



Department
of Health

The UK Strategy for Rare Diseases



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Llywodraeth Cymru
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The Scottish
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Ministerial foreword

The UK Strategy aims to ensure no one gets left behind just because they have a rare disease. We want to put the patients' needs first. To do this, we will bring together the talent, skills and professionalism of all relevant sectors. This will bring real, positive change in how we deal with rare diseases and how we help people with complex conditions.

There are between 5,000 and 8,000 rare diseases. Each one affects less than 0.1% of the UK's population, but together they affect the lives of 3 million people.

The Strategy aims to ensure that people living with a rare disease have the best quality of evidence based care and treatment that our health and social care systems, working with charities and other organisations, our researchers and industry can provide.

The UK is a recognised leader in research, treatment and care for rare diseases. It is at the forefront of the genomics revolution which could radically transform the way we diagnose and treat patients with rare diseases. We are already starting to drive this work forward, through initiatives such as the programme that will map the whole genome of 100,000 NHS patients which has

rare disease as one of its key priorities. This Strategy illustrates the UK commitment to build on our successes to date.

The diagnosis, treatment and management of rare diseases also require the highest level of partnership working to remove unnecessary barriers. We will build upon the best research, diagnosis and service provision that already takes place in the UK and elsewhere. We will improve understanding of rare diseases and increase the chances of finding effective and sustainable treatments and therapies. We will continue to encourage and develop collaboration at all levels and wherever possible.

All 4 UK countries will work together to achieve these goals. However, it is recognised that there will be certain areas where each country may wish to take a different approach on delivery, such as delivery of patient services, data sharing, national commissioning and priority setting. Separate plans for England, Scotland, Wales and Northern Ireland will be published to support and facilitate the implementation of this UK Strategy.

The plans will build upon current services following best practice and achieving value for money through the effective use of resources. They will support the UK Strategy and give people more detailed information on what is needed and how it will be delivered locally and nationally for the Strategy to succeed.

To develop the UK Strategy for Rare Diseases, the Rare Diseases Stakeholder Forum was established. We will ask that this

Forum continues to work with all 4 countries of the UK to monitor the implementation of this Strategy to ensure work in this vital area is driven forward.



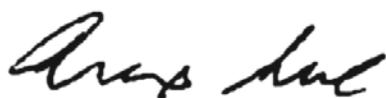
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Introduction

A rare disease is a life-threatening or chronically debilitating disease that affects 5 people or fewer in 10,000 and requires special, combined efforts to enable patients to be treated effectively.

The total number of rare diseases is steadily increasing because genetic research is beginning to explain disease patterns that we did not understand before. Research shows that 1 in 17 people will suffer from a rare disease at some point.¹ In the UK, this means more than 3 million people will have a rare disease – so rare diseases are not actually rare. They represent a significant cause of illness, making considerable demands on the resources and capacity of the NHS and other care services.

At least 80% of rare diseases have an identified genetic origin and 50% of new cases are in children.² Other causes of rare disease are infections, allergies, deterioration of body tissues and organs and teratogenic effects (disorders that occur to a foetus in the womb, for example through exposure to the drug Thalidomide).

As well as their main disease, some patients have other conditions that make treating and managing their disease even more difficult.

Why do we need a UK Strategy?

In the UK, there are many examples of excellent and world-class services for people with rare diseases. However, we want to see further improvement across the whole ‘patient journey’: the patient’s experience from their first contact with the NHS through to reaching a diagnosis and onto managing their condition and on-going care.

It can still take too long for patients to get a diagnosis for a rare disease. Around 4 in every 10 patients say they found it difficult to get a correct diagnosis.³ The coordination of care after diagnosis could also be improved, especially for genetic testing and services that help with diagnosis.

This Strategy does not just focus on patient services. It also covers scientific research, which is important for improving our understanding, diagnosis and treatment of rare diseases. The UK has a vibrant life sciences sector, which means we could be at the forefront in the development of new technology that improves services and opportunities for people with rare diseases.

Across all 4 countries of the UK, considerable work is being carried out to develop services for patients and to encourage and fund research. There are systems to identify and treat rare diseases including NHS

¹ <http://www.rare-disease.org.uk/about-rare-diseases.htm>

² http://www.eurordis.org/sites/default/files/publications/Fact_Sheet_RD.pdf

³ http://webarchive.nationalarchives.gov.uk/20130107105354/http://www.dh.gov.uk/en/Publicationsandstatistics/Publications/AnnualReports/DH_113912

genetics services, research programmes, and education and training for healthcare professionals.

Each country also has a longstanding and productive relationship with patient groups. This has allowed people with a rare disease to have a say in how services have been developed. It has also given policymakers valuable insight into the barriers that people have to overcome when living with their condition.

Background to the Strategy

Over recent years, the way in which rare diseases affect the lives of individuals, their families and carers and the cumulative impact they have on health and social care systems have become increasingly prominent in policy development, including:

- In 2009, a Recommendation of the Council of the European Union called for each EU State to have in place a rare diseases plan or strategy by the end of 2013 (2009/C 151/02).⁴
- In 2010, the ‘Annual Report of the Chief Medical Officer (England)’ highlighted the need for action on rare diseases and their effects on health.
- In 2012, the UK Health Departments carried out a consultation on the development of a UK plan for rare diseases.⁵ There were more than 300 responses.⁶ They suggested ways of building on the UK’s current services,

expert clinical leadership and world-class research.

What’s in the Strategy?

This Strategy is the overarching framework document that sets out a shared vision for improving the lives of all those with rare diseases. The focus throughout is patients and families.

