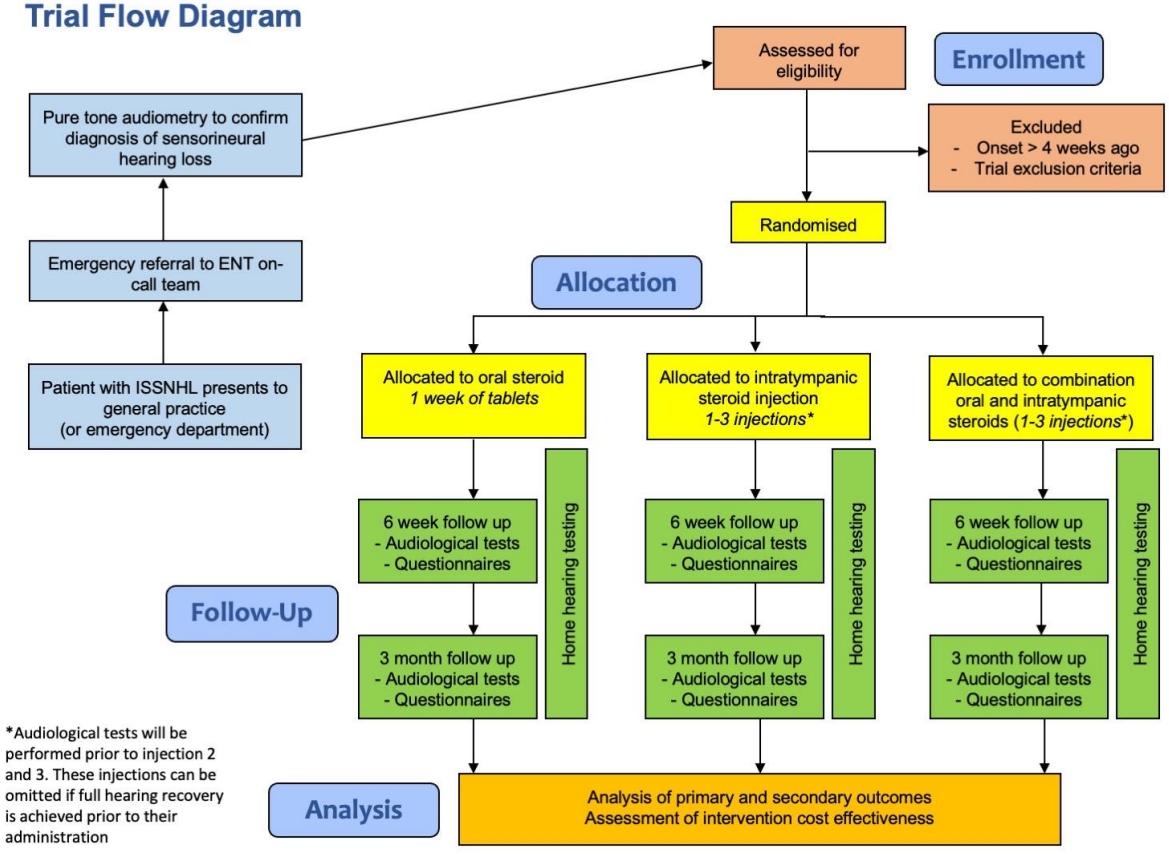
STARFISH Trial Summary

Title	STARFISH: STeroid Administration Routes For Idiopathic Sudden sensorineural Hearing loss
Trial Design	A pragmatic, multicentre, assessor-blinded, parallel 3-arm intervention, superiority, randomised controlled trial (1:1:1) with a 9-month internal pilot.
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 2 days of the start of oral steroids. **injections 2&3 may be withheld in the event of full hearing recovery prior to administration*
Outcome Measures	**Primary Outcome** ● The absolute improvement in pure tone audiogram average at 12-weeks following treatment initiation (calculated at 0.5, 1.0, 2.0, 4.0 kHz dBHL). Conducted by an audiologist blinded to the treatment allocation. **Secondary Outcomes** ● Functional hearing: ○ SSQ (Speech, Spatial and Qualities of hearing questionnaire) ○ Pure tone audiogram average at 6-week ○ Pure tone audiogram average across 4.0, 6.0 and 8.0 kHz, ○ AB phoneme score ● High frequency hearing threshold measured by the absolute improvement in pure tone audiogram average across 4.0, 6.0 and 8.0 kHz. ● Extent of hearing recovery ● Time to recovery ● Associated Symptoms: dizziness and tinnitus (VRBQ & TFI). ● Adverse Events ● Health Economics (HUI3, ICECAP-A, Resource usage) **Optional** ● Weekly home hearing tests (speech and pure tone thresholds) online
Trial duration per participant	Overall trial period 12 weeks: clinic follow up at 6 weeks to collect secondary outcomes, and 12 weeks to collect primary and secondary outcomes. Optional weekly home hearing test using online testing.
Estimated total trial duration	41 months (6 months setup, 25 months recruitment, 3 months follow up, 7 months analysis and write up)
Recruitment start date	Anticipated September 2022

Setting	Approximately 75 NHS hospital ENT units in the UK
Sample Size	525 participants

Eligibility Criteria	**Inclusion Criteria**
	● Adults aged 18 years or over.
	● Diagnosis of new-onset ISSNHL occurring within a 3-day period (based on patient-reported history) with a sensorineural hearing loss of 30 decibels (dBHL) or greater over 3 contiguous pure-tone frequencies (out of 0.5, 1.0, 2.0, 3.0, 4.0 kilohertz (kHz)) confirmed with a pure tone audiogram
