ISRCTN10535105 https://doi.org/10.1186/ISRCTN10535105

A research study to find out whether steroids given by mouth, an injection through the ear drum, or a combination of both treatments is best at improving hearing after unexplained sudden hearing loss.

Submission date
02/07/2022

Recruitment status
Recruiting

Registration date
02/12/2022

Overall study status
Ongoing

Last Edited
08/10/2024

Condition category
Ear, Nose and Throat

[X] Prospectively registered
[X] Protocol
[_] Statistical analysis plan
[_] Results
[_] Individual participant data
[X] Record updated in last year

Plain English Summary
Background and study aims
Hearing loss is a common and disabling condition that may result from problems with the cochlea, the inner ear structure that senses sound and sends information to the brain. Loss of hearing due to damage to the cochlea can occur suddenly and without an obvious cause, a condition described as sudden sensorineural hearing loss (SSNHL). SSNHL can range from a mild hearing loss to a completely deaf ear, which can make it difficult to understand people talking on the affected side. Recovery of hearing following SSNHL may be helped by urgent treatment with steroids, but crucially we do not know if these work best given as tablets or by an injection through the ear drum. If SSNHL is identified more than a few weeks after it occurs, steroids may have little effect. A major problem is that patients with SSNHL may not be referred to Ear, Nose and Throat (ENT) surgeons in time to benefit from steroid treatment (within four weeks), due to delays in the hearing loss being recognised or referred by general practitioners (GPs). Sudden hearing loss is rare and we usually do not know why it happens. Steroids are the best treatment to try and improve hearing, but we do not know whether it is best to give them by mouth or by an injection through the ear drum.

Who can participate?
Adults aged 18 years or over with ISSNHL in the last 4 weeks.

What does the study involve?
People with sudden hearing loss of unknown cause will be randomly chosen to have steroid treatment by mouth, injection into their ear, or both together. They will have a hearing test and fill in questionnaires before treatment and then six weeks and three months later to see how well their hearing recovers, as well as measure their dizziness and ringing in their ears. One of the main problems with a trial like this is reaching patients with sudden hearing loss to encourage them to see their GP, and making sure their GPs refer them quickly to their local Ear

Nose and Throat department for treatment. We will use a Facebook campaign to reach people with sudden hearing loss and encourage them to see their GP. We will use teaching sessions to remind GPs to refer straight away to their local hospital ENT department. As these patients are usually seen by junior ENT doctors, we will use a national group of junior ENT doctors to let patients know about the trial.

What are the possible benefits and risks of participating?
Benefits:
This group have already been very successful if previous work at recruiting patients to research studies. We have worked with a group of patients who had sudden hearing loss to make sure that this research study is designed well and measures the issues that they felt were important. They thought that it would be a good idea to be able to test their hearing at home during the study as well as coming into the hospital for their hearing tests. We therefore included some hearing tests that can be performed on a smartphone, tablet or desktop computer at home for those patients who have one of these devices. The results of the research study will be shared with the public through our Facebook group, a website and newsletters as well as GPs, emergency doctors and ENT doctors through talks at meetings and changing guidelines for the treatment of sudden hearing loss.
Risks:
Interventions:
- Both oral and injected steroid are commonly used treatments for ISSNHL in the UK with a good safety profile.
- Short-course high dose oral steroids have few risks if given according to the protocol. The most common side effects are altered mood or poor sleep, and these resolve when treatment finishes.
- Exclusion criteria ensure that patients at greater risk of side effects (e.g. pregnant women) are excluded.
- Intratympanic injection also has an established safety profile. It may be briefly uncomfortable, cause vertigo and occasionally infection and patients will be warned of these risks during the consent process and in specific patient information sheets for each treatment arm.
- Very rarely transtympanic injection could cause further permanent hearing loss, usually technique-related. Investigators performing injection will be required to review training material (written and video) and trainees/surgeons new to the technique will be supervised.
- Written instructions will be provided to participants regarding their allocated treatment, including information on side effects and who to contact in the event of a problem.
- GPs will be informed of the allocated treatment.
Research procedures:
- Additional research procedures include in-hospital speech hearing tests, questionnaires, and for some patients home hearing assessment.
- The main burden on participants is that slightly longer appointments will be required than those of standard of care. Follow up has been reduced to the minimum possible, and designed to coincide with standard care appointments.
- Although the questionnaires do not address sensitive issues, participants may find completing the questionnaires slightly distressing, or a burden on time. This risk will be explained during consent.
- Participants will be encouraged to perform online hearing tests weekly. Given potential time burdens or difficulty with internet access, these are optional. The tests are provided by an established developer of online hearing assessment tools and are designed to be simple to use with personal electronic devices and headphones.
Comprehension:
- Trial information will be made available in video and written format to maximise accessibility. The information sheet has been reviewed by patients to ensure accessibility.
Confidentiality:

