Prognostic factors for outcomes of idiopathic Sudden onset Sensorineural Hearing Loss: the SeaSHeL national prospective cohort study

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INTRODUCTION

Each year, approximately 20 people per 100,000 experience sudden loss of hearing that is sensorineural in nature.(1-3) 'Sensorineural' indicates an abnormality of the cochlea, the auditory nerve, or higher central auditory pathways.(4) When the hearing loss is of 30 dB (decibel) or more, over at least 3 contiguous frequencies and within 3 days, the condition is termed sudden onset sensorineural hearing loss (SSNHL).(4,5) SSNHL is predominantly unilateral and the hearing loss can range from mild to profound. Reported causes of SSNHL include infectious and otologic diseases; trauma, including noise-induced, barotrauma or head trauma; vascular or haematological; neoplastic; and other. In 71% to 90% of cases, the cause is unknown despite investigation, and these cases are termed idiopathic.(6,7)

Associated symptoms include tinnitus, vertigo and aural fullness. Idiopathic SSNHL is a serious condition, adversely impacting people's lives(8) with research indicating associations with emotional distress, depression, difficulties at work and impaired social integration(9,10). Its prognosis is poorly understood and may depend on age, comorbidities, degree of hearing loss, audiometric configuration, presence of vertigo, treatment received, time between onset of hearing loss and treatment and other factors. It is estimated that 32% to 65% of cases of idiopathic SSNHL recover spontaneously, although clinical experience suggests that this may be an overestimation, with further research required in this area.(1-3,11)

Current care pathways for patients suffering from idiopathic SSNHL appear to vary considerably in terms of the type of service patients first present to, their subsequent referral, length of time between onset of symptoms, presentation and start of treatment, the treatment plan as well as follow-up. Treatment options for idiopathic SSNHL include systemic and intratympanic steroids, antiviral agents, rheological agents, diuretics, hyperbaric oxygen treatment, and observation alone.(5) The lack of evidence regarding the comparative effectiveness of these treatments is recognised by clinical guidelines published by National Institute for Health and Care Excellence (NICE), the American Academy of Otolaryngology-Head and Neck Surgery (ORL-HNS),(5) and the British Academy of Audiology.(5,7,12,13)

Based upon recent discoveries in the molecular mechanisms that lead to sensorineural hearing loss, biotechnology and pharmaceutical companies are developing new treatments for patients with idiopathic SSNHL.(14,15) These treatments require rigorous testing in clinical trials before they can become available for application in a clinical service setting. To allow for such trials to be run effectively reliable information is required on where patients with idiopathic SSNHL present and can be recruited from within the optimum timeframe from onset of symptoms to start of treatment based upon the preclinical profile of the drug. This means that there is an urgent need for

information on patient numbers, geographical distribution, demographics, patient and treatment pathways, as well as outcomes.
This study proposes to collect these data through an ENT trainee and Audiologist led nationwide prospective cohort study of adult patients presenting with SSNHL within the NHS. Importantly, this study will not only provide key data to inform future trial design and delivery, but also a unique dataset to develop a prediction model to predict recovery for patients with SSNHL.

AIM

To develop a prediction model to predict recovery for patients with SSNHL.

PICO

P – Adult patients diagnosed with idiopathic SSNHL in NHS ENT and hearing services
I – Demographic and disease-specific variables (of which treatment is one variable)
C – None
O – Hearing levels, quality of life

OBJECTIVES

1. To map the patient pathway and identify the characteristics of adult patients presenting to NHS ENT and hearing services with SSNHL.

2. To develop a prediction model to predict recovery for patients with SSNHL.

3. Establish the impact of idiopathic SSNHL on patients' quality of life (QoL)

METHODS

Study design
National multicentre prospective observational cohort study. The study will be reported in accordance with STROBE and 'Transparent Reporting of a multi variable prediction model for Individual Prognosis or Diagnosis' (TRIPOD) reporting guidelines for observational studies.(16,17)

Setting
A multicentre study taking place at NHS centres providing ENT and Hearing Services.

Inclusion criteria
- Adult patients (male or female) aged over 16 years of age presenting to NHS ENT and hearing services with SSNHL

AND

- Diagnosed with a hearing loss in one or both ears of 30 dB HL or more, over at least 3 contiguous frequencies, between 250, 500, 1000, 2000, 4000 and 8000 Hz.
  AND
- Willing and able to provide written informed consent.

Exclusion criteria

- Patients with mixed or conductive hearing loss (CHL). CHL will be defined as a 'true' air-bone gap of 15 dB HL or more in 3 or more contiguous frequencies between 500, 1000, 2000, 4000 Hz.

