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

Submission date
14/02/2025

Recruitment status
No longer recruiting

Registration date
03/04/2025

Overall study status
Completed

Last Edited
14/02/2025

Condition category
Musculoskeletal Diseases

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

Plain English summary of protocol

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

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Additional identifiers

Integrated Research Application System (IRAS)
343181

Study information

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

Study objectives
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

Primary study design
Observational

Study design
Observational cross-sectional multicentre study

Study type(s)
Screening

Health condition(s) or problem(s) studied
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(s)
Type 1 Stickler syndrome genetic test, EDTA 1ml blood sample for COL2A1 long range PCR at baseline

Key secondary outcome(s)
Screening tool results, past medical and family history of Stickler syndrome, obtained via questionnaire at baseline in all participants

Completion date
02/10/2026

Eligibility

Key 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

Healthy volunteers allowed
No

Age group
All

Lower age limit
0 Years

Upper age limit
99 Years

Sex
All

Key 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

Date of first enrolment
01/03/2025

Date of final enrolment
01/06/2026

Locations

Countries of recruitment
United Kingdom

England

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
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Sponsor information

Organisation
Cambridge University Hospitals NHS Foundation Trust and University of Cambridge

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

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
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