- The trial is designed in accordance with the Birmingham Clinical Trials Unit (BCTU) Standard Operating Procedures.
- Site researchers will follow local NHS Trust policy on Data Protection.
- In correspondence, identifiers will be limited to Trial ID ± partial date of birth.
- Home hearing testing data will be associated with a code separate to the trial ID to ensure effective pseudo-anonymisation.

Where is the study run from?
University of Birmingham (UK)

When is the study starting and how long is it expected to run for?
June 2022 to May 2027

Who is funding the study?
National Institute for Health and Care Research (NIHR) (UK)

Who is the main contact?
starfish@trials.bham.ac.uk

Study website
See study outputs table

Contact information

Type(s)
Public

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Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number
2022-000085-17

IRAS number
1004878

ClinicalTrials.gov number
Nil known

Secondary identifying numbers

RG_21-145, IRAS 1004878, CPMS 53517

Study information

Scientific Title
A randomised controlled trial of STeroid Administration Routes For Idiopathic Sudden sensorineural Hearing loss: The STARFISH Trial

Acronym
STARFISH

Study hypothesis
Primary objective:
To establish the relative effects of oral, intratympanic, or combined oral and intratympanic steroids on hearing recovery in ISSNHL, when used as first line management.

Other objectives:
Hearing outcome
To use participant submitted data to explore the rate of hearing recovery.
Economic Aims and Objectives
To establish the cost-effectiveness of oral, intratympanic or combined oral and intratympanic steroids as the first line of treatment for ISSNHL.
Exploratory Objectives
To improve the early identification and onward referral of ISSNHL in primary care.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 07/11/2022, London - Harrow Research Ethics Committee (Level 3, Block B, Whitefriars, Lewins Mead, Bristol, BS1 2NT, UK; +44 207 104 8246; harrow.rec@hra.nhs.uk), ref: 22/LO/0532

Study design
Interventional single-blind randomized parallel-group controlled trial

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet
See study outputs table

Condition
Idiopathic sudden sensorineural hearing loss

Interventions
Oral steroid (Prednisolone) 1mg/Kg/day up to 60mg/day for 7 days
or
Intratympanic steroid (Dexamethasone) three intratympanic injections 3.3mg/ml or 3.8mg/ml spaced 7±2 days apart
or
Combined oral (Prednisolone) and intratympanic (Dexamethasone) steroid as described above, with the first intratympanic injection occurring within four days of starting oral steroids

Intervention Type
Drug

Phase
Phase III

Drug/device/biological/vaccine name(s)
Prednisolone, dexamethasone

Primary outcome measure
The absolute improvement in pure tone audiogram average (calculated at 0.5, 1.0, 2.0, 4.0 kHz) at 12 weeks after randomisation

Secondary outcome measures
At 6 and 12 weeks post randomisation:
1. Functional hearing
1.1. Hearing related to speech: using The Speech, Spatial and Qualities of hearing scale (SSQ). SSQ is a validated measure, in the form of a short questionnaire, known to provide a good representation of the functional relationship with speech in everyday life and has been used to assess the disability of unilateral hearing loss seen in ISSNHL, providing disability scores associated with different aspects of hearing.
1.2. The absolute improvement in pure tone audiogram average (calculated at 0.5, 1.0, 2.0, 4.0 kHz).
1.3. Actual hearing thresholds measured by pure tone audiogram average following treatment initiation (calculated at 0.5, 1.0, 2.0, 4.0 kHz).
1.4. High frequency hearing threshold measured by the absolute improvement in pure tone audiogram average across 4.0, 6.0 and 8.0 kHz.
1.5. Recovery of speech perception: using Arthur Boothroyd (AB) word lists scored by phoneme.
1.6. Extent of hearing recovery: using an established classification of recovery (complete/partial /none) based on pure tone audiogram and speech perception
1.7. Time to hearing recovery: using online digits-in-noise and pure tone tests (Optional and recommended weekly where done).