Candidate predictors

Age; gender; social class, presence of vestibular symptoms; precipitating illness; pattern of hearing loss; severity of hearing loss; time between onset of symptoms and treatment; treatment(s) received.

Pattern of hearing loss will be defined as: low frequency loss (250, 500 Hz), mid frequency loss (1000, 2000 Hz), high frequency loss (4000 Hz and 8000 Hz), flat (all frequencies), sloping (progressive loss across frequencies).

Severity of hearing loss (on presentation) will be defined as follows: Pure tone average (PTA) across 6 points, classified as: mild (25-40 dB loss), moderate (41-70 dB loss), severe (71-95 dB loss) and profound (>95 dB loss).

Primary outcome:

The change in auditory function in the affected ear from initial presentation to follow-up (at any one time between 6 and 16 weeks from onset of symptoms). Auditory function will be defined as the PTA of air conduction thresholds at 250, 500, 1000, 2000, 4000 and 8000 Hz. If multiple pure tone audiograms have been carried out between 6 and 16 weeks, the most recent pure tone audiogram will be used for the calculation of auditory function.

Change in auditory function classified as:

1) Full recovery: Final PTA in affected ear within 10dB of PTA of unaffected ear (≤10dB)
2) Partial to no recovery: Final PTA in affected ear ≥ 10dB of PTA of unaffected ear.

Secondary outcomes:

Degree of change in auditory function:

- Complete recovery: Final PTA in affected ear within 10dB of PTA of unaffected ear (≤10dB)

- Marked recovery: PTA improvement ≥30 dB (and final PTA in affected ear ≥ 10dB of PTA of unaffected ear)
- Slight recovery: PTA improvement ≥10dB and <30 dB (and final PTA in affected ear ≥ 10dB of PTA of unaffected ear)
- No improvement: PTA improvement <10 dB (and final PTA in affected ear ≥ 10dB of PTA of unaffected ear)

Quality of life:
Change in QoL score from initial presentation to follow-up at any one time between 6 and 16 weeks following treatment. QoL will be measured using the Hearing Handicap Inventory for Adults (HHIA) (for patients under 60 years of age) or Hearing Handicap Inventory for Elderly (HHIE) (for patients over 60 years of age) (see Appendix 1) and the Health Utility Index Mark 3 (HUI3) (see Appendix 2). QoL data will be only be collected in a selection of sites (see below).

Statistical analysis
Prognostic model:
The total sample size required to develop a binary logistic regression model has been estimated as per TRIPOD recommendations(17) and Ogundimu et al(18). The number of events per variable (EPV) has been set at 15, producing a minimally required sample size of 550 patients (number of parameters = 15).

We will develop a multivariable prognostic model to predict recovery for patients with SSNHL in NHS ENT and Hearing services. Analyses will be conducted on the candidate predictors specified above (n=15). Missing outcome data at study end will be imputed using multiple imputation by a chained equations procedure. Internal validation will be performed to quantify optimism in the predictive performance (calibration and discrimination) of the developed model using bootstrapping techniques. Bootstrapping techniques provide information on the performance of the model in comparable datasets and generate a shrinkage factor to adjust the regression coefficients.(19,20) Statistical analysis will be carried out using R software (version 3.5.1).

QoL:
The mean change in HHIA, HHIE and HUI3 scores will be calculated from initial presentation to follow up (any one time between 6 and 16 weeks). We will use the non-parametric Wilcoxon and McNemar–Bowker tests with a significance level of 5% to compare results at patients' initial presentation and at their final follow up. Statistical data analysis will be carried out using the SPSS program 19.0 (SPSS, Chicago, IL, USA). QoL data will be collected from a sub-set of sites (20%, n=20).

STUDY PROCEDURES

Working group
A working group will be established that will be responsible for study design, recruitment and delivery. This will consist of an Academic and Operational Team. All roles will last for the duration of the study, estimated at 18-24 months.

Academic Team
The Academic Team will be responsible for study design, methodology, ethics application, acquiring of research funding, NIHR CRN Portfolio adoption, data analysis and write-up (collaborative authorship). The Academic Team will also be responsible for secure data storage and compliance with General Data Protection Regulation (GDPR) requirements. The Academic Team will ensure that each Site: ENT Lead, Audiological Lead and Clinical Research Nurse has the up-to-date study protocol, consent form, patient information sheet (PIS), data collection sheet, QoL questionnaires and advertisement material. The Academic Team will obtain input from the INTEGRATE trainee collaborative and the NIHR CRN Audiology Champion Network on optimising data completion as well as efficient data processing and transfer. The Academic Supervisors will provide overall academic supervision for the study.

