

A17/S(HSS)/g

**2013/14 NHS STANDARD CONTRACT
FOR WOLFRAM SYNDROME SERVICE (ALL AGES)**

PARTICULARS, SCHEDULE 2 – THE SERVICES, A – SERVICE SPECIFICATION

Service Specification No.	A17/S(HSS)/g
Service	Wolfram syndrome service (All Ages)
Commissioner Lead	
Provider Lead	
Period	12 months
Date of Review	

1. Population Needs

The aim of the service is to provide 'one stop' multi-disciplinary clinics from the service's 'hub' at Birmingham Children's Hospital NHS Foundation Trust (BCH), plus additional multi-disciplinary outreach clinics in locations appropriate to patients' needs. The service will provide expert diagnosis and on-going monitoring in addition to formulating management plans for local implementation. The service will also liaise with local services on the application of the management plan.

Although primarily an outpatient service, children requiring ileal conduit surgery for neuropathic bladder will be operated on at BCH as an integral component of the specified service.

WellChild are equal partners in the Wolfram service providing practical and emotional support to patients and their families. The WellChild Wolfram Syndrome Family Liaison Officer will have responsibility for coordinating the children's' and transition clinics, updating patient databases, inviting children and their families to clinics and arranging their transport and overnight accommodation.

1.1 National/local context and evidence base

The median age at death for patients with Wolfram Syndrome is 30 years, although some patients have been known to survive into their sixth decade.

Diagnostic criteria for diabetes mellitus are based on plasma blood glucose measurements and the presence or absence of symptoms. Diabetes is diagnosed when:

- a fasting plasma glucose (FPG) is ≥ 7.0 mmol/L (126mg/dl) (on two occasions if there are no symptoms of diabetes);

- **or** the post challenge plasma glucose is >11.1mmol/L (200mg/dl) 2 hours after a glucose load containing the equivalent of 1.75mg/kg (max 75g) of anhydrous glucose dissolved in water;
- **or** there are symptoms of diabetes and a random plasma glucose \geq 11.1mmol/L (300mg/dl). The symptoms may include polyuria, polydipsia, and unexplained weight loss.

The diagnosis of diabetes mellitus is usually confirmed quickly in symptomatic children by measurement of an elevated blood glucose level. In this situation, if ketones are present in the blood or urine, treatment is urgent.

Optic atrophy is defined as generalised pallor of the optic discs on direct fundoscopy. The presenting symptoms are decreasing visual acuity and loss of colour vision, and affected patients commonly complain of 'everything going grey'. The optic atrophy classically occurs before 15 years of age, and is progressive, leading to reduced visual acuity less than 6/60 within a median of eight (8) years (ref Barrett Eye). Visual evoked responses show normal latency but very low amplitudes (Mtanda).

The diagnosis of Wolfram Syndrome is made on clinical criteria above. Molecular genetic testing is confirmatory only. In the presence of childhood onset diabetes mellitus and progressive optic atrophy of onset before 15 years, at least one mutation will be identified in the causative gene in over 90% of patients (ref Khanim). Wolfram Syndrome is caused by mutations in the (WFS1) gene, which encodes an endoplasmic reticulum protein, Wolframin, involved in endoplasmic reticulum stress pathways and calcium homeostasis (refs). In the families of British, Pakistani, and Arab / African origin, WFS1 mutations were subsequently identified in 17 of 19 probands (Hardy et al 1999). A small number of patients, all of Middle Eastern origin, have been found to have mutations in a second gene, WFS2, encoding a mitochondrial protein ERIS/ZCD2/. The diagnosis of Wolfram Syndrome can usually be confirmed by molecular genetic testing of the causative gene, WFS1. In a series of 90 patients from one laboratory, 82 had mutations in WFS1 and one, of Jordanian descent, in WFS2.

2. Scope

2.1 Aims and objectives of service

The aim of the service is to provide 'one stop' multi-disciplinary clinics from the service's 'hub' in BCH plus additional multi-disciplinary outreach clinics in locations appropriate to patients' needs. The service will provide expert diagnosis and on-going monitoring in addition to formulating management plans for local implementation. The service will also liaise with local services on the application of the management plan.

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specified service.

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The key objectives of the Wolfram service are to:

- monitor and manage disease progression;
- coordinate care and management of children and adults with Wolfram Syndrome;
- provide expert support for local healthcare providers;
- establish a disease specific centre of excellence and expertise;
- provide a national genetic testing service and prenatal diagnosis (as required).

In addition the infrastructure will provide an opportunity for families to meet, share experiences and offer each other emotional support. Although not a primary objective, the service will also facilitate audit and evaluation of research into optimal therapies to prevent or delay the onset of complications.