2. Associated Symptoms
2.1. Dizziness: using the Vestibular Rehabilitation Benefit Questionnaire (VRBQ).
2.2. Tinnitus: using the Tinnitus Functional Index (TFI).

3. Adverse Events (AEs)
3.1. Adverse events relevant to the interventions

4. Health Economic Assessment
4.1. Two tools will be used to assess health economics: the Health Utilities Index 3 (HUI3), a participant reported assessment of health-related quality of life suited to hearing loss, and ICEpop CAPability measure for Adults (ICECAP-A), a participant reported measure of capability for the adult population
4.2. Resource usage

Overall study start date
01/12/2021

Overall study end date
31/05/2027

Eligibility

Participant inclusion criteria
1. Adults aged 18 years or over
2. Diagnosis of new-onset ISSNHL- sensorineural hearing loss of 30 decibels (dBHL) or greater occurring within a 3-day period and including 3 contiguous pure-tone frequencies (out of 0.5, 1.0, 2.0, 4.0 kilohertz (kHz)) confirmed with a pure tone audiogram occurring within a 3-day period (based on participant reported history)
3. Onset of hearing loss within 4 weeks prior to randomisation
4. English spoken as a first or second language

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
525

Participant exclusion criteria
1. Identified cause for hearing loss (not idiopathic)
2. Bilateral ISSNHL
3. Received prior steroid treatment for the same episode of ISSNHL
4. Medical contraindication to high dose systemic steroids
5. Previous history of psychosis
6. On oral steroid therapy for another condition
7. Known adrenocortical insufficiency other than exogenous corticosteroid therapy
8. Hypersensitivity to the active substance or to any of the excipients
9. Has a systemic infection unless specific anti-infective therapy is employed
10. Has ocular herpes simplex

11. Has ipsilateral acute or chronic active middle ear disease (including acute otitis media, chronic suppurative otitis media and cholesteatoma, excluding dry perforation)
12. Does not have the capacity to provide written informed consent

Recruitment start date
01/02/2023

Recruitment end date
30/11/2026

Locations

Countries of recruitment
England

Northern Ireland

Scotland

United Kingdom

Wales

Study participating centre
Aberdeen Royal Infirmary
Foresterhill Road
Aberdeen
United Kingdom
AB25 2ZN

Study participating centre
Addenbrookes
Addenbrookes Hospital
Hills Road
Cambridge
United Kingdom
CB2 0QQ

Study participating centre
Broomfield Hospital
Court Road
Broomfield
Chelmsford
United Kingdom
CM1 7ET

Study participating centre
Charing Cross Hospital
Fulham Palace Road
London
United Kingdom
W6 8RF

Study participating centre
Colchester General Hospital
Colchester District General Hosp.
Charter Way
Turner Road
Colchester
United Kingdom
CO4 5JL

Study participating centre
Countess of Chester Hospital
Countess of Chester Health Park
Liverpool Road
Chester
United Kingdom
CH2 1UL

Study participating centre
Freeman Road Hospital
Freeman Road
High Heaton
Newcastle upon Tyne
United Kingdom
NE7 7DN

Study participating centre
Furness Hospitals NHS Trust
Furness General Hospital
Dalton Lane
Barrow-in-furness
United Kingdom
LA14 4LF

Study participating centre
West Wales General Hospital
Glangwili
Carmarthen
United Kingdom
SA31 2AF

Study participating centre
Glasgow Royal Infirmary
84 Castle Street
Glasgow
United Kingdom
G4 0SF

Study participating centre
Gloucestershire Royal Hospital
Great Western Road
Gloucester
United Kingdom
GL1 3NN

Study participating centre
Great Western Hospitals NHS Foundation Trust
Great Western Hospital
Marlborough Road
Swindon
United Kingdom
SN3 6BB

Study participating centre
Hinchingbrooke Hospital
Hinchingbrooke Park
Huntingdon
United Kingdom
PE29 6NT

Study participating centre
The James Cook University Hospital
Marton Road
Middlesbrough

United Kingdom
TS4 3BW

Study participating centre
James Paget University Hospital
Lowestoft Road
Gorleston
Great Yarmouth
United Kingdom
NR31 6LA