It makes commitments in a number of different areas and each UK country will need to show how these will be achieved in their own national plans which are due to be published by the end of February 2014. There are 5 areas where all 4 countries of the UK will take action, either together or individually:

- empowering those affected by rare diseases
- identifying and preventing rare diseases
- diagnosis and early intervention
- coordination of care
- the role of research

To achieve the Strategy’s aims, we will need to make the best use of current scientific, technological, medical and social resources. We will also need to build on and complement current initiatives, including:

- the ‘Strategy for UK Life Sciences’ and Innovation, Health and Wealth initiatives in England⁷
- ‘A Route Map to the 2020 Vision for Health and Social Care in Scotland’⁸, linking the ‘Healthcare Quality Strategy

⁴ <http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:C:2009:151:0007:0010:EN:PDF>

⁵ https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/215141/dh_132883.pdf

⁶ <http://webarchive.nationalarchives.gov.uk/20130107105354/http://www.dh.gov.uk/health/2012/11/response-rare-disease/>

⁷ https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/32457/11-1429-strategy-for-uk-life-sciences.pdf

⁸ <http://www.scotland.gov.uk/Topics/Health/Policy/Quality-Strategy/routemap2020vision>

for NHS Scotland⁹ and the Scottish Government's health and healthcare research strategy, 'Investing in Research, Improving Health'¹⁰

- 'Together for Health: a five year vision for the NHS in Wales'¹¹, linking the strategy documents 'Our Healthy Future'¹² and 'Fairer Health Outcomes for All'¹³
- 'Transforming your Care' in Northern Ireland¹⁴

All 4 UK countries have agreed to use the UK Strategy to improve services and research and to bring real, positive change for people with rare diseases.

⁹ <http://www.scotland.gov.uk/Resource/Doc/311667/0098354.pdf>

¹⁰ <http://www.cso.scot.nhs.uk/Publications/research.pdf>

¹¹ <http://www.wales.nhs.uk/sitesplus/documents/829/togetherforhealth.pdf>

¹² <http://wales.gov.uk/topics/health/cmo/healthy/?lang=en>

¹³ <http://wales.gov.uk/topics/health/publications/health/reports/fairer/?lang=en>

¹⁴ <http://www.dhsspsni.gov.uk/index/tyc.htm>

1. A UK-wide vision for rare diseases

1.1. All 4 UK countries will:

- promote equity of access – allowing everyone with a rare disease to follow a clear, well defined care pathway, providing high quality services for every individual through integrated personal care plans
- offer a patient centred, coordinated approach to treatment services, specialist healthcare and social care support which takes into account the needs of patients, their families and others who provide essential support
- deliver evidence-based diagnosis and treatment of rare diseases, developed through the best use of regional and national resources that are easily accessible by patients and professionals
- support specialised clinical centres to provide expert, high quality clinical care and expertise to patients their families and carers and the patient's, multi-professional health care team
- promote excellence in research and develop our understanding of and treatments for rare diseases
- deliver rapid and effective translations of advances in the understanding of rare diseases into clinical care by creating appropriate infrastructure, care pathways and clinical competences
- deliver effective interventions and support to patients and families quickly, equitably and sustainably
- promote collaborative working between the NHS, research communities, academia and industry wherever possible to facilitate better understanding about rare diseases and how they can be best treated
- support education and training programmes that enable health and social care professionals to better identify rare diseases to help deliver faster diagnosis and access to treatment pathways for patients
- promote the UK as a first choice location for research into rare diseases as a leader, partner and collaborator

2. Empowering those affected by rare diseases

2.1. Whilst expert clinical teams can offer advice and treatment in many cases, only those living with a rare disease have the direct experience of how it has affected them and their families. We must acknowledge how important the patient's experience and views are to:

- getting a diagnosis
- creating a care pathway
- developing services for people with a rare disease
- improving our understanding of rare diseases

2.2. In the UK, there are a wide range of patient organisations that offer help and support to people with a rare disease. Patient groups have an important role in helping patients and their families feel less isolated. Most patient organisations offer advice and support through websites, leaflets and personal contact. Many of them have specialist staff, including nurses and patient advocates (people who can act on a patient's behalf in health and care services). This range of support provides a lifeline to people who have a rare disease, and it complements the services that health and social care organisations provide.

2.3. The Health Departments of the UK have a long history of working closely with patient organisations. In the area of rare diseases this has provided exceptional mutual benefit through close working with organisations such as Genetic Alliance UK, Rare Disease

UK and the Specialised Healthcare Alliance, as well as organisations that deal with specific diseases.

2.4. Locally, most teams that provide specialised services are (or should be) keen to get the advice of their patients. As part of their usual routine, NHS services have surveys to find out patients' experiences. The results give useful information on what is going well and where things need to be improved.

2.5. For everybody's benefit (especially patients and their families), these relationships must continue, and we must build on them. They are especially important for making sure that patients, their families and professionals can get the information they need.

2.6. For a patient to make informed choices they must have access to reliable, correct information about their condition. Individual patient groups are a valuable source of help. But it is important that patients get information when they need it, so that they and their families can make sense of unusual and difficult situations. People want information about:

- how to find and contact support groups
- what their treatment options are
- relevant research

2.7. It is not just patients who need access to high quality information. The very fact that these diseases are rare means that health and social care professionals are

also unlikely to have previous experience of the patient's condition. This is particularly true in primary care (a patient's first point of contact, for example a GP). So it is important that professionals also have access to reliable information, including what treatment pathways are available. This situation is also likely to apply to other professional groups, such as pharmacists and teachers.

2.8. There are already some good sources of information, such as patient organisation websites and others such as Orphanet, which provides information on rare diseases and drugs to help improve the diagnosis, care and treatment of patients with rare diseases.¹⁵

2.9. The UK is a member of the international consortium that supports Orphanet. We believe it is a valuable resource for information sharing. The UK will work with its Orphanet partners to promote the site to people with rare diseases and to make it more accessible.

2.10. Patients must also know how to manage their own care and to take part in research. We address these issues later.

¹⁵ <http://www.orpha.net/consor/cgi-bin/index.php>

3. Identifying and preventing rare diseases

3.1. Many rare diseases are present at birth and are either caused by:

- a genetic problem (for example sickle cell disease) or
- deficiencies or exposures to substances around the time of conception or during pregnancy (for instance, spina bifida is associated with a folic acid deficiency around conception and early pregnancy)

3.2. The World Health Assembly resolution in 2010 emphasised that birth defects are still significant and that early diagnosis and action can prevent complications and illness.¹⁶

3.3. It will be important that the countries maintain an overview of prevention and management of rare diseases at a number of levels through different service providers and with different population groups.

