

# IIH Intervention: A clinical trial comparing two treatments (shunts and stents) to preserve vision for people with idiopathic intracranial hypertension

<b>Submission date</b> 10/11/2022	<b>Recruitment status</b> Recruiting	<input type="checkbox"/> Prospectively registered
		<input type="checkbox"/> Protocol
<b>Registration date</b> 02/02/2023	<b>Overall study status</b> Ongoing	<input type="checkbox"/> Statistical analysis plan
		<input type="checkbox"/> Results
<b>Last Edited</b> 02/07/2025	<b>Condition category</b> Nervous System Diseases	<input type="checkbox"/> Individual participant data
		<input checked="" type="checkbox"/> Record updated in last year

## Plain English summary of protocol

### Background and study aims

Idiopathic intracranial hypertension (IIH) is a neurological condition characterised by increased pressure inside the skull, called intracranial pressure (ICP). It is more common in women of reproductive age with obesity. Common symptoms of IIH include headaches, blurred vision and ringing in the ears. If left untreated, the disorder may cause blindness. The majority of patients with IIH are managed with weight loss and medications. Fewer than 10% of patients develop progressive visual loss and require urgent intervention to reduce ICP and preserve vision. This trial will compare the two most common interventions performed in the UK and evaluate their clinical and cost-effectiveness. The first is called cerebrospinal fluid (CSF) shunting and involves a procedure where a thin tube called a shunt is implanted in the body to drain brain fluid. The second is called dural venous sinus stenting (DVSS) and involves a procedure where a metallic mesh tube called a stent is implanted inside a brain blood vessel. Both procedures can preserve vision, but there is no strong evidence to support one over the other. Participants will have the same chance to be treated with CSF shunting or DVSS. The aim of the trial is to know which intervention is the most effective to save the vision and the most cost-effective.

### Who can participate?

Adults with a diagnosis of IIH at risk of permanent sight loss

### What does the study involve?

The trial will be conducted in NHS hospitals located in England, Wales and Scotland. Participants are randomly allocated to undergo cerebrospinal fluid (CSF) shunting or dural venous sinus stenting (DVSS). Afterwards the participants will be asked to attend 11 hospital appointments and one telephone appointment. This follow-up will take 2 years from start to finish. Participants will be closely monitored for any side effects and potential device failure, and for changes in vision, headaches and quality of life. The researchers will also collect health data from NHS Digital (the national custodian of NHS health and social care data).

What are the possible benefits and risks of participating?

There are no direct benefits from taking part in the trial but the information gained from this trial may help improve treatment for adults with IIH in the future. Participants may be seen more often and/or feel more supported as a consequence of their involvement in the trial. As with any intervention, there are risks and complications, but there are no additional disadvantages or risks involved in taking part in this trial. Both CSF shunting and stenting are treatments for IIH (shunting is widely used internationally, and in some hospitals, stenting is used as part of the standard of care). Participants require an intervention to prevent sight loss. None of these treatments is experimental but at present, there is not enough information to determine which treatment is most suitable and provides the higher level of health benefits to the individual.

Where is the study run from?

University of Birmingham (UK)

When is the study starting and how long is it expected to run for?

September 2021 to February 2029

Who is funding the study?

National Institute for Health Research (NIHR, grant number: NIHR131211) (UK)

Who is the main contact?

IIH Intervention Trial manager, IIHIntervention@trials.bham.ac.uk (UK)

### **Study website**

<https://www.birmingham.ac.uk/research/metabolism-systems/translational-brain-science/iih>

## **Contact information**

### **Type(s)**

Public

### **Contact name**

Dr . IIH Intervention Trial Office

### **Contact details**

D3B Clinical Trial Team

5th Floor

Open Plan East

Institute of Translational Medicine

Mindelsohn Way

Birmingham

United Kingdom

B15 2TH

-

IIHIntervention@trials.bham.ac.uk

### **Type(s)**

Scientific

### **Contact name**

Mr Darren Barton

**ORCID ID**

<https://orcid.org/0000-0003-0106-5861>

**Contact details**

D3B clinical trial team  
Office 15, 5th Floor  
Open Plan EAST, ITM  
Heritage Building  
Mindelson Way  
Edgbaston  
Birmingham  
United Kingdom  
B15 2TH  
+44 (0)121 371 8027  
d.barton@bham.ac.uk

