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- Approbation du document final par un membre ERN-RND qui est à la fois membre du groupe d'experts respectif et du work package pour les guides cliniques.

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GUIDE CLINIQUE

Management of the ataxias
towards best clinical practice

Third edition

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ATAXIA

ATAXIA

Ataxia UK

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1. Introduction

This document aims to provide recommendations for healthcare professionals on the diagnosis and management of people with progressive ataxia.

The progressive ataxias are rare neurological conditions, and are often poorly understood by healthcare professionals. Diagnosis has generally been a long process because of the rarity and complexity of the different ataxias[1]. In addition, many healthcare professionals are unsure how best to manage the conditions and there is sometimes a feeling that little can be done for these patients[1,2]

Although there are no disease-modifying treatments for the majority of the progressive ataxias, there are many aspects of the conditions that are treatable and it is thus important that this is recognised by the relevant healthcare professionals. The diagnosis and management of the few treatable causes is also of paramount importance. All this highlights the importance of producing these guidelines: in order to increase awareness and understanding of these conditions, and lead to their improved diagnosis and management.

With new developments in genetic technologies and the discovery of more genes, diagnosis is improving and has great scope to continue to do so. In addition, research is advancing and many human trials to test medications are taking place, making us more optimistic that disease-modifying treatments will be found for the progressive ataxias.

Conditions covered in these guidelines

Ataxia means 'lack of coordination' and it is a symptom of many conditions. These guidelines focus on the progressive ataxias, and exclude disorders where ataxia is an epiphenomenon of another neurological condition *(see Table 1a and 1b)*.

Table 1a: Conditions covered in these guidelines

Hereditary ataxias
- including Friedreich's ataxia, spinocerebellar ataxias and episodic ataxias (but excluding ataxia-telangiectasia*).

Idiopathic progressive ataxias
- forms of cerebellar ataxia associated with neurodegeneration of unknown aetiology.

Specific neurological disorders
- in which progressive ataxia is the dominant symptom eg: cerebellar variant of MSA.

** Information about the extra neurological features of ataxia-telangiectasia (AT) is not included in this document. For more in depth knowledge about this condition please refer to the Ataxia-Telangiectasia Society who produce guidelines on AT.*

Table 1b: Other causes of ataxia

Vascular	Inflammatory (eg: multiple sclerosis)
Traumatic	Metabolic
Developmental	Toxic / drug-related (eg: alcohol)
Neoplastic / paraneoplastic	Epilepsy (in children)
Infectious	

Epidemiology of the ataxias

Epidemiological studies of the progressive ataxias in the UK are sparse, data from the UK are thus summarised with information from studies in other countries *(see Box 1)*. In the UK, the latest estimates based on the studies below suggest there are at least 10,000 adults and 500 children with progressive ataxia[3,4].

Although the progressive ataxias are rare conditions, when taken together they are more common than other better known neurological conditions. These studies suggest that the prevalence of the progressive ataxias is higher than conditions that are generally better known such as Huntington's disease[5] and motor neurone disease[6].

Box 1: Epidemiological studies

European studies:

- The most common inherited ataxia in Europe is Friedreich's ataxia; the estimated disease incidence based on carrier frequency of 1 in 85 is **1:29,000**[7]. Generally in Europe prevalence is quoted as between 1 in 20,000 to 1 in 50,000, with some geographical variability[8]. It is the most common inherited ataxia in the Caucasian population.
- The minimum prevalence of childhood ataxia in Europe was estimated at 26 in 100,000 in a recent systematic review[4]. This included conditions not covered in these guidelines (e.g. ataxic cerebral palsy), thus the estimate for progressive inherited ataxias covered in these guidelines is 4.61 in 100,000.

UK studies:

- Estimated minimum prevalence: 10.2 in 100,000 adults with late onset cerebellar ataxia in South Wales[9].

Guideline development

These guidelines have been developed by the patient support organisation, Ataxia UK, through extensive consultation with numerous UK healthcare professionals with experience in ataxia.

Contributors for each section were selected due to their clinical expertise in ataxia in the relevant discipline. They reviewed the medical literature for their section, provided scientific evidence for the efficacy of different interventions and graded the level of evidence following the procedure of the Guideline International Network (GIN)[10].

The information on the level of evidence was then used to give a grading to each recommendation made in these guidelines. Table 2 details the level of evidence and grading system used.

A Guideline Development Group consisting of neurologists with expertise in ataxia and representatives of Ataxia UK reviewed all the sections and discussed any changes with contributors until consensus was reached.

Table 2: Evidence grading scheme for these guidelines

Level of evidence (categorisation of reference materials)[11]

I Evidence obtained from a systematic review of all relevant randomised controlled trials.

II Evidence obtained from at least one randomised controlled trial.

III-a Evidence obtained from one or more controlled trials, pseudo-randomised by alternate allocation, birth date or other planned method.

III-b Evidence obtained from prospective or retrospective cohort studies with concurrent controls, case-control studies, or interrupted time-series with a control group.

III-c Evidence obtained from cohort studies with historical controls, two or more single-arm studies, or interrupted time-series without a parallel control group.

IV Evidence comprises opinions based on clinical experience, descriptive studies or reports by clinical bodies or committees.

Grading of recommendations in the guidelines based on the level of evidence[12]

A. Body of evidence can be trusted to guide practice; includes one or more level I studies, or several at level II directly applicable to the target population, and demonstrating overall consistency of results.

B. Body of evidence can be trusted to guide practice in most situations; includes one or two studies rated as level II or several level III studies, directly applicable to the target population, and demonstrating overall consistency of results.

C. Body of evidence provides some support for recommendation(s) but care should be taken in its application; includes studies rated as III-c, or level I or II with a moderate risk of bias, some inconsistency and applicable to target population with caveats. Population studied is not the target population, however, it would make sense clinically to apply this evidence to target population.

D. Body of evidence is weak and recommendation must be applied with caution; includes level IV, or level I to IV studies with high risk of bias, inconsistent evidence and that are not applicable to target population.

GPP. Good practice point: Recommended best practice based on clinical experience and expert opinion.

(Adapted from Reference)

2. Diagnosis

2.1. Presentation

The presentation of a patient with ataxia can be diverse. The ataxia may be transient (e.g. following a viral infection, also known as post-viral cerebellitis), episodic (eg: episodic ataxias due to genetic causes) or progressive (eg: in Friedreich's ataxia, the most common ataxia in the UK[13]). Onset may be acute (eg: in a patient with stroke) or it may be gradual. Most of the progressive ataxias are of gradual onset. Rapidity of progression is an important consideration, because such rapid progression of ataxia (over weeks) may indicate paraneoplastic cerebellar degeneration and the need to hunt for covert cancer[14]. Rapid progression may also be a sign of multiple system atrophy in its cerebellar form, or of prion diseases, thus the need for fast referral[15–17]. Finally the age of onset should be considered; diseases presenting with ataxia in children or young adults – often developmental, metabolic or inherited – tend to differ from the neurodegenerative or immune-mediated ataxias presenting in older people. The clinician therefore has to consider all aspects of the history in coming up with a differential diagnosis for each patient.

Family history is crucial in patients with ataxia in view of the frequency with which genetic/inherited factors cause ataxia. Almost all forms of genetic transmission are recognised, but generally speaking early-onset ataxias, under 20 years of age, tend to be of autosomal recessive (AR) inheritance (e.g. Friedreich's ataxia) whereas the spinocerebellar ataxias (SCAs) are autosomal dominant (AD) and tend to present mostly after 20 years of age; although both recessive and dominant can occur at any age. With AR inheritance there is a one in four risk of further siblings also being affected, but the parents of the patient, whilst carriers of the mutated gene, are usually themselves clinically unaffected. Parental consanguinity is sometimes identified. With AD transmission, one of the parents is likely to be affected but may have much milder clinical features. In some AD ataxias, paternal transmissions in particular tend to lead to dramatically reduced age of onset and more severe clinical phenotypes in offspring (eg:SCA1, SCA2, SCA3, SCA7, DRPLA). Ataxias due to mitochondrial disease may be an under-diagnosed cause of 'inherited' ataxia, but the pattern of inheritance may be complex, including maternal transmission, AR and AD inheritance[18,19]. Premutations of the fragile-X gene may be a cause of adult-onset ataxia ('fragile X-associated tremor/ataxia syndrome' or FXTAS) that affects both men and women[20].

Patients with ataxia complain of incoordination and unsteadiness, slurred speech and clumsiness. Rarely, oscillopsia (due to nystagmus) is reported. The clinical signs seen in patients with ataxia can be summarised as follows[21]:

- Gait ataxia and in some cases impaired sitting balance
- Gaze-evoked and/or resting nystagmus, hypermetropic /hypometropic saccades and jerky pursuit
- Speech may be slurred (dysarthric) and have a staccato quality
- Intention tremor
- Dysmetria or 'past-pointing'
- Dysdiadochokinesis

Patients with disorders limited to midline cerebellar disease may only show ataxia when gait is tested, especially heel-to-toe/tandem gait. It is also important to recognise that impairment of sensation (joint position sense) can produce (sensory) ataxia. Depending on the underlying cause of the ataxia, there can be additional neurological features that manifest themselves during the course of the illness. These can include ophthalmoplegia, parkinsonism, visual disturbance, peripheral neuropathy, urinary symptoms, spasticity and cognitive decline[21].

2.2. Referral process

Patients presenting with ataxic symptoms should be referred to secondary care, where they should ideally be seen by a paediatrician, if under 16, or adult neurologist. Depending on the clinical state of the patient, this referral may need to be urgent. For example, in a case with a suspected brain tumour, the patient may have to be admitted or seen within two weeks. In children, following referral to a paediatrician, the recommended pathway then involves being referred to a paediatric neurologist.

A referral to a neurology centre specialising in ataxia is then recommended particularly for patients where a diagnosis of the cause of ataxia has not been achieved. In selected cases (adults) it may be possible for the general practitioner (GP) to refer directly to Specialist Ataxia Centres (eg: in cases where a diagnosis of a progressive ataxia has already been made).

There are currently three Specialist Ataxia Centres in the UK accredited by Ataxia UK. These are centres specifically involved in the diagnosis and management of patients with progressive ataxia[22]. Patients attending these Accredited Specialist Ataxia Centres would be seen by an ataxia specialist neurologist, receive continuity of care, support by a specialist nurse and streamlined referrals to other named specialists as appropriate. The service provided is highly valued by patients (data from London Specialist Ataxia Centre, Ataxia UK). A list of these Accredited Specialist Ataxia Centres is found in the Appendix. In addition the Appendix also lists other clinicians with expertise in ataxia in the UK. More information is available from Ataxia UK.

2.3. Investigations

2.3.a. Adults

Details of appropriate investigations for adults are found in Table 3. Primary care investigations to be done by the GP comprise those that are relatively inexpensive, common and widely available. Their purpose is to exclude medical and neurological conditions that may contribute to ataxia. Secondary care investigations are generally done by a neurologist, with referral and input from other specialists as appropriate.

It is important to consider genetic tests for common inherited ataxias, particularly if there is a family history. In certain cases the potential diagnosis may be apparent following the first clinical consultation and therefore a ‘third line’ genetic test, for example, may be undertaken immediately. *See also section 2.4 for genetic tests.*

Table 3: Diagnostic investigations in adults			
Primary care	U&Es Creatinine FBC ESR/CRP	Liver enzymes γ-GT TFT Vitamin B12	Folate Random blood sugar CXR
Secondary care (first line)	α –FP Blood film Caerulopasmin/copper Coeliac screen[a] Creatine kinase Genetic tests for FA, SCA1, 2, 3, 6, 7 (12, 17)	Lactate Lipid-adjusted Vitamin E and lipoproteins electrophoresis Lumbar puncture (cells, protein, glucose*, cytology, oligoclonal bands*, Lactate, Ferritin) MRI brain and cervical spine	Anti-Hu/Yo and other paraneoplastic antibodies† Anti-GAD Anti-VGCC† CT (chest, abdomen, pelvis) 14-3-3 and other proteins in CSF (prion diseases)† [b]
Secondary care (second line)	Cholestanol Coenzyme Q_{10} (ubiquinone)[c] Electroencephalography Electromyography Long chain fatty acids	Muscle biopsy Neuropsychology testing Ophthalmology tests Peripheral nerve conduction studies Phytanic acid	Remaining genetic tests Total body PET scan White cell enzymes

*With blood

† In patients with rapid progression

All the diagnostic tests in Table 3 should be readily available in primary or secondary care. Tests marked a-c are only available in certain laboratories:

a. If testing for gluten ataxia is not readily available clinicians can contact Professor Marios Hadjivassiliou who runs a specialised gluten ataxia clinic. Contact details: Sheffield Teaching Hospitals NHS Foundation Trust, Sheffield S10 2JF. Tel: 0114 271 2502.
Also see section 4.2.a. on gluten ataxia.

b. Testing for 14-3-3 protein in the CSF can be carried out at the National Creutzfeldt-Jakob Disease Research & Surveillance Unit, Western General Hospital, Edinburgh. Contact details: Main office telephone: 0131 537 1980/2128/3103; website: www.cjd.ed.ac.uk.

c. Coenzyme Q10 (CoQ10) levels to test for ataxia with CoQ10 deficiency. Testing of CoQ10 deficiency can be performed on skeletal muscle samples or on blood mononuclear cells[23]. Testing is available at the Neurometabolic Unit, National Hospital for Neurology and Neurosurgery, London. Contact Dr Iain Hargreaves or Prof Simon Heales: iain.hargreaves@uclh.nhs.uk or simon.heales@uclh.nhs.uk Tel: 0203 44 83844.

2.3.b. Children

If a child presents with ataxic symptoms, an urgent referral to local paediatric services is necessary. Targeted investigations will then depend on the clinical assessment. This includes obtaining details such as family history, whether the ataxia is acute, intermittent or chronic, any precipitants and associated conditions. It is important to consider examination findings, especially those distinguishing central from sensory ataxia. *See Table 4 for differential diagnoses of ataxia that guide the choice of appropriate diagnostic tests.*

The investigation of acquired ataxia in children is generally more urgent because of the necessity of excluding posterior fossa and brainstem tumours. It is also important to consider that there is a need for investigation in children as there is a risk that the cause will be genetic, and their parents may wish to have further children.

Table 4: Differential diagnoses of ataxia to guide diagnostic investigations in children

Acute	Intermittent	Chronic
Inflammatory	Episodic ataxias	Hereditary ataxias
Intoxication	Glut1 deficiency	Space occupying lesion
Metabolic	Metabolic	Structural
Vascular	Epileptic	Leukodystrophies
Trauma	Structural	Lysosomal storage
Raised intra-cranial pressure	Psychogenic	Metabolic
Epileptic		Vitamin deficiencies
Sensory		Auto-immune
Vertigo		Sensory
Psychogenic		Psychogenic

Table 5 is not exhaustive but covers diagnostic investigations in children for most conditions. These investigations are generally carried out in tertiary care. Local paediatric services should only investigate in the light of clinical judgment and in consultation with the local tertiary paediatric neurology service. Urgent referral to tertiary paediatric neurology services is almost always necessary to complete investigations and for advice about management.

In first line investigation neuroimaging is mandatory, to exclude a tumour and to look for a white matter disorder or structural condition. MR imaging of the brain (+/- spine) is the best way to view the posterior fossa[24], but if urgent MR imaging is not available, a CT scan will help to exclude a tumour. If possible MR spectroscopy should be obtained as well. In acute ataxia MR angiography might be indicated.

For further information on the availability of diagnostic tests see Adults section above and section 2.4.

Table 5: Diagnostic investigations in children within tertiary care	
First line	MRI brain (+/- spine) including 3DT1 MPRAGE, T2w in all planes, coronal FLAIR (except neonates) and DTI CT scan (if magnetic resonance imaging [MRI] is unavailable) MR spectroscopy (if possible) MR angiography (in acute ataxia)
Second line (acute)	***Acute central ataxia without encephalopathy*** Blood: serology (viral, mycoplasma) Viral cultures (throat swab, urine, stool) EEG ***Acute central ataxia with encephalopathy*** Blood: serology (viral, mycoplasma); culture; toxicology including heavy metals; metabolic (liver function tests, ammonia, amino acids, blood gas, lactate, pyruvate, glucose, biotinidase); antithyroid antibodies. Urine: viral culture; toxicology; amino acids; organic acids. CSF: pressure; cell count, glucose, protein; viral and bacterial studies (culture including TB, serology, PCR); oligoclonal bands; lactate and pyruvate. Throat swab, and faeces (or rectal swab): viral and bacterial culture Mantoux test EEG ***Sensory ataxia*** Nerve conduction studies and electromyography Cerebrospinal fluid protein Blood: anti-GM1 and anti GQ1b antibodies; Viral cultures (throat swab, urine, stool) Viral and mycoplasma serology Stool culture or rectal swab (esp. C. jejuni) ***Opsoclonus myoclonus:*** Neuroblastoma (consult oncologist): Chest Xray Ultrasound scan of neck, abdomen and pelvis I^{123} metaiodobenzylguanidine (MIBG) scintigraphy scan Urine catecholamine metabolites–if negative do MR imaging of neck, chest and abdomen
Second line (intermittent)	***All ataxias*** Blood: DNA for episodic ataxias, Glut 1 deficiency and metabolic disorders; lactate, amino-acids Urine: organic acids CSF: fasting glucose and lactate, both with simultaneous blood values EEG
Second line (chronic)	***Depending on clinical features*** ***Suspected Friedreich's ataxia:*** DNA for FXN gene EMG and nerve conduction studies (NCV) Echocardiography Fasting glucose Exclude vitamin E and vitamin B12 deficiencies (lipid corrected vitamin E level, vitamin B12 level, plasma homocysteine, urine methylmalonic acid) ***Suspected Ataxia-telangiectasia:*** Plasma α-fetoprotein level Immunoglobulin levels DNA for ATM gene ***Other conditions*** Blood: Full blood count with vacuolated lymphocytes (light and electron microscopy); lipid adjusted vitamin E, vitamin B12, biotinidase, white cell CoQ10, α-fetoprotein, immunoglobulins, copper, caeruloplasmin, phytanic acid, cholestanol, lipid electrophoresis, cholesterol, thyroid function, acyl-carnitines, white cell lysosomal enzymes, very long chain fatty acids, transferrin IEF, red cell purine nucleotide species, thyroid and antigliadin antibodies. Micro-array testing (or karyotype, FISH 22q and Angelman deletions); chromosomal radiation fragility; DNA (for specific tests and to store). Urine: organic acids, purine and pyrimidines. CSF: fasting glucose, lactate and amino-acids, with simultaneous blood values ECG Echocardiogram Electromyography and nerve conduction studies Tissue biopsies; muscle CoQ10 level

2.4. Genetics

2.4.a. Referral to Genetics Services

When requesting genetic investigations it is essential to discuss the implications of the test with the patient prior to testing. In view of the potential implications for family members of patients who undergo testing, it is essential that neurologists liaise with their clinical genetics counterparts (as highlighted in the National Service Framework for long-term conditions; quality requirement 2.10)[25].

The situation is simplest in the case of symptomatic patients, when the test is being performed primarily for diagnostic purposes. However, even in these situations testing can be complex, for example where there are other children at risk or where there may be extreme anticipation which may result in a pre-symptomatic test in the parent of the child. Therefore it is important that the patient and their family are informed about the potential implications in case the test is positive and the availability of genetic counselling should be indicated to the patient and their family. This service should be provided by healthcare professionals with expertise in genetic counselling (eg, clinical geneticists, genetic counsellors or neurologists with expertise in this field). Consultations should include discussions on the implications of having a genetic test for the individual with ataxia and their family and any reproductive choices they may make.

The situation is more complicated in the case of 'at-risk' subjects, where an individual is clinically unaffected at that point in time. These people should also be offered genetic counselling from a suitable healthcare professional to discuss whether they wish to undergo genetic testing. In the case of at-risk minors this should be done by the regional genetic service. However, testing of at-risk minors is not generally recommended, but should be considered on a case by case basis. In cases of recessive ataxias it is important to consider the implications of the carrier status of the patient's family members who may at some point be making reproductive decisions. Genetic counselling should thus be offered to these individuals too.

It is important to consider that there are approaches for pre-natal testing and pre-implantation genetic diagnosis available for some inherited ataxias. This is generally provided by genetic services in conjunction with local obstetrics or prenatal units.

In cases where genetics services are not already involved and when a genetic mutation is found, the individuals should be referred in a timely way to collaborating clinical geneticists, with all of the available data (including the genetic diagnosis of the index case if available and the patient agrees to the release of this information). Good communication between the different specialties and professionals is vital.

When samples for genetic tests are being obtained from patients and their families, informed consent must be sought, preferably in written form using routine consent forms available from genetics centres. Consent should include access to information to assist family members.

Clinicians who take samples for genetic tests should be made aware of guidelines on best practice for the ataxias produced by the European Molecular Genetics Quality Network: www.emqn.org.

Many genetic tests are available on a research basis (eg: by exome sequencing) and almost invariably the ethics committee submission in connection with the study will have clarified the appropriate consent to be obtained. It is important that patients understand the implications of any genetic test. Usually participant patients are given the option of being informed about any results that may emanate from studies, especially were this to be of relevance to them and their family members. Any genetic results from research studies would need to be validated by an accredited genetics laboratory before a formal result is given to the patient.

2.4.b. Genetic tests available

Table 6 shows the currently available genetic tests, grouped according to modes of inheritance and Harding classification types I to III *(see section 2.4.c for an explanation of this classification)*. Some of these are available via the UK Genetics Testing Network (www.ukgtn.org), and their website gives details of accredited laboratories across the UK where the tests are undertaken along with turnaround times. These genetic tests are performed individually using Sanger DNA sequencing or PCR techniques.