Screening

3.4. One of the most widely known screening programmes is newborn blood spot screening. This programme is offered to all parents in all 4 UK countries, and it tests babies for a range of conditions including phenylketonuria, congenital hypothyroidism, sickle cell disease, cystic fibrosis and medium chain acyl-CoA dehydrogenase deficiency. With all of the above diseases, early action can lead to better results for the patient or prevent serious illness.

3.5. Screening programmes raise complex ethical, legal and social issues for the people who are offered screening – either as an adult for their own information or as a parent on behalf of their child.

3.6. The UK National Screening Committee advises ministers and the NHS in all 4 UK countries on all aspects of screening.

3.7. Using research evidence, pilot programmes and economic evaluation, the Committee assesses the evidence for national screening programmes against a set of internationally recognised criteria covering:

- the condition
- the test
- the treatment options
- the effectiveness and acceptability of the screening programme

3.8. Assessing screening programmes in this way is intended to ensure that they are both helpful and cost effective.

3.9. The Committee regularly assesses current screening programmes and new evidence for screening for other conditions.

¹⁶ http://apps.who.int/gb/ebwha/pdf_files/WHA63/A63_R17-en.pdf

Case study

When we fast (go without feeds/food) our body uses its own fat stores for energy. People with Medium-chain acyl-CoA dehydrogenase deficiency (MCADD) have a problem in producing energy from their body fat stores. During illness the body uses fat as its main supply of energy.

If a baby / child with MCADD becomes unwell and feeds poorly, or has vomiting or diarrhoea they will become drowsy, irritable or will not respond normally. This happens because they are not able to make enough energy from their body fat stores. We can prevent this by giving 'glucose polymer powder' to supply energy.

3.13. For example, there are many women who carry major X-linked disease like Duchenne muscular dystrophy. They are usually discovered by family testing when a boy in the family has developed the disease.

3.14. Testing for carrier status of abnormal genes is used in affected families and high risk populations. In the future, increasing experience with large genomic panels is likely to mean an expansion of capability for carrier testing with potential utility for detection of a range of genetic conditions in adults.

3.15. This will allow more informed choices about having a family, pre-conception or foetal screening or testing a child in early life. Naturally, this raises serious questions in the area of ethics, patient information and management of the results of any testing.

Carrier testing

3.10. Carrier testing involves testing people who are known to be at increased risk of being carriers of a specific inherited disorder. This may be because a relative is known to be a carrier or has the condition or certain genetic conditions might be more prevalent in their community.

3.11. Whilst not part of the general population screening programme in the UK, the availability of predictive testing is important for reproductive choice for adults, for example in ethnic groups who are at increased risk of recessively inherited disorders. These include conditions such as Tay Sachs and Thalassaemia.

3.12. Most of us who may carry a rare disease in our genes do not know that we do. If we happen to conceive with a partner who also carries the same gene, then the child may inherit the faulty gene from both parents and be affected by the disease. Only then do we find out that we are carriers.

Preconception and antenatal care

3.16. We can help to reduce the number of babies born with congenital disorders (disorders that are there from birth) and give parents reproductive choice through continuing programmes that:

- encourage pregnant women to eat well (for example by supplementing their diet with folic acid)
- encourage women to avoid exposure to harmful substances or organisms before and during pregnancy (for example by having the rubella immunisation)
- screen women during pregnancy

Antenatal and new born screening

3.17. Even those with severe rare diseases can sometimes be identified and treated at an early stage to reduce the impact of their disease (for example through surgery, nutrition or medication). Antenatal and new

born screening (for example newborn blood spot screening) has an important role to play.

3.18. The new-born period is a particular focus of attention in addressing these conditions, mainly because of their extreme rarity but also due to the non-specific nature of their presentation.

3.19. Early, effective screening means that parents can be immediately referred to specialist centres for diagnosis and onward management.

Cascade testing for severe genetic conditions

3.20. Early diagnosis and early evidence based treatment are also important in reducing the impact of a disease on adult lives.

3.21. Cascade testing involves testing 'at risk' relatives for a genetic condition. Used effectively, it can reduce morbidity (how common a condition is) and mortality (the death rate). For example, after someone dies as a result of long QT syndrome (a rare inherited heart condition), cascade testing can identify relatives who may benefit from drug treatments or implantable defibrillators, preventing cardiac episodes and sudden death.

4. Diagnosis and early intervention

4.1. Delays in diagnosis mean that opportunities for timely interventions can be missed. In addition, relatively common symptoms can hide underlying rare diseases, leading to misdiagnosis. In 2004, a survey of 8 rare diseases revealed that 25% of patients said there was a gap of between 5 and 30 years between getting their first symptoms and diagnosis.¹⁷

4.2. Sometimes it is obvious that a person has a health problem. But diagnosis may require specific expertise. For example, if someone loses sensation in their hands and feet, a probable diagnosis is peripheral neuropathy. There are many common causes of peripheral neuropathy. However, there are also some very rare causes that can only be identified by a person with specialised expertise and laboratory tests.

4.3. Rare diseases are covered in undergraduate and postgraduate medical training in the UK. But it is unrealistic to expect primary care staff such as GPs (who are very often the first point of contact) to recognise all rare diseases. Many diseases are so rare that a GP is unlikely to see a single case in their whole career. Timely and accurate referral is therefore a crucial skill.

4.4. In 2008, a review identified 5 aspects of diagnosis that are particularly difficult for GPs.¹⁸

- atypical presentations
- non-specific presentations
- very rare conditions
- co-morbidity (more than one disease present)
- perceptual features that could be missed

4.5. Often these features occur together, making it hard to make an accurate diagnosis. Despite the best efforts of the NHS, it may still prove extremely difficult, or indeed impossible, to agree a diagnosis.

4.6. All 4 UK countries need to find ways to identify and help the significant number of patients who have no definite diagnosis, especially children with developmental delay that has no known cause. The UK may have to work with other countries to find a solution to this challenge. Methods that may help to ensure speedy diagnosis in people with a rare disease are addressed below.