2.2 Service description/care pathway

The primary element of the service is a multi-disciplinary team (MDT) assessment and monitoring programme that is delivered through a mixture of clinics held at the bases for the service and through outreach clinics.

BCH will provide four clinics per annum, one of which will be a transition clinic, held jointly with University Hospitals Birmingham NHS Foundation Trust (UHB). Each clinic must be able to accommodate up to five (5) children (i.e. maximum 20 children per annum).

UBH will hold three (3) adult clinics, one of which one will be a transition clinic. Each clinic must be able to accommodate up to six (6) patients (i.e. maximum 18 patients per annum).

The service is resourced to provide one outreach MDT Wolfram clinic per year, jointly run by the paediatric and adult services. The Wolfram service MDT will travel to the host hospital to conduct a half-day outpatient clinic in partnership with the local medical doctor, nurse and dietician. Outreach clinics will be run in locations appropriate to the geography of the patient group.

The Wolfram service MDT will:

- review investigations;
- discuss and develop the patient's management plan;
- offer social support in terms of benefits and community care advice.

The care of individual patients will remain under the responsibility of the local team and is not part of the nationally commissioned Wolfram service.

Each child or adult will have access to at least four (4) specialists at each outpatient or outreach visit from the following list:

- clinical geneticist
- ophthalmologist
- endocrinologist
- neurologist
- clinical psychologist
- urologist (for children)
- psychiatrist with expertise in dementia (for adults)
- multicultural worker
- deaf / blind communicator.

The clinics will be supported by dedicated paediatric and adult nurses with specific specialised training and experience in rare diabetes syndromes. The clinics, both in Birmingham and outreach, will be supported by multicultural workers for ethnic minority groups (primarily Mirpuri Pakistani) and interpreters to support signing and other deaf / blind communication.

Role of The Third Sector Partner

WellChild is a full partner in the Wolfram service. WellChild representatives will provide a blend of information and advice along with practical and emotional support to children and young people diagnosed with Wolfram Syndrome and their families. WellChild also currently funds a network of children's nurses, who work in a key worker capacity with children and young people with long term complex care needs. Because of the complex nature of Wolfram Syndrome, it is anticipated that some of the children under the care of the Wolfram service will also have access to a WellChild nurse

Specifically, WellChild will provide a Wolfram Syndrome Family Liaison Officer service who will:

- be a main point of contact for families, especially following diagnosis;
- develop a parent support network;
- work with the Wolfram team at BCH to coordinate the children's and transition clinics;
- update the patient databases;
- liaise with families re: attendance at clinics including arranging transport and overnight accommodation;
- update the BCH clinic team on any issues arising from the families clinic attendance or during specific times during the child's health 'journey'.

With the patient's consent, the WellChild Family Liaison Officer will be present at each children's and transition clinic appointment to provide:

- support and information;
- practical advice about financial support such as disability allowances,

equipment and local services.

Wolfram service clinic notes and correspondence will be stored at each NHS centre (computerised where possible) rather than incorporated into existing hospital notes. The trusts will have responsibility for ensuring safe storage and adherence to the Data Protection Act (1998) for computerised data. Off-site back-up storage will also be arranged.

Investigations

These are detailed in the care pathway and will include:

Annual blood haematology and chemistry in all patients plus further endocrine, neurological or urology investigations based on clinical assessments (as required)

Table 1



Education

The service will provide education sessions for patients and their families at every MDT clinic to address diet and insulin issues.

Service model and care pathways

This care pathway has been developed for patients attending NHS England commissioned specialist Wolfram Syndrome service comprised of centres in Birmingham (Birmingham Children's Hospital and Queen Elizabeth Hospital Birmingham NHS Foundation Trust (a part of University Hospitals Birmingham NHS Foundation Trust)). The service is delivered in partnership with the WellChild charity (which will help families establish a patient support group). The purpose of the service is to improve the quality of care for patients with Wolfram Syndrome by offering dedicated MDT outpatient review to patients and their families on an annual basis. The service is being developed because the syndrome is rare, inherited and complex. Diagnosis of the condition is often delayed until early to mid-teens, only when visual impairment emerges in combination with insulin-dependent diabetes mellitus. Wolfram Syndrome gives rise to multiple problems, some of which are life threatening and therefore require the input of many medical specialist and several non-clinical services. Affected families often feel isolated with few opportunities to benefit from the emotional support of others.

Modified diagnostic criteria: Two primary features with or without secondary features are required for diagnosis (adapted from Barrett T et al 1995).

