

D12/S(HSS)/d

**2013/14 NHS STANDARD CONTRACT  
FOR STICKLER SYNDROME DIAGNOSTIC SERVICE (CHILDREN)**

**SECTION B PART 1 - SERVICE SPECIFICATIONS**

<b>Service Specification No.</b>	D12/S(HSS)/d
<b>Service</b>	Stickler syndrome diagnostic service(Children)
<b>Commissioner Lead</b>	
<b>Provider Lead</b>	
<b>Period</b>	12 months
<b>Date of Review</b>	

**1. Population Needs**

**1.1 National/local context and evidence base**

Stickler syndrome (SS) is a dominantly inherited disorder of connective tissue associated with retinal detachment, myopia (short-sight), cleft palate, deafness, and arthropathy.

It is the commonest inherited cause of rhegmatogenous retinal detachment in childhood. Although the systemic features are widespread, the sight-threatening complications are perhaps the most serious, particularly the risk of giant retinal tear (GRT) which is frequently bilateral and, if untreated, leads to blindness.

Patients with Stickler syndrome may also have associated hearing loss which is typically congenital and frequently undiagnosed. It may be sensorineural, conductive or a mixture of both [1].

The incidence of premature arthropathy in Stickler syndrome has been variously estimated at between 75% - 90%. All sub-groups can be affected [1].

Stickler syndrome is one of the genetic conditions associated with cleft palate and up to 80% of patients exhibit some form of midfacial clefting abnormality.

**Evidence base**

This service will provide a multi-disciplinary team (MDT) clinical assessment with subsequent molecular genetic analysis. Research has demonstrated that this

approach not only reduces the time and costs of laboratory analysis, but also increases the efficiency. More importantly, results published recently in peer reviewed literature for Collagen type II alpha 1 (COL2A1) analysis according to the European protocol analysing blood samples alone without prior specialist clinical assessment returned only 41% rate of positive mutation identification [2]. The strategy being adopted by this service has consistently returned over a 95% positive mutation identification with a much faster turnaround time using a pre-assessment algorithm (see sub-section 3.1 below) to direct the laboratory analysis [3,4].

The risk of retinal detachment varies considerably depending on the sub-type of Stickler syndrome. In a study of over 200 patients with type 1 Stickler syndrome (the most common sub-group), 83% of untreated patients had suffered retinal detachment and 66% of cases had bilateral detachment or retinal tears (the precursor to retinal detachment). Of those who had received prophylactic surgery only 3% had detached over a mean follow up of 14 years and none of these had bilateral involvement, thereby eliminating the incidence of blindness in that series, blindness being conventionally defined as “severe visual loss in both eyes”. An equally important outcome was that the treatment was safe with no serious associated adverse events [5, 6].

## **2. Scope**

### **2.1 Aims and objectives of service**

- to provide accurate clinical and molecular genetic diagnosis and sub-classification of Stickler syndrome for patients and families in England. Stickler syndrome is a dominantly inherited disorder of connective tissue associated with cleft palate, deafness, and arthropathy. It is the commonest inherited cause of rhegmatogenous retinal detachment in childhood;
- to develop a central patient registry and repository of data for longitudinal outcomes of all patients with Stickler syndrome in England to facilitate advancements in risk assessment, prophylaxis and treatment of the long-term ophthalmic, auditory, oro-facial and articular complications of this disorder.

### **2.2 Service description/care pathway**

#### **Service description**

The service will receive referrals from healthcare professionals for diagnosis and sub-classification of Stickler syndrome. Patients and families will be seen and assessed in a MDT clinic to evaluate the ophthalmic, audiometric, musculo-skeletal and radiological features for each individual patient/family. This assessment will record baseline or historic clinical problems and will guide subsequent molecular genetic

analysis according to the algorithm shown below.