High quality training

4.7. Tools to reduce the time it takes to diagnose a rare disease will not be effective unless there is the right level of education,

¹⁷ <http://www.eurordis.org/publication/survey-delay-diagnosis-8-rare-diseases-europe-%E2%80%98eurordiscare%E2%80%99>

¹⁸ Kostopoulou O, Delaney BC, Munro CW. Diagnostic difficulty and error in primary care—a systematic review. *Family Practice* (2008) 25(6): 400-413

training and awareness promotion of rare diseases and how many people have one.

4.8. The NHS has a good reputation for high quality training, but rare diseases require additional skills.

4.9. We need to ensure that all doctors are alert to the possibility of a rare disease when they see patients, even if they are not able to diagnose specific diseases. This means including better training on rare diseases on university courses (undergraduate and postgraduate) and in professional development at work. Health professionals do not need detailed knowledge of every rare condition. But all medical specialties and multi-professional care teams should have a general awareness of rare diseases, so that they can make rapid referrals to specialists in the appropriate field.

Clearly defined care pathways

4.10. It is essential to have clear, easily accessible and effective care pathways. These are likely to include primary care, local hospitals, regional centres and specialist clinical centres. There should be common protocols for identifying patients at risk of rare diseases, or who have no diagnosis. Patients should receive a focused, coordinated diagnostic service so that they can get a quick diagnosis rather than having to start again every time there is an inconclusive test result.

The role of the patient

4.11. It is important to acknowledge that many patients with access to well signposted sources of reliable information can help clinicians with decisions about referral and diagnosis.

Assessing treatments

4.12. So that patients with rare diseases get the most effective treatments, it is important that we have appropriate procedures for evaluating the benefits and costs of treatments as they become available. These procedures should be transparent and robust enough to be able to take account of the particular challenges that occur when evaluating treatments for rare diseases.

4.13. For effective evaluation, there needs to be processes to let people know when new treatments become available. UK Pharmascan is the UK-wide source of information about new medicines.¹⁹ It provides valuable information for NHS organisations to help them plan effectively for the introduction of new treatments.

Genetic testing

4.14. The UK Genetic Testing Network (UKGTN) promotes equal access to laboratory services and ensures the quality of that genetic testing for inherited conditions. One of its key functions is to evaluate genetic tests for rare disorders. If a test fulfils the UKGTN evaluation criteria, it is suitable for commissioning purposes.²⁰

4.15. The process evaluates the care pathway for the rare disorder and the guidance to clinicians as to when they should request a test. On its website, UKGTN also has an online directory of UK laboratories that provide genetic tests for rare diseases and the clinical criteria for their use.

¹⁹ <https://www.ukpharmascan.org.uk/>

²⁰ <http://ukgtn.nhs.uk/resources/testing-criteria/>

Case study

The Molecular Genetics Laboratory at the Southern General Hospital in Glasgow has the lead interest in infantile epilepsy. In 2005 it introduced tests for mutations in the SCN1A gene which cause infantile epilepsy. The laboratory has close links with the Yorkhill Hospital Paediatric Neurology Department. Over the past 8 years this collaboration has led to the service expanding the cohort of genes that it tests for. Testing is now available for 12 genes that account for some of the commonly associated infantile onset epilepsy syndromes. Almost 500 children a year are tested for genetic abnormalities.

The identification of a mutation and confirmation of a genetic epilepsy syndrome can have a positive influence on treatment options and clinical outcome for these children. This is because early diagnosis and subsequent targeted treatment can prevent co-morbidities of the syndrome by reducing seizure frequency.

Without genetic testing it can take several years to get a correct diagnosis. By this time developmental delay (due to prolonged and recurrent seizures) is severe and irreversible.

The laboratory receives specimens from the 4 Scottish Molecular Genetic Consortium centres as well as referrals from the rest of the UK and many international destinations. The testing service for infantile onset epilepsy syndromes has established the Molecular Genetics Laboratory as a centre of excellence for these conditions.

Coding and classification

4.16. High quality healthcare, diagnosis and intervention relies upon accurate methods of recording genetic information to detail the incidence and prevalence of disease, and to enable service planning and international collaboration.

4.17. The standard system for coding and classification of disease is the World Health Organisation's International Classification of Diseases (ICD). The ICD is a global standard that has been used for 100 years, so it has proved its worth in the classification of common disorders. Now in its 10th revision (ICD-10), it is used to code hospital activity and death statistics in the UK.

4.18. Whilst accurate – a recent review showed that coding of primary diagnosis was accurate in 96% of cases in hospital statistics – its value for rare diseases is extremely limited. This is because it is not good at separating out the thousands of rare diseases and disorders. However, systems such as Orphanet provide a more comprehensive approach to collecting, archiving and sharing data on rare diseases.²¹

4.19. The ICD is currently being revised with the aim of publishing an 11th revision (ICD-11) in 2015.²² There is a specific working party to address the challenges of coding for rare diseases. The European Commission has acknowledged there is a need for a group of experts in this area, and it has said it will

²¹ Orphanet (<http://www.orpha.net/consor/cgi-bin/index.php>) is a freely accessible online rare disease catalogue which includes clinical phenotype information. It is used as a rare diseases reference database in Europe and beyond.

²² <http://www.who.int/classifications/icd/revision/en/>

establish a Commission expert group on rare diseases.²³

4.20. Changing the basic system of classification and coding requires training for medical coding staff in all NHS hospitals and in the national statistics organisations. It also requires software to be updated. Therefore, changing a fundamental coding system can create significant challenges.

4.21. Any changes in coding practice must be evidence based. Along with other funders, the Department of Health in England is supporting several large scale alternative coding initiatives for rare diseases (for example the use of the Human Phenotype Ontology coding in the Deciphering Developmental Disorders programme).²⁴ Existing software can make integration into computerised clinical coding systems easier.