Study participating centre
John Radcliffe Hospital
Headley Way
Headington
Oxford
United Kingdom
OX3 9DU

Study participating centre
Kettering General Hospital Laboratory
Kettering General Hospital
Rothwell Road
Kettering
United Kingdom
NN16 8UZ

Study participating centre
Kingston Hospital
Galsworthy Road
Kingston upon Thames
United Kingdom
KT2 7QB

Study participating centre
Leicester Royal Infirmary
Infirmary Square
Leicester
United Kingdom
LE1 5WW

Study participating centre
Leeds General Infirmary
Great George Street
Leeds
United Kingdom
LS1 3EX

Study participating centre
Lincoln County Hospital
Sewell Road
Lincoln
United Kingdom
LN2 5QY

Study participating centre
Lister Hospital
Coreys Mill Lane
Stevenage
United Kingdom
SG1 4AB

Study participating centre
Liverpool University Hospitals NHS Foundation Trust
Royal Liverpool University Hospital
Prescot Street
Liverpool
United Kingdom
L7 8XP

Study participating centre
Manchester Royal Royal Infirmary
Cobbett House
Oxford Road
Manchester
United Kingdom
M13 9WL

Study participating centre

Morriston Hospital
Heol Maes Eglwys
Cwmrhydyceirw
Swansea
United Kingdom
SA6 6NL

Study participating centre
Taunton Hospital
Musgrove Park Hospital
Taunton
United Kingdom
TA1 5DA

Study participating centre
Ninewells Hospital
Ninewells Avenue
Dundee
United Kingdom
DD1 9SY

Study participating centre
North West London Hospitals NHS Trust
Northwick Park Hospital
Watford Road
Harrow
United Kingdom
HA1 3UJ

Study participating centre
Peterborough City Hospital
Edith Cavell Campus
Bretton Gate
Bretton
Peterborough
United Kingdom
PE3 9GZ

Study participating centre
Poole
Poole Hospital

Longfleet Road
Poole
United Kingdom
BH15 2JB

Study participating centre
Princess Royal Hospital
Apley Castle,
Grainger Drive
Apley
Telford
United Kingdom
TF1 6TF

Study participating centre
University Hospital Birmingham
Queen Elizabeth Hospital
Edgbaston
Birmingham
United Kingdom
B15 2TH

Study participating centre
Queen Alexandras Hospital
Southwick Hill Road
Cosham
Portsmouth
United Kingdom
PO6 3LY

Study participating centre
Queen Elizabeth University Hospital
1345 Govan Road
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G51 4TF

Study participating centre
Queens Hospital
Belvedere Road
Burton-on-trent

United Kingdom
DE13 0RB

Study participating centre
Queens Medical Centre
Nottingham University Hospital
Derby Road
Nottingham
United Kingdom
NG7 2UH

Study participating centre
Royal Berkshire Hospital
Royal Berkshire Hospital
London Road
Reading
United Kingdom
RG1 5AN

Study participating centre
Royal Blackburn Hospital
Haslingden Road
Blackburn
United Kingdom
BB2 3HH

Study participating centre
Bolton Royal Hospital
Minerva Road
Farnworth
Bolton
United Kingdom
BL4 0JR

Study participating centre
Royal Derby Hospital
Uttoxeter Road
Derby
United Kingdom
DE22 3NE

Study participating centre
Royal Devon and Exeter Hospital
Royal Devon & Exeter Hospital
Barrack Road
Exeter
United Kingdom
EX2 5DW

Study participating centre
Royal Free London NHS Foundation Trust
Royal Free Hospital
Pond Street
London
United Kingdom
NW3 2QG

Study participating centre
Royal Hallamshire Hospital
Glossop Road
Sheffield
United Kingdom
S10 2JF

Study participating centre
Royal Lancaster Infirmary
Ashton Road
Lancaster
United Kingdom
LA1 4RP

Study participating centre
Royal Stoke University Hospital
Newcastle Road
Stoke-on-trent
United Kingdom
ST4 6QG

Study participating centre

Royal United Hospitals Bath NHS Foundation Trust
Combe Park
Bath
United Kingdom
BA1 3NG

Study participating centre
Royal Victoria Hospital
274 Grosvenor Road
Belfast
United Kingdom
BT12 6BA