**Additional identifiers****EudraCT/CTIS number**

Nil known

**IRAS number**

314408

**ClinicalTrials.gov number**

Nil known

**Secondary identifying numbers**

CPMS 54221, IRAS 314408

**Study information****Scientific Title**

Intervention to preserve vision in idiopathic intracranial hypertension: evaluation of clinical effectiveness and cost-effectiveness

**Study objectives**

To ascertain if the progression of visual function over 12 months, as measured by perimetric mean deviation, differs for idiopathic intracranial hypertension patients (IIH) undergoing dural venous sinus stenting compared to IIH patients undergoing cerebrospinal fluid shunting

**Ethics approval required**

Old ethics approval format

**Ethics approval(s)**

Favourable opinion 12/012/2022, West Midlands - South Birmingham Research Ethics Committee (Meeting held by video-conference via Zoom; +44 (0)207 104 8345, (0)207 104 8068, (0)207 104 8143; southbirmingham.rec@hra.nhs.uk), ref: 22/WM/0230

**Study design**

Randomized interventional study

**Primary study design**

Interventional

**Secondary study design**

Randomised controlled trial

**Study setting(s)**

Hospital

**Study type(s)**

Treatment

**Participant information sheet**

<https://www.birmingham.ac.uk/research/metabolism-systems/translational-brain-science/iih/participants>

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

Idiopathic intracranial hypertension

**Interventions**

Participants are randomized to undergo either cerebrospinal fluid (CSF) shunting or dural venous sinus stenting (DVSS).

The null hypothesis, which the researchers aim to disprove, is that dural venous sinus stenting (DVSS) is equivalent to cerebrospinal fluid (CSF) shunting in terms of the long-term trajectory of perimetric mean deviation for the treatment of idiopathic intracranial hypertension (IIH). CSF shunting represents the standard of care treatment for these patients and so makes the natural comparator. The secondary and exploratory outcomes will help the researchers to ascertain how these treatments affect different parts of the lives of patients with IIH.

The researchers have chosen a randomized design (randomized 1:1) to provide an unbiased comparison and to avoid the potential confounding factors implicit in non-randomised comparisons.

Once a potential participant has completed the screening process and is deemed eligible for study inclusion, they will be randomized on a 1:1 basis using computer-generated randomization via the Trial eRDC system. Patient treatment allocation will be stratified by the following criteria:

1. Presence of or intention to insert CSF lumbar drain prior to the protocol-defined intervention
2. Duration of IIH diagnosis (diagnosis  $\leq 28$  days from randomisation or diagnosis  $> 28$  days from randomisation)
3. The degree of papilloedema defined by the Frisén grade being  $< 4$  or  $\geq 4$  in the most affected study eye

To avoid any possibility of the treatment allocation becoming too predictable, a random factor will be included within the algorithm whereby for a proportion of the allocations true randomisation will be implemented rather than by using the minimisation allocation. 80% of

randomisations will be ascertained using the minimisation allocation, with the remaining 20% being true randomisation. In this manner the local responsible clinician will not be able to predict or influence the treatment allocation.

## **Intervention Type**

Procedure/Surgery

## **Primary outcome measure**

Perimetric mean deviation (PMD) is measured using a Humphrey Visual Field (HVF) over 12 months (analysed using repeated measures methods) using data collected at baseline, and then 1 week, 2 weeks, 1, 2, 3, 4, 6 and 12 months post-intervention, and at any unscheduled visit for revision/device failure between Visit 2 and 12 months post-intervention.

## **Secondary outcome measures**

Secondary outcome measures have been listed by category for clarity. Analysis will be over the time period stated (analysed using repeated measures methods). The primary efficacy analysis will use an interval of baseline to 12 months (analysis occurring once the final patient has completed their 12-month assessment) with longer-term follow-up using an interval of baseline to 24 months (occurring once the final patient has completed their 24-month assessment).