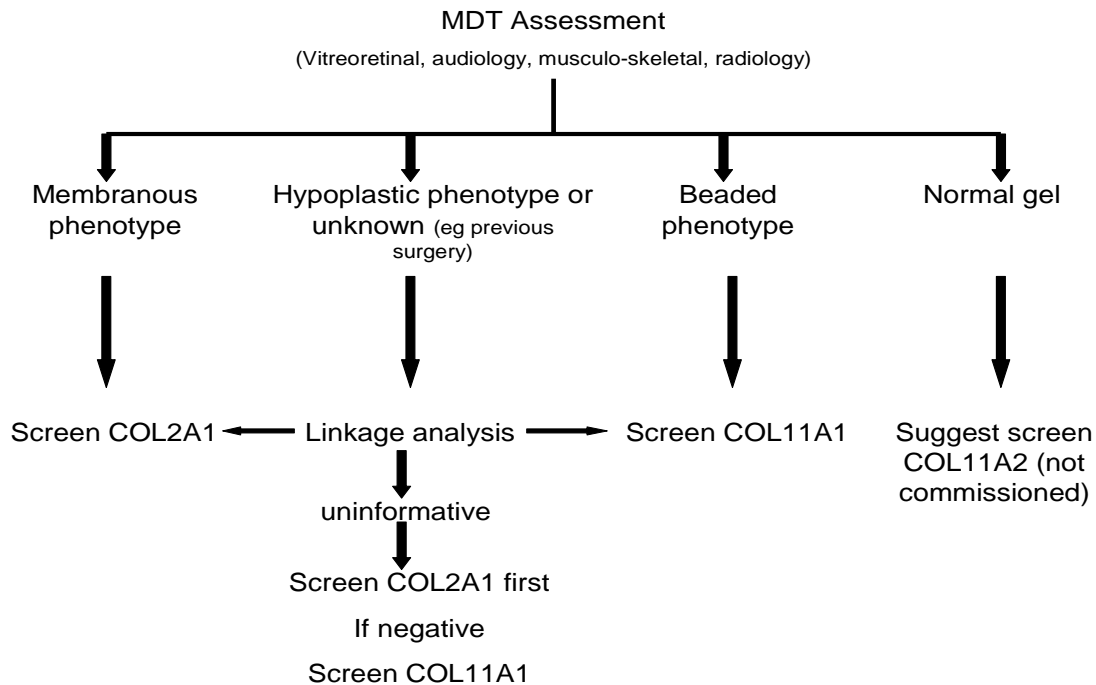
Where indicated, blood samples will be taken for deoxyribonucleic acid (DNA) extraction from peripheral lymphocytes and subsequent mutation analysis. For rare cases where transport or access for primary multidisciplinary team (MDT) assessment is difficult, we would adopt a direct laboratory screening protocol according to clinical data provided and the screening algorithm.

Tests are performed in the Molecular Genetics Laboratory at Cambridge University NHS Foundation Trust (Clinical Pathology Accreditation (CPA) accreditation ref. 1275) and the Department of Health reporting timescales will be adhered to for standard sequencing using the high-throughput system within our laboratory including MLPA (dosage) analysis capable of detecting large deletions/insertions. Expected reporting times are:

- 8 weeks for mutation analysis for collagen type II alpha 1 (COL2A1)
- 8 weeks for mutation analysis for collagen type XI alpha 1 (COL11A1)
- 2 weeks for predictive testing of relatives.

For a minority of patients and families the use of additional minigene/splicing technology will be required and with current technology the expected turnaround for this is approximately 12 weeks. Based on current experience, additional minigene/splicing analysis are likely to be required in 5-10% of patients [4, 5].

Following initial multi-disciplinary assessment to direct mutation analysis, patients would be seen again at approximately 2-4 months for discussion and counselling of results, following which unaffected patients are discharged. Affected patients would continue with day to day care at their local hospital (see subsection 5). This local management is expressly excluded from the scope of this service and individual needs will be communicated by the provider lead to all allied healthcare workers associated with each affected patient. In every case this communication will include their General Practitioner but may also include (but not exclusively) genetic counsellors, ophthalmologists, orthoptists, rheumatologists, orthopaedic and spinal surgeons, ear nose and throat (ENT), cleft and orthodontics teams, educational and special needs and occupational healthcare workers



### 2.3 Population covered

NHS England commissions the service for the population of England. NHS England contract includes provision for the service to treat eligible overseas patients under S2 [Under European Union (EU) regulations, patients can be referred for state funded treatment to another European Economic Area (EEA) member state or Switzerland, under the form S2 (for EU member states) or the form E112 (for Iceland, Norway, Liechtenstein and Switzerland)] referral arrangements. Providers are reimbursed for appropriately referred and recorded activity as part of NHS England contract.

Trusts performing procedures on EU-based patients outside of S2 arrangements will need to continue to make the financial arrangements directly with the governments involved, separately from their contract with NHS England.

With regard to S2, the mechanism for recovery of costs has been via the Department for Work and Pensions Overseas Healthcare Team. They are responsible for agreeing reconciliation and recovery of costs with European administrations. These arrangements were implemented in October 2009, though a similar process existed previously. The financial flows are therefore back into the Treasury rather than back to Trusts.

## 2.4 Any acceptance and exclusion criteria

Referrals will be made to the service and triaged by either the:

- provider lead;
- nominated Vitreoretinal Consultant;
- Stickler specialist nurse.