Study participating centre
Salford Royal Hospital
Stott Lane
Eccles
Salford
United Kingdom
M6 8HD

Study participating centre
Sandwell General Hospital
Lyndon
West Bromwich
United Kingdom
B71 4HJ

Study participating centre
Inhealth - Southend Pet/ct
Southend University Hospital
Prittlewell Chase
Westcliff-on-sea
United Kingdom
SS0 0RY

Study participating centre
St Johns Hospital
Howden Road West

Livingston
United Kingdom
EH54 6PP

Study participating centre
Stepping Hill Hospital
Poplar Grove
Hazel Grove
Stockport
United Kingdom
SK2 7JE

Study participating centre
Tameside General Hospital
Fountain Street
Ashton-under-lyne
United Kingdom
OL6 9RW

Study participating centre
Thomas Linacre Centre
Parsons Walk
Wigan
United Kingdom
WN1 1RU

Study participating centre
Torbay Hospital
Newton Road
Torquay
United Kingdom
TQ2 7AA

Study participating centre
University College London Hospitals NHS Foundation Trust
250 Euston Road
London
United Kingdom
NW1 2PG

Study participating centre
University Hospital Coventry & Warwickshire
Clifford Bridge Road
Walsgrave
Coventry
United Kingdom
CV2 2DX

Study participating centre
Monklands Hospital
Monkscourt Avenue
Airdrie
United Kingdom
ML6 0JS

Study participating centre
University Hospital of Wales
Heath Park
Cardiff
United Kingdom
CF14 4XW

Study participating centre
Wexham Park Hospital
Wexham Street
Wexham
Slough
United Kingdom
SL2 4HL

Study participating centre
Wrexham Maelor Hospital
Croesnewydd Road
Wrexham Technology Park
Wrexham
United Kingdom
LL13 7TD

Study participating centre

Wythenshawe Hospital
Southmoor Road
Wythenshawe
Manchester
United Kingdom
M23 9LT

Study participating centre
Ysbyty Gwynedd Day Hospital
Ysbyty Gwynedd
Penrhosgarnedd
Bangor
United Kingdom
LL57 2PW

Sponsor information

Organisation
University of Birmingham

Sponsor details
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researchgovernance@contacts.bham.ac.uk

Sponsor type
University/education

Website
http://www.birmingham.ac.uk/index.aspx

ROR
https://ror.org/03angcq70

Funder(s)

Funder type
Government

Funder Name
National Institute for Health and Care Research

Alternative Name(s)
National Institute for Health Research, NIHR Research, NIHRresearch, NIHR - National Institute for Health Research, NIHR (The National Institute for Health and Care Research), NIHR

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Results and Publications

Publication and dissemination plan
Peer reviewed scientific journals
Internal report
Conference presentation
Publication on website
Other
Data sharing of individual patient data will be via submission of a request to the Trial Management Group.

Intention to publish date
31/07/2027

Individual participant data (IPD) sharing plan
The final dataset will be available to members of the TMG and co-applicant group who need access to the data to undertake the final analyses. Any request for data generated in this trial will be considered by BCTU. Data will typically be available 6 months after the primary publication unless it is not possible to share the data (for example: the trial results are to be used as part of a regulatory submission, the release of the data is subject to the approval of a third party who withholds their consent, or BCTU is not the controller of the data).
Only scientifically sound proposals from appropriately qualified Research Groups will be considered for data sharing. The request will be reviewed by BCTU Data Sharing Committee in discussion with the CI and deputy CI and, where appropriate (or in the absence of the CI and deputy CI) any of the following: the trial sponsor, TMG and independent TSC.
A formal Data Sharing Agreement (DSA) may be required between respective organisations once release of the data is approved and before data can be released. The data will be fully de-identified (anonymised) unless the DSA covers transfer of participant identifiable information. Any data transfer will use a secure and encrypted method.

IPD sharing plan summary

Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Participant information sheet	version 2.0	07/10/2022	15/11/2022	No	Yes
Protocol file	version 3.0	10/10/2022	15/11/2022	No	No
Study website			15/11/2022	No	No
Study website	INTEGRATE link		15/11/2022	No	No
Protocol (other)			01/12/2022	No	No
HRA research summary			26/07/2023	No	No
Protocol article		29/02/2024	01/03/2024	Yes	No