### **Vision:**

1. Perimetric mean deviation (PMD) is measured by Humphrey Visual Field (HVF) over 24 months (analysed using repeated measures methods) using data collected at 24 months post-intervention, and at any unscheduled visit for revision/device failure.
2. Retinal nerve fibre layer (RNFL) thickness is measured using Optical Coherence Tomography (OCT) over 12 and 24 months (analysed using repeated measures methods) using data collected at baseline, and then 1 week, 2 weeks, 1, 2, 3, 4, 6, 12 and 24 months post-intervention (the latter only pertinent to the 24-month analyses), and at any unscheduled visit for revision/device failure.
3. Optic nerve head size is measured using Optical Coherence Tomography (OCT) over 12 and 24 months (analysed using repeated measures methods) using data collected at baseline, and then 1 week, 2 weeks, 1, 2, 3, 4, 6, 12 and 24 months post-intervention (the latter only pertinent to the 24-month analyses), and at any unscheduled visit for revision/device failure.
4. Macular ganglion cell layer/complex thickness is measured using Optical Coherence Tomography (OCT) over 12 and 24 months (analysed using repeated measures methods) using data collected at baseline, and then 1 week, 2 weeks, 1, 2, 3, 4, 6, 12 and 24 months post-intervention (the latter only pertinent to the 24-month analyses), and at any unscheduled visit for revision/device failure.
5. Visual acuity is measured by logarithm of the minimum angle or resolution (LogMAR) units over 12 and 24 months (analysed using repeated measures methods) using data collected at baseline, and then 1 week, 2 weeks, 1, 2, 3, 4, 6, 12 and 24 months post-intervention (the latter only pertinent to the 24-month analyses), and at any unscheduled visit for revision/device failure.

### **Intervention reporting:**

1. Proportion of patients representing to hospital within 30 days of primary trial intervention, calculated as the percentage of patients who present over all patients in the arm and will be measured at 1 week, 2 weeks and 1 month, and at any unscheduled visit for revision/device failure during that period.
2. Proportion of patients being re-admitted to hospital within 30 days of primary trial intervention, calculated as the percentage of patients who are re-admitted over all patients in the arm and will be measured at 1 week, 2 weeks and 1 month, and at any unscheduled visit for

revision/device failure during that period.

3. Proportion of major complication, defined as the incidence of complications graded between III and V or major anaesthesia problems (including complications from revision procedures) according to the Clavien-Dindo classification of surgical complications reported at intervention, and then 1 week, 2 weeks, 1, 2, 3, 4, 6, and 12 months post-intervention, and at any unscheduled visit for revision/device failure between Visit 2 and 12 months post-intervention.

4. Proportion of major complication, defined as the incidence of complications graded between III and V or major anaesthesia problems (including complications from revision procedures) according to the Clavien-Dindo classification of surgical complications reported at intervention, and then 1 week, 2 weeks, 1, 2, 3, 4, 6, 12, 18 and 24 months post-intervention, and at any unscheduled visit for revision/device failure.

5. Proportion with minor complications, defined as Clavien-Dindo grade I-II during hospital stay, measured at intervention, and then 1 week, 2 weeks, 1, 2, 3, 4, 6 and 12 months post-intervention, and at any unscheduled visit for revision/device failure between Visit 2 and 12-month post-intervention.

6. Proportion with minor complications, defined as Clavien-Dindo grade I-II during hospital stay, measured at intervention, and then 1 week, 2 weeks, 1, 2, 3, 4, 6, 12, 18 and 24 months post-intervention, and at any unscheduled visit for revision/device failure.

7. Proportion of patients requiring revision in whom the revision intervention is the same as the primary intervention over 12 and 24 months post-intervention, measured at intervention, and then 1 week, 2 weeks, 1, 2, 3, 4, 6, 12, 18 and 24 months post-intervention, and at any unscheduled visit for revision/device failure.