New technologies for sequencing genes are being developed and this means genetic testing is undergoing a major revolution. Most genetic tests have been done "in series", ie: one test after another. Next generation sequencing (NGS) is a different technology that allows massively parallel sequencing and has resulted in the identification of many new genes associated with ataxia, new patterns of inheritance and new diagnostic pathways. Targeted "panel" tests are increasingly used and are highly reliable, but only have limited numbers of genes. A next generation sequencing panel is now available as an NHS diagnostic service from the Oxford Molecular Genetics Service. This panel includes around 99 genes causing ataxia (with more genes being added as new genes are found). More information on this service can be found here: www.ouh.nhs.uk/services/referrals/genetics/genetics-laboratories/molecular-genetics-laboratory/services-by-disorder/documents/InheritedAtaxiasNGS-98gene.pdf . An NGS panel including hereditary ataxias is also available at the Sheffield Children's NHS Foundation Trust, for more details see: www.sheffieldchildrens.nhs.uk/our-services/sheffield-diagnostic-genetics-service/next-generation-sequencing.htm

Research studies involving whole exome sequencing or whole genome sequencing are ongoing and patients could be informed of these as potential studies they may wish to consider taking part in. Exome sequencing targets the coding parts of genes, whereas genome sequencing obtains information on most (but not all) of the entire genome. In England, the 100,000 genomes project run by Genomics England and delivered by Genomic Medicine Centres, aims to increase the diagnostic rate, and patients with ataxia who have so far eluded a genetic diagnosis may be invited. Patients from Northern Ireland can also participate and the project will be rolled out to Scotland and Wales. Further information see: www.genomicsengland.co.uk . Interpretation of NGS data can be very complex and clinicians should seek advice about performing such tests and how to interpret the data before embarking on them.

For more information on ataxia research studies contact Ataxia UK (www.ataxia.org.uk). A number of inherited ataxias have been identified although not all genes have yet been found. More information on inherited ataxias can be seen in selected research publications[26,27].

Table 6: Genetic tests (underlined tests available 'routinely' via the UK Genetic Testing Network)		
Autosomal recessive	FRDA	
	AT[a]	
	AOA1[b] and AOA2[b]	
	Ataxia with Vitamin E deficiency	
	POLG1	
	ARSACS	
Autosomal dominant	Type I	SCA1, SCA2, SCA3, SCA10, SCA12, SCA13, SCA17, SCA23 (or type III), SCA27, SCA28, SCA35, SCA36
	Type II	SCA7
	Type III	SCA5, SCA6, SCA11, SCA14, SCA15
	EA type 1 EA type 2 DRPLA GSS[c] POLG 1	
Mitochondrial[d]	NARP, MELAS, MERRF	
'X-linked'	FXTAS (Fragile X associated Tremor and Ataxia Syndrome)	

Genetic tests marked a-d are also available; contact details for arranging these tests are given.

a **Testing for A-T** – The national ataxia-telangiectasia service provides a laboratory testing service for A-T and related disorders through Prof Malcolm Taylor's laboratory at the University of Birmingham. It also provides both paediatric (Nottingham City Hospital, Director Dr Mohnish Suri) and adult (Papworth Hospital, Director Dr Nick Oscroft) Centres of expertise. Referral for testing or clinics can be made either via the A-T Society (Tel: 01582 760733, email info@atsociety.org.uk) or directly with the appropriate Centre.

b **Testing for AOA1 and AOA2** – Professor Malcolm Taylor, School of Cancer Studies, University of Birmingham (a.m.r.taylor@bham.ac.uk) or Dr Penny Clouston, Oxford Regional Genetics Laboratories, Churchill Hospital, Oxford, OX3 7LJ. (penny.clouston@ouh.nhs.uk). At the Oxford Regional Genetics Laboratories testing for AOA1 and AOA2 is offered as part of a gene panel including multiple ataxia genes; for clinical advice contact andrea.nemeth@eye.ox.ac.uk.

c **Testing for GSS syndrome** (Gerstmann-Straussler-Scheinker syndrome) and other prion-related genetic disorders can be carried out can be carried out at the National Creutzfeldt-Jakob Disease Research & Surveillance Unit, Western General Hospital, Edinburgh. Contact details: Main office telephone: 0131 537 1980/2128/3103; website: www.cjd.ed.ac.uk. Testing for prion-related disorders is also available at the National Prion clinic at the National Hospital for Neurology and Neurosurgery. www.uclh.nhs.uk/OurServices/ServiceA-Z/Neuro/NPC.

d **Rare mitochondrial disease service.** This service has been nationally commissioned by the National Commissioning Group (www.mitochondrialncg.nhs.uk). There are three designated sites: London - National Hospital for Neurology and Neurosurgery, Newcastle upon Tyne - Royal Victoria Infirmary and Oxford – John Radcliffe Hospital and Churchill Hospitals.

For further details of other laboratories in European countries providing diagnostic tests go to www.orpha.net (ORPHA97).

2.4.c. Guidance for genetic testing

With the numerous autosomal dominant (AD) spinocerebellar ataxias that have been identified, the Harding classification of considering these as types I, II or III is of some utility, and may inform genetic testing. Type I is so-called 'complicated' disease, where in addition to the ataxia, other neurological findings such as dementia, ophthalmoplegia, pyramidal signs and extrapyramidal features may be present. In type II disease there is progressive retinopathy and resulting blindness, and most cases to date have been associated with SCA7. Type III disease is reasonably 'pure' spinocerebellar ataxia. In Table 7, the currently available AD ataxia genes are tabulated, and the corresponding Harding group and any especially distinguishing clinical characteristics are indicated.

Table 7: The autosomal dominant spinocerebellar ataxias (SCAs) in which causative genes have been identified

SCA	Harding type	Gene	Clinical/other features
SCA1	I	*ATXN1*	Pyramidal involvement, ophthalmoplegia
SCA2	I	*ATXN2*	Slow saccades, peripheral neuropathy
SCA3	I	*ATXN3*	Also known as Machado-Joseph. Bulging eyes, ophthalmoplegia, peripheral neuropathy, pyramidal involvement, in a subgroup Parkinsonian phenotype,
SCA5	I	*SPTBN2*	Adult onset ataxia; a more severe childhood onset ataxia with intellectual disability can be caused by de novo missense mutations.
SCA6	III	*CACNA1A*	Allelic with EA2 / Familial Hemiplegic Migraine, mild ataxic syndrome
SCA7	II	*ATXN7*	Macular degeneration
SCA8	III	*ATXN8OS*	Not specific test*
SCA10	I	*ATXN10*	Seizures, Mexican origin
SCA11	III	*TTBK2*	Adult onset ataxia
SCA12	I	*PPP2R2B*	Tremors, common in India
SCA13	I	*KCNC3*	Some have intellectual disability
SCA14	III	*PRKCG*	Adult onset ataxia
SCA15	III	*ITPR1*	Very variable age of onset, slowly progressive; some have intellectual disability.
SCA16		Now known to be SCA15	
SCA17	I	TBP	Psychiatric features, dementia, chorea
SCA19/22	I or III	*KDND3*	Slowly progressive adult onset ataxia, occasionally pyramidal signs and urinary symptoms
SCA23	I or III	*PDYN*	Some have neuropathy, limb spasticity, cognitive decline, myoclonus or seizures
SCA27	I	*FGF14*	Variable age of onset, dyskinesias, learning difficulties
SCA28	I	*AFG3L2*	Slow saccades, ophthalmoplegia
SCA31	III	*BEAN1*	Pyramidal signs, hearing difficulties, decreased vibration sense, occasionally tremor
SCA35	I	*TGM6*	Dystonia
SCA36	I	*NOP56*	Motor neuron signs
SCA38	III?	*ELOVL5*	Slowly progressive ataxia, nystagmus
SCA40	III	*CCDC88C*	Only one family reported, adult onset
SCA41	III	*TRPC3*	Only one case reported, adult onset

The table above lists the SCA type, the gene causing the condition, Harding classification and some distinguishing clinical features[19,28].

***SCA8** – The clinical validity of genetic testing for SCA8 by CAG repeat sizing, has not yet been established, thus SCA8 testing should not be offered as a routine genetic test if family history is unknown. However, SCA8 testing may be appropriate in large pedigrees where the expansion has been proven to be segregating with the disease. It is still important to note that finding an expansion for SCA8 in a patient does not exclude the presence of another causative mutation.

Some of the distinguishing clinical features for the more common recessively inherited ataxias can be found in Table 8[27]. *For information on treatable inherited ataxias see section 4.2.*

Table 8: Distinguishing clinical features for more common autosomal recessive ataxias

Ataxia type	Gene	Clinical/other features
Friedreich's ataxia	*FXN*	Mixed cerebellar and sensory ataxia; cardiomyopathy, spasticity, diabetes, scoliosis and pes cavus may develop
Ataxia oculomotor apraxia type 1	*APTX*	Extrapyrimidal signs, mild cognitive impairment, variable oculomotor apraxia, peripheral neuropathy
Ataxia oculomotor apraxia type 2	*SETX*	Similar to AOA1 but presents later
ARSACS	*SACS*	Pyramidal signs and peripheral sensorimotor neuropathy with amyotrophy, spasticity
Ataxia caused by mutation in SPG7 gene	*SPG7* †	Increasingly recognised as a relatively common cause of both childhood and adult onset ataxia, often (but not always) with spasticity
Ataxia telangiectasia	ATM	For information on ataxia telangiectasia refer to the AT Guidelines obtained via the AT Society.

† Mutations in *SPG7*, a gene causing recessive hereditary spastic paraplegia, has emerged as a relatively common cause of ataxia (often with spasticity) [29].

Prevalence of inherited ataxias

There is limited information on the prevalence of inherited ataxias in the UK, however some are believed to be rarer than others and the information below may provide some guidance on diagnostic testing.

Recessive ataxias

- Friedreich's ataxia – the most common inherited ataxia in Caucasian populations[30].
- Ataxia with oculomotor apraxia type 2 and ataxia telangiectasia – the two second most common recessive ataxias worldwide[31].

Dominant ataxias

- Common spinocerebellar ataxias – SCA3 is thought to be the most common dominant ataxia worldwide, followed by SCA2. SCAs 1 and 6 are also found in many populations worldwide[31]. The most common SCA in the UK is SCA6. There is high prevalence of SCA3 in Portugal, Brazil and Japan[32], SCA7 in South Africa and SCA2 in Cuba and parts of Spain[31].

- Dentatorubral Pallidoluysian Atrophy (DRPLA) – was thought to be rare in Caucasian populations and most commonly reported in Japan. However, a recent study in Wales suggests that DRPLA may not be as geographically restricted as thought and the diagnosis should be considered in UK patients[33].
- SCA13 and SCA14 – in a recent UK screening study no SCA13 families were found, although it has been reported in a sporadic case[34]. At least seven SCA14 families have been identified in the UK[35].

X-linked ataxias

- Generally rare, but Fragile X associated Tremor and Ataxia Syndrome is increasingly recognised, and may mimic other patterns of inheritance. Genetics testing should be specifically requested,as it is usually a repeat disorder and will not be detected using sequencing technologies. There are major implications for family members.

Recommendations	Grade
1. The clinical context (speed of evolution, episodic/fluctuating versus progressive etc) should determine the investigation of individual cases.	GPP
2. Ataxia in adults can arise due to serious neurological disease and urgent referral for secondary care (to a neurologist) should be made without delay following primary care investigation.	GPP
3. Children presenting with ataxic symptoms should be referred urgently for paediatric assessment (usually by local specialists, who may liaise with paediatric neurologists, clinical geneticists etc).	GPP
4. Rapid progression (over weeks or months) can denote a paraneoplastic cause, prion disease or multiple system atrophy, thus urgent investigations are required.	GPP
5. When a diagnosis of progressive ataxia is made referral to a Specialist Ataxia Centre is encouraged.	GPP
6. Neurologists should liaise with their clinical genetics counterparts given the potential implication for family members of patients who undergo genetic testing.	GPP
7. Informed consent should be sought from all those undergoing genetic testing.	GPP
8. It is essential to offer genetic counselling to patients and discuss the implications of a genetic test prior to testing.	GPP
9. Genetic counselling should include the implications of having a genetic test for the individual and their family and any reproductive choices they may make.	GPP
10. Asymptomatic ‘at risk’ subjects should be offered genetic counselling.	GPP
11. Genetic testing of asymptomatic ‘at-risk’ minors is not generally recommended, but should be considered on a case-by-case basis.	GPP
12. Any genetic test results from research studies need to be validated by an accredited laboratory before a formal result is given to the patient.	GPP

3. Patient pathways

3.1. Referrals

Following the referral to a neurologist, in many cases it may be relevant for either the GP or the neurologist to refer patients to other specialists. Depending on the symptoms experienced, and the type of ataxia a patient is diagnosed with, a variety of different specialists will be involved in their care. Section 4 on Medical Interventions gives an overview of some of the symptoms people with ataxia can experience and the referrals recommended. Section 5 highlights the importance of allied health professionals in the care of patients with ataxia and early referral is recommended.

A summary of referrals is shown below:

- **Community paediatric multidisciplinary team**
  Children should be referred to the community paediatric multidisciplinary team.
- **Spinal surgeon/orthopaedic surgeon/orthotist**
  Patients with Friedreich's ataxia often develop scoliosis. Referral to spinal surgery and/or orthopaedic surgery may therefore be appropriate in some cases; referral to physiotherapy may also be helpful. Patients with Friedreich's ataxia may develop *pes cavus*, therefore referral to an orthopaedic surgeon with specialty in foot and ankle surgery and to an orthotist may be appropriate. *See section 4.1.d.*
- **Cardiologist**
  Cardiac abnormalities are common in Friedreich's ataxia, therefore a referral to a cardiologist is required. Other ataxias are not normally associated with cardiological problems. *See section 4.1.f.*
- **Urologist**
  Bladder problems can be a feature of some of the ataxias. They occur, for example, in multiple system atrophy. Also, in later stages of various spinocerebellar ataxias urinary incontinence can sometimes be experienced. *See section 4.1.g.*
- **Audiology services**
  Some people with ataxia (eg: Friedreich's ataxia and some spinocerebellar ataxias) experience hearing problems so referral to Audiology services, hearing therapist and/or speech and language therapist is recommended. *See section 4.1.m.*
- **Neuro-ophthalmologist**
  Many of the ataxias are associated with eye symptoms such as reduced vision, diplopia or oscillopsia due to nystagmus. A referral to a neuro-ophthalmologist and other specialist services is recommended since in some cases treatment may be available. *See section 4.1.n.*
- **Neuropsychologist/ neuropsychiatrist**
  Some ataxias may be associated with cognitive problems; therefore in selected cases a referral to Neuropsychology department is recommended. *See section 4.1.o.* Referral to a neuropsychiatrist is recommended in patients with ataxia and severe cases of dementia or psychosis. *See section 4.1.p.*
- **Allied health professionals**
  Patients would benefit from a referral for neurorehabilitation at the early stage of the disease in order to establish strategies to maintain function (eg: balance, upper-limb coordination, speech and swallowing).

Physiotherapy is often valuable, particularly to preserve mobility, and to avoid other problems, such as ones associated with being in a wheelchair. Regular follow-up is important. Patients will also need

advice on walking aids at the different stages of their condition. Referral to a wheelchair clinic for specialist seating advice is important at the appropriate stage of the disease. *See section 5.2.*

Patients with progressive ataxia often experience dysarthria, which later in the disease may cause communication difficulties. A referral to a **speech and language therapist** is therefore important. Dysphagia becomes more common as the disease progresses; therefore this should also be assessed by a speech and language therapist or other appropriately trained professional. *See section 5.1.*

Ataxia patients benefit from regular assessments by an **occupational therapist**. Occupational therapists have expertise in assessment of daily tasks and providing specific interventions which may include teaching strategies, recommending equipment or adaptations. Occupational therapists work in various health and social care settings. As a general rule, local authority based (social services) occupational therapists have a prime focus on home adaptations and equipment provision. A referral to a community rehabilitation team or neurological outpatient setting should be considered for further assessment of specific areas. Specialist neurological hospitals may offer expert assessment via clinics. *For further information on referrals contact the College of Occupational Therapy (www.cot.co.uk). See section 5.3.*

- **Specialist palliative care team**
  When an individual with ataxia has a limited lifespan and/or distressing symptoms it may be relevant to refer to a specialist palliative care team. *See section 6.*

Patient Support groups

Referral to a patient support organisation is recommended.

- Ataxia UK provides support to people with all ataxias (apart from ataxia telangiectasia where there is a dedicated charity).
- The AT Society supports people with ataxia-telangiectasia
- The MSA Trust provides support solely to people with multiple system atrophy
- The Niemann-Pick Disease Group supports people with Niemann-Pick Disease.

When progressive ataxia is first diagnosed often patients will not have heard of the condition and will not know anyone else with it. At this stage the support that can be provided by patient support organisations can be crucial. The possibility of meeting others in the same situation, receiving emotional support and information from a Helpline and finding out how others cope with the symptoms, can be of much benefit to people with ataxia. Although each support organisation provides its own services, many will also provide the opportunity for patients to be informed about research developments and take part in research projects.

Contact details

- Ataxia UK (registered charity in England and Wales (number 1102391) and in Scotland number (SC040607).12 Broadbent Close, London N6 5JW ***www.ataxia.org.uk Helpline: 0845 644 0606***
- MSA Trust for multiple systems atrophy (registered charity number 1062308) MSA Trust 51, St. Olav's Court, SE16 2XB ***www.msaweb.co.uk Tel: 0333 323 4591***
- Ataxia-Telangiectasia Society (registered charity number 1105528) IACR-Rothamsted, Harpenden, Herts AL5 2JQ ***www.atsociety.org.uk Tel: 01582 760733***
- Niemann-Pick Disease Group (UK) (registered charity number 1061881) 11 Greenwood Close, Washington, NE38 8LR ***www.niemannpick.org.uk Tel: 0191 415 0693***

3.2. Reviews and follow-up

Patients should be offered 6-12 monthly reviews from a neurologist or a specialist ataxia neurologist *(see Section 2.2 and Appendix 1 for information on Specialist Ataxia Centres)*. If it is difficult for patients to travel to the hospital, follow-up appointments could be less frequent. Regular follow-up reviews are important for a number of reasons. Firstly, it enables the neurologist to monitor the progression of the condition and identify any new symptoms that may need treatment. Secondly, if patients are discharged and not offered a follow-up appointment they are not likely to benefit from medical advances. For example, new diagnostic tests are regularly becoming available, especially as new genes are identified, thus increasing the possibility of identifying a diagnosis for patients with 'idiopathic' cerebellar ataxia. In addition, new treatments may be developed, both ones that may affect disease progression and ones for symptomatic relief. Clinicians should consider the use of validated ataxia-specific rating scales for measuring progression of the ataxias *(see Research section for details of these scales).*

Regular follow-up of patients with Friedreich's ataxia is necessary, specifically to monitor for the development of cardiomyopathy, diabetes, scoliosis and other treatable symptoms. Annual urine/blood tests for diabetes are also recommended.

For the majority of patients with ataxia, for most of the time, their ongoing management can be provided at the primary care level. In addition to regular input from their GPs, other professionals including community therapists are likely to be involved. Specific community nursing needs may be delivered by district nurses.

The hospital-based neurologist/ ataxia specialist will, however, remain involved as a coordinator and instigator of services. Effective communication between primary and secondary care is therefore vital. Multi-disciplinary, multi-professional working practices that are mutually supportive are important, as recommended by the National Service Framework for long-term conditions[25]. As ataxia is usually chronic and progressive, an even greater reliance on community services with the passage of time is likely. The establishing of durable networks of care at an early stage is therefore crucial. In line with recent recommendations in the National Service Framework for long-term conditions, involvement of symptom and palliative care professionals is recommended,[25] especially as the disorder progresses. The remit at this stage may include providing practical and emotional support for carers, who are often family members *(see section 6).*

4. Medical interventions

This section aims to provide an overview of the medical interventions available for people with progressive ataxias. Section 4.1 focuses on the treatment of symptoms experienced by people with ataxia, whereas section 4.2 describes the management of the few treatable forms of ataxia in adults and children.

4.1. Symptomatic treatments

Patients with progressive ataxias may experience a variety of symptoms, some of which can be treated medically. This section describes the most common symptoms and provides advice on specific treatments. There are currently no approved treatments to improve the underlying ataxia in the majority of the progressive ataxias, although research advances may result in medications in the future. Medications are available to treat ataxia episodes in episodic ataxia *(see section 4.1.q).*

4.1.a. Muscle spasticity, spasms and joint contractures

Spasticity is the presence of increased muscle tone or hypertonia, caused by a lesion of the upper motor neurones which can cause muscle stiffness, spasms and pain. Persistently raised muscle tone can result in abnormal posturing of body parts which if prolonged can result in muscle and tendon shortening, fixed deformities and ultimately contractures[36]. **Contractures** are characterized by permanent reductions in the range of motion of joints and resistance to passive stretch. This is mediated by neural factors, principally spasticity, and non-neural factors such as structural changes in soft tissues[37]. **Spasms** are sudden, involuntary and often painful muscle contractions which are often associated with spasticity and provoked by muscle stretch or other stimuli[36]. They may be transient or prolonged.

From a pathophysiological point of view, spasticity has been defined as a velocity-dependent increase in tonic stretch reflexes with exaggerated tendon jerks, resulting from hyper-excitability of the muscle stretch reflex[38]. More recently, the influence of afferent pathways on spasticity has been appreciated so that it may be thought of as a condition of disordered sensorimotor control presenting with intermittent or sustained involuntary activation of muscles[39]. This is important, since a first step in the treatment of spasticity may be the reduction or elimination of increased afferent input such as that caused by pain, infection, diarrhoea, constipation, urinary retention, tight clothing or poor posture.

Ataxia and spasticity may coexist in a large number of congenital, genetic or acquired conditions including common conditions such as stroke, multiple sclerosis, cerebral palsy and head injury. Spasticity is prominent at presentation in some cases of the following conditions and these are sometimes referred to as spastic ataxias[40].

- Late-onset Friedreich's ataxia (LOFA)
- Autosomal recessive Spastic Ataxia of Charlevoix-Saguenay (ARSACS)
- Hereditary spastic paraplegia type 7 (HSP7)
- Adult-onset Alexander disease
- Spinocerebellar ataxia type 3 (SCA3; Machado-Joseph disease)
- Cerebrotendinous xanthomatosis
- Fatty acid hydroxylase-associated neurodegeneration

Spasticity has also been described more rarely in a range of other autosomal recessive ataxias, spastic paraplegias and autosomal dominant ataxias including SCAs 1–3, 6–8, 10–12, 17, 23, 28, 30, and 35. Metabolic causes include:

- Ataxia with Vitamin E deficiency
- Ataxia with Coenzyme Q_{10} deficiency
- Abetalipoproteinaemia
- Metachromatic leukodystrophy
- Adrenomyeloneuropathy
- Vanishing white matter leukodystrophy
- Krabbe disease
- Gaucher's disease type III
- 3-methylglutaconic acidaemia type III
- Non-ketotic hyperglycinaemia
- GM2 gangliosidosis[40].