Academic Team Lead:
- Mr Rishi Mandavia. (SFO Academic & Careers Lead, INTEGRATE Otology Subcommittee Member, NIHR CLAHRC BRC Clinical Research Fellow UCL Ear Institute)
- Junior Academic Lead: Dr Yaamini Premakumar, Academic Foundation Year 2 Doctor, London North West

Academic Team Members:
- Miss Maha Khan - ENT ST5 Health Education North West, SFO Committee Member, INTEGRATE Collaborator Engagement Officer;
- Mr Nishchay Mehta -ENT ST8 North London, INTEGRATE Otology Committee Chair;
- Miss Tanjinah Ferdous - Audiologist Royal National Throat Nose and Ear Hospital (RNTNEH) and NIHR CRN North Thames Audiology Champion;
- Patient representative - The patient representative will advise on study design, the PIS, patient consent form as well as interpretation and dissemination of study findings
- Mr Timothy Chu – Data Collection Lead.

Academic supervisors:
- Professor Anne GM Schilder - Professor of Otorhinolaryngology UCL Ear Institute;
- Dr Gerjon Hannink - Methodologist, Radboud UMC Nijmegen, The Netherlands.

Academic-Operational Liaison:
- Mr Rishi Mandavia

This role will involve ensuring effective communication between the Academic and Operational Teams so that patient recruitment and data collection will take place as per study design. The Academic-Operational Liaison will chair working group meetings.

Operational Team:
The INTEGRATE ENT Trainee Collaborative, and Student and Foundation Doctors in Otolaryngology (SFO-UK) will help recruit Operational/Regional leads and ENT Site Leads and advertise the study through their networks. Operational/ Regional leads and ENT site leads will be of Grade F2 and above.

The NIHR CRN Audiology Champions Network will similarly help recruit Audiology Site Leads and advertise the study through their networks.

Each Operational/Regional Lead will be responsible for coordinating patient recruitment and data collection in approximately 5 hospital sites. This role will involve monthly meetings with the Academic-Operational Liaison as well as Site Leads to evaluate monthly data collection and implement strategies to maximise data capture and accuracy.

The Publicity Officers will be responsible for working with Academic Team to develop and disseminate material for the study including presentations and publications. The Publicity Officers will also work with the Academic Team to organise local dissemination of project findings upon study completion. The Publicity Officer will work with the SFO UK website lead (Dheeraj Karamchandani) and INTEGRATE Collaborator Engagement Officer (Maha Khan); to establish the study on the SFO UK and INTEGRATE Websites. The Publicity Officers will also be responsible for organising working group meetings as well as documenting and circulating meeting minutes.

Site Leads:
Each site will have an ENT and an Audiological Site Lead who will be responsible for registering the study for approval in each of their respective Research and Development (R&D) departments, advertising the study locally through presentations at departmental meetings, posters in ENT and Audiology outpatient departments, and through Trust websites and email notifications. ENT and Audiological Site Leads will also be responsible for recruiting patients for the study at their site; checking data accuracy as well as entering study data anonymously on Research Electronic Data Capture (REDCap) software (in accordance with data governance procedures - see below). In centres where QoL data will be collected (20 centres), ENT and Audiological Site Leads will require an up-to-date Good Clinical Practice (GCP) certificate and will be responsible for consenting patients.

NIHR CRN Research Nurses:

Adoption of the study onto the NIHR CRN Portfolio will give access to LCRN Research Nurses, who can assist in identifying potential patients and in consenting and recruiting patients into the study.

Study sponsor
University College London (UCL)

Study site Recruitment
Eligible sites across the United Kingdom will be identified via SFO-UK (The Student and Foundation Doctors in Otolaryngology), INTEGRATE (The National ENT Trainee Research Network), The NIHR CRN Audiology Champion Network, and the NIHR CRN. Ninety-seven sites will be recruited in total.

Study period
The study will be ongoing until the inclusion of 550 patients. It is estimated that the study period will be 32 months (from participant recruitment to dissemination of findings).

Participant Recruitment
For centres where QoL data are collected (20 of 97 sites), patients that meet the inclusion criteria and who are willing to discuss participation will be referred to: The ENT or Audiology Site Lead or NIHR CRN Research Nurse, who will provide eligible patients with a Participant Information Sheet (PIS) describing the study (see Appendix 3), and will take informed written consent (see Appendix 4). Patients will receive the usual assessment and treatment provided at the study site for SSNHL; in addition, they will be requested to complete two QoL questionnaires (see Appendix 1,2):

- HHIA or HHIE.
- HUI-3

For centres where QoL data are not collected, patients that meet the inclusion criteria will receive the usual assessment and treatment provided for SSNHL. Neither patient consent or PIS will be required.