4.22. Current and future ICD coding systems will require connectivity, between ICD on the one hand and Human Phenotype Ontology²⁵ and SNOMED²⁶ on the other, if we are to deliver improvements in the coding of rare diseases and disorders that can support health policy and care delivery. Improved coding can also build on systems like Orphanet, which is also connected to genotype coding carried out by the UK-based European Bioinformatics Institute.

4.23. As part of this Strategy, the UK will examine whether ICD-11 can complement other coding systems that are more relevant to rare diseases, to support the planning and delivery of care.

4.24. We also need to take account of coding in general practice (for example doctors'

surgeries). In Scotland 'Read Codes' are used in general practice. In England there is a planned move to a new system of coding by 2014. Clarity is needed on how these general practice coding systems will link with the ICD codes used in hospitals and the Orphanet codes.

Effective IT support

4.25. There needs to be a different approach to diagnosis in cases where a rare disorder is not even suspected, often because the rare disorder mimics common conditions.

4.26. For example, a patient may have 2 symptoms which are common separately but only very rarely occur together. A computer prompt could alert a doctor to the risk if a patient reports the 2 symptoms together. The UK will examine how information held in patient records and in databases such as Orphanet can be adapted to improve the diagnosis of rare diseases within existing healthcare services.

²³ http://ec.europa.eu/health/rare_diseases/docs/dec_expert_group_2013_en.pdf

²⁴ <http://www.ddduk.org/>

²⁵ <http://www.human-phenotype-ontology.org/>

²⁶ <http://www.connectingforhealth.nhs.uk/systemsandservices/data/uktc/snomed>

5. Coordination of care

5.1. Some patients need expertise from a number of specialists, making a multi-disciplinary and coordinated team approach important. Well coordinated care is essential when several specialists and hospital departments are involved in a patient's care. It is not the best use of time or resources if patients have to visit different departments at the same hospital on different days, particularly if the hospital is not close to their home. Problems can also occur if possible interactions between different treatments are not properly managed.

5.2. Primary care services often manage a patient's day-to-day care. It is therefore important that GPs feel supported and that they can manage care efficiently. Following diagnosis, a patient should have an evidence based care plan that identifies the anticipated course of the condition and sets out the responsibilities of specialist, general and primary care services in care management. Good communication between patients, their families and professionals is essential to ensure that the primary care plan is agreed and the care team has information and appropriate specialist support. The ultimate aim will be to ensure that the agreed care plan is delivered effectively.

Case study

Outreach clinics, held in Child Development Centres, enable families to be seen in one place at one time by the local paediatrician, the regional neurologist, therapists from both local and regional services and a representative of the Muscular Dystrophy Campaign. This is a model that seems to work with a number of different very rare conditions where the symptoms and anticipated problems are fairly similar. It would seem problematic and perhaps unnecessary, to have separate clinics for each of these conditions.

5.3. It is essential to coordinate care across the 'boundaries' between different services, so that care is effective, accessible and convenient to patients (for example, it should not disrupt their work or education). People coordinating care should consider the boundaries between:

- primary, secondary, tertiary and quaternary healthcare services (from the point of visiting a GP to the provision of highly specialised medical care)
- healthcare, social care and voluntary sector services
- child, adolescent, adult and older people's health services, especially in regard to multi-system disorders
- different medical disciplines

- service delivery and academia, which can help to sustain services and attract good experts from across the UK

5.4. Improving coordinated care requires a joined-up approach by all concerned, to find a suitable balance or an innovative way forward. This should include discussions with patients, their family and their carers. For example, healthcare professionals are already using telemedicine and IT to coordinate care. Telemedicine especially means geographical distance does not have to be a barrier to coordinated care. It can improve access to specialist medical services that might not be available in some areas.

5.5. Telemedicine expands consultation techniques beyond face-to-face meetings. It is now progressing to sophisticated clinical examinations and imaging using secure broadband links; connecting patients and experts irrespective of their geographical location.

5.6. There are also potential benefits to using IT to help staff meet agreed standards of care and to manage data.

Case study

Tim Goodship, Professor of Renal Medicine at Newcastle University, played a central role in describing the genetic basis for a rare and severe kidney disease called atypical haemolytic uraemic syndrome. As he is in constant demand across the country for assistance in patient management, he now consults from his office with a secure encrypted video-consulting platform. Colleagues and patients load the necessary software onto either a PC or mobile device, and a broadband internet connection allows them to have consultations without the need to travel.

5.7. Responsibility for coordination will depend on the case and the circumstances. For those receiving complex treatment where only one discipline is involved, a highly specialised professional might have responsibility for coordinating their care. Where there are many disciplines, the clinical geneticist may have responsibility. In any case, the aim should be to ensure that care is always coordinated.

5.8. Patients should have an overall care plan to manage coordination of care between health and social services. The care plan should also involve the extended family of a patient, who may have health problems themselves. The plan might address a range of issues, including:

- sources of information and support
- access to tools and services that help with diagnosis
- access to expertise in clinical specialist centres
- links between the GP and experts
- how treatment will be managed, including the role of the patient
- how the patient might take part in research programmes
- involvement of social services and other agencies

5.9. The care plan might also identify a person who can liaise, on behalf of the patient, with the professionals involved in a person's care. But each country will need to take its own view on this. To ensure consistent and coordinated care in managing rare diseases, there is likely to be a role for guidelines and protocols which may need to be based on mutual agreement where there is no hard evidence to say what works best. These might also cover care that is not directly related to the rare disease. It may be useful to get an idea of what is needed from places that have already adopted this approach.

5.10. To improve services in the longer term, there is a place for coordinating and integrating data nationally and internationally – particularly for rare diseases that affect very few people. This could be based on a standard approach to data collection to compensate for the small numbers of cases.

Case study

In Northern Ireland, for some lysosomal storage disorders (LSDs) there is a twice yearly clinic where a consultant from the Manchester LSD Centre comes to see patients jointly with the local consultants. The patients benefit from his expertise without having to travel to England. Some patients with these disorders do attend designated centres if this is considered their best course of management. These different options ensure that patients in Northern Ireland access the same level of expertise as they would in England. Bringing in a consultant has the benefit of minimising travel for patients who may have multiple health problems. It also helps to share knowledge with local clinicians.