Spasticity can affect many parts of the body contributing to a range of symptoms seen in progressive ataxia including dysarthria and dysphagia as well as limb problems such as clumsiness, lack of manual dexterity and difficulty with walking.

Treatment of spasticity

The purpose of treating spasticity is to optimize mobility, standing capacity and upper limb function; to reduce symptoms of pain and spasms, especially those at night which impair sleep and contribute to daytime fatigue; to improve transferring, sitting posture, washing and dressing, and so promote independence and reduce carer reliance; to prevent skin ulceration and the formation of pressure sores; and to prevent contractures and so reduce the development of chronic disability. Treatments may be non-pharmacological (therapy-based), pharmacological or surgical, usually proceeding from one to the next in that order if the previous has failed or provided incomplete benefit.

It is vital that pharmacological and surgical techniques are used in association with patient education and timely physiotherapy to maximize efficacy and maintain benefit.

Non-pharmacological therapies

Physiotherapy has a vital role to play in educating patients and carers in correct posture, muscle use and the avoidance of spasticity triggers such as pain and infection.

Pharmacological Treatments

Although there is little evidence of the efficacy of anti-spasticity interventions specifically in cases of spastic ataxia, a greater evidence base exists in commoner conditions causing spasticity, particularly stroke, multiple sclerosis, cerebral palsy, head injury and spinal injury. Since the underlying

neurophysiological mechanisms generating spasticity and spasms are similar, treatment decisions have to be made pragmatically by extrapolation of such evidence and on the basis of expert experience. Cochrane Reviews describing the management of spasticity exist for multiple sclerosis[41,42], cerebral palsy[43,44], spinal cord injury[45] and amyotrophic lateral sclerosis[46].

Most clinicians start with the following oral medications for generalised spasticity (usually in this order due to the profile of side effects and better tolerability): baclofen, tizanidine, gabapentin, clonazepam, dantrolene sodium or diazepam. It is advisable to start at a low dose for all medications and increase the dose slowly. Chronic use of diazepam is not recommended apart from in very severe cases. If these are not successful or not tolerated, greater CNS concentrations of baclofen can be achieved with reduced peripheral exposure to side effects by the use of an intrathecal baclofen infusion, although this requires careful patient selection, planning and an expert centre to undertake the procedure and follow-up[47].

Many other oral medications have shown some evidence as anti-spasticity agents including methocarbamol, levetiracetam, lamotrigine, pregabalin, progabide, clonidine, piracetam, vigabatrin, prazepam, cyproheptidine, L-threonine, thymoxamine, orphenadrine and 3,4-diaminopyridine. However, these are rarely used in practice. Intrathecal phenol has also been used but because of the destructive nature of the agent, its use is restricted to those patients with severe lower limb spasticity who cannot be managed by alternative means[36].

Anecdotally, it is known that patients with ataxia sometimes gain benefit from the use of cannabis products in reducing pain and spasticity. Studies of *Cannabis sativa* extract and synthetic cannabinoids in MS and other neurological conditions have shown significant reductions in pain, spasms and spasticity[48]. However, the largest of these trials[49,50] failed to show significant reductions in objective markers of spasticity, so further research is required.

In all cases, there can be paradoxical worsening of mobility or other functions by unmasking of underlying weakness[51]. Patients should therefore be warned of this possibility beforehand. In addition, it highlights the importance of titrating the dosage of medications slowly in order to avoid this, and the medication should be stopped or reduced if worsening of mobility or other functions occurs.

Focal spasticity, particularly in small muscles, is probably best treated with intramuscular botulinum toxin injections for which numerous well-controlled, randomized trials have shown benefit[52]. It is advisable to be referred to a specialised clinic for such treatment. There is evidence that this benefit is prolonged by adjunctive therapies such as stretching, taping, casting, dynamic orthoses or electrical muscle stimulation. It is therefore very important that such injections are accompanied by a course of physical therapy at the time or immediately after injection.

Spasticity can be associated with painful nocturnal cramps. In the elderly, quinine sulphate has been used extensively to try and alleviate this. However, it has been associated with serious adverse events (particularly cardiac ones) and so its use is not generally recommended for patients with cardiac conditions and for patients with Friedreich's ataxia.

Surgical Treatments

Surgical treatments are generally considered options to be taken only when physical and pharmacological interventions have not worked. However, they may be considered in exceptional cases, particularly in the case of fixed, non-reducible deformities or where ablation of specific nerve fibres will result in improvement in a specific focal symptom. Surgical treatments include orthopaedic procedures such as tendon lengthening, tenotomy or tendon transfer; and neurosurgical procedures such as peripheral neurotomies, dorsal rhizotomies and microsurgical ablation of the dorsal root entry zone ('DREZotomy')[53].

Recommendations	Grade
1. Careful assessment by a neurologist, with advice from a physiotherapist, is required to decide on the type of treatment of spasticity.	GPP
2. Consider physiotherapy first to treat spasticity, and if that does not provide complete benefit use pharmacological treatment. Surgery should be considered in cases where physiotherapy and pharmacological treatments have not worked.	GPP
3. For pharmacological treatment of generalised spasticity consider using the following oral medications (usually in this order due to the profile of side effects and better tolerability): baclofen, tizanidine, gabapentin, clonazepam, dantrolene sodium or diazepam.	GPP
4. To treat focal spasticity, particularly in small muscles, refer to a specialised clinic for treatment with intramuscular botulinum toxin injections, followed by physiotherapy.	GPP

4.1.b. Tremor

Tremor can be an intrusive complaint in some patients with ataxia, and is classically described as being of “intention” type (with the amplitude of shaking increasing as the target is approached). “Maintained posture” tremor can also be encountered. Although tremor is especially notable in Fragile X-associated tremor/ataxia syndrome and SCA12, it can be present in virtually any form of progressive ataxia. The co-presence of sensory disturbance (and especially joint position loss) can further exacerbate tremor.

Treatment is difficult, and the variety of pharmacologically unrelated agents promoted as potential therapies is a testament to their general lack of efficacy. The published data up to 2005 have been reviewed[54]. Generally speaking, good quality randomised controlled trial data for the use of any of the agents suggested in the management of cerebellar tremor is lacking. A conventional approach to the medical management of tremor in ataxia is shown in table 9.

Table 9: Pharmacological treatment of tremors in patients with progressive ataxia

(listed in the order of general usage)

Drug	Starting dose (daily)	Usual maintenance dose
Propranolol	20mg	80-160mg daily (using a long-acting formulation)
Primidone*	50mg	125- 250mg twice daily
Propranolol and Primidone combined		
Topiramate*	12.5mg	25mg twice daily
Clonazepam	0.5mg	0.5mg
Gabapentin	200mg	400-800mg three times a day

*Additional caution to be exercised in the elderly with the use of these medications for possible side effects.

Physiotherapy may be helpful in the management of tremors and should be considered *(see section 5.2)*.

In patients where tremor is extremely debilitating and not responsive to medication, a referral to a centre specialising in functional neurosurgery should be considered.

This is because there may be a useful role for functional neurosurgery, including deep brain stimulation (DBS), in the management of tremor, although here too studies specifically for the management of cerebellar tremor are lacking. In a study of a patient with SCA2, chronic thalamic stimulation was shown to improve severe resting and action tremor[55]. Improvement in unilateral cerebellar tremor in a single subject has been described after Vim (nucleus ventralis intermedius) and latterly PSA (posterior subthalamic area) DBS[56]. Benefit has also been reported from the use of DBS (of Vim) in a single subject with abetalipoproteinemia[57], and in FXTAS[20].

For information on dystonic tremor see section 4.1.c. on Dystonia.

Recommendations	Grade
1. Patients with ataxia who have tremors should be offered pharmacological treatment using the drugs described in table 9 to be tried in the order they are listed until symptom relief is achieved.	GPP
2. In patients where tremor is extremely debilitating and not responsive to medication a referral to a centre specialising in functional neurosurgery should be considered.	D

4.1.c. Dystonia

Dystonia is characterised by sustained co-contractions of agonist and antagonist muscle groups in different parts of the body, resulting in abnormal postures and twisting/repetitive movements, and can be focal, segmental or generalised. Dystonia can be an accompanying feature of many ataxic conditions. Patients with ataxia who develop dystonia most commonly have a focal form of dystonia. An “idiopathic” form characterised by predominantly (focal) cervical dystonia and ataxia has been reviewed[58]. Even this clinically relatively homogeneous entity is thought to be aetiologically heterogeneous.

A number of treatment options for dystonia, including oral drugs, botulinum toxin injections, surgical techniques (globus pallidus interna stimulation) and physiotherapy are available. Oral drugs are unfortunately often ineffective. The first treatment option for focal dystonia is botulinum toxin injections. For generalised dystonia, a trial of oral medications should be offered first, followed by surgery if this is not successful.

In patients with dystonic tremor, physiotherapy and pharmacological intervention with drugs such as trihexyphenidyl and orphenadrine should be the first treatment options, followed by surgery if these are ineffective. A number of reviews of the treatment of dystonia are available, and these strategies can be adapted in the management of this complication in patients with ataxia[59–61].

Recommendations	Grade
1. Focal dystonia should be treated with botulinum toxin injections.	GPP
2. Generalised dystonia should be treated with oral medications, followed by surgery if this is not effective.	GPP
3. Patients with dystonic tremor should be offered physiotherapy and oral medications followed by surgery if the former are ineffective.	GPP

4.1.d. Scoliosis

Scoliosis is derived from the Greek word *'Scolios'* meaning crooked. It is the lateral curvature of the spine associated with twisting of bony elements (vertebrae) along with deformation of chest cage producing 'rib hump' deformity. If left untreated, the scoliosis may progress with time and cause rigid 'C' or 'S' shaped curvature of the back with compression of lungs and other internal organs resulting in severe pain with shortness of breath. It may also result in having difficulties with sitting properly in a wheelchair due to pelvic obliquity (ie: tilting of the pelvis).

Scoliosis is a common feature in people with Friedreich's ataxia; with up to 60% developing spinal deformity (scoliosis / kypho-scoliosis)[62]. If left untreated, this may become severe with time due to the underlying progressive neurodegenerative disorder and worsening of spinal deformity with growth[62–65]. It is therefore important for neurologists and paediatricians to carry out an evaluation of the spine and regularly monitor the potential development of scoliosis in Friedreich's ataxia patients, especially in children.

If scoliosis is detected, referral to a spinal surgeon is recommended. The urgency of referral is determined by severity of curvature and co-existent pain / discomfort.

Spinal assessment: On referral to a spinal unit, patients are seen by a specialist spinal deformity surgeon who will request an x-ray of the whole spine (standing or sitting) to determine the magnitude / severity of spinal curvature. This measurement (Cobb angle) is recorded and overall spinal balance in both frontal (ie: coronal) and sideward (ie: sagittal) planes is evaluated. A detailed neurological assessment is also undertaken and findings documented. An assessment of posture and seating ability (in wheelchair users) along with degree of constriction of rib cage by pelvis (costo-pelvic impingement) is determined[64–66].

Treatment: If scoliosis is diagnosed a referral to a physiotherapist to advise on posture and exercises is recommended. For mild deformities, the curvature is kept under close observation and the spinal surgeon may discuss bracing (i.e. a rigid plastic corset is worn like a garment)[65,66]. The brace holds the spine straight by three-point contact pushing on muscles and correcting the spinal curvature. It is important to follow the advice of the specialist spinal surgeon and for the patient to wear the brace diligently as advised[64,65].

For severe deformities, the surgeon may discuss the need for an operation and explain the risks / benefit of surgery in greater detail[62,67]. Further special investigations may be requested to thoroughly evaluate patient(s) prior to surgery. These investigations may include:

- CT Scan
- MRI Scan
- Cardiac ECHO: Assessment of cardiac function
- PFT: Pulmonary (ie: lung) function tests
- Sleep studies

Surgery: The operation may involve one or two surgeries to straighten the spine and hold it in corrected position by using rods, screws and wires[62,65]. These implants act as scaffolds holding the spine straight until the bony elements knit together (fusion occurs). One would be several inches taller after the operation and anticipated stay in hospital is likely to be a few weeks. The anticipated time to recover from surgery is likely to be a few weeks to a couple of months. The outcome of the surgery can be rewarding for the patient with improved quality of life and seating ability in a wheelchair, and reduction

in pain[62,67]. Liaison between the surgeon, anaesthetist and cardiologist is important when surgery is planned, and careful consideration should be given to fluid management and monitoring during surgery. This is particularly relevant if patients with Friedreich's ataxia already have cardiac problems.

Further follow-up and continuity of care: The rods / implants will stay inside the body for the rest of the person's life and it is important for the surgeon to continue to see the patient regularly in out-patient follow-up clinics every few months for the first year and every 6-12 monthly after the first year. Serial x-rays of the whole spine are done at each visit and assessed for progression to bony union / fusion. Life-long follow-up may be needed to ensure there are no untoward events (rod breakage / screw backout which may happen infrequently)[62,67].

Complications: Any concerns from the patients with surgical wounds or any other issues should be discussed with the GP initially. On evaluation the GP would arrange a referral to a specialist if appropriate.

Recommendations	Grade
1. Regular surveillance of the development of scoliosis in Friedreich's ataxia patients (especially children) is recommended as it is important for it to be treated.	GPP
2. If scoliosis is detected, referral to a physiotherapist and spinal surgeon is recommended.	GPP
3. For mild scoliosis the patient should be kept under close observation and the spinal surgeon should consider treatment with bracing.	B
4. For severe scoliosis consider surgery to straighten the spine.	B
5. Regular follow-up by a spinal surgeon is recommended after an operation on the spine.	B

4.1.e. Pain

Chronic pain in patients with ataxia can arise through musculoskeletal or neuropathic (peripheral and central) causes. It can be a distressing complaint particularly in advanced ataxia, where in addition to neuropathic pain, pain can also arise from joint/spinal deformity and abnormal positioning. A variety of interventions, including physiotherapy, are available for pain management. A number of drugs are available to treat neuropathic pain, with the most commonly used drugs being Amitriptyline, Nortriptyline, Carbamazipine, Pregabalin, Gabapentin and Duloxetine[68].

Referral to a pain management clinic may be necessary in some cases, where inter-disciplinary input including physiotherapy and psychological therapies can be used for the management of pain[68].

Recommendations	Grade
1. Treat pain with physiotherapy and/or pharmacological treatments.	GPP
2. Consider use of the following drugs to treat neuropathic pain: Amitriptyline, Nortriptyline, Carbamazipine, Pregabalin, Gabapentin and Duloxetine.	GPP
3. Consider referral to a pain management clinic if pain is severe or limiting daily activities.	GPP

4.1.f. Cardiac involvement in Friedreich's ataxia

Cardiac involvement in Friedreich's ataxia is frequent, exceeding 90% of the patients in some studies and reports[69] (this applies to ECG measures rather than structural/functional changes). It is therefore essential to involve a cardiologist in the screening of patients with Friedreich's ataxia for the early diagnosis of cardiac problems and the management of cardiac complications, where required. A broad clinical spectrum is seen with cardiac pathology.

As in all other cardiomyopathies, increased awareness is paramount for the recognition, diagnosis and management of patients who suffer from these abnormalities. Although the cardiac abnormalities are gradual and progressive and cardiac risk does not appear to precede symptoms, the overlapping aetiologies of their symptoms may justify preventative cardiac screening. Expert opinion would suggest that it would be advisable for patients to be screened once every two years before any cardiac disease is documented, and at least annually after manifesting features of asymptomatic cardiac disease.

Clinical presentation

Friedreich's ataxia patients report breathlessness, and less frequently chest pain. It is sometimes difficult to discriminate the origin of these symptoms between cardiac or respiratory/neuromuscular origin. They may also report palpitations, which may be non-specific or attributed to atrial arrhythmias.

Specific aspects of the cardiac phenotype seen in Friedreich's ataxia can be detected by:

- **ECG** –There is usually evidence of electrocardiographic abnormalities mainly in the form of non-specific repolarisation changes,[70–72] T wave inversion and also deep S-wave in V1 and V2, and high R-wave in V5 and V6 (LVH)[72]. The QRS and QTc duration are expected to be normal. Conduction abnormalities, which would require intervention are rare[73,74].
- **Echocardiographic abnormalities** – More than 50% of the patients have abnormalities on cardiac imaging[75]. The typical pattern is concentric left ventricular hypertrophy with an end-diastolic wall thickness in most patients of less than 15 mm, and absence of outflow tract obstruction[74,76].

Patients with an earlier diagnosis (and presumably onset) of disease generally also show more severe cardiac involvement[76]. With time, it is likely that there will be some degree of regression of the hypertrophy in these patients resulting in thinning and dilatation of the left ventricle. This does not represent a variation of the phenotype but rather a progression of the cardiomyopathy. Consequently some patients progress to the dilating phase of the condition and this is associated with severe systolic dysfunction with dilation of the ventricle; it occurs especially at older ages, but is infrequent[77].

Diastolic dysfunction is associated with the stage of the condition. There is inadequate volume of data to suggest that there is early or disproportional diastolic dysfunction in patients with FRDA[73]. A paper has described various clinical features of the FRDA cardiac phenotype but there is no association at present with prognosis and outcome[78].

Diagnosis and monitoring

Transthoracic Echocardiography is the method of choice for the diagnosis and monitoring of the myocardial changes. The cardiac MRI as an alternative or complimentary imaging modality has not been widely used so far but it might be helpful to assess the cardiac mass in a more accurate way compared to echocardiography[75]. It also has the potential to detect areas of expansion of the extracellular volume using Gadolinium imaging which are suggestive of fibrosis in other disease settings.

As part of the cardiac screening it is relevant to test levels of troponin, as a study has shown elevated

levels of troponin in 47% of people with Friedreich's ataxia who did not have active arrhythmia, chest pain or features of acute coronary syndrome at the time of sampling. Although long-term longitudinal studies have not been yet published, it could be helpful to measure levels at baseline for future follow-up of patients and in particular if chest pains occur[79].

Cardiac rhythm monitoring – Holter monitors can be helpful for the detection of silent cardiac arrhythmias or the association of symptoms (such as palpitations, shortness of breath) with the underlying rhythm. Arrhythmia is predominantly supraventricular[70]. The prevalence of atrial fibrillation correlates with the severity of the cardiac disease and therefore has negative prognostic implications[76]. There is no evidence from the literature that ventricular arrhythmia occurs in early stages or disproportionately to the stage of underlying cardiac condition. Severe arrhythmia is associated with severe dilated cardiomyopathy (DCM)[74,80].

Some data suggest an association between electrocardiographic and echocardiographic changes and the size of the GAA expansion in the FRDA gene and the neurologic deficit in Friedreich's ataxia; however this is not confirmed by all datasets[71,74,81–84].

Management

The management of the manifestation of cardiac involvement is symptomatic and also aims to prevent further complications. Depending on the phenotype of patients with Friedreich's ataxia, guidelines for treatment of hypertrophic cardiomyopathy[85] and heart failure[86] should be applied and individualised. Although not validated specifically in clinical studies with Friedreich's ataxia patients, a cardiologist would consider beta-blockers, ACE inhibitors/other vasodilators, spironolactone and loop diuretics for the management of patients who present with heart failure symptoms attributed to myocardial dysfunction. Amiodarone and digitalis have roles in the management of atrial fibrillation; rate control can be achieved also with beta-blockers or calcium antagonists, depending on the clinical circumstances. Treatment may also include implantation of pacing devices with the optional additional capacity of a defibrillator.

An issue which often requires multidisciplinary discussion is the indication and type of anticoagulation for atrial arrhythmias in these patients, who are prone to falls and injury. The decision is usually individualised. The standard treatment is warfarin. The use of the newer novel oral anticoagulants have not been studied in Friedreich's ataxia, but they may prove a superior option due to the lack of a need for regular monitoring and reduced risk of intracranial hemorrhage.

Cardioverter defibrillator implantation: For all patients, including those with neuromuscular disorders, guidelines on device implantation[87] and sudden death prevention should be followed. For individual patients, risks and benefits related to the intervention and its short, medium and long-term consequences should be considered.

Transplantation: Although it is appropriate to consider patients with Friedreich's ataxia with advanced heart failure for transplantation, the complexity of the underlying condition and multi-organ involvement count as risk factors for a successful transplantation so the patients need to be considered with great caution and on individual basis.

Other drugs: The role of antioxidant agents, such as idebenone and CoQ10 for the treatment of cardiac changes in Friedreich's ataxia is yet unclear *(see Research section).*

Standard guidelines for assessing cardiovascular risk factors should be used in all patients and treated accordingly. In the case of statins, despite suggestions that statins lower CoQ10, this should not affect the choice of the treatment of hypercholesterolaemia with statins. Moreover, the number of patients with Friedreich's ataxia who require treatment with statins is expected to be low in the first four decades of their life.

Conclusion

Although clinical observations and research have offered new insights into the disorder, the natural course of the cardiomyopathy in Friedreich's ataxia is largely unknown.

Therefore, systematic study and follow-up of patients with Friedreich's ataxia who exhibit cardiac abnormalities will provide the longitudinal data required to shed light on many aspects of the cardiac manifestation of this disorder, and may help prevent complications and/or delay their progression.

Recommendations	Grade
1. When Friedreich's ataxia is diagnosed a referral to a cardiologist is recommended for the early diagnosis of cardiac problems and the management of cardiac complications, where required.	GPP
2. Regular screening by a cardiologist is recommended in Friedreich's ataxia patients; once every two years before any cardiac disease is documented, and at least annually after manifesting features of asymptomatic cardiac disease.	GPP
3. Transthoracic Echocardiography and ECG should be used for the diagnosis and monitoring of the myocardial changes.	GPP
4. Holter monitoring should be undertaken to detect silent cardiac arrhythmias or the association of symptoms (such as palpitations, shortness of breath) with the underlying rhythm.	GPP
5. A cardiologist should consider pharmacological treatment (including the use of anticoagulants), and in some cases the implantation of pacing devices, in collaboration with the neurologist.	GPP

4.1.g. Bladder problems – lower urinary tract dysfunction

From the limited data available, lower urinary tract symptoms appear to be common in people with ataxia. Symptoms occur most prominently In Multiple System Atrophy (MSA), and may even manifest prior to other neurological symptoms[88]. In Friedreich's ataxia, a prevalence of 23% was seen in a study of 140 patients[89]. The most common symptoms relate to problems with storage and include urinary urgency, frequency and incontinence (overactive bladder symptoms). Urodynamics may demonstrate uninhibited detrusor contractions and altered bladder capacity[90,91]. Problems with voiding may occur as well, especially in multiple system atrophy[88] and Spinocerebellar ataxia type 3, and individuals may report urinary hesitancy, poor stream, sensation of incomplete bladder emptying and double voiding, or may be in retention[88,92]. Incomplete bladder emptying may result in recurrent urinary tract infections.