Primary features	Secondary features
Childhood onset diabetes mellitus (up to 15 years) Childhood onset progressive optic atrophy (up to 17 years)	Diabetes insipidus Sensorineural deafness Neuropathic bladder Loss of sense of taste and smell Cerebellar ataxia Exaggerated startle response to loud noise Myoclonic epilepsy Neuromuscular incoordination of swallowing mechanism Central sleep apnoea Loss of short term memory, alteration of mood

The Wolfram Syndrome medical clinic

This will be outpatient based; staffed by the designated consultants (endocrine, neurology, genetics) and specialist nurse; dietician; clinical psychologist; and WellChild family liaison officer. Each specialist will be allocated a clinic room in which they will remain for each of their consultations with families. This system works well

as it allows patients to meet in the waiting area with the family liaison officer; and support each other. In addition, the clinicians will meet in the team room at the beginning and end of the clinic to discuss clinical management issues.

The specialist nurse will weigh and measure the patient, and plot on growth charts if appropriate. Blood pressure will be measured. The genetics consultant or nurse counsellor will take a family history and complete the structured history sheet. The patient will be consented for deoxyribonucleic acid (DNA) storage and gene testing. The ophthalmologist (if required) will place pupil-dilating drops in each eye prior to fundoscopy. The endocrinologist will evaluate the growth velocity if a child and review the requirements for hormonal supplementation (e.g. insulin, anti-diuretic hormone). The presence of any other hormone deficiency (thyroid, testosterone) will also be considered and appropriate tests sought. The urologist/urodynamics team will seek evidence of bladder dysfunction and implement bladder capacity tests. The neurologist will perform a full neurological examination and arrange neuroimaging (magnetic resonance imaging (MRI) brain).

At the end of the clinic the patient will be invited to have a snack together with a dietary assessment. Blood samples if required will be drawn by the clinic nurse. Assessment by a clinical psychologist will be made as appropriate.

Investigations:

Each patient should receive the following baseline investigations:

- **Laboratory:**
Biochemistry: renal function, liver function, fasting paired serum and urine osmolarities and sodium; HbA1c.
- **Haematology:**
Full blood count
- **Urodynamic (children):**
Bladder function tests (residual urine volume after bladder emptying)
- **Imaging:**
Biennial renal ultrasound scan (ureteric dilatation)
Brain MRI (cerebellar and mid brain atrophy)

Genetic Testing:

Two genes are associated with Wolfram Syndrome and mutation testing will be available for each patient, following appropriate consent. A dedicated NHS genetic testing service is already funded for WFS1 based in the Regional Genetics Laboratory, Birmingham Women's Hospital Foundation Trust (BWHCT) and approximately 75% of mutations are expected to be discovered in this manner. If mutations are not forthcoming, then the sample will proceed to Phase II as summarised (Table 1 above).

Analysis and reporting

The senior scientist will analyse the data and, in consultation with the lead clinician, will prepare a clinical report. The service will be based within the West Midlands Regional Molecular Genetics Clinical laboratory, BWHCT. Although the Wolfram diagnostic service will be managed by the senior scientist, the service will fall under the general management of the Genetics Service and be subject to common audit.

Management of syndrome

As a genetic disease, overall cure is not possible but treatment aimed at alleviating organ-specific problems is achievable. These will include the following within the realms of the Wolfram service;

- identifying and treating diabetes insipidus;
- optimising insulin treatment for diabetes mellitus;
- provision of low vision aids/ low vision learning skills;
- identification and management of neuropathic bladder;
- identification of neurological complications and treatment where indicated of myoclonic epilepsy.

Other specialist treatments and management will be sought through appropriate referral to other specialties outside of the Wolfram service. The costs of those subsequent therapies will not be borne by the Wolfram service.

Days/hours of operation

- Adult clinics – held three (3) times per annum including one transition clinic jointly with BCH;
- Children's clinics – held four (4) times per annum including one (1) transition clinic jointly with UHB.

Discharge Criteria

The intention of this service is to provide disease surveillance and annual follow-up with tailored management of Wolfram Syndrome in collaboration with other healthcare providers. Patients will be discharged to local care providers:

- where development of severe disability or chronic morbidity precludes travel, the service will liaise with local services to provide advice on management and transfer of clinical information. Arrangements for ongoing data collection will be made.

Transition to Adult Services

Transition arrangements are an important part of the service. Each adolescent approaching his / her 17th year may attend a transition clinic (it is expected that up to four (4) per year will move over to the adult clinic) and familiarise themselves with the different environments, personnel and travel arrangements.

Risk Management

Care delivered by the Wolfram service providers must be of a nature and quality to meet the care standards, specification and agreement for the service. It is the trust's responsibility to notify the commissioner on an exceptional basis should there be any breaches of the care standards. Where there are breaches, any consequences will be deemed as being the trust's responsibility.

Patients must be managed in line with the specification and care standards. Any deviation from these which has not been approved by NHS England is at the trust's risk both clinically and financially. It is the trust's responsibility to inform the commissioners of any such non-approved deviations on an exceptional basis.