The ENT or Audiology Site Lead or NIHR CRN Research Nurse will undertake a daily review of ENT and audiology clinics to identify eligible patients.

Data collection
A data collection proforma will be completed that will guide the recording of routine clinical information in patient notes. This proforma will be affixed into the patients' clinical notes.

<u>Data to be collected:</u>

- Site: Trust/CCG
- Service: ENT Emergency Clinic, ENT Outpatient Department, Audiology Department
- Age
- Gender (M/F)
- Family history of hearing loss (Y/N)
- Ethnicity (code)
- Education level (Primary education or less; Secondary education; Tertiary / further education = 3)
- Occupation
- Region (code)
- Co-morbidities
- Laterality
- Date of onset of symptoms of SSNHL
- Before hearing loss onset, was there any difference in hearing between the 2 ears?
- Date of first treatment for SSNHL (if applicable)
- Details of 1st treatment (route, drug name, drug dose, duration)
- Where first treatment given (GP/A&E/ENT clinic)
- Date patient referred to ENT or Audiology
- Patient referred by (GP, A&E, on-call ENT, Audiology, Other (specify)
- Date(s) seen in ENT Emergency Clinic /ENT outpatient clinic/ Audiology clinic
- Presentation: first, follow up.
- Treatments given so far (route, drug name, drug dose, duration, prescriber, date Initiated)
- Associated aural fullness.
- Associated tinnitus
- Associated vertigo
- Associated otalgia
- Associated discharge
- Other associated symptoms (specify)
- Precipitating illness
- Identifiable cause for SSNHL (Meniere's disease/ Retrocochlear disease/ autoimmune hearing loss/ trauma/ radiation-induced hearing loss/ noise-induced hearing loss/ or any other identifiable aetiology responsible for loss)
- Otoscopic examination findings (abnormal/normal)
- Dates of hearing tests
- Audiometry results (Collected at initial presentation and at any one time between 6 to 16 weeks) at six frequencies (250, 500, 1000, 2000, 4000 and 8000 Hz)
- Imaging (specify modality and date)
- Laboratory tests (specify test[s] and date[s])
- Treatment plan (medication name, route, dose, duration)

- Follow up (timing and type of planned follow-up) until primary endpoint reached
- HHIA or HHIE score and HUI-3 Score (Collected at initial presentation and any one time between 6 and 16 weeks)
- Adverse treatment events

Site-specific data

- How referrals are made and taken
- How patients are booked
- Who triages referrals and how often
- What grade(s) of clinician assess patients with SSNHL
- How follow-up is arranged for ENT Emergency Clinic, ENT Outpatient Department and Audiology Department for patients with SSNHL

Audiometry

Audiograms will be performed in soundproofed chambers. Air and bone conduction threshold audiometry as well as masking will be performed according to study site protocols.

Quality of life measures

Health Utility Index Mark 3 (HUI3). The HUI3 instrument consists of eight attributes (vision, hearing, speech, ambulation, dexterity, emotion, cognition and pain), with five to six levels and leads to 972,000 possible health states. Its multiplicative scoring function results in possible utility scores varying from −0.36 to 1.00. (21,22)

Hearing Handicap Inventory for Adults (HHIA) or Hearing Handicap Inventory for Elderly (HHIE). The HHIA and HHIE (for participants aged 60 years or over) are validated diagnostic tools for quantifying social and emotional consequences of hearing loss in adults and the elderly.(23-25) Both tools include two subscales: the social subscale comprises 12 questions addressing the social effects of hearing loss, and the emotional subscale comprises 13 questions addressing the emotional effects of hearing loss. Each question has three possible answers (yes, no or sometimes), with point values ranging from 0 to 4 points; total scores range from 0 to 100. Scores are classified as follows: no hearing handicap (total score ≤16), mild/moderate hearing handicap (total score from 18 to 42) and severe/ significant hearing handicap (total score >42).(23,26) Patients will be requested to complete the HHIA or HHIE questionnaires at their initial presentation and at their final follow up.

Data Entry

Participants will be assigned a unique study identification (ID) number that will be affixed to their clinical proformas. Once all data for a patient has been gathered, data from each participant's clinical proforma will be uploaded by the Site Lead using the

patient's unique ID number onto a secure online REDCap form. For data security, once data has been entered and submitted there will be no option to re-enter and edit the information recorded. Each ENT or Audiology Site Lead or NIHR CRN Research Nurse will be required to submit a monthly update on numbers of included patients to their respective Operational/Regional Lead.

