ISRCTN86229394 https://doi.org/10.1186/ISRCTN86229394

# Early diagnosis of Stickler syndrome using a screening tool in children with Perthes disease

**Submission date**
14/02/2025

**Recruitment status**
Recruiting

**Registration date**
03/04/2025

**Overall study status**
Ongoing

**Last Edited**
14/02/2025

**Condition category**
Musculoskeletal Diseases

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

**Plain English Summary**
Background and study aims
Stickler syndrome is a genetic condition passed from parents to children that affects collagen, a key protein in the body's connective tissues. This can lead to problems with joints, the roof of the mouth, hearing, and eyes. The most common type, type 1 Stickler syndrome, can cause retinal detachment, leading to sight loss and potential blindness. While there is a treatment to prevent retinal detachment, early diagnosis is crucial to offer this treatment before sight is lost.

Our study aims to create a screening tool to identify important medical and family history associated with Stickler syndrome. We will test this tool in patients already diagnosed with Stickler syndrome and compare it to children without the condition. We will then use the tool in children with Perthes disease, a separate rare disease affecting the hip joint, to see if any have signs of Stickler syndrome. If successful, this tool could help diagnose patients earlier and offer treatment to prevent sight loss.

Who can participate?
Participants with Stickler syndrome will be selected from patients under our team and through the Stickler Syndrome UK charity's membership survey. A random sample of paediatric patients will also be selected from the general paediatric clinic in Cambridge. For testing in the Perthes disease population, participants will be selected from the paediatric orthopaedic Perthes disease clinic in Liverpool.

What does the study involve?
Participants will complete a screening tool, which takes about 10 minutes and includes a short examination of the child's mouth and joints. Children with Perthes disease will also have a blood test to check for a genetic variant causing type 1 Stickler syndrome.

What are the possible benefits and risks of participating?
The study aims to benefit future patients by identifying Stickler syndrome earlier and providing sight-saving treatment. For children with Perthes disease, the study may diagnose Stickler syndrome, leading to urgent assessment and management. The risks are minimal, with the screening tool being non-invasive and the blood test having the usual risks of distress and bruising.

Where is the study run from?
The study is run by the Vitreoretinal Research Group in the Department of Clinical Neurosciences at the University of Cambridge, in collaboration with the Paediatric Orthopaedic Department at Alder Hey Hospital in Liverpool (UK)

When is the study starting and how long is it expected to run for?
October 2024 to October 2026

Who is funding the study?
Addenbrooke's Charitable Trust Clinical Research Fellowship
Cambridge Trust Cambridge Masters & Churchill College Studentship (UK)

Who is the main contact?
Robert Smyth, rs815@cam.ac.uk

# Contact information

### Type(s)
Public, Scientific, Principal Investigator

### Contact name
Dr Robert Smyth

### ORCID ID
http://orcid.org/0000-0001-9482-5123

### Contact details
Vitreoretinal Research Group
John van Geest Centre for Brain Repair, University of Cambridge,
Forvie Site, Robinson Way
Cambridge
United Kingdom
CB2 0PY
+44 1223 331160
rs815@cam.ac.uk

### Type(s)
Principal Investigator

### Contact name
Mr Martin Snead

### ORCID ID
http://orcid.org/0000-0003-0042-8659

### Contact details
Vitreoretinal Research Group
John van Geest Centre for Brain Repair, University of Cambridge,
Forvie Site, Robinson Way
Cambridge

United Kingdom
CB2 0PY
+44 1223 331160
mps34@cam.ac.uk

# Additional identifiers

### EudraCT/CTIS number
Nil known

### IRAS number
343181

### ClinicalTrials.gov number
Nil known

### Secondary identifying numbers
Nil known

# Study information

### Scientific Title
A cross-sectional study screening for Stickler syndrome in children diagnosed with Perthes disease

### Study hypothesis
Stickler syndrome is present in the paediatric Perthes disease population and can be identified with a screening tool

### Ethics approval required
Ethics approval required

### Ethics approval(s)
Not yet submitted

### Study design
Observational cross-sectional multicentre study

### Primary study design
Observational

### Secondary study design
Cross sectional study

### Study setting(s)
Hospital, Medical and other records

### Study type(s)
Screening

### Participant information sheet
See outputs table

### Condition
Screening for Stickler syndrome in paediatric Perthes disease patients

### Interventions
A screening tool for Stickler syndrome will be developed using past medical and family history for patients under Cambridge University Hospitals NHS Trust (CUH) and identified by Stickler Syndrome UK charity patient membership survey, who have been co-diagnosed with Stickler syndrome and Perthes disease. This tool will then be ratified using paediatric patients with and without Stickler syndrome in CUH. Finally, the screening tool will be applied to paediatric patients with Perthes disease in Alder Hey hospital, Liverpool, with a genetic blood test for type 1 Stickler syndrome (COL2A1) collected at the same time. Patients' genetic results will be compared to their screening tool results, and the identification of any Stickler syndrome patients amongst this cohort will be considered a successful study outcome.