8. Proportion of patients requiring revision in whom the revision intervention crosses over to the alternative intervention over 12 and 24 months post-intervention, measured at intervention, and then 1 week, 2 weeks, 1, 2, 3, 4, 6, 12, 18 and 24 months post-intervention, and at any unscheduled visit for revision/device failure.

9. Time to first revision measured as the average number of days between primary trial intervention and first revision over 12 and 24 months, measured at intervention, and then 1 week, 2 weeks, 1, 2, 3, 4, 6, 12, 18 and 24 months post-intervention, and at any unscheduled visit for revision/device failure.

10. Number of revisions per patient as captured on an unscheduled revision CRF and/or a valve adjustment CRF over 12 and 24 months. Data pertinent for this outcome may be completed anytime from the time of intervention, to 24 months post-intervention (including 1 week, 2 weeks, 1, 2, 3, 4, 6, 12, 18 and 24 months post-intervention, and at any unscheduled visit for revision/device failure).

11. Proportion of patients with adverse events as measured by the CTCAE version 5 at intervention, and then 1 week, 2 weeks, 1, 2, 3, 4, 6, 12, 18 and 24 months post-intervention, and at any unscheduled visit for revision/device failure.

#### Headache:

1. Monthly headache days (MHD) in a 28-day period over 12 and 24 months (analysed using repeated measures methods) using data collected at baseline/screening, 1, 2, 3, 4, 6, 12, 18 and 24 months post-intervention, and at any unscheduled visit for revision/device failure.

2. Headache severity measured by numeric rating scale 0-10, where 10 is the worst pain, in a 28-day period over 12 and 24 months (analysed using repeated measures methods) using data collected at baseline/screening, 1, 2, 3, 4, 6, 12, 18 and 24 months post-intervention, and at any unscheduled visit for revision/device failure.

3. Monthly moderate to severe headache days, defined as the number of days when the headache is moderate to severe in intensity (numeric rating scale scores of 4-10), and lasts for more than 4 hours or that requires acute headache analgesia, in a 28-day period over 12 and 24 months (analysed using repeated measures methods) using data collected at baseline/screening, 1, 2, 3, 4, 6, 12, 18 and 24 months post-intervention, and at any unscheduled visit for revision

/device failure.

4. Moderate to severe headache severity measured by NRS ( $\text{NRS} \geq 4$ ) in a 28-day period over 12 and 24 months (analysed using repeated measures methods) using data collected at baseline /screening, 1, 2, 3, 4, 6, 12, 18 and 24 months post-intervention, and at any unscheduled visit for revision/device failure.

5. Monthly use of acute headache analgesics calculated in 28-day periods over 12 and 24 months (analysed using repeated measures methods) from reported concomitant medications at baseline, intervention visit, 1 week, 2 weeks, 1, 2, 3, 4, 6, 12, 18 and 24 months post-intervention, and at any unscheduled visit for revision/device failure.

#### Patient-Reported Outcome Measures (PROM):

1. Quality of recovery is measured using the Quality of Recovery 15 questionnaire (QoR-15) at time of discharge

2. Satisfaction with intervention is measured using a 5-point Likert scale at time of discharge

3. Visual function is measured using the Visual Function Questionnaire (NEI-VFQ-25) with 10-Item Neuro-Ophthalmic Supplement) over 12 and 24 months (analysed using repeated measures methods) using data collected at baseline, intervention visit, 1 week, 2 weeks, 1, 2, 3, 4, 6, 12, 18 and 24 months post-intervention, and at any unscheduled visit for revision/device failure if not completed in the previous 8 weeks.

4. Headache disability is measured using the Headache Impact Test (HIT-6) over 12 and 24 months (analysed using repeated measures methods) using data collected at baseline, 1, 2, 3, 4, 6, 12, 18 and 24 months post-intervention, and at any unscheduled visit for revision/device failure if not completed in the previous 8 weeks.