GOVERNANCE

All study staff recruiting patients in centres where QoL Data will be collected will require an up-to-date GCP certificate. The study will be conducted in compliance with the protocol, GCP and applicable regulatory requirements. Site Leads will be required to register the study with their local Research & Development (R&D) department, Caldicott Guardian and Information Governance department where available.

In line with GDPR, the sponsor, UCL, will be registered with the Information Commissioner's Office. At the conclusion of the study, electronic files will be transferred and stored in accordance with UCL's guidelines for electronic and hard copy records.

This research will comply with the: Data Protection Act (2018), Freedom of Information Act (2000); Human Rights Act (Article 8) (1998). The research will adhere to the Information Governance Framework of UCL.

FUNDING

Funding has been requested from Industry to support the study. The principal costs will be for:

- Questionnaires for QoL outcome measures for national cohort study
    - 100 questionnaire packs with return postage at £3 each = £300
- Information packs for patients for national cohort study. £2 each x 100 = £200
- Consent forms, postage and return postage. £3 each x 100 = £300
- Dissemination conference = £1200

ETHICS

For centres where QoL data are collected, patients will be required to give written informed consent.

In centres where no QoL data are collected, there will be no deviation from the usual standard of care for any patient, and patient data will be anonymised; therefore consent is not required.

An application will be made to the NHS Research Ethics Committee. It is anticipated that this study will be eligible for proportionate review.

<u>Participant Information Sheet (PIS) (Appendix 3)</u>

The PIS will be provided to patients in centres where QoL data will be collected.

Consent form (Appendix 4)
For centres where QoL data are collected, patients will be required to give consent. The person taking consent will be recorded on a delegation log.

Two copies of the written and signed consent form will be completed; one for the participant and the second for the participant's medical notes.

Anticipated benefits:
Though there are no direct benefits for the participant, their participation will provide information that could potentially improve the care patients with SSNHL in the future.

Potential hazards:
There are no anticipated risks to the patients who consent to their anonymous data being recorded and submitted for the study. QoL questionnaires will take approximately twenty minutes to complete; and with an additional ten minutes for the consent process, the participant's appointment may take thirty minutes longer overall. To mitigate this, Site Leads will arrange for QoL questionnaires to be completed whilst participants are waiting for their appointment.

DISSEMINATION
Results will be presented at local and inter(national) meetings and published for the attention of a professional and scientific audience. Publication and presentation of the final results will be on behalf of all study sites and collaborators. A lay summary report will be published for participants and their families and friends.

Findings will be discussed at a dissemination conference, involving patients and their family members, clinicians, commissioners, guideline developers as well as industry. This will be a unique learning event, bringing together patients, the public and professionals to identify and prioritise areas for future research. This conference will also serve to raise awareness of SSNHL as an ENT emergency to patients and professionals.

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Appendices

Appendix 1 HHIA/HHIE Questionnaires

Appendix 2 HHUI3 Questionnaire

Appendix 3 Participant Information Sheet

Appendix 4 Consent form

Appendix 1: HHIA/ HHIE

Hearing Handicap Inventory for Adults (HHIA) (<65 years of age)

INSTRUCTIONS: The purpose of the scale is to identify the problems your hearing loss may be causing you. Check YES, SOMETIMES, or NO for each question. DO NOT skip a question if you avoid a situation because of your hearing problem. If you use a hearing aid, please answer the way you hear WITHOUT your aid.

		Yes (4)	Sometimes (2)	No (0)
S-1	Does a hearing problem cause you to use the phone less often than you would like?			
E-2	Does a hearing problem cause you to feel embarrassed when meeting new people?			
S-3	Does a hearing problem cause you to avoid groups of people?			
E-4	Does a hearing problem make you irritable?			
E-5	Does a hearing problem cause you to feel frustrated when talking to members of your family?			
S-6	Does a hearing problem cause you difficulty when attending a party?			
S-7	Does a hearing problem cause you difficulty hearing/understanding coworkers, clients, or customers?			
E-8	Do you feel handicapped by a hearing problem?			
S-9	Does a hearing problem cause you difficulty when visiting friends, relatives, or neighbors?			
E-10	Does a hearing problem cause you to feel frustrated when talking to coworkers, clients or customers?			
S-11	Does a hearing problem cause you difficulty in the movies or theater?			
E-12	Does a hearing problem cause you to be nervous?			

