inferences when data are assumed missing at random. The model will also include a random effect for recruiting site, while site size will be adjusted for using fixed effects. The model will be fit using an unstructured variance-covariance. If the model fails to converge, a simpler covariance structure will be used.

The between group effect will be reported using an adjusted difference in means along with a corresponding 95% confidence interval.

The comparative statistical analyses described above will be performed for the total questionnaire score while each subscale will be summarised by treatment group in terms of the mean, standard deviation, median, lower & upper quartiles, minimum, maximum and number of observations. A summary of participant reported questionnaires and their subscales is provided in Table 4.

For the impact on families outcome (SOS-HEAR), which is measured at 12 months only, a linear mixed effects model will be utilised with a random effect for recruiting site, while treatment allocation and participant-level characteristics (age, sex, socio-economic status)will be adjusted for using fixed effects.

The between group effect will be reported using an adjusted difference in means along with a corresponding 95% confidence interval.

The SOS-HEAR total score and subscales will be reported similarly to the participant reported questionnaires. Further details can be found in Table 4.

**Table 4:** Participant reported questionnaires and subscales.

| Trial Outcome | Questionnaire | Subscales |
|---|---|---|
| Hearing related quality of life | IOI-HA | 1) Benefit subscale<br>2) Residual difficulty subscale<br><br>Disability score (Scores can range from 1 to 15)<br>Benefit score (Scores can range from 1 to 15)<br>Total score (Scores can range from 7 to 35) |
| Impact on Families | SOS-HEAR | 1) Communication changes (Scores can range from 0 to 24)<br>2) Communicative burden (Scores can range from 0 to 24)<br>3) Relationship changes (Scores can range from 0 to 12)<br>4) Going out and socializing (Scores can range from 0 to 16)<br>5) Emotional reactions (Scores can range from 0 to 20)<br>6) Concern for partner (Scores can range from 0 to 12)<br><br>Total Score (Scores can range from 0 to 108)<br>Factor Score (Score ranges vary across factors) |
| Hearing related quality of life | HHI | None -Total score only<br>Total score ranges from 0 to 88 |
| Barriers and facilitators to behaviour change within standard practice e.g., capabilities, opportunities and motivations | 6-item COM | 1) Physical Capability<br>2) Psychological Capability<br>3) Physical Opportunity<br>4) Social Opportunity<br>5) Reflective Motivation<br>6) Automatic Motivation<br><br>Item Score (Score ranges from 0 to 10 for all items)<br>Total score will not be presented |

## 7.5. Other follow-up data

Individual site adherence to the intervention is described in Section 6.2, however this does not describe whether participants within sites are receiving the intervention, so it is also important to assess the fidelity of the intervention. Therefore, participants within the sites randomised to the intervention will be described with respect to the following measures:

- Whether the day 7 appointment was offered and accepted
- Whether the day 7 appointment was attended
- Format of the day 7 appointment
- Whether the week 6 appointment was offered and accepted
- Whether the week 6 appointment was attended
- Format of the week 6 appointment
- Whether unscheduled appointments were needed (any appointment between and not including the day 7 and week 6 appointments)
- Number of unscheduled appointments needed

The number of unscheduled appointments will be summarised using the median, lower & upper quartiles, minimum and maximum.

Follow-up visits will be offered to all participants within the FAMOUS trial. Therefore, participants will be described by treatment group with respect to the following measures:

- Total number of appointments offered and accepted within 12 months post fitting
- Total number of appointments attended within 12 months post fitting

Both measures will be summarised using the mean, median, lower & upper quartiles, minimum and maximum.

### 7.6. Withdrawal and discontinuation

Consenting participants' withdrawal from questionnaire completion will be measured throughout the trial. The number and percentage of patients who have withdrawn will be tabulated by treatment group and the time from fitting to participant withdrawal will be summarised using the mean, median, lower & upper quartiles, minimum and maximum by treatment group.

Site discontinuation from their randomised intervention will also be collected with the number and percentage of sites discontinuing and number of weeks from randomisation to site discontinuation summarised using the mean, median, lower & upper quartiles, minimum and maximum by treatment group.

## 8. ANALYSIS OF SAFETY

The occurrence of an adverse event as a result of participation within this trial is not expected and no adverse event data will be collected, therefore, no analysis of safety data will be carried out.

## 9. FINAL REPORT TABLES AND FIGURES

See 1936FAMOUS Dummy Tables for final analysis v1.0 22Jun2023 for the full final analysis dummy table document.

## 10. REFERENCES

Sullivan TR, W. I. (Epub 2016 Dec 19). Should multiple imputation be the method of choice for handling missing data in randomized trials? . *Stat Methods Med Res. 2018*, 27(9):2610-2626.