	● Onset of hearing loss within the preceding 4 weeks.
	Exclusion Criteria
	● Identified cause for hearing loss (i.e. not idiopathic)
	● Bilateral ISSNHL
	● Received prior oral or intratympanic steroid treatment for the same episode of ISSNHL
	● Medical contraindication to high dose systemic steroids:
	  ○ Previous psychiatric history of psychosis
	  ○ Known adrenocortical insufficiency other than exogenous corticosteroid therapy
	  ○ Systemic infections unless on treatment
	  ○ Ocular herpes simplex
	● Hypersensitivity to the active substance or to any of the intervention excipients
	● Pregnant
	● On oral steroid therapy for another condition
	● Ipsilateral acute or chronic active middle ear disease (including acute otitis media, chronic suppurative otitis media and cholesteatoma, excluding dry perforation).
	● Does not have the capacity to provide written informed consent
	● English not spoken as a first or second language

Trial Flow Diagram



Schedule of Assessments

	Visits						
Assessments	**Screening**	**Baseline / Interven-tion**	**2nd IT injection (week 1 ±2 days)**	**3rd IT injection (week 2 ±2 days)**	**Weekly (for 12 weeks)**	**Week 6 ±7 days**	**Week 12 ±7 days**
Eligibility check	All						
Valid informed consent		All					
Relevant medical history taken		All					
Concomitant medication		All					
Demographic information		All					
Randomisation		All					
Pure tone audiogram		All	2,3	2,3		All	All
AB word lists		All				All	All
Online home hearing tests (optional)					All		

Speech, Spatial and Qualities of hear scale (SSQ)		All				All	All
Vestibular Rehabilitation Benefit Questionnaire (VRBQ)		All				All	All
Tinnitus Functional Index (TFI)		All				All	All
Health Utilities Index 3 (HUI3)		All				All	All
ICECAP-A		All				All	All
Resource usage						All	All
Adverse Events monitoring						All	All
Compliance reporting						2,3	
Prescription use monitoring						1,3	
Oral steroid provision		1,3					
Intratympanic injection		2,3	2,3	2,3			

**For participants who have a smartphone or tablet.*

1 = for arm 1 (oral steroid), 2 = for arms 2 (intratympanic injection), 3 = for arm 3 (combined treatment)