5. Health status is measured using the 36-item Short form health survey (version 2, SF-36v2) over 12 and 24 months (analysed using repeated measures methods) using data collected at baseline, 1, 2, 3, 4, 6, 12, 18 and 24 months post-intervention, and at any unscheduled visit for revision /device failure if not completed in the previous 8 weeks.

6. Health-related utility values measured using the EuroQol 5 dimension 5 level (EQ5D-5L) instrument over 12 and 24 months (analysed using repeated measures methods) using data collected at baseline, 1 week, 2 weeks, 1, 4, 6, 12, 18 and 24 months post-intervention, and at any unscheduled visit for revision/device failure.

7. Time to return to work (if working) measured by a study-specific question added to the Work Productivity and Activity Impairment Questionnaire – General Health (WPAI-GH) over 24 months (analysed using repeated measures methods) using data collected at baseline, 2, 6, 12, 18 and 24 months post-intervention.

8. Impairments in work and activities are measured using the Work Productivity and Activity Impairment Questionnaire – General Health (WPAI-GH) over 12 and 24 months (analysed using repeated measures methods) using data collected at baseline, 2, 6, 12, 18 and 24 months post-intervention, and at any unscheduled visit for revision/device failure if not completed in the previous 8 weeks.

9. Healthcare resource use over 12 and 24 months, measured using a study-specific questionnaire at baseline, 1 week, 2 weeks, 1, 4, 6, 12, 18 and 24 months post-intervention, and at any unscheduled visit for revision/device failure if not completed in the previous 8 weeks.

#### Overall study start date

01/09/2021

#### Completion date

28/02/2029

## Eligibility

## **Key inclusion criteria**

List of principal criteria:

1. Diagnosis of idiopathic intracranial hypertension (IIH) by the IIH consensus guideline with bilateral papilloedema and a risk of permanent visual loss
2. Visual loss in at least one eye (study eye), secondary to papilloedema that cannot be explained by other ocular or central nervous system (CNS) pathology
3. Participants will be suitable for both cerebrospinal fluid (CSF) shunting and dural venous sinus stenting (DVSS)
4. Age 18 to <64 years at the time of consent
5. Able to provide written informed consent

## **Participant type(s)**

Patient

## **Age group**

Adult

## **Lower age limit**

18 Years

## **Upper age limit**

64 Years

## **Sex**

Both

## **Target number of participants**

Planned Sample Size: 138; UK Sample Size: 138

## **Key exclusion criteria**

List of principal criteria:

1. Presence of current venous sinus thrombosis on diagnostic brain imaging by either Magnetic Resonance Imaging (MRI), Magnetic Resonance Venography (MRV) or Computed Tomography Venography (CTV)
2. A completely normal CTV (or MRV) with clear visualisation of the whole sinus with no evidence of stenosis(es)
3. Previous surgery for IIH including, optic nerve sheath fenestration, CSF shunting procedures, sub-temporal decompression and DVSS.
4. Previous bariatric surgery within the last 3 months
5. Patients with a past ophthalmic history affecting the eligible eye(s) that could affect the vision (e.g. prior optic atrophy)
6. History of any clinically significant disease or disorder which, in the opinion of the investigator, may either put the subject at risk because of participation in the study, or influence the results or the subject's ability to participate in the study
7. Have participated in any other interventional study within 1 month prior to the screening visit (of note participation in the IIH Life database or other observational studies will not prevent enrolment in this study)
8. Previous randomisation for treatment in the present study
9. Pregnant
10. Absolute or serious contraindication to standard anti-thrombotic regimen peri- and post-

stenting

11. Other secondary causes of raised intracranial pressure, including: haematological (e.g. moderate to severe anaemia); causes of venous obstruction (e.g. cerebral venous sinus thrombosis); medications (e.g. quinolones); systemic disorders (e.g. chronic kidney disease); endocrine (e.g. Addison's disease); and syndromic (See Protocol Appendix 3 for a full list)