Diagnostic Approach

Lower urinary tract dysfunction should be managed by a suitably trained healthcare professional who is knowledgeable both about ataxias as well as managing the neurogenic bladder. The post-micturition residual urine should be measured as part of the initial assessment and preferably before antimuscarinic medications are started. This measurement can be made either using ultrasound or in-out catheterization. Urinary tract infections (UTI) may mimic overactive bladder symptoms and can themselves worsen neurological disability. 'Dipstick' tests of the urine using reagent strips to test for UTIs should be used to exclude infection. Urodynamics are not routinely performed unless bladder symptoms are refractory to treatment or intravesical treatments are being planned. It is also important for urological/gynaecological causes for lower urinary tract symptoms such as prostate enlargement or stress incontinence, to be appropriately ruled out.

Treatment

In the majority of cases, the bladder can be successfully managed using a simple algorithm which has been adopted from treatment guidelines for bladder dysfunction in patients with Multiple Sclerosis[93] (figure 1). Practical advice should be given about cutting down caffeine, fizzy drinks and alcohol, as well as information about timed voiding and bladder retraining whenever appropriate. The fluid intake should be individualized, particularly taking into consideration possible concurrent cardiac issues; however a fluid intake of between 1 to 2 litres a day is recommended[93]. Pelvic floor exercises may be helpful especially when symptoms are mild.

Most individuals with overactive bladder symptoms will require antimuscarinic medications *(table 10).* The most often experienced side-effects are dry mouth and constipation. If the former is too uncomfortable, artificial saliva may be prescribed. Antimuscarinics may increase heart rate, which may be relevant in individuals with cardiomyopathy (eg: in some patients with Friedreich's ataxia). Cognitive problems can occur in some individuals with ataxia and in the rare situation where cognitive impairment is a feature, antimuscarinics should be prescribed with caution. It would be sensible to use more selectively-acting medications such as trospium or darifenacin. If symptoms continue to be refractory, intradetrusor injections of botulinum toxin A is likely to be an option, though it remains to be unlicensed for this indication. More recently, percutaneous tibial nerve stimulation has emerged as an option for managing overactive bladder symptoms.

In individuals with persistently elevated post-void residual volumes in excess of 100 mL, clean intermittent self catheterisation (CISC) is indicated. This should be taught by a urology specialist nurse or continence advisor. Manual dexterity and vision need to be assessed when considering CISC. With advancing disease, a long-term indwelling catheter may be required, preferably suprapubic rather than urethral.

Referral to specialist urology services is indicated in cases of haematuria, suspicion of a concomitant urological condition, eg: prostate enlargement, recurrent urinary tract infections, symptoms refractory to medical management, or for consideration of Botulinum toxin or suprapubic catheterization.

Figure 1.

Algorithm for management of neurogenic lower urinary tract dysfunction. (UTI – urinary tract infection, PVR – post-void residual volume, CISC – clean intermittent self catheterization).

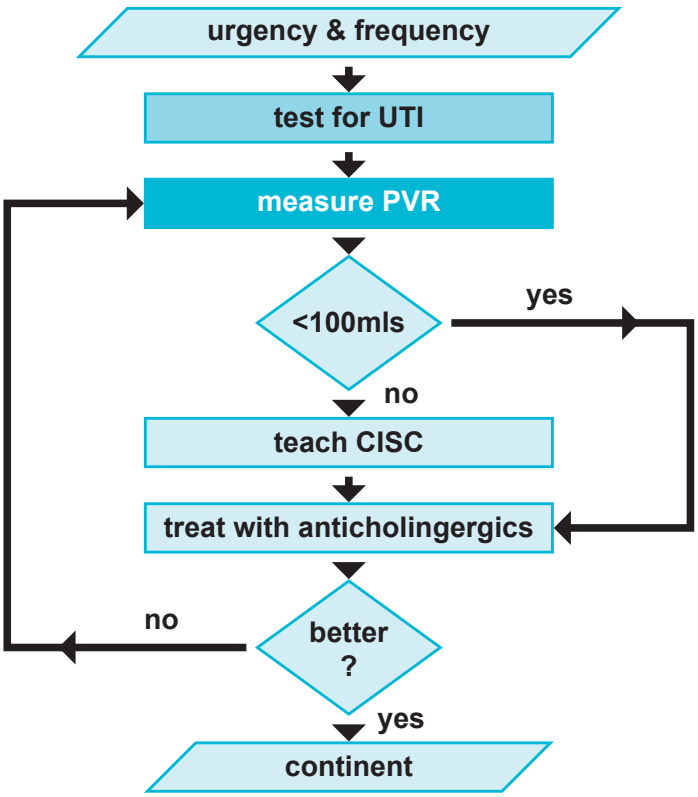

Table 10: Antimuscarinic medications that can be used to manage overactive bladder symptoms

(reproduced from treatment guidelines for bladder dysfunction in multiple sclerosis) [93]

Generic name	Trade Name	Dose (mg)	Frequency
Tolterodine tartrate	Detrusitol	2	bd
Tolterodine tartrate	Detrusitol XL	4	od
Oxybutynin chloride	Ditropan	2.5 - 5	bd - qds
Oxybutynin chloride XL	Lyrinel XL	5 - 30	od
Propiverine hydrochloride	Detrunorm	15	od - qds
Darifenacin	Emselex	7.5 - 15	od
Solifenacin	Vesicare	5 - 10	od
Fesoterodine	Toviaz	4-8	od

Legend: od – once daily; bd – twice daily; tds – three times daily; qds – four times daily, XL – extended life.

In addition to the medications listed in table 10, trospium could also be considered as a treatment option, at a dosage of 20mg bd (with reduced dosage in cases of renal impairment) - *see treatment section above*.

Recommendations	Grade
1. In primary care, test for urinary tract infection and measure PVR (to exclude common causes of urgency and frequency). If these are normal, check for other common causes such as prostate enlargement.	GPP
2. Practical advice should be given about cutting down caffeine, fizzy drinks and alcohol, as well as information about timed voiding and bladder retraining whenever appropriate. The fluid intake should be individualized; a fluid intake of between 1 to 2 litres a day is recommended (taking into consideration possible concurrent cardiac issues).	GPP
3. Advice on pelvic floor exercises should be given as it may be helpful especially when symptoms are mild.	GPP
4. Most individuals with overactive bladder symptoms will require antimuscarinic medications *(table 10).*	GPP
5. In patients with cardiac complications and/or cognitive problems caution is advised when using antimuscarinic medications.	GPP
6. In patients with cognitive problems, more selectively-acting antimuscarinic medications, such as trospium chloride or darifenacin should be considered.	GPP
7. In some instances referral to an urologist is recommended eg: in cases of haematuria or suspicion of concomitant urological condition.	GPP

4.1.h. Gastroenterological problems

Bowel complications can be present in ataxia as in other chronic conditions. For example, this is well described in Friedreich's ataxia[63]. Whilst most commonly presenting as constipation, faecal urgency and incontinence also occur and represent a significant intrusion to quality of life[94]. Development of faecal urgency and incontinence may be contributed to by other medications, mobility difficulties, age, previous childbirth (especially if forceps deliveries or large babies) and co-existent medical conditions[95].

Constipation which does not resolve with lifestyle intervention (diet, fluid and mobility assistance) may need laxatives or suppositories. In patients with faecal soiling, the possibility of severe constipation and overflow incontinence needs to be considered. Urgency and faecal incontinence warrants specialist assessment: treatment options include loperamide, behavioral and pelvic floor directed therapies, and consideration of digital anorectal stimulation, depending on specific cause identified at such an assessment. More specific guidance can be found in the NICE guidelines for faecal incontinence in adults[95].

Recommendations	Grade
1. Suggest changes in lifestyle (eg: diet, fluid and mobility assistance) for patients with constipation, followed by the use of laxatives or suppositories.	GPP
2. Consider referral for specialist assessment if patients have urgency and faecal incontinence.	GPP

4.1.i. Sexual Dysfunction

Erectile dysfunction is common and may be the first manifestation of autonomic dysfunction in multiple system atrophy[96]. Erectile dysfunction can also occur in patients with other ataxias and discussion about sexual function should therefore be included in their consultation. Phosphodiesterase-5 inhibitors are the mainstay of treatment, eg. sildenafil, tadalafil and vardenafil. Treatment decisions should balance the needs of the person and potential side effects of medications, eg: hypotension. Caution should be exercised in patients with cardiac pathologies (eg: Friedreich's ataxia), thus a consultation with a cardiologist is advised.

Recommendations	Grade
1. Consider discussing sexual function with male patients due to the potential for erectile dysfunction.	GPP
2. Treat erectile dysfunction where appropriate with phosphodiesterase-5 inhibitors. Treatment decisions should balance the needs of the person and the potential side effect of medications eg: hypotension.	GPP
3. If patients have cardiac pathologies caution should be exercised when considering medication, and consultation with a cardiologist is recommended.	GPP

4.1.j. Swallowing and dysphagia

Dysphagia is a common problem seen amongst patients with ataxia, however, it is important for other causes to be excluded. Questions about swallowing difficulties and coughing or choking episodes when eating or drinking should be asked at every clinic appointment. Where symptoms of dysphagia exist, a referral to a speech and language therapist should be made for assessment *(see section 5.1)*. Difficulties with swallowing may result in a narrowing of the patient's diet and it is important to strike a balance between providing safe eating/swallowing advice and allowing the enjoyment of food. Significant dysphagia can ultimately result in unintentional weight loss if patients struggle to maintain an adequate caloric intake. High-calorie, nutritional supplements may be of use in these circumstances and early referral to a dietician is recommended. If calorie intake cannot be maintained despite supplements, a discussion about the possibility of a percutaneous gastronomy (PEG) should take place in order to provide a secure means of feeding. This should involve a multidisciplinary team (including a speech and language therapist, dietician and surgeon).

Recommendations	Grade
1. If patients show symptoms of dysphagia a referral to a speech and language therapist should be made *(see section 5).*	GPP
2. If there is unintentional weight loss due to dysphagia consider the use of nutritional supplements and refer to a dietician.	GPP
3. If calorie intake cannot be maintained despite supplements, discuss the possibility of a percutaneous gastronomy (PEG) to provide secure feeding.	GPP

4.1.k. Nutrition

It is important for patients with ataxia to maintain a healthy, balanced diet. There are a number of issues that arise in these patient groups that can make this difficult and it is important to discuss these with patients during clinical reviews.

Frequently, patients with ataxia can report issues with weight gain. Whilst the aetiology of this is multifactorial, many patients will report that reduced mobility and an inability to undertake regular exercise is a significant contributing factor. Excessive weight gain can lead to a vicious cycle of deteriorating mobility and it is important therefore to support patients in maintaining a steady weight or in weight management where appropriate. Where possible, facilitated exercise at a gym can be a useful adjunct to dietary measures but this may not be practicable in patients with significant mobility impairment. Diet planning can be facilitated with support from the patient's GP or community dietician.

It is important that dietary advice be tailored to the individual however there are some general recommendations that can be made. The WHO lists 5 general points that are universally applicable:

- Achieve an energy balance i.e. consume roughly the same number of calories that you burn off through exercise and exertion
- Limit energy intake from saturated to unsaturated fats
- Increase consumption of fruits and vegetables
- Limit the intake of free sugars
- Limit salt intake

Additional advice on a balance diet can be found on the NHS Choices website[97].

Specific dietary interventions include the following:

Gluten Ataxia

This is a specific type of ataxia caused by a sensitivity to gluten and there is evidence that a strict gluten-free diet can improve ataxia in these patients *(see section 4.2.a).*

Vitamin E deficiency

Vitamin E deficiency can lead to or exacerbate ataxia. It can be seen as a result of malabsorption (eg: in coeliac disease) or be nutritional, most commonly seen in patients with ataxia due to alcohol. Treatment is with oral vitamin E (100mg daily). There is also a specific inherited form called Ataxia with Vitamin E

deficiency in which a higher dose of vitamin E supplementation is required *(see section 4.2.b).* Treatment can be difficult in malabsorption syndromes and the underlying causes should be treated where possible. There is no evidence that vitamin E supplementation is effective in ataxia patients with a serum vitamin E level in the normal range.

Ataxia with Coenzyme Q10 deficiency

Ataxia with Coenzyme Q10 deficiency is another rare recessively inherited ataxia which can be caused by mutations in a number of genes involved in the biosynthesis of ubiquinone (CoQ10). CoQ10 levels can be measured on muscle biopsy and on blood samples and if they are significantly reduced then supplementation with CoQ10 can be an effective treatment *(see section 4.2.d).*

For more information on specific dietary interventions see section 4.2 on treatable ataxias. Further dietary advice is also found within other subsections of 4.1, as some symptoms require dietary changes.

4.1.I. Sialorrhea (excess salivation)

Excess salivation is a common and distressing problem for patients with ataxia, especially in later stages. Saliva that remains pooled in the mouth may become an aspiration source and thus could result in choking and pneumonia[98]. On a psychological level it is very distressing to patients who find themselves dribbling and is often quoted by patients as a major factor in withdrawing from social situations[98]. Patients sometimes get skin lesions from prolonged dribbling at night when they are lying on their side and this can also be embarrassing and distressing for them.

Sometimes patients experience a thick secretion rather than excessive production of saliva. It is important to evaluate the type of secretion as that informs the treatment *(see table 11)*. Sialorrhea is normally associated with dysphagia, thus a referral to a speech and language therapist is recommended for assessment of swallow *(see section 5.1).*

Table 11: Summary of treatments to be considered

(listed in the order that the treatments are often trialed)

Excessive thin secretion	Thick secretion
Postural changes	Ensure adequate hydration (2L/day)
Support collars	Avoid mucus thickening foods (dairy)
Natural products: sage (capsules, tea tinctures), dark grape juice	Avoid caffeinated drinks and alcohol
	Suck sweets to stimulate saliva production
	Steam inhalation/ humidifiers / nebulisers
Medications:	Pineapple puree/ juice
Transdermal hyoscine (scopaderm)	
Amitriptyline	
Atropine 0.5% drops sublingual	
Benztropine	
Glycopyrrolate	
Benzhexol	
Botulinum toxin injections	
Manually assisted cough technique	

The table is adapted from Bavikatte et al 2012[99]

Recommendations	Grade
1. Sialorrhea is normally associated with dysphagia, thus a referral to a speech and language therapist is recommended for assessment of swallow.	GPP
2. Treat sialorrhea and thick secretions according to the treatment pathway in table 11.	GPP

4.1.m. Audiology and Hearing

Problems

Hearing loss is a known symptom of the progressive ataxias. It is common in Friedreich's ataxia[100] and those ataxias involving peripheral neuropathies. It is therefore important that when an ataxia is diagnosed and there is a hearing problem that the patient is referred for Audiology testing, in order to establish the nature of the hearing loss, establish hearing thresholds and functional abilities (i.e. speech perception). Routine monitoring should be put in place.

Assessment

The assessment of the ataxic patient can be challenging, and it is important to consider the possibility of Auditory Neuropathy Spectrum Disorder (ANSD), which is a known manifestation in conditions such as Friedreich's ataxia[101] and has recently been shown to be a feature of the spinocerebellar ataxias too[102].

A typical assessment should include pure tone audiometry using both air conduction and bone conduction, tympanometry, otoacoustic emissions and acoustic reflex testing. Most importantly, in this clinical population, functional assessments such as speech testing, both in quiet and in noise, should be undertaken[103].

Discrepancy between hearing thresholds and speech perception is indicative of ANSD and objective testing such as auditory brainstem response, and in case the otoacoustic emissions are absent, cochlear microphonic are necessary to confirm the diagnosis of ANSD[104]. Cortical auditory evoked potentials testing is also recommended. Referral to otorhinolaryngology should be made where appropriate.

Management

In case of ANSD, hearing aids are often unsuitable[105], but a hearing aid trial should be considered. Other assistive devices, such as FM hearing devices, have been shown to be of benefit in Friedreich's ataxia[100,106] and spinocerebellar ataxias[102] and results of further trials are awaited. At the time of writing these devices are not available routinely in the UK although they are in other countries eg: in Australia people with ataxia are offered FM hearing devices, such as the *Roger pen* system, as part of the National Health service. Dexterity may be an issue, and therefore appropriate devices should be chosen.

For those who do not achieve any benefit from appropriate aiding with hearing aids, it is appropriate to refer for further assessment to the local cochlear implant centre. Mild improvement was seen in a small study of non-ataxic patients with ANSD with a cochlear implant even if the hearing thresholds do not meet NICE TAG 166 criteria (profound at 2 and 4 kHz bilaterally). [107]

Where possible, referral to hearing therapist or speech and language therapist should be made upon diagnosis of a hearing loss *(See also section 5.1)*. Hearing therapists can offer guidance in communication tactics, hearing aid management and advice on assistive listening devices to help both at work and in the home.

Recommendations	Grade
1. If a patient is experiencing hearing problems refer to Audiology services for a battery of hearing tests.	GPP
2. A hearing aid trial should be considered although it is often not suitable for this patient population.	GPP
3. A trial with an FM hearing device is recommended in cases of ataxia with ANSD.	C
4. Refer to hearing therapist or speech and language therapist for guidance on communication tactics.	GPP
5. For those who do not achieve any benefit from hearing aids, consider to a cochlear implant centre.	D
6. In specific cases (eg: ADNS) a referral to a neuro-otologist should be considered.	GPP

4.1.n. Eye symptoms

Many of the ataxias are associated with eyes symptoms such as oscillopsia due to nystagmus, diplopia or reduced vision. A referral to a neuro-ophthalmologist is recommended if eye symptoms are present.

Nystagmus

Nystagmus can be a symptom experienced by patients with ataxias and it can sometimes also cause oscillopsia (a disabling subjective sensation of movement of the visual world). These involuntary eye movements do not require treatment if patients are not affected, however therapy should be considered when visual disability is present. There have been a few randomised placebo-controlled treatment trials; these have shown the efficacy of gabapentin in treating symptomatic pendular or gaze-evoked jerk nystagmus[108,109] and sometimes downbeat nystagmus[109]. Downbeat nystagmus can also be treated with 3,4-diaminopyridine and baclofen[109,110]. A number of other studies (non-randomised controlled trials) have shown the efficacy of other medications such as clonazepam and valproate for pendular nystagmus and of 4-aminopyridine for downbeat nystagmus[111].Orbital injections of botulinum toxin to weaken the extraocular muscles have also been reported to be beneficial in some patients, although there are limitations to this approach (discussed in a review in 2002)[112].

Diplopia

Diplopia (seeing ‘double’) is not a common symptom associated with the ataxias but may occur. The images are usually separated horizontally (rather than vertically), as a result of a manifest exo - or eso deviation of the visual axes, and is concomitant in all directions of gaze. Single vision can be restored optically using prisms, so eye muscle surgery is rarely necessary.

Visual impairment

Degeneration within the retina or optic nerves is well recognised in association with several of the ataxias. For example, approximately half of patients with Friedreich’s ataxia have clinically apparent optic atrophy, although patients may not be aware they have subnormal vision and severe visual loss is uncommon[113,114]. Progressive deterioration in visual acuity is often seen in patients with SCA7 because of bilateral (and usually symmetrical) maculopathy.

At this stage there is still no known treatment either to prevent or to treat the retinal or optic nerve manifestations of ataxic disorders. However, patients can benefit from a wide range of low vision aids as well as having their visual disability registered.

Recommendations	Grade
1. A referral to a neuro-ophthalmologist is recommended if ataxia patients have any eye symptoms.	GPP
2. If disabling nystagmus or oscillopsia is present treatment is recommended, often with either gabapentin or baclofen.	B
3. Refer to an optometrist or neuro-ophthalmologist for restoration of single vision with prisms in cases of diplopia.	GPP
4. Patients with visual impairment should be offered low vision aids and the possibility of having their visual disability registered.	GPP

4.1.o. Cognition

There is emerging research to suggest that patients with ataxia are at risk of cognitive impairment, as with most patients with other neurological conditions. However, relatively little research has been conducted so far in trying to determine the specific cognitive impairments in ataxia. Ataxia is a symptom of a number of conditions, and it may be possible that the different genetic mutations as well as the extent of degeneration underlying the different conditions may lead to different patterns of deficits.

Research in Friedreich's ataxia and various different types of spinocerebellar ataxia suggest some impairments in executive skills[15,115–127], attention[115–117,126,127], memory[119,122–124,126,128,129], speed of information processing[120,121,124,127,128,130,131] and, possibly only in some types of spinocerebellar ataxia, social cognition[115,116,132]. In this instance, social cognition refers both to 'Theory of Mind' skills, which is the ability to attribute mental states to others and understand that the beliefs and knowledge of others may be different from your own[115,116], as well as to the ability to recognize different emotions in others[133]. There is a lack of homogeneity within the conditions; thus, patients with certain subtypes of spinocerebellar ataxia may be more impaired cognitively[115,116].

The delineation of a patient's cognitive strengths and weaknesses is important for the management of their condition, and forms the basis for which recommendations of rehabilitation strategies can be made. Even mild impairments can have a significant impact upon a patient's daily function at home and at work, and thus patients can benefit from cognitive rehabilitation, as demonstrated in patients with Friedreich's ataxia[132].

To identify cognitive symptoms one needs to administer a detailed and comprehensive neuropsychological evaluation. Thus, referral to a Neuropsychology Department is recommended. Neuropsychological evaluation can not only screen for cognitive impairment occurring in the different types of ataxia, but can also monitor the progression of any such impairment over time. One study has tracked the longitudinal course of cognitive impairment in patients with ataxia[121], but there is generally lack of research in this area. Characterising the course of the impairment is of paramount importance to inform the likely prognosis.