Where a patient's presentation challenges the assumptions that underpin the specification, service standards and contractual arrangements, it is the trust's responsibility to inform the commissioners on an exceptional basis, prior to any treatment (except for emergency treatment) so that the implications of the patient's requirements can be considered. This does not affect situations where the Individual Funding Request (IFR) process applies.

2.3 Population covered

This service covers patients registered with an English General Practitioner, resident in Scotland, resident in the European Union and eligible for treatment in NHS under reciprocal arrangements.

Patients from Wales and Northern Ireland are not part of this commissioned service and the Trust must have separate arrangements in place in order to accept patients from these countries.

2.4 Any acceptance and exclusion criteria

The service is accessible to all patients with Wolfram Syndrome regardless of sex, race, or gender.

Modified diagnostic criteria. Two primary features with or without secondary features are required for diagnosis.

Primary features	Secondary features
Childhood onset diabetes mellitus (up to 15 years) Childhood onset progressive optic atrophy (up to 17 years)	Diabetes insipidus Sensorineural deafness Neuropathic bladder Loss of sense of taste and smell Cerebellar ataxia Exaggerated startle response to loud noise Myoclonic epilepsy

	Neuromuscular incoordination of swallowing mechanism Central sleep apnoea Loss of short term memory, alteration of mood
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Children (up to 18 years) and adults who fulfil the Wolfram Syndrome diagnostic criteria will be recruited from the existing known patients. Referrals from clinicians throughout the UK will be accepted.

Exclusion criteria

Patients may be excluded from the service if:

- the individual clearly has an alternative diagnosis;
- the individual has Alström syndrome (differential diagnosis) – he/she will be referred directly to the Alström service in BCH;
- the patient is resident outside England and Scotland; for other devolved administrations (Wales and Northern Ireland), the provider must seek to make alternative arrangements with referrers;
- there is a very low index of suspicion.

Accessibility/acceptability

The provider will require staff to attend mandatory training on equality and diversity and the facilities provided will offer appropriate disabled access for patients, family and carers.

When required, the providers will use interpreters and printed information will be available in multiple languages.

The provider has a duty to co-operate with the commissioner in undertaking Equality Impact Assessments as a requirement of race, gender, sexual orientation, religion and disability equality legislation

Interdependencies with other services

The Wolfram Syndrome service lies within two NHS Foundation Trusts: Birmingham Children's Hospital NHS Foundation Trust for paediatric patients and Queen Elizabeth Hospital Foundation Trust (a part of University Hospitals Birmingham NHS Foundation Trust) for adults.

The service will serve as a national centre of expertise to which primary care teams or hospital-based services may seek advice or refer patients for diagnosis and management.

The service will work closely with schools, education services, social services, speech and language therapy services, physiotherapy, child development teams and services for the blind.

As each patient is assessed annually, the service will rely on close communication

and more frequent monitoring by general practitioners and other specialist services (e.g. nephrology in the case of renal failure or transplant). The service in general, and the Wellchild charity in particular, will play a role in educating patients, carers and healthcare professionals.

2.4 Relevant networks and screening programmes

None

3. Applicable Service Standards

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

The Wolfram service providers must be fully integrated into their trust's corporate and clinical governance arrangements.

The commissioners and service will conduct a formal Joint Service Review at least every six months with each provider. This may be a joint meeting at the commissioner's discretion.

4. Key Service Outcomes

<i>Quality Performance Indicator</i>	<i>Threshold</i>	<i>Method of measurement</i>	<i>Consequence of breach</i>	<i>Report Due</i>
QoL to be maximised as long as possible: measured by pedsqol or equivalent	TBC			
Hba1c	TBC			
Renal function maximised as long as possible	TBC			

The outcomes of the service will be to reflect morbidity / mortality.

- quality of life to be maximised as long as possible: measured by PedsQL (paediatric quality of life inventory™) or equivalent;
- HbA1c (glycosylated haemoglobin);
- renal function maximised as long as possible.

Key performance indicators (KPIs): these are process indicators:

- all patients to be screened for diabetes insipidus two yearly;
- guidelines for patient management to be developed;
- all patients over 15 years to be screened for neurological abnormalities with examination and investigations, including use of MRI brain scans as baseline;
- the age at diagnosis of referred patients to fall with better recognition of the syndrome by health professionals;
- development of a family outcome tool.

5. Location of Provider Premises

Birmingham Children's Hospital NHS Foundation Trust
Steelhouse Lane
Birmingham
B4 6NH

University Hospitals Birmingham NHS Foundation Trust
Queen Elizabeth Medical Centre
Queen Elizabeth Hospital
Birmingham
B15 2TH

Adopted