### Intervention Type
Other

### Primary outcome measure
Type 1 Stickler syndrome genetic test, EDTA 1ml blood sample for COL2A1 long range PCR at baseline

### Secondary outcome measures
Screening tool results, past medical and family history of Stickler syndrome, obtained via questionnaire at baseline in all participants

### Overall study start date
02/10/2024

### Overall study end date
02/10/2026

## Eligibility

### Participant inclusion criteria
We will have different cohorts at each stage of our study:

1. Design of screening tool:
1.1. Stickler syndrome patients participating in the SSUK patient membership survey
1.2. Stickler syndrome patients with a diagnosis of Perthes disease

2. Ratification of screening tool:
2.1. Stickler syndrome patients aged 4-10 years
2.2.General paediatric patients without a diagnosis of Stickler syndrome aged 4-10 years

3. Screening of Perthes disease population:
3.1. All paediatric patients attending paediatric orthopaedic Perthes disease clinics

### Participant type(s)
Healthy volunteer, Patient

### Age group
All

### Lower age limit
0 Years

### Upper age limit
99 Years

### Sex
Both

### Target number of participants
Total sample size: 300. 1) Design of screening tool: use of patients from Perthes case series plus others diagnosed with Perthes disease (estimated 30), and patients from Stickler Syndrome UK patient membership survey (estimated 50). 2) Ratification of screening tool: 26 paediatric Stickler syndrome patients and 26 general paediatric patients. 3) Screening of Perthes disease population: paediatric patients from Perthes disease cohort (estimated 100-200).

### Participant exclusion criteria
We have different cohorts at each stage of our study:

1. Design of screening tool
1.1. Paediatric patients in SSUK patient membership survey without a Perthes disease diagnosis (as will be used in cohort 2)

2. Ratification of screening tool
2.1. Patients with a diagnosis of Perthes disease, being investigated for Perthes disease
2.2. General paediatric patients under investigation for a connective tissue disorder other than Stickler syndrome

3. Screening of Perthes disease population:
3.1. Previous genetic diagnosis of Stickler syndrome

### Recruitment start date
01/03/2025

### Recruitment end date
01/06/2026

## Locations

### Countries of recruitment
England

United Kingdom

### Study participating centre
**Cambridge University Hospitals NHS Foundation Trust**
Cambridge Biomedical Campus
Hills Road
Cambridge
United Kingdom
CB2 0QQ

### Study participating centre
**Alder Hey Children's NHS Foundation Trust**
Alder Hey Hospital
Eaton Road
West Derby
Liverpool
United Kingdom
L12 2AP

## Sponsor information

### Organisation
Cambridge University Hospitals NHS Foundation Trust and University of Cambridge

### Sponsor details
Research and Development Department
Cambridge University Hospital
Hills Road
Cambridge
England
United Kingdom
CB2 0QQ
+44 1223 348490
cuh.research@nhs.net

### Sponsor type
Hospital/treatment centre

### Website
https://www.cuh.nhs.uk/our-research/get-involved/become-a-researcher/

### ROR
https://ror.org/04v54gj93

## Funder(s)

**Funder type**
Charity

**Funder Name**
Addenbrooke's Charitable Trust, Cambridge University Hospitals

**Alternative Name(s)**
Addenbrooke's Charitable Trust, Cambridge University Hospitals NHS Foundation Trust, ACT

**Funding Body Type**
Private sector organisation

**Funding Body Subtype**
Other non-profit organizations

**Location**
United Kingdom

**Funder Name**
Cambridge Commonwealth European and International Trust

# Results and Publications

**Publication and dissemination plan**
Planned publication in a peer-reviewed journal.
Planned presentation at relevant conferences.
Publication of results on SSUK website, newsletter and social media.

**Intention to publish date**
01/10/2027

**Individual participant data (IPD) sharing plan**
The datasets generated and/or analysed during the current study will be published as a supplement to the results publication. Prior to publication the datasets generated during and/or analysed during the current study will be available upon request from Robert Smyth on rs815@cam.ac.uk. All shared data will be anonymised to protect patient confidentiality, and any data that may compromise patient confidentiality will be withheld.

**IPD sharing plan summary**
Available on request, Published as a supplement to the results publication

**Study outputs**

| Output type | Details | Date created | Date added | Peer reviewed? | Patient-facing? |
|---|---|---|---|---|---|
| Participant information sheet | 1 - Perthes-Stickler Case Series | | 14/02/2025 | No | Yes |

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|---|---|---|---|---|---|
| Participant information sheet | 2 - Ratification | | 14/02/2025 | No | Yes |
| Participant information sheet | 3 - Perthes Screen | | 14/02/2025 | No | Yes |
| Protocol file | version 1 | 13/02/2025 | 14/02/2025 | No | No |