Recommendations	Grade
1. When cognitive impairment is suspected (even if mild) referral to a Neuropsychology department is recommended.	GPP
2. Cognitive rehabilitation is recommended for those patients with cognitive impairment.	C
3. Characterising the course of the cognitive impairment is advisable in order to inform the likely prognosis.	GPP

4.1.p. Depression and other psychiatric symptoms

Patients with ataxia, as those with other neurological conditions, are susceptible to depression[134,135]. Practical and effective treatment of symptoms of depression can be carried out in primary care, without the need for specialist psychiatric input. In addition to pharmacological interventions, psychological and psychosocial interventions including counselling and cognitive behavioural therapy (CBT) can offer significant benefits. In some cases, more input from secondary level psychiatric services may be indicated, especially if depression is severe, there is a significant risk of self harm or the depression has not responded to an adequate course of antidepressant medication. Although there is a lack of evidence for treatment and management of depression specifically in patients with ataxia, NICE have produced Guidelines for the treatment and management of depression in adults with a chronic physical disorder including neurological disorders, and it is recommended these should be followed[136].

Dementia or psychosis are less common in patients with ataxia. These can normally be managed in primary care. However, depending on severity and risk the patient may require input from specialist psychiatric services. Again there is a lack of evidence into the treatment and management of these symptoms specifically in patients with ataxia.

Recommendations	Grade
1. In many cases depression can be treated in primary care using medications, counselling or cognitive behavioural therapy.	GPP
2. In more severe or complex cases of depression and other psychiatric symptoms a referral to a psychiatrist/neuropsychiatrist in secondary care is recommended.	GPP
3. For adults consult NICE Guidelines for the treatment of depression in patients with a chronic physical disorder[136].	GPP

4.1.q. Inherited episodic ataxias

Some patients experience ‘episodes’ of ataxia and may be diagnosed with an inherited episodic ataxia. Episodic ataxia type 1 and 2 (EA1 and EA2 respectively) are the best characterized genetically and the most well-known, but other rarer forms (constituting EA3 to EA8) have been identified in single kindreds and associated with mutations in known genes and/or linked to potential genetic loci[137].

The most common form is EA2 in which patients present with attacks of cerebellar dysfunction lasting hours to several days, and can be associated with other neurological features such as hemiplegic migraine, migraine with or without aura and epilepsy, all of which merit treatment in their own right. A second stage may develop later in the life in which the condition becomes progressive[138]. Triggers should be identified and avoided, including stress, caffeine and alcohol consumption. Attacks can be precipitated by exertion. However, regular but modest exercise should be encouraged[138].

Acetazolamide, a sulfa-containing carbonic-anhydrase inhibitor, is used as a first line drug for the prevention or reduction in frequency of episodic ataxia attacks. It has been used effectively in clinical practice for many years, but because of the rarity of the condition there have been no randomized-controlled trials, and its mechanism of action is unknown. Long-term use of acetazolamide is associated with dose-related side effects, such as renal calculi, gastrointestinal symptoms, paraesthesiae, fasciculations and fatigue.

Following an international consensus meeting GA is now accepted as one of the three commonest manifestations of autoimmunity to gluten ingestion which are: Coeliac disease (also known as gluten sensitive enteropathy), Dermatitis Herpetiformis and GA[144]. The term Gluten-Related Disorders has been proposed to encompass all these entities.

Whilst antigliadin antibodies can be used in aiding the diagnosis of GA, these are found in up to 12% of healthy population[145]. Therefore it is important not to rely solely on testing for antigliadin antibodies. More specific antibodies have been identified and in particular antibodies against TG6 appear to be very promising in the diagnosis of GA[146,147]. This test is not yet widely available. However, it should be considered if gluten ataxia is suspected *(see Diagnosis section 2)*. Neurologists are often faced with weighing up the options of whether or not to recommend a gluten-free diet in the context of a patient with idiopathic sporadic ataxia (when all other causes excluded) and positive antigliadin antibodies in the absence of enteropathy.

For those patients with gluten ataxia who also have an enteropathy, the recommendation is that they should go on a gluten-free diet without delay. For those patients with ataxia and no enteropathy, but who have serological evidence of gluten sensitivity, it is advisable to recommend a gluten-free diet with dietetic advice and close monitoring.

The trial mentioned above did demonstrate that even those patients without enteropathy benefited from a gluten-free diet. Patients should however be made to understand that such benefit can only be seen with strict adherence to the diet, with evidence of elimination of the antibodies (that need to be tested on a six-monthly basis). Any improvement in ataxia or stabilisation of symptoms usually manifests within a year on a strict diet.

In some patients where there is evidence of cerebellar atrophy the expected benefit will be in the form of stabilisation rather than improvement. Monitoring can take the form of the 'Scale for the Assessment and Rating of Ataxia' *(see Research section 7)*[148].

Some patients have shown benefit from the use of intravenous immunoglobulin therapy, however this has only been shown in case reports or small trials[149].

Recommendations	Grade
1. It is recommended that patients with idiopathic cerebellar ataxia are tested for gluten sensitivity.	GPP
2. Consider testing for antibodies against TG6 as a more sensitive test for gluten ataxia.	C
3. Ataxia patients with or without enteropathy who have serological evidence of gluten sensitivity should be advised to start a gluten-free diet without delay.	C
4. Patients who are starting a gluten-free diet should be advised about strict adherence and given dietetic advice.	GPP
5. Close monitoring is recommended with six-monthly testing to ensure for elimination of antigliadin antibodies.	GPP

4.2.b. Ataxia with Vitamin E deficiency

Ataxia with Vitamin E deficiency (AVED) is a rare recessively inherited form of ataxia caused by mutations in the TTPA gene that often results in similar symptoms to Friedreich's ataxia. A genetic test can confirm the diagnosis. In these patients, serum vitamin E levels are significantly reduced. Vitamin E

deficiency can also be caused by malabsorption of fat-soluble vitamins, as can be seen in a syndrome called abetalipoproteinemia, which also has ataxia as one of its symptoms.

Diagnosis of Vitamin E deficiency needs to be made in the context of serum lipid levels, also known as lipid adjusted vitamin E, as estimation of free levels of vitamin E is not reliable and can be misleading (normal range for lipid adjusted vitamin E is 3.9-5.9 units but may vary between labs). Patients diagnosed with Ataxia due to Vitamin E deficiency should be given vitamin E supplements. The daily dose of vitamin E required is much higher than what is used for other deficiency states (doses range from 800mg/day to 1500mg/day or 40mg/Kg per day in children)[150]. Treatment of presymptomatic children can prevent the development of ataxia. Studies have shown treatment leads to cessation of progression of neurological symptoms and mild improvement in certain patients, especially in the early stages of the disease[150]. Abetalipoproteinemia can also be treated with vitamin E supplements[151].

Diagnosis of this type of ataxia is very important so that early treatment with supplements can commence *(see Diagnosis section 2).*

Recommendations	Grade
1. Patients diagnosed with ataxia with vitamin E deficiency or abetalipoproteinemia should be treated with Vitamin E supplements.	C

4.2.c. Ataxia with Vitamin B12 deficiency

Patients who are deficient in Vitamin B12 can sometimes have similar symptoms to Freidreich's ataxia, hence it is important to test Vitamin B12 levels *(see Diagnosis section 2)*. This condition can be treated with Vitamin B12 supplements[152]. If a patient is diagnosed with ataxia with Vitamin B12 deficiency they should be referred to a haemotologist, who will administer treatment. Depending on severity of symptoms treatment can be parenteral or oral with cyanocobalamin or hydroxocobalamin.

Recommendations	Grade
1. Patients diagnosed with ataxia and Vitamin B12 deficiency should be treated with Vitamin B12.	GPP

4.2.d. Ataxia with CoQ10 (ubiquinone) deficiency

Ataxia with primary Coenzyme Q10 (CoQ10) deficiency is an autosomal recessive condition associated with mutations in the *ADCK3* gene [153](also known as the *CABC1* gene[154]). The level of CoQ10 in skeletal muscle in these patients is usually below the normal range (variable between laboratories). Classification as ARCA2 (Autosomal Recessive Cerebellar Ataxia-2) has been suggested[153]. Originally characterised by childhood onset ataxia and exercise intolerance[155], recently patients with adult onset ataxia have also been identified[156]. Severity is variable; some individuals develop seizures and mild mental impairment.

Patients with this form of ataxia may improve with CoQ10 supplementation, hence the importance of early diagnosis[155–157]. The exact dose and form of supplementation is not clear to date. However,

a high dose of CoQ10 supplementation (500-1000 mg/day) is suggested in these patients. Although not all patients respond, given it is a potentially treatable condition, it is advisable to treat with CoQ10 supplementation.

Some patients with AOA1 (*APTX* gene mutations) and mutations in the *ANO10* gene have also responded to CoQ10 therapy (200-500 mg/day)[158,159]. In these forms of ataxia the CoQ10 deficiency is secondary, and not due to a defect in its biosynthesis.

Testing of CoQ10 deficiency can be performed on skeletal muscle samples or on blood mononuclear cells[23]. *For details on testing see Diagnosis section 2.*

Recommendations	Grade
1. Patients diagnosed with ataxia with CoQ10 deficiency should be treated with CoQ10 supplements.	D
2. Consider treatment of patients diagnosed with AOA1 with CoQ10 supplementation.	D

4.2.e. Cerebrotendinous xanthomatosis

Cerebrotendinous xanthomatosis is a sterol storage disorder characterized by the accumulation of cholestanol and cholesterol in tendons, the central nervous system and the lenses. It is an autosomal recessive condition that can affect children and adults. Chronic diarrhoea from infancy may be the earliest clinical manifestation. In approximately 75% of affected individuals, cataracts are the first finding, often appearing in the first decade of life[160]. Diagnosis is by clinical and biochemical testing; a genetic test is also available *(also see Diagnosis section 2)*.

Treatment with chenodeoxycholic acid may result in stabilisation or partial reversal of the neurological symptoms in some patients[160]. Early diagnosis and initiation of therapy is important because some patients with established cholestanol deposits in the brain continue to deteriorate despite treatments[160,161].

Recommendations	Grade
1. Prompt diagnosis of cerebrotendinous xanthomatosis is advised in order to initiate treatment.	GPP
2. If cerebrotendinous xanthomatosis is diagnosed treatment with chenodeoxycholic acid is recommended.	B

4.2.f. Niemann-Pick type C (NPC)

NPC is a rare multi-system disease caused by accumulation of cholesterol and glycosphingolipids in the brain and other organs and ataxia may be a presenting symptom. A mean delay from onset to diagnosis of 6 years reflects its varied presentation. However, with the emergence of treatment that may slow the neurodegenerative aspects, international guidelines were updated in 2012 summarising presentation, diagnosis and management[162].

Presentation

Severe cases present in infancy with cholestatic jaundice or acute respiratory failure. However, a more 'typical' presentation is in the second or third decade with one or more of:

- visceral signs that are readily missed at the bedside but frequently present on imaging (hepatomegaly in >50% and/or splenomegaly >90%)
- psychiatric disturbance (depression, acute psychosis or cognitive changes)
- a neurological syndrome that may include ataxia (limb and gait ataxia, dysarthria, dysphagia), an eye movement disorder (classically a vertical supranuclear gaze palsy), dystonia, myoclonus, epilepsy, cataplexy, or cognitive decline.

Cases have been reported with onset as late as mid sixth decade or the neurological features are missed or erroneously ascribed to side effects of psychotropic medication. A tool, the NP-C Suspicion index, has been developed to help clinicians diagnose this treatable condition[162] *(see www.npc-si.com)*.

Investigation

Diagnosis has been is hampered by the lack of a simple, reliable test. Chitotriosidase (frequently available as part of white cell enzymes panel) may be mildly elevated. MR brain scans are normal or non-specifically abnormal with cortical or cerebellar atrophy mirroring the clinical picture. Tissue diagnosis of bone marrow biopsy (foam cells) is unreliable, as is the gold standard of skin biopsy, culture and filipin staining–that can be normal in variant cases which are more likely to present later in adulthood.

Genetic testing of the two causative genes (NPC1 in 95% of cases and NPC2 in 5% of cases) provides a more definitive diagnosis. In addition, measurement of plasma oxysterols shows promise as an inexpensive screening tool[163]. This diagnostic test is now available for the diagnosis of NPC at the Willink Biochemical Genetics Laboratory (Central Manchester University Hospitals NHS FT) and also the laboratory at Great Ormond Street Hospital.

Management

Symptomatic treatments for the psychiatric manifestations (antidepressants and/or antipsychotic medication) and the neurodegenerative aspects (anticonvulsants, gastrostomy feeding) have historically been the mainstay. However, it is now known that administration of Miglustat has been shown in studies to reduce the accumulation of glycosphingolipids and may slow the neuropsychological decline as well as stabilizing the progression of other neurological manifestations[164–168]. It is the approved disease-modifying treatment for the treatment of paediatric and adult NPC and is available in the UK via Specialist Centres *(see below for a list).*

Details of Specialist NPC Centres:

Paediatric Niemann-Pick Disease patients:

- Great Ormond Street Hospital for Children NHS Foundation Trust
- Central Manchester University Hospitals NHS Foundation Trust
- Birmingham Children's Hospital NHS Foundation Trust

Adult Niemann-Pick Disease patients:

- Salford Royal NHS Foundation Trust
- University Hospitals Birmingham NHS Foundation Trust
- University College London Hospitals NHS Foundation Trust
- Royal Free Hampstead NHS Trust

At the time of writing arrangements are in place for patients from Scotland, Wales and Northern Ireland to be seen within the designated Centres in England for diagnosis and clinical management. Decisions on funding treatment/access remain with the patient's local health authority.

Recommendations	Grade
1. If NPC is suspected based on clinical investigations, perform diagnostic tests described above. Early diagnosis is important as it is a treatable condition.	GPP
2. If NPC is diagnosed refer promptly to a Specialist Centre for treatment and management.	GPP
3. Treatment with Miglustat is recommended in both adult and paediatric cases and is available in Specialist Centres.	B

4.3. Treatable causes in children

Some of the treatable conditions mentioned above are seen in children, including:

- CoQ10 (ubiquinone) deficiency; (the most common presentation of this is in children)
- Episodic ataxia type 2 (intermittent ataxia)
- Vitamin E deficiency
- Cerebrotendinous xanthomatosis.

In addition, the following conditions are also treatable causes of childhood ataxia. In some cases the ataxia is an epiphenomenon of another condition, so brief summaries are provided and further sources of information are included.

4.3.a. Glucose transporter 1 deficiency (often intermittent) (Glut-1 DS)

Impaired glucose transport across the blood-brain barrier results in Glut-1 deficiency syndrome, characterised by infantile seizures, developmental delay, acquired microcephaly, hypoglycorrhachia[169,170]. A wider phenotype is now recognized, including ataxia, spasticity and paroxysmal movement disorders which can be triggered by exertion or fasting. A ketogenic diet has been found to be effective treatment for epilepsy, but may not help gait problems[169,171] *(For further information see www.ncbi.nlm.nih.gov/omim; OMIM number 606777; also contact CLIMB (www.climb.org.uk)*

Recommendations	Grade
1. If Glut-1 DS is diagnosed treat with a ketogenic diet.	D

4.3.b. Hypobetalipoproteinemia

Hypobetalipoproteinemia is a rare disorder characterized by low levels of fats, beta-lipoproteins and cholesterol[172]. Familial hypobetalipoproteinemia can be severe with early onset (abetalipoproteinemia/homozygous familial hypobetalipoproteinemia), or benign (benign familial hypobetalipoproteinemia). Severe early familial hypobetalipoproteinemia is often associated with growth delay, diarrhoea with steatorrhea, and fat malabsorption. Spastic ataxia, atypical retinitis pigmentosa, acanthocytosis, a low level of liposoluble vitamins (A, E, K), major cytolysis, and even cirrhosis can occur[173].

Recent guidelines on the diagnosis and management of this treatable disorder have been published[172] *(For further information see www.orpha.net ORPHA426; also contact CLIMB www.climb.org.uk.)* Management of the moderate form includes reduction of the proportion of fat in the patient's diet and vitamin E supplementation.

Recommendations	Grade
1. Consider management of the moderate form of hypobetalipoproteinemia by reducing the proportion of fat in the patient's diet and vitamin E supplementation.	GPP

4.3.c. Hartnup disease

Intermittent ataxia, photosensitive rash, psychotic behaviour and intellectual disability are possible features of this condition.

Patients benefit from a high-protein diet, sunlight protection, and avoidance of photosensitizing drugs[174]. Treatment includes nicotinamide supplements; some patients may respond to a tryptophan-rich diet[174].

(For further information see www.ncbi.nlm.nih.gov/omim; OMIM number 34500. Also contact CLIMB www.climb.org.uk)

Recommendations	Grade
1. Consider treating Hartnup disease with nicotinamide or tryptophan-rich diet, and advise patients on a high protein diet, sunlight protection and avoidance of photosensitizing drugs.	GPP

4.3.d. Biotinidase deficiency

This is a metabolic disorder characterised primarily by cutaneous and neurologic abnormalities. This condition should be treated with biotin[175,176].

(For further information see www.ncbi.nlm.nih.gov/omim; OMIM number 253260. Also contact CLIMB www.climb.org.uk)

Recommendations	Grade
1. Treat patients diagnosed with biotinidase deficiency with biotin.	GPP

4.3.e. Pyruvate dehydrogenase deficiency

This is a metabolic disorder which can cause ataxia in some affected males. Treatment is generally aimed at stimulating the PDH complex or providing an alternative energy source for the brain. It can respond to treatment with thiamine, carnitine, and lipoic acid. A ketogenic diet may be indicated especially for those presenting with a dystonic disorder. Dichloroacetate has been used, but significant side effects, such as peripheral neuropathy, may limit effectiveness[177].

(For further information see www.orpha.net ORPHA765 or contact CLIMB www.climb.org.uk)

Recommendations	Grade
1. Consider treatment with thiamine, carnitine or lipoic acid and advising on a ketogenic diet.	GPP

4.3.f. Structural disorders

If ataxia is caused by structural disorders these are usually surgically treatable. Brain tumours can cause ataxia but usually other symptoms such as headache, vomiting and personality change are present. *(For more information see www.directorycancer.com/brain-tumours.)* Hydrocephalus can have similar symptoms and can be due to a wide variety of causes.

(For more information contact the Association for Spina Bifida www.asbah.org). Arnold-Chiari malformation is a congenital malformation at the back of the brain. *(For more information contact the Association for Spina Bifida www.asbah.org)*

Recommendations	Grade
1. If ataxia is due to structural causes a referral for surgical treatment may be recommended.	GPP

4.3.g. Acute encephalopathies

Intoxication, either from recreational or medically prescribed drugs, can cause acute or intermittent ataxia, but is not always immediately recognised.

For more information about metabolic encephalopathies, such as branched chain amino-acidurias, contact CLIMB (www.climb.org.uk).

4.3.h. Non-convulsive status epilepticus / other epilepsies

Can rarely present as intermittent ataxia (combined with altered consciousness) but seen more commonly in the context of a known epilepsy syndrome[178].

For more information contact Epilepsy Action (www.epilepsy.org.uk).

4.3.i. Sensory ataxias

Refsum syndrome and chronic inflammatory demyelinating neuropathy (CIDP) are conditions affecting the nerves. Refsum syndrome also involves the cerebellum and can sometimes result in ataxia.

For more information see the National Institute of Neurological Disorders and Stroke (www.ninds.nih.gov) and contact CLIMB (www.climb.org.uk)[179].

5. Allied health professional interventions

This section is aimed at providing information to physiotherapists, speech and language therapists and occupational therapists to help manage their ataxia patients. In depth reviews are provided, as this information is not available elsewhere. Medical professionals may be interested in the recommendation tables at the end of each section.

A full range of therapies should be available for patients with ataxia. These should include: physiotherapy, speech and language therapy and occupational therapy.

Recommendations	Grade
1. Referral to a full range of therapies including speech and language therapy, physiotherapy and occupational therapy should be made available to patients with ataxia.	GPP

5.1. Speech and language therapy (SLT)

The progressive ataxias may affect communication and/or swallowing function. The most obvious communication difficulty encountered is that of dysarthria which is a motor speech disorder resulting in altered voice quality, speech clarity, naturalness and intelligibility. Communication may also be affected in cases where there is an associated cognitive impairment impacting on language processing. In addition, any difficulties with executive functions may result in changes in communication behaviour.

Difficulty in swallowing is a common symptom of ataxia, particularly as the disease advances. Depending on the pathophysiology of the disease, swallow dysfunction (dysphagia) may occur at the oral, pharyngeal and/ or oesophageal stage of swallowing. For example, when there is cerebellar involvement, dysphagia may be characterised by reduced coordination of the oro-pharyngeal muscles involved in swallowing food and drink.

a. Communication problems

General Assessment

SLTs undertake a comprehensive assessment of each patient's communication in the context of their life roles and wishes. Assessment may include perceptual and objective measures of motor speech function and cognitive linguistic functions. General guidance on speech assessment can be accessed through textbooks on motor speech disorders, as well as the clinical guidelines published by the Royal College of Speech and Language Therapists (www.rcslt.org). Cognitive linguistic problems can be screened through verbal fluency tasks.

It is also highly important to consider the impact of communication difficulties on the individual's participation in activities of daily living and life roles. Obtaining the views of the family and/ or carers where appropriate is also recommended. Management may be targeted at the level of impairment, activity limitation or participation restriction, or any combination of these, based on the ICF framework[180]. A wide range of impact and quality of life assessments that have been developed for other patient groups, are also suitable for people with ataxia.

i. Speech problems (dysarthria)

Overview

Dysarthria is a common symptom of the progressive ataxias. The main features vary, and may include any, or a combination of articulatory imprecision, excess and equal stress, harsh and/or tremulous voice quality, and slowed speech rate[181–183]. Ataxic dysarthria appears to be related to a disturbance in the neural mechanisms that underlie the coordination, temporal regulation, and quasi-automatic control of respiratory, phonatory, and articulatory movements for speech[184]. Some researchers view ataxic dysarthria as reflecting a global impairment of the respiratory, laryngeal, and articulatory subsystems of speech, although individual variations may be seen in the relative severity of these impairments according to the type of ataxia and disease duration[185,186].

Deterioration in dysarthria in the spinocerebellar ataxias (SCAs) tends to be slow (eg in one study deterioration was observed over a period of three years.)[181] Furthermore, patients with early disease onset (before age 24) are reported to have more deterioration in voice quality as compared to patients with late disease onset (after age 43).[181] In addition to ataxic dysarthria, patients may also present with features of spastic, bulbar or flaccid dysarthria reflecting a more diffuse pathophysiology. Features of spastic dysarthria have been noted in studies, including perceptions of a strained-strangled voice quality as part of the presentation[181,187]. It should be noted that the occurrence of symptoms other than those associated with an ataxia is variable, both across individuals as well as disease progression[188].