The referral criteria are those detailed in the COL2A1 and COL11A1 gene dossiers (for molecular genetics laboratories) and those published in a current clinical review 2011 (copy attached, for clinicians).

In brief, this will be clinically affected individuals with congenital vitreous abnormality typically (but not exclusively) from the following four groups:

1. neonates with Pierre-Robin / cleft and myopia;
2. infants with spondyloepiphyseal dysplasia associated with myopia or deafness;
3. patients with a family history of retinal detachment and joint hypermobility, midline clefting, or deafness
4. Sporadic cases of retinal detachment associated with joint hypermobility, midline clefting, or deafness

This service does **not** cover clinical or molecular genetic analysis of the allied type II/XI collagen connective tissue disorders Spondyloepiphyseal Dysplasia Congenita (SEDC), Spondyloperipheral dysplasia, Kniest Dysplasia and Otspondylomegaepiphyseal dysplasia (OSMED)

This service does **not** cover clinical or molecular genetic analysis of other allied non-type II/XI collagenopathies such as Knobloch Syndrome, Wagner syndrome, Multiple Epiphyseal Dysplasia (MED) and Metatropic dysplasia

Clinical and molecular genetic analysis for patients with these disorders may be requested, commissioned and provided separately or on an individually negotiated basis outside the scope of the national service.

## 2.5 Interdependencies with other services

The Stickler Syndrome Support Group ([www.stickler.org.uk](http://www.stickler.org.uk), Registered Charity Number 1060421) is run by patients with Stickler syndrome for patients with Stickler syndrome. They have been closely involved in all stages of the development of this service and with many of the research projects that have been responsible for an improved understanding of the various aspects of this disorder.

The patient support group holds annual or bi-annual two day meetings across the UK at which progress is presented to patients and in which the service has regularly, and will continue to participate, in addition to various satellite meetings around the UK to inform healthcare professionals in both primary care and the allied sub-specialties.

### 3. Applicable Service Standards

#### 3.1 Applicable national standards e.g. NICE, Royal College

The providers of the Stickler diagnostic service must ensure they are fully integrated into their trust's corporate and clinical governance arrangements and must comply fully with CNST and CQC requirements in terms of quality and governance.

Each centre will ensure that:

- regular meetings take place with patient representatives;
- all practitioners participate in continuous professional development and networking;
- patient outcome data is recorded and audited across the service.

### 4. Key Service Outcomes

<i>Activity Performance Indicators</i>	<i>Threshold</i>	<i>Method of measurement</i>	<i>Report Due</i>
New patient referrals	Within the maximum waiting times as outlined within the NHS Constitution	Electronic tracking of pathways via JCIS software within the Trust	
Molecular Genetic Analysis (i) Index diagnosis COL2A1	40 working days	Clinical Pathology Accreditation-accredited lab database	
Molecular Genetic Analysis (ii) Index diagnosis COL11A1	40 working days	Clinical Pathology Accreditation - accredited lab database	
COL2A1 and COL11A1 predictive tests (mutation known)	14 working days	Clinical Pathology Accreditation - accredited lab database	

<b>5. Location of Provider Premises</b>
Cambridge University Hospitals NHS Foundation Trust

Adopted

**Change Notice for Published Specifications and Products**  
**developed by Clinical Reference Groups (CRG)/Programme of Care(PoC)**

**Change of Clinical Reference Group requiring a change to the Published Products**

<b>Current Product Name</b>	Stickler Syndrome Diagnostic Service (Children)	<b>Current Ref No</b>	E01/S(HSS)/a
<b>Current Programme of Care</b>	Women & Children's	<b>Current CRG</b>	Medical Genetics

**Describe why change required**

Change of CRG agreed by CRG chairs as Stickler Syndrome has serious sight threatening complications, particularly the risk of giant retinal tear which is frequently bilateral and if untreated leads to blindness

**Confirmation that changes been agreed by the relevant CRG Chairs and Accountable Commissioners:**

Name of current CRG Chair: Frances Flinter	Name of new/proposed CRG Chair: Alison Davis	Name of current Accountable Commissioner: Ann Jarvis	Name of new/proposed Accountable Commissioner: Iain Mellis
Agreed: Yes	Agreed: Yes	Agreed: Yes	Agreed: Yes

<b>New Product Name</b>	Stickler Syndrome Diagnostic Service (Children)	<b>New Ref No</b>	D12/S(HSS)/d
<b>New Programme of Care</b>	Trauma	<b>New CRG</b>	Specialised Ophthalmology

**Date: 16<sup>th</sup> December 2013**



**Authorised by: Frances Flinter & Alison Davis**  
**Proforma completed by Iain Mellis**

Adopted