Specialist clinical centres

5.11. The UK wants to support the sharing of information, data, knowledge and best practice in treatment nationally, across Europe and further afield.

5.12. Specialist clinical centres can provide an opportunity to acquire and maintain knowledge through research and interaction with patients. They bring together multi-disciplinary teams of health and social care professionals to manage patient care and local resources effectively and efficiently. The centres are not necessarily specific locations but may be 'virtual', using appropriate technologies to bring experts together.

5.13. Timely referrals to appropriate centres can be important in reducing the time it takes to receive a diagnosis. The use of new technologies such as telemedicine will increasingly mean that patients can access expert services remotely. This reduces the need for patients to travel and allows the creation of networks of experts who work together across hospitals.

5.14. In providing specialist health and care services, they help with the coordination of professional care and reduce the time that patients spend seeking help. They can also provide information and advice to patients and professionals, identifying where the care pathway can be improved. These centres are uniquely placed to provide a focal point for undertaking research and for implementing evidence based practice across all aspects of the patient pathway. Centres should have connections to others across the UK and in Europe.

5.15. Although specialist clinical centres may provide all the essential expertise, in almost all cases most of the care is provided locally – by local hospitals, primary care teams, social care and education teams, and in the patient’s home. Therefore, centres must have protocols in place to share their expertise with local services. This will require the development of shared protocols for effective communication and information sharing between the centre, local teams and the patient.

5.16. It would not be practical to have expertise in every disease at every specialist centre. A hub and spoke model, however, could ensure that expertise can be collated at the centres, no matter where the expertise is located.

6. The role of research

Increasing the evidence base

6.1. The UK is a trusted and respected leader in research into rare diseases. Improving the link between research and services for patients we will promote a culture of innovation. This will then lead to faster access to evidence based care. The basic and translational research needed to achieve these benefits for society will also require international collaboration, particularly for extremely rare diseases.

6.2. There is currently a lack of robust epidemiological (related to the frequency, distribution and control of diseases), clinical and health economics data for most rare diseases. For example, the natural history of many rare diseases is still unknown, information is spread out across care providers and patient organisations, and there is a lack of longitudinal health outcome data (data on the long term changes in people's health).

6.3. Therefore, estimates about the health and social care 'burden' associated with rare diseases are inadequate. This stops commissioners implementing evidence based policies for providing care and measuring improvements in care against known benchmarks. All the UK countries are looking at ways to collect data to address this gap, and this work needs to continue.

6.4. More research is needed on the most effective approaches for delivering care for most rare disease. This will help prevent

patients affected by the same rare disease getting different care. Research to define the best care pathways for rare diseases must be carried out. This would complement the EU supported RARE-Bestpractices programme.²⁷

Engaging and involving patients in research

6.5. Input from patients and their families can improve both the quality and effectiveness of research. Their involvement should be encouraged at all stages of the research process. This can be done by working with patient groups and using new opportunities such as social media (for example Facebook, Twitter and PatientsLikeMe).

Case study

In Wales, the National Institute for Social Care and Health Research (NISCHR) is developing a delivery plan for patient and public involvement (PPI) in health and social research. This plan will outline NISCHR's vision for PPI in health and social care research and will set out its commitment to ensuring that the public, patients and users will be involved in all areas of its work.

6.6. The National Institute for Health Research (NIHR) in England ensures consideration of patient and public involvement is included within the assessment

²⁷ <http://www.rarebestpractices.eu/>

and awarding of all research across all its funding programmes. In addition, INVOLVE, a national advisory group funded by the NIHR, supports greater public involvement in the NHS public health and social care research.²⁸

6.7. The British Paediatric Surveillance Unit enables doctors and researchers to find out how many children in the UK and Republic of Ireland are affected by particular rare diseases or conditions each year.²⁹

Ethics and research governance

6.8. All research studies that involve human subjects follow national guidelines, regulations and laws, and must respect the dignity of research participants at all times. However, there is a need to ensure that governance and regulation are proportionate, so as to make research projects in the UK more cost-effective, speeding up research permissions and reducing the time it takes to get research started.

6.9. The Health Research Authority (HRA) has a role to streamline research approvals in the NHS, and is making considerable progress in this regard, working with NHS Research and Development, NIHR and the 4 countries of the UK. Pending legislation, it is intended that the HRA will take responsibility for the Research Governance Framework.

6.10. Unfortunately, an unintentional consequence of modern research governance has often meant the common practice of genetics teams, working on small projects, joining forces to investigate a particular rare disorder fall foul of the need for individual contracts and material transfer agreements. This situation can be frustrating for researchers, patients and families.

6.11. This issue is being addressed. In England, the National Institute for Health Research Office for Clinical Research Infrastructure has worked with NHS colleagues to develop a national agreement applicable to Non-CTIMP rare disease projects.³⁰ The NIHR UK Rare Genetic Disease Research Consortium Agreement provides a governance framework for rare disease Non-CTIMP projects that are developed by a regional genetics centre and supported by their NHS Trust (NHS Board in Scotland).³¹ Under this agreement, the research and development team responsible for all the other regional genetics centres will also sign off the project without a full review of protocol and the need for individual negotiations.

Improving diagnosis

6.12. There are 3,200 rare diseases for which the causative gene is known. One of the main barriers to providing testing in mainstream NHS services has been the cost of providing a DNA based diagnosis. New technology such as next generation sequencing (NGS) and falling sequencing costs are likely to mean that DNA-based diagnosis will become more affordable. Developments in NGS as part of routine diagnosis will give a better understanding of most rare diseases for which the causative gene is known, and more insight into the causative genes in many disorders for which the gene is not yet known.

6.13. In December 2012, the UK Government said up to £100 million could be used to make whole genome sequencing available to NHS patients over the next 3 to 5 years.