Changes in communication behaviour can occur at any point, and research into a range of neurological speech disorders suggest that patients' perceptions of their speech impairment is not necessarily related to its severity as assessed by the SLT. Reports of patients feeling embarrassed about speaking, having difficulty talking on the telephone and having reduced confidence in communication leading to social isolation are commonly encountered in clinical practice[189].

Assessment

There are no specific assessment procedures for ataxic dysarthria, instead, clinicians need to establish a comprehensive picture of motor speech control and function through a range of structured and unstructured tasks (oromotor performance, single word assessment, connected speech assessment). Segmental as well as suprasegmental aspects of speech need to be considered, and particular attention should be paid to performance variations across speech tasks associated with different cognitive and motor demands as patients can show significant differences in severity and nature of impairment across such tasks.

Management

A recent Cochrane review of treatment of ataxic dysarthria found no controlled behavioural treatment studies specific to ataxic dysarthria. A number of pharmaceutical studies performed showed little effect on speech performance[190]. In the absence of evidence based guidance on the most effective treatment, the clinician will need to devise individualised treatment programmes based on the findings of a comprehensive assessment. A programme may target the presenting speech impairment, as well as issues relating to the patient's activity and/or participation[180]. Previous studies of therapy for ataxic dysarthria have shown only modest improvements in speech intelligibility when targeting individual speech parameters, such as respiratory support, speech rate, stress placement and clarity of articulation in isolation[182,191].

A study reported short and long-term improvement in phonatory and articulatory functions, speech intelligibility, and overall communication and job related activity following an intensive course of Lee Silverman Voice Treatment (LSVT) in a single case study of cerebellar dysarthria resulting from thiamine deficiency[184]. In addition, positive outcomes were reported for a combination of LSVT and gradually

increasing utterance length and complexity in a case of ataxic dysarthria following brain injury from boxing[192]. The LSVT programme focuses on training patients to maximise their phonatory efficiency and increase articulatory effort by speaking loud[193]. In the absence of properly controlled evidence that LSVT is suitable for administration to degenerative ataxias, care should be taken that no adverse effects are introduced through its application.

As alternatives to LSVT, the patient can be advised of strategies to improve intelligibility, including over-articulation (clear speech), production of shorter phrases and more frequent breath top-ups. Management may also involve assisting patients to develop increased self-monitoring of their speech quality and identification of helpful speech strategies.

When speech intelligibility levels fall below 50% or when reduced intelligibility has a significant impact on functional communication, alternative and augmentative means of communication (AAC) should be considered[194]. The SLT should discuss AAC options with each individual, their communication partners, and the multidisciplinary team. The individual's language skills, cognitive functioning, motor and perceptual skills, and communication environment are all taken into consideration. AAC can take the form of simple systems such as pen and paper or use of an alphabet chart to supplement speech. Some patients may benefit from a high technology aid such as a Lightwriter with a choice of written and/or voice output. Switch activated communication aid systems should be trialled in cases where there is severe upper-limb and truncal ataxia which cannot be adequately alleviated by appropriate seating and set up. SLTs are frequently involved in sourcing funding for AAC equipment for individual patients.

ii. Cognitive problems

Overview

There is emerging research to suggest that patients with ataxia are at risk of cognitive impairment which, in turn, may impact on communication. There is a more detailed description of cognitive impairment and ataxia in the medical interventions section of these guidelines *(see section 4.1.o)*. Altered communication associated with executive dysfunction includes difficulty in organising and planning verbal messages resulting in disrupted narrative sequences, also difficulty in generating ideas, judging and weighing options and forming inferences on information heard and read. The need for clinical prudence in being on the alert for cognitive disturbances when assessing, treating, and rehabilitating patients with cerebellar disease has been reported[195]. Speech and language therapists (SLTs) should therefore be looking for any signs of cognitive difficulties in patients with progressive ataxia that might impact on communication.

Management

Speech and language therapy management of cognitive communication difficulties will encompass education about the underlying impairments impacting on communication. The SLT will identify strategies to manage communication breakdown with the individual and their key communication partners. These strategies are practised within a supportive, therapeutic environment. Strategies include verbal and visual prompts which can be used by the individual or the communication partner in conversations to assist with topic management and turn-taking[196,197]. If an individual presents with word finding difficulties, general strategies as reported in the aphasia literature can be helpful.

iii. Hearing problems

Overview

Hearing problems are a known symptom of the progressive ataxias and can significantly impact on communication. Hearing problems including assessment, management and services available are described in more detail of these guidelines in the medical interventions section *(see section 4.1.m)*.

Management

Management of the hearing difficulties associated with people with ataxia is challenging. The provision of conventional hearing aids (which are designed to make sounds louder, rather than make signals clearer), tend not to be useful. Provision of communication training including the use of listening strategies and lip-reading may be helpful in optimising understanding as well as increasing awareness of the importance of quiet listening conditions. Radio-frequency FM listening devices have been reported to improve signal to noise ratio in some patients *(see Hearing section 4.1m)*. SLTs are best placed to advise patients on communication strategies. Additional support is available from hearing therapists attached to audiology departments or sense teams in the community.

b. Swallowing problems (dysphagia)

Dysphagia in the progressive ataxias is often gradual and insidious in its onset. Studies indicate the cerebellum's role in controlling the speed of oral muscle movements, and clinical experience is that the oral phase of the swallow is frequently affected[198]. Abnormal pharyngeal and oesophageal function were identified in a small group of patients with hereditary sensory ataxia[199].

Symptoms of dysphagia are listed in Table 12 and include difficulties controlling food or drink in the mouth, chewing, dribbling, coughing or choking on food or drink. Swallowing difficulties may be exacerbated when there are co-existing postural or hand-to-mouth coordination difficulties. Patients with dysphagia are at risk of malnutrition, dehydration, and recurrent chest infections[198]. Co-occurring cognitive impairment may place patients at additional risk due to their reduced ability to self-monitor and maintain a safe approach to eating and drinking, including compliance with recommended textures and safe swallowing strategies. Dysphagia can have a significant impact on quality of life, with patients reporting taking extra time for meals, embarrassment associated with eating and drinking leading to avoidance of social gatherings, and fear of choking[200].

Assessment

The SLT will take a case history from the patient and/or family/carers. A comprehensive case history includes identification of signs and symptoms of dysphagia; current eating and drinking behaviour including individual dietary preferences; nutritional status and food supplementation. Given the progressive nature of dysphagia associated with ataxias, there may be under-reporting of swallowing difficulties as patients adopt compensatory approaches to their oral intake, including avoidance of particular food or liquid types. Rigorous questioning and a thorough examination for all signs and symptoms of dysphagia are therefore recommended *(see Table 12 for signs and symptoms of dysphagia)*.

SLTs conduct a full clinical examination of swallowing function comprising oral motor and sensory examination and observation of the patient during oral intake. An instrumental examination of swallowing is indicated when information gained from clinical examination is not sufficient to guide management of the presenting dysphagia. Instrumental examinations include videofluoroscopy (radiographic procedure) and/or a fibreoptic endoscopic evaluation of swallowing (FEES).

Table 12: Signs and symptoms of dysphagia
Signs of dysphagia • Recurrent chest infections • Weight loss • Dehydration • Poor oral hygiene • Observed coughing or choking during oral intake **Symptoms of dysphagia** • Dribbling • Difficulty chewing food • Food pocketing in the mouth or sticking in the throat • Coughing • Choking during oral intake • Nasal regurgitation • Avoiding specific food or liquid consistencies • Anxiety associated with oral intake • Taking long time to complete meals • Avoidance of social eating

Treatment

Following comprehensive assessment, the SLT advises on management of the dysphagia. Dysphagia management is best conducted within a multidisciplinary team (MDT). The SLT works closely with the dietician, to ensure optimal nutrition and hydration via the oral and/or alternative route, as well as the physiotherapist / occupational therapist, to ensure optimal feeding/positioning and use of aids or adaptations to deliver food to mouth. There is growing clinical interest in the use of oral muscle strengthening exercises for swallowing in degenerative conditions although the evidence base is not well established. Strengthening exercises should specifically target underlying swallowing pathophysiology e.g. the use of the Shaker exercise to target reduced anterior hyoid tilt. *Examples of management techniques are listed in Table 13.*

Table 13: Dysphagia management techniques
Dysphagia management techniques • Modification of consistency of food or drink • Introduction of safe swallow strategies including use of a chin tuck position, double swallow, throat clear • Advice regarding sitting posture and set up for oral intake • Introduction of carer-initiated prompts to maintain safety eg: slow rate, small sips, avoiding talking with food or drink in mouth • Advice on oral hygiene care

Management of severe dysphagia should include consideration of alternative feeding routes when the oral route is no longer a viable option for maintaining adequate nutrition and hydration. Alternative feeding options, for example, percutaneous endoscopic gastrostomy tube (PEG) feeding should be discussed with the individual, their family and the MDT. The use of assistive devices developed for swallowing problems in the stroke population is currently not advisable due to lack of evidence for their effectiveness.

c. Speech and language therapy service

It is clinically accepted that patients benefit from being seen at any stage during the disease progression and when they are experiencing specific difficulties with either their communication and/or swallowing. Provision of relevant and timely information is integral to the patient developing an understanding of their disease and supports the 'expert patient role', empowering patients to take responsibility for managing their condition effectively[201]. It is recommended that an open referral system should be in place where patients are able to access help from a SLT as and when required. Due to the nature of the progressive ataxias, speech and language therapy input needs to change over time in line with patient need. The newly diagnosed patient and their families may benefit from information regarding help that is available in the future should they require this, and symptoms to be aware of that would warrant assessment and advice from a SLT. When symptoms become more disabling, the SLT will take an active role in providing appropriate exercises or strategies to optimise communication and/or swallow function. Later in the disease, the SLT may be involved in advising on augmentative communication systems and/or alternative routes for nutrition and hydration.

Recommendations	Grade
1. If patients experience specific difficulties with either their communication and/or swallowing a referral to an SLT is recommended. An open referral system should be in place where patients are able to access help from a SLT as and when required.	GPP
2. It is important that SLTs undertake a comprehensive assessment of each patient's communication, which takes into consideration the impact of communication difficulties on the individual's activities of daily living and life roles.	GPP
3. Speech and language therapists should be vigilant for any signs of cognitive and/or hearing difficulties in patients with ataxia that might impact on communication and the management strategy should be modified accordingly.	GPP
4. In the absence of evidence based guidance on the most effective treatment, the speech and language therapist will need to devise individualised treatment programmes for dysarthria based on the findings of a comprehensive assessment.	GPP
5. When speech intelligibility levels fall below 50% or when reduced intelligibility has a significant impact on functional communication, alternative and augmentative means of communication should be considered.	D
6. A comprehensive case history should be taken by the SLT including the identification of signs and symptoms of dysphagia and detailed current eating and drinking behaviour and individual dietary preferences.	GPP
7. An instrumental examination of swallowing is indicated when information gained from clinical examination is not sufficient to guide management of the presenting dysphagia.	GPP
8. A multidisciplinary approach is recommended to dysphagia management between the SLT and dietician, to ensure optimal nutrition and hydration, as well between the SLT and the physiotherapist / occupational therapist to ensure optimal feeding position and use of aids or adaptations *(see table 13).*	GPP
9. Muscle strengthening exercises can be indicated and if so they should specifically target underlying swallowing pathophysiology.	GPP

5.2. Physiotherapy

This section aims to provide guidance to physiotherapists and other healthcare professionals mostly for people with progressive ataxia, although it may also be of some value for the non-progressive cerebellar ataxias. There has been little research assessing physiotherapy interventions in people with progressive ataxia therefore some of the evidence has also been drawn from studies in people with ataxia as part of other conditions such as multiple sclerosis. The reality of clinical intervention trials is that the nature of disease pathology is varied (i.e. patients do not just typically present with isolated cerebellar ataxia but often also with symptoms such as spasticity, weakness and sensory loss). Whilst gaining an understanding of evidence-based options for people with ataxia from these guidelines it remains important to be mindful of how concomitant non-ataxia symptoms may have affected the findings presented, or conversely the extent to which physiotherapists may generalise findings to patients with ataxia who feature additional significant non-ataxia signs.

Although the focus of this section is on findings from intervention studies, recent qualitative studies with people with idiopathic and inherited ataxias have highlighted the need to also consider the social impact of the condition on the rehabilitation approach[202].

5.2.a. Physiotherapy services

Patients with progressive ataxia should be referred to see a physiotherapist or neuro-physiotherapist at an early stage of the disease in order to establish strategies to maintain function (eg: balance, upper limb coordination, posture). Ideally the service provision would involve automatic referral for any patient with progressive ataxia and provision of open-access regular follow-up and long-term care[2].

Physiotherapy is often valuable to preserve mobility and to avoid other problems, such as those associated with being in a wheelchair. The management of specific impairments, such as muscle spasms and contractures, and tremors should involve a multidisciplinary approach including a physiotherapist who can advise on exercises *(see muscle spasms and contracture section 4.1.a)*. Patients with Friedreich's ataxia who may develop scoliosis should also see a physiotherapist for prevention strategies *(see scoliosis section 4.1.d)*. As mobility becomes impaired a physiotherapist will be involved in providing advice on walking aids or wheelchairs.

5.2.b. Approaches to physiotherapy

Rehabilitation for people with ataxia may adopt a compensatory or restorative approach. A compensatory approach (which includes orthotics and devices, movement retraining, reducing the degrees of freedom and optimising the environment) seems valuable for teaching people practical, everyday strategies and ways of managing the condition. It may be particularly important for those with severe upper limb tremor. Restorative approaches aim to improve function by improving the underlying impairment. Indeed, despite cerebellar damage, some improvement in symptoms can occur with practice in people with chronic and progressive conditions[203–214].

It is envisaged that physiotherapists will employ a combination of restorative and compensatory approaches guided by the patient's clinical presentation and context. This guidance aims to assist physiotherapists in this clinical decision making process.

Rehabilitation

Physiotherapy can improve gait, balance and trunk control for people with ataxia, and can reduce activity limitations and support increased participation[204,205,210,211,215,216]. The prevention of falls is important

to consider in patients with progressive ataxia given the high frequency and fall-related injuries being common[217,218]. Careful assessment is required to avoid falls.

For people with cerebellar dysfunction, dynamic task practice that challenges stability, explores stability limits and aims to reduce upper-limb weight bearing seems an important intervention to improve gait and balance[203–205,209,210,213,215,219–224]. Strength and flexibility training may be indicated in conjunction with the above. Therapeutic equipment is often provided to support function. Intensity of training seems to be important as studies have shown that higher training intensities being associated with greater improvements in clinical outcome[211,216]. There is some evidence to suggest that improvement is greater in people with less severe ataxia and it is also related to the ability to learn the task[225,226].

Targeted coordination and gait training over a four-week period resulted in improvements in people with cerebellar ataxia as measured by the Scale for the Assessment and Rating of Ataxia *(SARA – see Research section)* that was sustained after one year[211,216]. Daily training improved outcome. This particular training showed a more sustained improvement in people with cerebellar dysfunction compared to people with afferent ataxias such as Friedreich's ataxia and sensory ataxic neuropathy.

Balance training exercises undertaken in front of standardised moving visual images resulted in improvements in balance scores in some patients with SCA6 (a pure cerebellar ataxia) in a pilot trial but results were mixed[227].

5.2.c. Specific interventions for balance and gait

i. Video-game based coordinative training

Intensive coordination training using whole-body controlled videogames can be an effective and motivational therapy for children with progressive ataxia[228]. In a trial of ten children with progressive ataxia (who could walk without support) the use of an 8-week training programme resulted in improvements in various signs of ataxia as measured by the Scale for the Assessment and Rating of Ataxia of ataxia *(see Research section)*, Dynamic Gait Index, and Activity-specific Balance Confidence Scale. The training programme consisted of three commercially available Microsoft Xbox Kinect videogames ('Table tennis', 'Light race' and '20,000 Leaks'). This intervention has not been tested in adults or in children who are not able to walk unaided. Supervision from a physiotherapist is essential to ensure the correct movements are being performed and for safety.

ii. Treadmill training

Treadmill training can be an effective intervention for people with ataxia due to brain injury[206,208,214]. Intensity and duration of training seem to be significant factors. Consistent intensive training over many months combined with over-ground training may be required. This intervention has not been tested in people with progressive ataxias.

iii. Visually guided stepping

Oculomotor and locomotor control systems interact during visually guided stepping in that the locomotor system depends on information from the oculomotor system during functional mobility for accurate foot placement[229]. Marked improvements in oculomotor and locomotor performance have been seen following eye movement rehearsal in a small study in patients with mild cerebellar degeneration[230]. Rehearsal of intended steps through eye movement alone, i.e. looking at foot target placement for each step, before negotiating a cluttered room, might improve performance and safety. This simple strategy, although task specific and short lived in nature, is promising and relatively quick and easy to apply in a functional setting.

iv. Balance and mobility aids

No studies have specifically evaluated the role of balance and mobility aids for people with ataxia. Clinical experience suggests walking aids should be considered on a case-by-case basis.

In terms of postural control, somatosensory cues from the fingertips – using light touch contact or a walking aid as a means of balance – can provide a powerful reference orientation even when contact force levels are inadequate to provide physical support for the body[231]. Indeed, clinical observation suggests that some individuals with ataxia find light touch contact more useful as a strategy than a conventional walking aid. This may explain why some people prefer to use Nordic poles, which help encourage light touch contact, rather than traditional walking sticks that tend towards force contact and a reduction in muscular forces acting through the lower limbs.

Upper extremity weight bearing during ambulation may perpetuate deterioration or worsening of gait parameters. Therefore, it is important for people with ataxia to decrease their dependency of weight bearing through the upper limbs (eg: not leaning on furniture to assist in their walking)[204]. Furthermore, individuals with cerebellar hemisphere lesions, who are more likely to have dysmetria and tremor, may find balance and mobility aids hard to use. This is because placing and controlling a stick can be as difficult as trying to accurately place legs during swing phase. Careful assessment is required for those with dysmetria, dysdiadochokinesia and tremor.

Walking aids also have the potential to compromise the ability to respond to balance disturbances through impeding lateral compensatory stepping and can thus affect safety[232]. Thus it is important to ensure the appropriate walking aid is recommended for each patient.

v. Axial weighting

There is a very limited theoretical basis for axial weighting, and no evidence to support the use of axial weights to improve gait in people with ataxia.

vi. Lycra garments

The use of lycra to affect postural sway, walking effort and speed in adults with ataxia has had mixed results that may depend on the individual (unpublished data: M.Watson@uea.ac.uk). Insufficient data are available to support the use of lycra garments for children with ataxia.

vii. Biofeedback for balance and gait

Some forms of biofeedback may be beneficial. For example, the biofeedback of head position delivered using a tongue-placed electro-tactile system resulted in improvements in postural sway with eyes closed in a small study of people with cerebellar ataxia[207]. However, findings are variable and from studies with a low number.

5.2.d. Specific interventions for spasticity

Physiotherapy has a vital role to play in educating patients and carers in correct posture, muscle use and the avoidance of spasticity triggers such as pain and infection.

Muscle lengthening is a fundamental feature of the physical therapy management of spasticity which aims to maintain and improve range of movement and prevent the formation of contractures. This can involve physical exercises which antagonize the overactive spastic muscle and also improve muscle strength; passive stretching by the therapist or carer; or physical positioning techniques. Active exercise is generally more effective than passive exercise if the patient is able; increased fitness can also reduce

fatigue and permit further exercises.

Positioning can involve splinting, casting, orthoses, standing or the use of weights, resistive devices, wedges, cushions or T-rolls. More prolonged splinting can involve firm materials such as metal or plastic, or softer supportive materials such as foam or sheepskin. Orthoses should be of good quality, well-fitted and prepared in a specialist Orthotics Department.

Electrical stimulatory devices have some evidence in the treatment of spasticity, including the Functional Electrical Stimulator, the Foot Drop Stimulator and the Transcutaneous Nerve Stimulator[36,233]. However, a recent Cochrane Review of stretch for preventing contractures concluded that there was moderate to high quality evidence that stretch does not have clinically important effects on joint mobility, and there was little or no effect of stretch on pain, spasticity, activity limitation, participation, restriction or quality of life[234]. None of the studies considered specifically studied patients with ataxia and no studies used the intervention for longer than 7 months, therefore it is difficult to comment on longer-term treatments.

5.2.e. Specific interventions for upper-limb tremor

Lesions affecting the cerebellar hemispheres give rise to ipsilateral limb symptoms including tremor in addition to dysynergia, dysdiadochokinesia and rebound phenomenon. An action tremor occurs during movement, i.e. it is produced by voluntary contraction of muscle, and includes postural tremor (occurs when voluntarily maintaining a position against gravity, e.g. holding an arm out straight) and kinetic tremor (occurs during any type of voluntary movement). Kinetic tremor is further subdivided into: simple kinetic tremor, which occurs during voluntary movements that are not target-directed (e.g. flexion/extension or pronation/supination), and intention tremor, which occurs during target directed, visually guided movements (e.g. finger nose test), and worsens at the terminal phase of the movement as the target is approached[235].

In addition to affecting activities of daily living, the psychosocial consequences of upper-limb tremor can be significant[236]. The treatment of upper-limb tremor, via the action of pharmacological agents and physiotherapy, remains wanting. *Also see tremor section 4.1.b.*

i. Manipulation of visual information

Individuals with intention tremor or other cerebellar deficits may have difficulty using visual information to control arm and hand movements[237]. Tremor amplitude may be reduced if target directed movements are performed from memory rather than under direct visual guidance[238] or if the primary saccade and the hand movement to reach the object are performed separately[239].

ii. Cold therapy

Transient tremor control using cooling could have important functional implications when performing discrete functional activities such as intermittent self-catheterisation, signing documents, working a PC and taking a meal, as has been found in MS[239,240]. Deep cooling may be more effective than moderate cooling in individuals with severe tremor. Upper-limb cooling in general may not be as useful for individuals who also have significant proximal tremor.

iii. Wrist weighting

Evidence in this area is equivocal[236,238,241–243]. It seems weighted wrist cuffs (of different weights) and weighted cutlery may be useful for some individuals under specific circumstances and should be assessed on a case-by-case basis. Patient goals and perspectives should be considered when assessing the value of the intervention. As some individuals show exaggerated tremor for a short time

on removal of weights, it is suggested that specific functions such as eating or writing are targeted. The long-term effects are not known; clinical observation suggests some people accommodate to the weight. Weighted cuffs may be too fatiguing or cumbersome to confer any functional or psychosocial benefit for some individuals, thus patient goals and perspectives are critical in assessing the value of this intervention.

iv. Robotics

Adaptive robotic therapy of upper limb reaching movements may be a potentially useful adjunct that may be tailored to the patient's level of ability, allow intensive training and that can transfer to real life tasks[244,245]. However, these are not widely available and at the time of writing not available in the UK.

