

# 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.

<b>Submission date</b> 02/07/2022	<b>Recruitment status</b> Recruiting	<input checked="" type="checkbox"/> Prospectively registered <input checked="" type="checkbox"/> Protocol
<b>Registration date</b> 02/12/2022	<b>Overall study status</b> Ongoing	<input type="checkbox"/> Statistical analysis plan <input type="checkbox"/> Results
<b>Last Edited</b> 08/10/2024	<b>Condition category</b> Ear, Nose and Throat	<input type="checkbox"/> Individual participant data <input checked="" type="checkbox"/> Record updated in last year

## Plain English summary of protocol

### 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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Principal Investigator

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**Type(s)**

Principal Investigator

**Contact name**

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**Type(s)**

Scientific

**Contact name**

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## **Additional identifiers**

**EudraCT/CTIS number**

2022-000085-17

**IRAS number**

1004878

**ClinicalTrials.gov number**

Nil known

**Secondary identifying numbers**

## Study information

### Scientific Title

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

### Acronym

STARFISH

### Study objectives

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

## **Health condition(s) or problem(s) studied**

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

#### Completion date

31/05/2027

## Eligibility

#### Key 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

#### Key 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

**Date of first enrolment**

01/02/2023

**Date of final enrolment**

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**

**Morrison 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  
Glasgow  
United Kingdom  
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  
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**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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England  
United Kingdom  
B15 2TT  
+44 121 4058011  
[researchgovernance@contacts.bham.ac.uk](mailto: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?
<a href="#">Participant information sheet</a>	version 2.0	07/10/2022	15/11/2022	No	Yes
<a href="#">Protocol file</a>	version 3.0	10/10/2022	15/11/2022	No	No
<a href="#">Study website</a>	INTEGRATE link		15/11/2022	No	No
<a href="#">Study website</a>			15/11/2022	No	No
<a href="#">Protocol (other)</a>			01/12/2022	No	No
<a href="#">HRA research summary</a>			26/07/2023	No	No
<a href="#">Protocol article</a>		29/02/2024	01/03/2024	Yes	No