²⁸ <http://www.invo.org.uk/>

²⁹ <http://www.rcpch.ac.uk/bpsu>

³⁰ Clinical Trial of an Investigational Medicinal Product

³¹ <http://www.bsgm.org.uk/genetics-healthcare-research/nih-uk-rare-genetic-disease-research-consortium-agreement/>

It is intended to generate 100,000 whole genome sequences. Rare diseases are one of the initial priority areas for the project, along with cancer and infectious disease. This project and others by the Medical Research Council, National Institute of Health Research and major charities are putting the UK at the forefront of the diagnosis, treatment and prevention of rare diseases. These initiatives are expected to lead to a revolution in diagnosis of rare diseases. As genomic technologies develop and costs fall, we expect the diagnosis time for many rare diseases to fall significantly.

6.14. New opportunities also lead to new challenges. The initial costs of diagnostic testing may be offset over time by reductions in unnecessary healthcare. But the increased use of genomic approaches in identifying millions of DNA variants of uncertain significance will demand sophisticated bioinformatic and clinical evaluation. How this can be achieved within defined budget limits will need careful consideration.

6.15. The UK is playing a leading role in the international initiatives such as the Human Variome Project³² and the Global Alliance aimed at solving this new challenge through confidential sharing of knowledge. In addition, RD-Connect, an initiative led by the University of Newcastle Upon Tyne, is developing a unique global infrastructure that links up databases, registries, biobanks and clinical bioinformatics data used in rare disease research into a central resource worldwide.³³

Case study

The DDD (Deciphering Developmental Disorders) project¹ is an innovative rare disease project funded by the Department of Health, England's Health Innovation Challenge Fund in conjunction with the Wellcome Trust Sanger Centre. With support from all 23 regional genetics centres in the UK, DDD collects samples from children and young adults with complex patterns of currently undiagnosed congenital malformation. Genomic testing of the subjects and their parents is identifying new genetic syndromes in up to a third of cases.

¹ <http://www.ddduk.org/>

Partnership in developing new treatments

6.16. The main aim of research into rare disease is to improve diagnosis and treatment for patients with a rare disease. To achieve this, support is required for basic, experimental medicine, clinical and health service research. There is continued commercial interest in rare diseases, especially from pharmaceutical companies and small and medium biotechnology/IT businesses. Companies are increasingly interested in using gene-based research to identify new drug targets and help reduce the risk of development failure.

6.17. Drug development and research into rare diseases can also help improve treatment for more common diseases. All 4 countries of the UK are working with industry to identify opportunities in this area.

³² <http://www.humanvariomeproject.org/>

³³ <http://rd-connect.eu/>

Case study

In Scotland, the Stratified Medicine Innovation Centre brings together Scottish Universities, NHS Scotland and industry partners to work together in the area of biomarkers and genomics. The focus on practical application should ensure that the results are relevant to the NHS.

6.18. For drug discovery to progress further, it is important to have close cooperation at all stages of translational research (research into the practical applications of basic research). The UK continues to contribute to and support projects such as the European Project for Rare Diseases National Plans Development (EUROPLAN)³⁴ and International Rare Diseases Research Consortium (IRDIRC), including its goal to develop 200 drugs for rare diseases by 2020.³⁵

6.19. The increase in knowledge of rare disease variants will ultimately enable innovative approaches to treatment. These might include evaluation of existing compounds, re-purposing of existing drugs, use of biological products or small molecules, gene therapy and stem cell derived approaches. As genomics knowledge increases, better use will be made of the rich clinical data sources available across the NHS, including using existing and new rare disease registries.

Coordination of rare disease research

6.20. Underpinning all of the above will be the on-going commitment of patients and their relatives, the NHS, the UK's research community and its funders. Coordination is essential in this work. Organisations such as the Office for Strategic Coordination of Health Research are vital in ensuring that funding in rare diseases is coordinated and joined up.

6.21. Despite the encouraging work of the major research funders, we still need to do more to improve coordination. We hope that putting this Strategy into action, through the national plans, will reduce fragmentation and ensure that the UK continues to have a leading role in rare disease research to ultimately improve the health and wealth of the nation.

³⁴ http://www.euoplanproject.eu/_newsite_986989/index.html

³⁵ http://www.irdirc.org/?page_id=1035

7. UK commitments

7.1. To achieve the UK-wide vision for rare diseases described in this document, all 4 countries of the UK commit themselves to the following actions:

Empowering those affected by rare diseases

1. strengthen the mechanisms and opportunities for meaningful and sustained patient involvement in rare disease service provision and research, recognising patient groups as key partners – including in the development of the four country plans to implement the Strategy
2. improve awareness amongst service providers and others of the effects that rare diseases can have on a person's education, family, social relationships and ability to work
3. encourage effective and timely liaison between the NHS and other public service providers, and encourage providers to consider the effects of rare diseases on people's lives when they are developing and managing services
4. make sure that patients and their families have a say in decisions about treatment and in the planning, evaluation and monitoring of services
5. consider how to give all patients with a rare disease clear and timely information about: their condition and its development; treatment and therapy options; practical support
6. improve access for patients (or where appropriate their parents or guardians) to their personal data
7. support patients to register on databases, where these exist
8. help patients to contribute to research and other activity related to rare diseases

Identifying and preventing rare diseases

9. continue to work with the UK National Screening Committee to ensure that the potential role of screening in achieving earlier diagnosis is appropriately considered in the assessment of all potential new national screening programmes and proposed extensions to existing programmes
10. initiate action to ensure carrier testing approved by the appropriate commissioning bodies, where the associated molecular tests are evaluated and recommended by UKGTN, is accessible for at risk relatives