S-13	Does a hearing problem cause you to visit friends, relatives, or neighbors less often than you would like?			
E-14	Does a hearing problem cause you to have arguments with family members?			
S-15	Does a hearing problem cause you difficulty when listening to TV or radio?			
S-16	Does a hearing problem cause you to go shopping less often than you would like?			
E-17	Does any problem or difficulty with your hearing upset you at all?			
E-18	Does a hearing problem cause you to want to be by yourself?			
S-19	Does a hearing problem cause you to talk to family members less often than you would like?			
E-20	Do you feel that any difficulty with your hearing limits or hampers your personal or social life?			
S-21	Does a hearing problem cause you difficulty when in a restaurant with relatives or friends?			
E-22	Does a hearing problem cause you to feel depressed?			
S-23	Does a hearing problem cause you to listen to TV or the radio less often than you would like?			
E-24	Does a hearing problem cause you to feel uncomfortable when talking to friends?			
E-25	Does a hearing problem cause you to feel left out when you are with a group of people?			

Thank you for completing this questionnaire.

Adapted from Newman, C.W., Weinstein, B.E., Jacobson, G.P. and Hug, G.A., Test-retest reliability of the Hearing Handicap Inventory for Adults, *Ear Hear*., 12, 355-357 (1991)

Interpretation – for member of research team

NO = 0 points Sometimes = 2 points YES = 4 points

Total # of points for Social / 48

Total # of points for Emotional /52

Total # of points /100

0 (no handicap) to 100 (total handicap)
Tick as appropriate:

0-16%	No handicap	
18-42%	Mild-Moderate Handicap	
44% +	Significant handicap	

Hearing Handicap Inventory for Elderly (HHIE) (>=65 years of age)

INSTRUCTIONS: The purpose of the scale is to identify the problems your hearing loss may be causing you. Check YES, SOMETIMES, or NO for each question. DO NOT skip a question if you avoid a situation because of your hearing problem. If you use a hearing aid, please answer the way you hear WITHOUT your aid.

		Yes (4)	Sometimes (2)	No (0)
S-1	Does a hearing problem cause you to use the phone less often than you would like?			
E-2	Does a hearing problem cause you to feel embarrassed when meeting new people?			
S-3	Does a hearing problem cause you to avoid groups of people?			
E-4	Does a hearing problem make you irritable?			
E-5	Does a hearing problem cause you to feel frustrated when talking to members of your family?			
S-6	Does a hearing problem cause you difficulty when attending a party?			
E-7	Does a hearing problem cause you to feel “stupid” or “dumb”?			
S-8	Do you have difficulty hearing when someone speaks in a whisper?			
E-9	Do you feel handicapped by a hearing problem?			
S-10	Does a hearing problem cause you difficulty when visiting friends, relatives, or neighbors?			
S-11	Does a hearing problem cause you difficulty when visiting friends, relatives or neighbours?			
S-12	Does a hearing problem cause you to attend religious services less often than you would like?			

E-13	Does a hearing problem cause you to be nervous?			
S-14	Does a hearing problem cause you to visit friends, relatives, or neighbors less often than you would like?			
E-15	Does a hearing problem cause you to have arguments with family members?			
S-16	Does a hearing problem cause you difficulty when listening to TV or radio?			
S-17	Does a hearing problem cause you to go shopping less often than you would like?			
E-18	Does any problem or difficulty with your hearing upset you at all?			
E-19	Does a hearing problem cause you to want to be by yourself?			
S-20	Does a hearing problem cause you to talk to family members less often than you would like?			
E-21	Do you feel that any difficulty with your hearing limits or hampers your personal or social life?			
S-22	Does a hearing problem cause you difficulty when in a restaurant with relatives or friends?			
E-23	Does a hearing problem cause you to feel depressed?			
S-24	Does a hearing problem cause you to listen to TV or the radio less often than you would like?			
E-25	Does a hearing problem cause you to feel uncomfortable when talking to friends?			
E-26	Does a hearing problem cause you to feel left out when you are with a group of people?			

Thank you for completing this questionnaire.

Adapted from Newman, C.W., Weinstein, B.E., Jacobson, G.P. and Hug, G.A., Test-retest reliability of the Hearing Handicap Inventory for Adults, *Ear Hear.*, 12, 355-357 (1991)

Interpretation- for members of research team

NO = 0 points Sometimes = 2 points YES = 4 points

Total # of points for Social / 52

Total # of points for Emotional /52

Total # of points /104

0 (no handicap) to 100 (total handicap)
Tick as appropriate:

0-16%	No handicap	
18-42%	Mild-Moderate Handicap	
44% +	Significant handicap	

Appendix 2: HHUI3 Questionnaire

Health Utilities Mark 3 (HUI3)

INSTRUCTIONS: The purpose of tis questionnaire is to describe your health status. Circle the number which corresponds to the best description of your current status. Please do not skip any questions- feel free to ask a member of the research team for clarification.