5.2.f. Wheelchair seating

Wheelchairs rank among the most important therapeutic devices used in rehabilitation and can make the difference between an active and efficient alignment and a postural catastrophe. Despite a lack of research studies, clinical observation suggests that powered wheelchair mobility with appropriate postural support is an option to provide people with ataxia with a means of independent mobility.

Power chairs may also help conserve energy that can then be used outside the wheelchair for carrying out activities of daily living in antigravity postures. Additionally an appropriate posture in the power chair may facilitate respiration and swallow in those patients who may be compromised in these areas. In the absence of other evidence, clinical experience and patients' needs should be used to guide clinical reasoning[246].

5.2.g. Exercise

In general people with ataxia should be encouraged to exercise as part of health promotion and as long as risk factors and health and safety considerations have been assessed. Exercise should be tailored towards what appeals most to participants and may involve exploring several different options as well as building motivation and sustainability into the exercise prescription[247,248].

Note of caution: Cardiac abnormalities are a common occurrence in people with Friedreich's ataxia. If patients have cardiac complications, advice from a cardiologist should be sought before embarking on an exercise program. (See cardiac problems section 4.1.f).

i. Hydrotherapy and swimming

Anecdotal evidence supports the value of hydrotherapy for people with ataxia as a form of exercise. Hydrotherapy and swimming, as water activities, offer risk and challenge and provide freedom of movement often not available on land[249]. Hydrotherapy is also considered to offer beneficial effects on health related quality of life.

ii. General fitness training

Anecdotal evidence advocates the benefits of general fitness training, yoga and Pilates for people with ataxia to help maintain strength, flexibility and balance. Activities such as horse riding and climbing[250] may also confer similar benefits. Psychosocial benefits have also been reported. In a case study in a patient with Friedreich's ataxia without cardiomyopathy, aerobic training was shown to have some benefits[251], but studies in this area are lacking.

5.2.h. Specific Impairments

People with ataxia can experience a number of specific impairments which physiotherapists should be aware of. Clinical experience and feedback from people with ataxia indicates that fatigue can be a common and at times an overwhelming issue[252]. Spasticity, contractures, dystonia and scoliosis can also occur. In the management of such complications, in addition to medical interventions, physiotherapy has an important part to play. *See the Medical interventions section of this document and the MS Society Guidance for Physiotherapists (2008)[253] for further direction about managing these symptoms.*

Bladder and bowel problems (such as frequency, urgency and incontinence) can also be a feature of the ataxias. For specialist advice and assessment referral to a gynaecologist or urologist may be required *(see Medical Intervention section 4.1.g)*. For further advice refer to the Association of Chartered Physiotherapists in Women's Health (ACPWH), which provide assessment and treatment for men and women with bladder and bowel impairment. A referral to a continence nurse may be useful. Finally, neuropathic pain can be a feature of the ataxias *(see section 4.1.e on pain).*

Recommendations	Grade
1. Patients with progressive ataxia should be referred to see a physiotherapist or neuro-physiotherapist at an early stage of the disease in order to establish strategies to maintain function (eg: balance, upper limb coordination, posture) and prevent falls.	GPP
2. Consider the potential use of rehabilitation approaches and the specific interventions for gait/balance and upper limb tremor as listed above for patients with ataxia on a case by case basis.	GPP
3. Consider suggesting rehearsal of intended steps through eye movement alone, i.e. looking at foot target placement for each step, before negotiating a cluttered room, as it might improve performance and safety.	D
4. Consider the use of video-game based coordinative programme in children with ataxia who are able to walk unaided under physiotherapist supervision.	C
5. The use of walking aids is recommended and should be assessed on a case by case basis. Light touch as a balance aid may be helpful for postural orientation and stability.	GPP
6. Advise people with ataxia to decrease their dependency of weight bearing through the upper limbs when walking.	GPP
7. Careful assessment is required when recommending walking aids to patients with dysmetria, dysdiadochokinesia and tremor.	GPP
8. People with ataxia should be encouraged to exercise as part of health promotion but ensure as risk factors and health and safety considerations are assessed.	GPP
9. In patients with Friedreich's ataxia and cardiac complications, advice form a cardiologist should be sought before embarking on an exercise program.	GPP
10. Assess seating position and posture when advising on a wheelchair.	GPP
11. Physiotherapists should be aware of a number of other specific impairments that people with progressive ataxia may have to treat accordingly.	GPP

5.3. Occupational therapy

a. Introduction

This section aims to provide occupational therapists working with ataxia patients with information about how common impairments impact on typical activities and occupations; and provide advice on interventions. In the absence of specific research, a philosophical approach, expert opinion and relevant progressive neurological conditions research will be drawn on.

This section has been reviewed by the College of Occupational Therapists Specialist Section – Neurological Practice, Long-term Conditions Forum and is endorsed by the College of Occupational Therapists.

Occupational therapy (OT) is widely recognised to be a valuable part of the multi-disciplinary care team in ataxia although primary research evidence is limited[220,254–256]. Occupational therapy is an important intervention for people with progressive neurological conditions in maintaining independence and quality of life[222,257,258] enabling them to participate in self-care, work and leisure activities that they want or need to perform[259]. When it is no longer possible to maintain usual activities, occupational therapists should support people to adapt their relationship with their physical and social environment to develop new valued activities and roles[260].

The focus of occupational therapists on 'engagement' in activity, rather than the disorder is important in progressive conditions. Occupational therapy intervention should focus on functional goals that support the person and their carers, to address occupational needs, thereby adding to quality of life[258]. Occupational therapists should draw on their core skills to assess and understand the impact of the illness on occupational engagement, utilising problem solving and clinical reasoning skills to provide effective intervention. This will likely require flexible use of different frames of reference depending on the stage of disease progression. For example, a rehabilitation and educative approach could support occupational engagement in the early stages, while compensation will likely be needed as the disease progresses. Use of a client centred model of practice can support this process, guiding understanding of the individual's key issues in a holistic manner.

Occupational therapists should use assessment and outcome tools that focus on occupational engagement and/or measure the person's satisfaction with the performance of an activity; as use of tools that measure impairment would not always demonstrate the effectiveness of OT intervention. Appropriate tools include, but are not limited to, Assessment of Motor and Process Skills (AMPS), Goal Attainment Scale (GAS), Canadian Occupational Performance Measure (COPM), self-efficacy tools and quality of life measures[261,262].

It must be emphasised that the guidance given here is mostly based on practice consensus, not research. A literature review only identified a small number of case studies and case series designs focused on OT intervention in ataxia.[220,254–256]

Due to the similarity of treatment approaches, to supplement this, wider evidence has been used from other progressive neurological conditions where more evidence is available, for example Multiple Sclerosis.[222,259,260,263,264] Therefore the current evidence base is insufficient to make strong recommendations to clinical practice with the methodological quality of the articles being weak (SIGN 2001), and further research is needed in this area. In addition, most of the studies reviewed describe multidisciplinary intervention and it is therefore difficult to separate the effects of OT specifically.

A compensatory model of practical and physically focussed OT in the management of SCA3 showed positive and statistically significant changes in depression in a small study (although other outcome measures did not show a statistically significant change)[256]. This intervention was provided via 6-month

individually tailored programmes focussed by client-centred goals addressing everyday difficulties, including feeding, work and social interaction. A combination approach to OT for the management of ataxia tremor has been suggested as useful. It is important to keep in mind the following domains when providing OT intervention to this population to ensure occupational engagement and wellbeing: promoting normal posture and movement, equipment provision and advice on activities of daily living, improving proximal stability and automatic equilibrium, and dampening/weighting[222]. A comprehensive overview of strategies relating to specific tasks advocated a combination of compensatory techniques including postural stability, splinting and assistive technology, using client-centred goals and a task-orientated approach[220,257]. Findings supported use of compensatory equipment and techniques that limit degrees of movement and dampen tremor in specific tasks.

Key findings from literature review:

- Client-centred, individually tailored OT programmes can have a positive effect on mood scales
- A short course of multidisciplinary rehabilitation, which includes OT, is beneficial compared to no treatment
- Client-centred goals along with a theoretical task-orientated approach may be useful to aid clinical reasoning
- Compensatory equipment and techniques that limit the degree of movement and dampened the tremor within specific functional tasks may improve occupational engagement for the individual
- Specialist seating can have positive and negative affects on posture but may improve comfort
- Further research is required.

Table 9 lists general considerations for OT interventions.

Table 9: General considerations for Occupational Therapy intervention

Using The Occupational Therapy Process, Creek, 2003 (GPP)[265]

- Gather as much background information as possible about the referral
- Complete a full occupational performance history/interview
- Prioritise occupational performance issues/areas of concern
- Acknowledge and address the carers' and family's needs within the assessment process
- Be mindful of the rate of disease progression and how this will impact on your intervention
- Identify the impairments or skills that are of concern and consider how the environment impacts on performance through observing performance within everyday tasks
- Identify the individual's strengths and their resources
- Establish a list of main concerns and prioritise treatment goals
- Decide the approach to your intervention with the person, i.e. adaptation, rehabilitation, compensation, education, sign-posting or a combination of these
- Implement intervention through performance of activities or environmental adaptations
- Evaluate your outcomes and re-evaluate a need for further input
- Consider the need for future assessment when occupational needs change and how that person can re-access yours or other appropriate services

b. Common issues encountered with activity and participation

The effects on a person's occupational performance are not predictable and will depend on the types of activities that the person needs and wants to participate in. It is important to take a person-centred approach to analysing the area of occupational need within performance of daily activities and roles.

Evidence suggests that people with ataxia may have a lower quality of life in the early and end stages of the condition[266]. It is therefore important to recognise that even at the early stage of the condition difficulties with roles and occupational engagement may benefit from support. As most ataxias are progressive an important consideration is proactive planning for future needs[25]. This can be a difficult situation to deal with in a sensitive manner, and occupational therapists must respect the individuals in their own journey of acceptance of this condition. If appropriate, occupational therapists should broach the expectation of future decline in occupational engagement when considering any major adaptations.

c. Common occupational therapy interventions

Common interventions and practical advice collected from clinical experience are outlined below *(these are listed in alphabetical order)*.

i. Computer use

There are many aids to compensate for ataxia when using a computer. This may require joint assessment with a speech and language therapist in considering whether voice-activated software may be appropriate for overcoming problems with using a keyboard to enter information; however, dysarthria may prevent voice-activated software from being useful. Importantly, Information Technology is a constantly changing area with new devices and solutions becoming available all the time. If the person is still at work, funding for a computer assessment should be gained through an Access to Work referral (AtW). Alternatively, occupational therapists should investigate charitable organisations that may provide funding to access these services and equipment.

Practical suggestions

- *A referral to IT solutions experts (such as AbilityNet) is strongly advised*
- *The AbilityNet website has free advice about IT adaptations for people with ataxia (www.abilitynet.org.uk)*
- *Keyboard and mouse modifications can be made to adjust the sensitivity and speed of response*
- *Alternatives to a standard mouse, such as a tracker ball, can be helpful*
- *Smaller keyboards or keyguards may help*
- *Consider the layout and location of equipment for ease of access*
- *Consider the impact of seating and ergonomic set up of the computer workstation*

ii. Control of the indoor environment

Control of the indoor environment can quickly become difficult for people with ataxia due to tremor and reduced coordination, for example use of electrical equipment with small switches or buttons. When assessing the person's control of their indoor environment, consider priority activities they wish to participate in. Remember that especially in the palliative stage the focus on meaningful activity can provide immense satisfaction and comfort to the person with ataxia and their family.

As the condition progresses, occupational therapists should consider a referral to their Regional Environmental Control Service. These services can provide electronic assistive technology to severely disabled people to enable them to live more independently at home. This may include an environmental control system which enables the person with ataxia to call for carer assistance or emergency help, manage door entry and access, use the telephone, control the television and other media devices and control the lights and electrical appliances.

Practical suggestions

- *Consider the use of 'big button' telephones and phones with autodial numbers or voice activation*
- *Consider use of a telephone with two way record to save conversations for replay later and to help keep messages*
- *Many telephone providers have inclusion phone services policies including a communications solutions guide obtainable online*
- *Light switches should be simple and easily reached from a standing or wheelchair position suitable to the person*
- *Appliance sockets are safest when located off the ground at waist level to avoid complex bending, squatting and reaching*

iii. Driving

If they are a driver, the newly diagnosed person with progressive ataxia is legally obliged to inform the DVLA and their insurance company of their diagnosis as soon as it is confirmed. Reporting the diagnosis may not mean cessation of driving. The DVLA will request information from the person and their medical team and may request attendance at a driving assessment centre before making a decision.

Some people will require driving adaptations to allow safe driving to be completed. Specialist centres provide assessment for suitable adaptations as well as driving ability (www.mobility-centres.org.uk). Where appropriate, the Motability scheme can assist people who receive the higher mobility rate of personal independence payment with minor adjustments, lessons or funding a vehicle (www.motability.co.uk). *For more information on driving see www.gov.uk/health-conditions-and-driving.*

There are some cases when the condition causes such difficulty with driving that it is unsafe for the person to continue with this role. When this is true, occupational therapists should explore alternative community mobility *(see section on outdoor and community mobility).*

Practical suggestions (to assist with car transfers):

- *Educate the person and carer on allowing the car door to be opened fully and to consider the height of the transfer being undertaken*
- *Ensure the person sits their bottom down first before moving their legs into the car*
- *Try inserting a swivel transfer mat and if the car seat is particularly low a firm foam cushion or blanket in a pillowcase*
- *Choose a model of car that optimises transfers, door access and storage space*

iv. Eating and drinking

Feeding needs to be considered due to multiple impairments impacting on safe and effective eating and drinking. Before commencing any feeding assessment, standard practice would be to ensure that the need for a speech and language therapy assessment is considered *(see section 5.1).* Joint working

may therefore be appropriate. Feeding solutions may be different depending on contextual factors, and solutions for eating at home may be different for social events. Altering positioning and/or seating will maximise posture and support core stability, thus reducing the impact of excessive limb movement[267].

Practical suggestions

- *Organise work spaces and utensils to reduce clutter and optimise performance*
- *Ensure individuals have appropriate postural control, use of a lumbar support will assist with optimal eating and drinking posture*
- *Non-slip matting can be used as a placemat to limit movement of the plate or cup, eg: Dycem® (www.dycem.com) or similar*
- *Plate guards can be useful to reduce the need to co-ordinate two movements, and rocker knives may make cutting food easier by limiting the degree of movement needed*
- *Weighted cutlery may be beneficial*
- *Use of lidded/insulated cups or cups with straws for drinking, especially hot liquids such as tea and coffee can be helpful*
- *Cups with anti-tremor insert devices can help as can Hotjo Mugs or similar products (www.neater.co.uk) which have a narrow neck and top to limit spills and a large non slip base which makes it easier to place on a work surface with uncontrolled movements*
- *For people with severe ataxia a sports bottle or camel pack may be helpful*
- *Use of the Neater-eater® or similar device with a dampening hydraulic mechanism can be very effective in aiding independent spoon or fork feeding (www.neater.co.uk)*

v. Falls management

Falls may occur in any area that a person mobilises. Occupational therapists should consider joint assessment with, or referral to a physiotherapist and referral to a falls management programme or group locally.

Practical suggestions:

- *Advice on clothing not being too long and shoes being well fitted should be given, to try and prevent falls*
- *Non-slip flooring is helpful in fall prevention*
- *The person should be taught fall recovery techniques and if there is a family member or carer involved, the occupational therapist should consider the safety of the carer.*
- *Where appropriate, consider the use of community care alarms, Telecare and techniques to avoid further injury e.g. pressure sores while waiting for help to arrive*

vi. Food preparation

Preparing food is a common concern in the early stages due to its obvious risks. Occupational therapists should carry out an activity analysis of food preparation tasks and suggest a variety of methods and aids that may compensate for difficult or unsafe aspects. This may include completing food preparation tasks in a seated position, having someone else do aspects of the task for them (but not the whole task), such as cutting hard vegetables; or use of devices to aid grip and maximise safety. Again, find out what is important to the person and offer individual assessment of these areas.

Practical suggestions

- *Kettle tipper devices or hot water dispensers can help making hot drinks safer*
- *Using a travel mug with a lid can sometimes assist with carrying a drink*
- *Waist-height ovens; use of full-length oven gloves; sliding food to a level surface (or level trolley) rather than lifting are all useful suggestions*
- *A microwave oven can provide a safer alternative to standard ovens*
- *Chopping boards with an attached cutting blade can be safer than a separate knife*
- *A food processor can help with slicing or chopping vegetables*
- *Ergonomic grip knives can be useful to limit the degree of movement needed when chopping food*

vii. Hand function

Individuals with Friedreich's ataxia often experience intrinsic muscle wasting in their hands, impacting on grip and dexterity and leading to a 'claw' deformity in the longer term. Assessment and education should be provided to manage this, with splinting explored as a method to maintain range of movement and improve occupational engagement as able[268].

viii. Handwriting

This can be an area of particular difficulty for someone with progressive ataxia. If the person is still at school or at university, it is important to work within the provisions of special educational supports such as those provided through support workers. For someone at work, consider a referral to AtW (www.gov.uk) for a full assessment. This may include an AbilityNet assessment for suggestions of alternative technological solutions for handwriting problems. Activity analysis may reveal the need for adaptations such as alternative positioning and/or seating, ergonomic desks and different pens.

Practical suggestions

- *Ensure work spaces and seating are set-up to provide maximum support and optimise posture*
- *Dictaphones or voice-activated computer software can be used to compensate for problems with handwriting*
- *Use of weighted pens and thick barrelled pens may help but there is limited supporting evidence*
- *Consider the type of pen nib and the pressure applied as some people experience fatigue affecting sustained pen grip*

ix. Household management

It is important to identify the household management priorities of the person and to recognise the cognitive and physical elements of these tasks. Most people with ataxia will continue to be able to cognitively manage the home but may have difficulty physically carrying out heavy housework such as vacuuming or heavy laundry. Occupational therapists may wish to discuss the impact of fatigue in order to help balance continued involvement in activities whilst recognising what is a priority to them.

Practical suggestions

- *Hiring a cleaner to assist with heavy household tasks can be beneficial to save energy for more enjoyable tasks*

Indoor mobility should ideally be assessed in the environments that the person frequently uses. For example, a person with progressive ataxia may walk well at home using walls and rails, but be unable to walk independently in a hospital, work or community setting. Mobility should be assessed jointly with physiotherapy colleagues if possible and consideration made of the use of walking aids.

Occupational therapists should consider the interaction of the person with their environment and the tasks that they want to perform once they have walked somewhere, as well as how the person plans to carry any items while walking. Use of walking frames may need to be reconsidered in very small areas and a combination of devices suggested in order to move from one area to another, eg: use of a walking frame to the bathroom and then hand rails once inside the bathroom.

When wheelchairs are required, close liaison with the local wheelchair service is recommended *(also see section on outdoor mobility)*. Consider the environment including access, door widths and interaction with furniture to ensure that the person can access areas they want and/or need to. Major home modifications may be required, if not in the first instance, as the condition progresses. This should be considered earlier, rather than later, with sensitive respect given to the person's psychological adjustment process.

Some people may choose what is considered an unconventional solution to help them navigate their home such as crawling. A compromise between safety, risk management and patient choice may be required.

Practical suggestions

- *Bags worn close to the body may be the most efficient and cause the least impact on balance. Later, it is advisable to avoid carrying items while walking*
- *Trolleys may help to transport items, especially food, drinks and heavy items at work or in the home and should be discussed and assessed if thought beneficial*
- *One-handed trays such as the Handitray® or similar products can help transportation of items*
- *Advise removal of items such as scatter rugs and loose electrical cables that may present as risks to mobility in the home environment*
- *Good lighting will help optimise performance of tasks and ensure that potential hazards in the home are avoided*

x. Leisure

Occupational therapists should bear in mind that if there is loss of other occupational roles, leisure could be an area that helps to redress this loss in a different capacity. It is an important area to consider during intervention, as participating in leisure activities can help to maintain physical and psychological wellbeing. Enjoying leisure time with family and friends should be encouraged, albeit in modified ways. For example, use of accessible holiday homes, use of a wheelchair when visiting outdoor areas such as parks and galleries, and ensuring social contact continues in the home or other spaces.

If the person has lost leisure roles such as participation in sport, consider that they may be able to continue their involvement in the activity with alternative roles such as score keeping, participation on committees, or attending social events at their local club. For hobbies such as horticulture, consider adaptations that can be made to maintain participation, for example visiting local garden centres, planning planting or maintaining raised beds.

Reading can present particular difficulty for people with ataxia due to difficulty holding a book and/or visual problems. Electronic books such as 'Kindles' can help with this as they are easier to hold, you can adjust the size of the text to suit and use talking text options.

Practical suggestions

- *Bookstands can be used to hold books*
- *Use of elastic bands around the loose pages of books can limit frustration caused by rustling pages where tremor exists*
- *Use of a rubber thimble can be useful to help turn pages where fine motor coordination is a problem*
- *Books may be downloaded online and use of zoom text can help where vision is a problem*
- *Talking books are available if preferred. The RNIB can be a useful support service in this area (see www.rnib.org.uk)*
- *Electronic page-turners can be purchased but are costly and take up space*

xi. Outdoor and community mobility

Mobilising outdoors can often present particular difficulty for the person with ataxia, as it may be an unfamiliar environment. Educate the carer and the person with ataxia about resting regularly whilst walking outdoors. Consider what and how the person plans to carry while walking *(see indoor mobility above)*. A wheelchair for outdoor use can help to reduce fatigue and/or maximise safety.