12. Absolute or serious contraindication for general anaesthesia

**Date of first enrolment**

01/02/2023

**Date of final enrolment**

28/02/2027

## **Locations**

**Countries of recruitment**

England

Scotland

United Kingdom

Wales

**Study participating centre**

**Queen Elizabeth Hospital**

Mindelsohn Way

Edgbaston

Birmingham

United Kingdom

B15 2GW

**Study participating centre**

**Worthing Hospital**

Lyndhurst Road

Worthing

United Kingdom

BN11 2DH

**Study participating centre**

**Gartnavel Royal Hospital**

J B Russell House

1055 Great Western Road

Glasgow  
United Kingdom  
G12 0XH

**Study participating centre**  
**St Thomas' Hospital**  
Westminster Bridge Road  
London  
United Kingdom  
SE1 7EH

**Study participating centre**  
**St James's University Hospital**  
Beckett Street  
Leeds  
United Kingdom  
LS9 7TF

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

**Study participating centre**  
**Kings College Hospital**  
Denmark Hill  
London  
United Kingdom  
SE5 9RS

**Study participating centre**  
**Royal Sussex County Hospital**  
Eastern Road  
Brighton  
United Kingdom  
BN2 5BE

**Study participating centre**  
**Bristol Eye Hospital**  
Lower Maudlin Street  
Bristol  
United Kingdom  
BS1 2LX

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

**Study participating centre**  
**Queen Elizabeth University Hospital**  
1345 Govan Road  
Glasgow  
United Kingdom  
G51 4TF

**Study participating centre**  
**St Thomas' Hospital**  
Westminster Bridge Road  
London  
United Kingdom  
SE1 7EH

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

**Study participating centre**  
**Manchester Royal Eye Hospital**  
Oxford Road  
Manchester

United Kingdom  
M13 9WL

**Study participating centre**  
**The Royal Victoria Infirmary**  
Queen Victoria Road  
Newcastle upon Tyne  
United Kingdom  
TS1 4LP

**Study participating centre**  
**National Hospital for Neurology & Neurosurgery**  
Queen Square  
London  
United Kingdom  
WC1N 3BG

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

**Study participating centre**  
**Southampton General Hospital**  
Tremona Road  
Southampton  
United Kingdom  
SO16 6YD

**Study participating centre**  
**Kings College Hospital**  
Denmark Hill  
London  
United Kingdom  
SE5 9RS

**Study participating centre**

**University Hospital of Wales**  
Heath Park  
Cardiff  
United Kingdom  
CF14 4XW

**Study participating centre**  
**York Hospital**  
Wigginton Road  
York  
United Kingdom  
YO31 8HE

**Study participating centre**  
**Hull Royal Infirmary**  
Anlaby Road  
Hull  
United Kingdom  
HU3 2JZ

**Study participating centre**  
**Sunderland Eye Infirmary**  
Queen Alexandra Road  
Sunderland  
United Kingdom  
SR2 9HP

**Study participating centre**  
**Sunderland Royal Hospital**  
Kayll Road  
Sunderland  
United Kingdom  
SR4 7TP

## **Sponsor information**

**Organisation**  
University of Birmingham

**Sponsor details**

C/o: Dr Birgit Whitman  
Head of Research Governance and Integrity  
Room 106  
Aston Webb B Block  
Edgbaston  
Birmingham  
England  
United Kingdom  
B15 2TT  
+44 (0)7814650003  
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

Planned publication in a high-impact peer reviewed journal.

If appropriate, in consultation with the investigators and the appropriate journal, a press release will be issued to the media upon publication of the results. The results of the study will be shared with study participants, staff members at research sites and investigators.

## Intention to publish date

31/07/2028

## Individual participant data (IPD) sharing plan

The datasets generated during and/or analysed during the current study are/will be available upon request from the CRUK clinical trials unit in accordance with the CRCTU data-sharing policy: <https://www.birmingham.ac.uk/research/crctu/Data-sharing-policy.aspx>. Any request to access clinical trial data needs to be requested in writing via the CRCTU data-sharing request form. These data will only be made available after the full analysis of the study data has been undertaken and published in addition to the generation of a complete study report.

## IPD sharing plan summary

Available on request

## Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
<a href="#">HRA research summary</a>			28/06/2023	No	No