Attribute	Level	Description
Vision (1-6)	1	Able to see well enough to read ordinary newsprint and recognize a friend on the other side of the street, without glasses or contact lenses.
	2	Able to see well enough to read ordinary newsprint and recognize a friend on the other side of the street, but with glasses.
	3	Able to read ordinary newsprint with or without glasses but unable to recognize a friend on the other side of the street, even with glasses.
	4	Able to recognize a friend on the other side of the street with or without glasses but unable to read ordinary newsprint, even with glasses.
	5	Unable to read ordinary newsprint and unable to recognize a friend on the other side of the street, even with glasses.
	6	Unable to see at all.
Hearing (1-6)	1	Able to hear what is said in a group conversation with at least three other people, without a hearing aid.
	2	Able to hear what is said in a conversation with one other person in a quiet room without a hearing aid, but requires a hearing aid to hear what is said in a group conversation with at least three other people.
	3	Able to hear what is said in a conversation with one other person in a quiet room with a hearing aid, and able to hear what is said in a group conversation with at least three other people, with a hearing aid.
	4	Able to hear what is said in a conversation with one other person in a quiet room, without a hearing aid, but unable to hear what is said in a group conversation with at least three other people even with a hearing aid.
	5	Able to hear what is said in a conversation with one other person in a quiet room with a hearing aid, but unable to hear what is said in a group conversation with at least three other people even with a hearing aid.
	6	Unable to hear at all.
Speech (1-5)	1	Able to be understood completely when speaking with strangers or people who know me well.
	2	Able to be understood partially when speaking with strangers

		but able to be understood completely when speaking with people who know me well.
	3	Able to be understood partially when speaking with strangers or people who know me well.
	4	Unable to be understood when speaking with strangers but able to be understood partially by people who know me well.
	5	Unable to be understood when speaking to other people (or unable to speak at all).
Ambulation (1-6)	1	Able to walk around the neighbourhood without difficulty, and without walking equipment.
	2	Able to walk around the neighbourhood with difficulty, but does not require walking equipment or the help of another person.
	3	Able to walk around the neighbourhood with walking equipment, but without the help of another person.
	4	Able to walk only short distances with walking equipment, and requires a wheelchair to get around the neighbourhood.
	5	Unable to walk alone, even with walking equipment. Able to walk short distances with the help of another person, and requires a wheelchair to get around the neighbourhood.
	6	Cannot walk at all.
Dexterity (1-6)	1	Full use of two hands and ten fingers.
	2	Limitations in the use of hands or fingers, but does not require special tools or help of another person.
	3	Limitations in the use of hands or fingers, is independent with use of special tools (does not require the help of another person).
	4	Limitations in the use of hands or fingers, requires the help of another person for some tasks (not independent even with the use of special tools).
	5	Limitations in the use of hands or fingers, requires the help of another person for most tasks (not independent even with the use of special tools).
	6	Limitations in the use of hands or finders, requires the help of another person for all tasks (not independent even with the use of special tools).
Emotion (1-5)	1	Happy and interested in life.
	2	Somewhat happy.
	3	Somewhat unhappy.
	4	Very unhappy.

	5	So unhappy that life is not worthwhile.
Cognition (1-6)	1	Able to remember most things, think clearly and solve day to day problems.
	2	Able to remember most things, but have a little difficulty when trying to think and solve day to day problems.
	3	Somewhat forgetful, but able to think clearly and solve day to day problems.
	4	Somewhat forgetful, and have a little difficulty when trying to think or solve day to day problems.
	5	Very forgetful, and have great difficulty when trying to think or solve day to day problems.
	6	Unable to remember anything at all, and unable to think or solve day to day problems.
Pain (1-5)	1	Free of pain and discomfort.
	2	Mild to moderate pain that prevents no activities.
	3	Moderate pain that prevents a few activities.
	4	Moderate to severe pain that prevents some activities.
	5	Severe pain that prevents most activities.

Thank you for completing this questionnaire.

Adapted from: Horsman J, Furlong W, Feeny D, Torrance G. The Health Utilities Index (HUI®): concepts, measurement properties and applications. Health Qual Life Outcomes. 2003; 1:54. doi: 10.1186/1477-7525-1-54

Appendix 3: Participant Information Sheet

Participant Information Sheet

Research Project: Prognostic factors for outcomes of idiopathic Sudden onset Sensorineural Hearing Loss: the SeaSHeL national prospective cohort study

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You have been invited to take part in a research study.

Before you decide whether to take part, it is important you understand why the research is being done and what this will involve. This information sheet explains the research study, what will be expected of you as a participant and what will happen during/after the research has taken place.

If you have any questions or need any clarification after reading this document, please approach a researcher or get in contact with us (details at the end). Please take the time you need to consider whether or not you would like to participate in this study. You may discuss this with other people if you wish.