Practical suggestions

- *Shop-mobility, taxi card schemes, mobility buses and dial a ride services can be helpful*
- *Public transport and rail providers offer subsidised fares for people with a disability and can provide a meet and greet service/access assistance for customers*
- *Outdoor motorised scooters or wheelchairs can maximise independence, but consideration should be made of transfer safety*

xii. Posture and seating

An assessment for optimal posture and seating can be useful even in the early stages, and is essential in the later stages of ataxia. Occupational therapists should consider a referral to local wheelchair services for expert assessment. Consideration should be given to stable cushions and back supports, as canvas backs/seats in standard wheelchairs do not encourage good posture, which may impact on function.

A study using a randomised crossover trial design examined the effects of an individually adapted wheelchair support compared with a standard wheelchair for young people with progressive neuromuscular disorders, including FA. Their findings demonstrated improved postural alignment, but not improved respiratory or upper limb function; however fatigue could have influenced the findings[267]. Therefore, a compromise between optimising occupational engagement and providing adequate support is important.

xiii. Self-care and toileting

Aims of treatment for self-care and toileting include minimising the impact of excessive movement and helping the person to optimise their independence where possible. Prioritisation of tasks may mean that the person is happy to accept assistance with dressing if it allows conservation of energy that can be used for other, higher priority activities such as leisure or work. It is important to discuss this with the person and to anticipate for the future. For example, early referral for level access showers may be

appropriate for the person with progressive ataxia.

Toileting is often an area that people with ataxia report as difficult and stressful. Rails can help the person to fix their arms and provide greater stability during transfers. Other problems encountered include dressing and undressing in the toilet, and managing perineal hygiene. Remember that assessment should be completed and aids trialled, as each person is unique.

Practical suggestions

- *Encourage sitting to bathe or shower and consider providing seating with support for the back and arms*
- *Use of thermo-regulation devices on taps can be an important safety consideration*
- *Lever taps may be easier to use than standard taps*
- *Level access showers can be a useful consideration if bath transfers become unsafe or dangerous*
- *Small aids such as 'zip pulls' and button hooks and replacing fastenings with Velcro can be beneficial to increase independence with dressing*
- *An add-on bidet or an automatic washing/drying toilet such as a Closo-mat® (www.clos-o-mat.com) or similar device may help with perineal hygiene*
- *Rails around the toilet may be of benefit and wherever possible these should be fixed to minimise risk of accidents*
- *Consider the height of the toilet seat and adapt this where required*
- *Consider the use of hygiene wipes and alcohol gel to maintain hygiene when away from home*
- *Register with RADAR for key access to their public toilets*

xiv. Specialised equipment

Organisations such as the Disabled Living Foundation (www.dlf.org.uk) or Remap (www.remap.org.uk) provide information and advice on equipment for disabled people and can be a useful resource for occupational therapists.

xv. Transfers (from bed, chair and toilet)

As with most client groups, ensure that the height of the chair is correct for the person to transfer easily on and off, with the hip and knee angle at 90 degrees and feet flat on the floor. Armrests greatly enhance the ease of chair transfers; ensure the chair is stable and that armrests are at a suitable height and position to enable the patient to push up. Educate the patient and carer on sit to stand techniques and always consider the carer's safety within this.

Some people will need hoist provision for transfers and occupational therapists should ensure that they and their carers are adequately trained to perform this, with training being undertaken by a relevant team member. In particular, where full body tremor presents, slings need to provide the maximum support available for safety reasons.

Practical suggestions

- *Consider the height of the bed, chair and toilet and location within the room to ensure the most efficient and safest transfers*
- *A bed lever can be beneficial to aid rolling and rising in bed*
- *Mattress variators, or profiling beds may be of benefit*
- *Firmer mattresses can aid bed mobility*
- *Pressure care needs should be considered if bed mobility is severely restricted*

xvii. Work

Occupational therapists should consider maintenance of working roles for as long as the person wants it to continue and for as long as that is possible. When work is no longer possible consider rebalancing the loss of working roles with other activities or help to access relevant benefits.

It is important to provide education on the person's rights and responsibilities under the Equality Act (2010). Support the individual regarding the disclosure of their diagnosis to others and their employers, if this is a concern. It should be remembered that intervention should allow the person to develop skills to manage ongoing liaison with the employer where possible. Occupational therapists may directly intervene by assessing and advising on reasonable adjustments to support people with ataxia to maintain their working role. This may include adapting work hours, environmental adjustments, advising assistance with specific tasks or travel and managing fatigue at work.

A work site visit may be required and this could be completed by the occupational therapist or via a referral to AtW if appropriate. AtW will help considerably with costs of aids required such as motorised wheelchairs, ergonomically appropriate seating and desks, IT devices, support workers and with taxi travel to/from work.

d. Fatigue Management

Fatigue can be a significant problem for people with ataxia and the impact of this on occupational engagement should be addressed within OT intervention. As with other progressive neurological conditions, using the principles of fatigue management can help people to maintain a consistent level of activity and engagement in tasks that are a priority for them. The basic principles of fatigue management are taking regular rest breaks, prioritising and pacing activities, maintaining a healthy lifestyle, organising work area and tools and maintaining exercise tolerance. It is useful to provide information on fatigue and discuss strategies, using activity analysis to help people look at alternative ways of completing tasks in a more energy efficient way. The need for support with fatigue, attention and accessing information was identified in a study exploring the physiotherapy experiences of people with cerebellar ataxia[252]. Although current research does not demonstrate that occupational therapists are providing such interventions for people with hereditary ataxia, it would not be unrealistic to assume that these are already part of practice. Fatigue management, cognitive strategies and providing support to access services and information are common OT practices for people with other neurological conditions and should be explored for people with ataxia.

e. Psychological support

The psychological impact of having a long-term condition such as ataxia can be significant, especially for teenagers transitioning into adulthood while coping with increasing disability. Individuals may not be

ready to accept advice or equipment and emotional support and anxiety management may be required within this process[258].

For all people with ataxia, it is important for occupational therapists to assess whether anxiety and/or depression are impacting on occupational engagement. If anxiety and depression are identified as areas of difficulty, occupational therapists should look to address this within their intervention to support people to manage their occupational needs. Tools such as a Wellness Recovery Action Plan (WRAP) or Personal Wellbeing Plan can be helpful, although consideration may need to be made of specific costs related to this. Referrals should be made onto appropriate psychological services such as counselling or CBT as appropriate. If possible, individuals with ataxia should be given the opportunity to re-access services when they feel ready to make changes.

f. Cognitive impairment

It is important to consider that some people with ataxia may have cognitive impairment, requiring more tailored interventions *(see section 4.1.o)*. Additional adaptations may therefore be required, eg: timetables to help with fatigue management, visual prompts to remember risks, and additional instructions may be needed about the use of equipment.

g. Conclusion

Despite the limited primary evidence of specific OT intervention, expert opinion highlights involvement of occupational therapists in the multi-disciplinary management of people with progressive ataxias. The above examples provide a guide to suggested OT intervention in this group based on the consensus of occupational therapists working in this area. Future research is recommended into OT intervention, within the context of a multi-disciplinary team, for people with progressive ataxia.

Recommendations	Grade
1. When it becomes increasingly difficult for people with ataxia to perform everyday activities referral to occupational therapy services is recommended.	GPP
2. Occupational therapy assessment tools should measure the person's occupational engagement and/or satisfaction with their performance of an activity.	GPP
3. When making an assessment for treatment and management, occupational therapists should refer to general considerations for intervention in table 9 of this document.	GPP
4. Following a complete OT assessment, when a list of main concerns has been considered and treatment goals prioritised, consult practical suggestions in this section for guidance.	GPP/D
5. Fatigue management should be considered as part of the OT assessment.	D
6. Provide information on fatigue and discuss strategies, using activity analysis to help people look at alternative ways of completing tasks in a more energy efficient way.	GPP
7. Occupational therapists should be mindful of the psychological state of the person with ataxia and refer to counselling or CBT as appropriate, and/or consider that anxiety management may be required.	D
8. Consider the need for future assessments when occupational needs changes and how the patient can re-access both OT and other appropriate services.	GPP

6. Palliative Care

This section addresses issues arising for individuals with progressive ataxia and their carers as a result of the currently incurable nature of these conditions. Little information is available in the literature on palliative or end-of-life care in the ataxias, so in the absence of this, the guidance in this section is drawn from literature pertaining to other progressive degenerative neurological conditions. Although degenerative neurological conditions vary in their presentation and life expectancy, there are parallels in symptoms and the need for services[269,270]. It seems reasonable therefore to apply evidence from the wider field of progressive neurological conditions to the ataxia population.

What is Palliative Care?

Palliative care is an approach that improves the quality of life of patients and their families facing the problems associated with a life-threatening illness. The aim of palliative care is the prevention and relief of suffering by means of early identification, impeccable assessment and treatment of distressing symptoms and other problems; physical, psychosocial and spiritual[271]. Although the term 'palliative care' is often used to mean 'end of life care', the two are not synonymous. Palliative care is often applicable earlier in the course of an illness, in conjunction with other therapies that are intended to prolong life. In this context, palliative care will enhance the patient's quality of life and support the patient to live as actively as possible with the condition. End of Life care refers to the care that patients need in the last phase of their illness, usually in the months or weeks before death.

Palliative care is a generic term which describes an approach to care that is the responsibility of all health care professionals. Most palliative care for patients with progressive ataxias is provided in the community by district nurses, GPs and other members of the primary care team. However, some patients with complex needs require help from palliative care specialists. Patients with specialist palliative care needs can thus be supported by doctors and nurses at home, during hospital admissions and within a day hospice or inpatient hospice environment.

The importance of palliative care for patients with progressive neurological disease was highlighted in the UK National Service Framework for long term neurological conditions[25]. It is estimated that 300,000 people living with neurological conditions in the UK do not receive the specialist palliative care input that they need[272]. The UK National Service Framework for long term neurological conditions promotes the need for coordination between neurologists, rehabilitation specialists and palliative care services in order to ensure patients receive the best possible care[273].

Advance Care planning for patients with ataxia

Advance Care Planning (ACP) is defined as "A voluntary process of discussion and review to help an individual who has capacity to anticipate how their condition may affect them in the future and, if they wish, set on record: choices about their future care and treatment and/ or an advance decision to refuse treatment in specific circumstances, so that these can be referred to by those responsible for their care or treatment (whether professional staff or family carers) in the event that they lose capacity to decide once their illness progresses[274].

ACP may involve an individual with ataxia (who has mental capacity) writing a legally binding document detailing an Advance Decision to Refuse Treatment (ADRT). This decision only comes into force should the person subsequently come to lack capacity. Other outcomes of ACP may be the appointment of a Lasting Power of Attorney, a documented decision not to attempt cardiopulmonary resuscitation (DNAR) or a written Preferred Priorities of Care document. It is worth noting that patients cannot request specific treatment as part of an ACP, only refuse certain treatments (such as artificial feeding or resuscitation).

ACP allows a person with a progressive ataxia to retain control over their future treatment and management. Talking and planning ahead can provide comfort and reassurance. However, not all individuals with ataxia are able to engage with advance care planning. Some patients will want only information that is required to live one day at a time and will not want to be part of discussions that focus on future deterioration and further loss of function. These people may find attempts by professionals to engage them in ACP conversations unwanted and distressing. Effective communication, carried out with compassion and sensitivity, is therefore fundamental to the process of providing good quality person centred care.

Only a person with capacity who chooses to do so can take part in advance care planning. Should an individual with capacity wish to record choices about their care and treatment, or an advance decision to refuse treatment, in advance of losing capacity, they should be guided by a professional with appropriate knowledge and this should be thoroughly documented. Patients should be encouraged to review regularly any care planning documentation, to update this as appropriate, and to ensure that revisions are shared with those they wish to involve in their care. Advance care plans should be recorded on an electronic end of life system (if available) such as 'Coordinate my care'. Where a person lacks capacity to decide, care planning must focus on determining their best interests and making decisions to protect these[275].

End of Life Care

The progressive ataxias often have a disease course spanning several decades. It can be hard to know when the end of life is approaching. In other conditions, identifying the patient's last year of life is important in order to begin advance care planning. However, with some of the progressive ataxias, it may be necessary to engage in advance care planning some time before the individual is in the last year of life; before poor quality speech and other communication barriers intervene. Whether or not ACP has taken place before, identifying the end stage of the illness is still essential to ensure individuals and their families are provided with the most appropriate support.

Accurately predicting prognosis is virtually impossible in most advanced diseases, so clinicians can use certain triggers to identify a person approaching the end of life. One such trigger is the 'surprise question': "Would you be surprised if this patient died in the next 12 months?" [276]. In addition to the intuitive surprise question, clinicians should consider general and specific clinical prognostic indicators for patients with ataxia:

General indicators (common across different diseases):

- progressive physical decline
- increasing need for support
- progressive weight loss
- repeated/ unplanned crisis admissions

Indicators specific to ataxia:

- complex symptoms which are difficult to control
- swallowing problems (e.g. choking with meals) leading to recurrent aspiration pneumonia, sepsis, breathlessness or respiratory failure
- Speech problems; increasing difficulty in communication plus progressive dysphasia, dysarthria and fatigue.
- Congestive Heart Failure New York Heart Association classification class 3 or 4. (Shortness of breath on minimal exertion or at rest.)

Answering 'no' to the surprise question and identifying general or disease specific clinical indicators of decline should alert the multi-professional team that an individual with ataxia is approaching the end of life.

While many patients, families and professionals do not want to talk about death and dying, discussion enables the best possible end of life care tailored to the individual. In recent years the concept of a 'good death' has emerged[277]. A 'good death' usually means:

- Being treated as an individual, with dignity and respect
- Being without pain and other symptoms
- Being in familiar surroundings and
- Being in the company of close family and/or friends.

Provision of high quality end of life care includes attention to the patient's preferred place of care (home, hospital or hospice) and the provision of spiritual and pastoral support. As the person enters the dying phase, the focus of treatment shifts and symptom control and comfort take precedence over life prolonging treatment such as enteral feeding. The five priorities of care defined by the 'Leadership Alliance for the care of dying people' must be followed at this phase, and an individualised plan of care agreed with the patient and/or family in the final days/hours of life[278].

Recommendations	Grade
1. All healthcare professionals should ensure patients are aware that Advance Care Planning is an option and advise patients consider doing it.	GPP
2. All healthcare professionals should facilitate advance care planning and documentation of advance care directives in individuals with ataxia.	GPP
3. Documented Advanced Care Planning for individuals with ataxia should be regularly reviewed by the individual in conjunction with their treating clinicians. Review may be instigated by the individual or care provider, can be part of regular review or may be triggered by a change in circumstances.	GPP
4. Consider referring to a specialist palliative care team when an individual with ataxia has complex distressing symptoms, psychological, social or spiritual needs, and/or a need for end-of-life planning.	GPP
5. Ensure an individual identified as approaching the end-of-life stage and their family have open access to specialist palliative care services.	GPP
6. If needed offer specialist input in the last few days of life, and aftercare and bereavement support to their families.	GPP

7. Research

Recent progress

There have been a number of advances in the last few years in the identification of new genes causing specific ataxias, largely due to recent developments in gene sequencing technologies. Worldwide research using next generation sequencing and whole exome/genome sequencing has led to the identification of many new forms of ataxia and these developments are beginning to be translated into clinical services available to patients[34].

Research is also progressing in understanding the basic biological mechanisms underlying the ataxias and many therapeutic targets have now been identified. This has then lead to pre-clinical studies of potential disease-modifying drugs in animal and cell models, and encouragingly a number of clinical trials in people with ataxia are ongoing.

A summary of recent published trials is found below *(Table 14)*. This is included to illustrate that a number of types of drug trials have taken place. There are also many more trials in the pipeline, either to confirm the studies of pilot studies listed or exploring new potential treatments *(see Ataxia UK website and www.clinical trials.gov)*. Although there are as yet no approved treatments for the majority of progressive ataxias, it is hopeful that due to this increased activity approved treatments will become available soon.

Table 14: List of recent published trials in ataxia

Medication	Type of ataxia	Type of drug/mode of action
Idebenone[279–286]	Friedreich's ataxia	Antioxidant
CoQ10/Vitamin E[287,288]	Friedreich's ataxia	Antioxidant
Carnitine/creatine[289]	Friedreich's ataxia	Antioxidant
Deferiprone[290]	Friedreich's ataxia	Iron chelator
Deferiprine and idebenone[291]	Friedreich's ataxia	Iron chelator & antioxidant
Triple therapy Idebenone, deferiprone and riboflavin[292]	Friedreich's ataxia	Iron chelator & antioxidants
EPO[293–295]	Friedreich's ataxia	Increases frataxin
Carbamylated EPO[296]	Friedreich's ataxia	Increases frataxin
A0001[297]	Friedreich's ataxia	Antioxidant
Nicotinamide[298]	Friedreich's ataxia	Increases frataxin
RG2833[299]	Friedreich's ataxia	Increases frataxin
Interferon gamma[300,301]	Friedreich's ataxia	Increases frataxin
Resveratrol[302]	Friedreich's ataxia	Antioxidant
Riluzole[303,304]	Mixed ataxias	Drug repurposing/unknown mechanism
Lithium[305,306]	SCA2, SCA3	Drug repurposing/ reduces protein aggregates
Varenicline[307–313]	SCA3, SCA14, Friedreich's ataxia, Fragile X tremor/ ataxia	Drug repurposing/ unknown mechanism
Memantine[314,315]	Fragile X tremor/ ataxia	Drug repurposing/unknown mechanism

Research has also focused on the development of tools to measure the severity and progression of ataxia for use in trials such as validated ataxia-specific rating scales *(detailed in Table 15, below)*.

Table 15: Ataxia rating scales	
International cooperative ataxia rating scale (ICARS)[316]	All ataxias
Scale for the Assessment and Rating of Ataxia (SARA)[148,317]	Spinocerebellar ataxias/Friedreich's ataxia
Friedreich's ataxia rating scale (FARS)[318]	Friedreich's ataxia
Friedreich's ataxia impact scale (FAIS)[319]	Friedreich's ataxia
Inventory of non-ataxia signs (INAS)[320]	Progressive ataxia disorders

Databases and natural history data is being collected by networks of researchers worldwide and this has been of immense use in the design and implementation of clinical trials[317,321]. Due to all these encouraging developments, and the incentives provided in legislation on research in rare disease generally, pharmaceutical and biotech companies are now engaging more in ataxia research and indeed many research trials are being run by pharmaceutical companies, often in collaboration with university researchers and patient groups, such as Ataxia UK.

Participating in research studies

It is good clinical practice to offer patients the opportunity to take part in research projects. For information on research studies recruiting participants in the UK contact Ataxia UK, the ataxia charity who supports people with ataxia and works towards developing treatments for the ataxias.

Ataxia UK

For more information on ataxia research contact Ataxia UK, which provides up-to-date information for patients and healthcare professionals on developments in the ataxia field, including opportunities for patients to take part in research. Healthcare professionals are encouraged to join Ataxia UK's Medical Registry and/or Researcher's Registry and receive regular electronic newsletters with information on any trials recruiting participants. Information on ataxia conferences and ataxia training days is also provided.

(Register online at: www.ataxia.org.uk)

Ataxia UK also provides funding for research projects and facilitates research (eg: by organising ataxia conferences/meetings, helping to recruit participants in research projects and advising on the research landscape) and is willing to work in partnership with interested parties from academia, industry, patient groups and other stakeholders (contact research@ataxia.org.uk).

For more information on research developments and taking part in research projects contact Ataxia UK (www.ataxia.org.uk).

8. Appendix

A list of neurologists at Ataxia UK Accredited Specialist Ataxia Centres and other Centres of expertise*.
The following are adult neurologists (and clinical geneticists where indicated).

Specialist Ataxia Centres

Prof Marios Hadjivassilliou
Ataxia UK Accredited Ataxia Centre, Royal Hallamshire Hospital, Sheffield Teaching Hospitals NHS Trust
Glossop Road, Sheffield S10 2JF

Dr Paola Giunti
Ataxia UK Accredited Ataxia Centre, National Hospital for Neurology and Neurosurgery
Queen Square, London WC1N 3BG

Prof Rita Horvath
Ataxia UK Accredited Ataxia Centre,Newcastle upon Tyne Hospitals NHS trust, Royal Victoria Infirmary
Queen Victoria Road, Newcastle upon Tyne NE1 4LP

Other Centres

Dr George Tofaris & Prof Andrea Nemeth
(Clinical Geneticist)
Ataxia Clinic
John Radcliffe Hospital, Oxford
OX3 9DU

Dr Richard Davenport
Western General Hospital
Crewe Road South, Edinburgh
EH4 2XU

Dr Rajith de Silva
Queen's Hospital
Rom Valley Way, Romford, Essex
RM7 0AG

Dr John Ealing
Salford Royal NHS Foundation Trust
Stott lane, Salford, Greater Manchester
M6 8HD

Dr Nick Fletcher
The Walton Centre for Neurology and Neurosurgery,
NHS Trust, Lower Lane, Liverpool
L9 7LJ

Dr Simon Hammans
St Richard's Hospital
Spitalfield Lane, Chichester, West Sussex
PO19 6SE

Dr Paul Hart
St Helier Hospital
Wrythe Lane, Carshalton, Surrey
SM5 1AA

Dr John McKinley & Dr Seamus Kearney
Royal Victoria Hospital
Grosvenor Road, Belfast
BT12 6BA

Dr Neil Robertson & Dr Mark Wardle
University Hospital Wales
Heath Park, Cardiff
CF14 4XN

Dr Alastair Wilkins
Southmead Hospital
Bristol
BS10 5NB

Professor Nicholas Wood
Institute of Neurology
Queen Square, London
WC1N 3BG

Dr Paul Worth
Cambridge University Hospitals
NHS Foundation Trust
Hills Road, Cambridge
CB2 0QQ

Paediatric neurologists & paediatric clinical geneticists

Prof Peter Baxter: Sheffield Children's Hospital, Western Bank, Sheffield, S10 2TH

Prof Andrea Nemeth *(Clinical geneticist, see details above)*

Dr V Ramesh: Great Northern Children's Hospital, Queen Victoria Road, Newcastle upon Tyne, NE1 4LP

**Please note that this is a list of specialists known to Ataxia UK and to the Guideline Development Group and is not an exhaustive list. We would welcome contact from other neurologists with expertise in ataxia (email: research@ataxia.org.uk)*

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