If you decide to participate, please fill out the accompanying consent form.

Summary of the important things you need to know:

- We are studying patients with sudden onset hearing loss to find out how patients are being treated and how they cope with the condition. This will help develop future treatments for patients.
- The study will involve completing 2 questionnaires, that will take approximately 20 minutes.
- The study will not impact your care in any way.
- You can stop taking part in the study at any time

What is the purpose of the study?

Each year, around 15,000 people in the United Kingdom experience sudden onset hearing loss. When the cause for this is not clear, the condition is called idiopathic 'sudden onset sensorineural hearing loss' (SSHNL). There is increasing research being conducted to develop new treatments for this condition. We are carrying out this study to identify how patients are being treated, and how they cope with the condition afterwards. This will help us understand the condition better and help the development of new treatments.

Why have I been invited?
You have been invited to participate in this study as you have been diagnosed with SSNHL.

Do I have to take part?
No, you are under no obligation to participate in this study. You may withdraw from this study at any point by contacting a member of the research team, and you do not have to give a reason. Your healthcare will not be affected by your decision to participate or not participate in this study.

What will I have to do?

You will have to fill out a consent form and two questionnaires before and after your treatment that measure how your sudden hearing loss has affected your quality of life.

Each questionnaire will take approximately ten minutes to complete.

What are the possible disadvantages and risks of taking part?
Each questionnaire will take approximately ten minutes to complete. There are no foreseeable physical or mental risks, or disadvantages of taking part in the study.

What are the possible benefits of taking part?
Though there are no direct benefits for participating in the study, your participation will provide very useful information that could potentially improve the care of patients with SSNHL in the future.

What if there is a problem?
If there is a concern regarding any aspect of this study, you may raise it with the researcher on site. Alternatively, you may contact the study supervisor Prof. Anne Schilder (a.schilder@ucl.ac.uk) or a University Research Ethics Co-ordinator on 020 7679 8717 or by email to ethics@ucl.ac.uk.

Will my taking part in the study be kept confidential?
All information collected about you during the course of the study will be fully anonymised (i.e. you cannot be identified) and kept confidential.

The information you provide will be handled and stored in keeping with the Data Protection Act 1998. Once this study is finished, your anonymised data may be used for future studies.

What will happen if I don't carry on with the study?
You may withdraw at any point of the study by expressing this wish to a member of the research team.

What will happen to the results of the research study?
When we have analysed the results, we would like to share our findings with patients, members of the public and healthcare professionals by written reports and presentations.

Who is organising or sponsoring the research?
The research is being organised by the evident (Evidence-based Ear, Nose and Throat) team, Ear Institute, University College of London (UCL). The sponsor of the study is UCL.

Further information and contact details
Please feel free to contact the following individuals should you wish to seek more information.

Further information regarding the study:

Mr Rishi Mandavia, r.mandavia@ucl.ac.uk

Prof Anne Schilder, a.schilder@ucl.ac.uk

Formal complaints:

University Research Ethics Co-ordinator on 020 7679 8717 or by email to ethics@ucl.ac.uk.

Appendix 4: Consent form

Informed Participant Consent Form

Research Project: Prognostic factors for outcomes of idiopathic Sudden onset Sensorineural Hearing Loss: the SeaSHeL national prospective cohort study

Thank you for taking an interest in participating in this research.
Please complete this consent form after you have read the Participant Information Sheet or after having the project explained by a Researcher. If you have any questions, please ask the researcher before you decide to join.
You will be given a copy of this Consent Form and the Participant Information sheet to keep and refer to.
Please answer the following questions by ticking the response that applies:

	Yes	No
1. I have read the Information Sheet (Version 1.0) for this study and/or have had details of the study explained to me and I understand what the study involves (i.e. I understand the risks and benefits of participating in the study).	☐	☐
2. My questions about the study have been answered to my satisfaction and I understand that I may ask further questions at any point	☐	☐
3. I wish to voluntarily participate in the study under the conditions set out in the Participant Information Sheet and I understand that I am free to withdraw from the study at any time. I do not need to give a reason for my withdrawal and there will be no effect on my medical care or legal rights.	☐	☐
4. I agree to provide information to the researchers with the understanding it will be treated as strictly confidential under the Data Protection Act 2018.	☐	☐
5. I consent to the information collected for the purposes of this research study, once anonymised (so that I cannot be identified), to be used for any other research purposes.	☐	☐

Participant's Signature: _____ Date: _____

Participant's Name (Printed):

_____

Researcher's contact details: (Name, address, contact number of investigator)

Please keep your copy of the consent form and the information sheet together.