Diagnosis and early intervention

11. work to achieve reduced times for diagnosis of rare diseases, whilst acknowledging that more needs to be done to ensure that undiagnosed patients have appropriate access to coordinated care e.g. to help disabled children who are thought to have a genetic syndrome or condition that science has not yet identified
12. work with the NHS and clinicians to establish appropriate diagnostic pathways which are accessible to, and understood by, professionals and patients, by
 - establishing clear, easily accessible and effective pathways between primary care, secondary care, regional centres and specialist clinical centres, as appropriate
 - putting protocols in place to identify patients with no diagnosis, ensuring that a lack of diagnosis does not create a barrier to treatment
 - drawing on patients' ability to help inform decisions about referral and diagnosis
 - creating effective clinical networks to support this process
 - making high quality diagnostic tests accessible through common, clinically agreed systems or pathway
 - embedding appropriate information in national data systems including measuring equity of access to molecular tests to maintain UKGTN diagnostic studies
13. ensure that there are appropriate procedures for evaluating the costs and benefits of treatments for patients
14. where appropriate, support the availability of computerised prompts to help GPs diagnose a rare disease when a rare disease has not previously been considered
15. improve education and awareness of rare diseases across the healthcare professions, including:
 - involving patients in the development of training programmes
 - encouraging medical, nursing and associated health professionals to get hands-on experience in specialist clinics
 - ensuring awareness of methods and clinical techniques used in differential diagnosis
16. monitor the development of ICD-11 in preparation for its adoption
17. work with colleagues in Europe on the development of the European Orphanet coding system and considering the adoption of Orphanet coding and nomenclature
18. standardise data collection, building upon existing NHS data standards, and develop standards where they do not exist, increasing the reliability of information for use in providing or commissioning care
19. explore options to improve the link between existing patient data and electronic health records

20. assess the potential for rare disease databases where they do not exist
21. agree international standards, building on existing NHS standards
22. support international links to UK databases and build on the work of current funded programmes that aim to link rare disease research internationally

Coordination of care

23. continue to develop service specifications for rare diseases. This will include country specific care pathways and a 'generic' care pathway that sets out best practice that can be applied to all patients with rare diseases in the UK (particularly where there are no disease specific pathways). The generic care pathway will include:
 - an appropriate care plan for all patients with a rare disease
 - clearly stated principles around the standards of care which patients with a rare disease can expect, including patients with no diagnosis
 - the development of seamless pathways for transition, from childhood to adolescence, and on to adulthood and older age
 - access criteria and measures of quality and outcomes
24. agree that specialist clinical centres should as a minimum standard:
 - have a sufficient caseload to build recognised expertise
 - where possible, not depend on a single clinician
 - coordinate care
 - arrange for coordinated transition from children's to adults' services
 - involve people with rare conditions, and their families and carers
 - support research activity
 - ensure their expertise is available to families and their healthcare teams
25. ensure that the relationship between the specialist clinical centres and science and research is explained to and understood and put into practice by: practitioners delivering local health and social care; the research community; industry; academia
26. set out clearly the connections to and communications with specialist clinical centres in molecular diagnostics and other forms of diagnostic support
27. ensure that specialist clinical centres are as concerned with research as with health and social care support, and that they develop networks that provide professional to professional dialogue and collaboration across a wide range of experts, including internationally (especially for those conditions that are ultra-rare)
28. work with international partners wherever possible and develop UK-wide criteria for centres to become part of an expert reference network to increase the flow of information between patients and professionals in a range of disciplines

29. improve systems to record genetic and other relevant information accurately to record the incidence and prevalence of disease and support service planning and international planning
30. identify how they can change systems to hold information about rare diseases, including information about the uptake of treatments

The role of research

31. look at how the 4 UK countries develop, change or expand information systems to capture, connect and analyse data about clinical and social care pathways
32. work together to identify a selection of the rare diseases most suited to the development of best-care pathways and propose other rare diseases for possible pathway development, taking on board the needs of patients and carers and the challenges faced during delivery of the first set of pathways
33. examine how they can encourage service providers to involve patients in research and to ensure appropriate funding for excess treatment costs for research in rare diseases
34. make better use of online applications to give patients information about their condition so that they can develop a personalised care path plan with their clinical and social care team
35. use portals to connect patients and relatives to enhance research participation and, where appropriate, promote self-enrolment to approved research studies with online consenting, self-reporting and use of social media
36. encourage patient groups to get involved with regulatory bodies
37. help patient organisations and community engagement events develop more formal partnerships with the NHS research-active organisations
38. explore the feasibility of the UK Clinical Trials Gateway including experimental medicine trials for rare diseases to provide information for patients and their families about research trials
39. work with the research community, regulators, providers of NHS services and research funders to develop risk-proportional permission systems
40. encourage researchers to use current guidance to produce generic participant information leaflets and consent forms and participate in future guidance reviews
41. promote good practice and the use of systems which facilitate a consistent and streamlined process to local NHS permissions of publically, charitably and commercially funded research with an aim to reduce timescales.
42. begin and complete next generation sequencing (NGS) demonstration projects to: evaluate their usefulness, acceptability and cost-effectiveness; develop effective health economic assessments (for example through Health Technology Assessments) and similar initiatives

43. evaluate different NGS platform configurations, for example:
 - NGS for clinical condition-specific sets of genes (such as 100–200 of the 22,000 genes)
 - whole exome sequencing (2% of the entire genome)
 - whole genome sequencing
44. support the introduction of NGS into mainstream NHS diagnostic pathways, underpinned by appropriate clinical bioinformatics, including clinical bioinformatics hubs supported by high performance computing centres, where appropriate
45. ensure that training and education are available to the NHS workforce, highlighting the importance of NGS to all aspects of rare disease care, including support for evidence based local counselling for patients and their relatives who receive NGS results
46. work with industry to set priorities and determine how best to support research into rare diseases and promote research collaboration
47. support initiatives to facilitate engagement between patients, clinical care teams, researchers and industry wherever practical
48. set out the benefits of collaboration (besides producing specific treatments) for all stakeholders
49. continue to build a cohesive infrastructure for implementation and coordination of rare disease research in the NHS
50. encourage major research funders to use current structures to coordinate strategic funding initiatives in rare diseases
51. improve engagement between key stakeholders, including:
 - patients and relatives
 - main funding providers
 - healthcare commissioners
 - NHS hospitals and specialist care units
 - industry (pharmaceutical, biotechnology, IT, diagnostics)

8. Next steps

8.1. Research and technology advances are progressing rapidly, both for single gene (genetics) and whole DNA (genomics). The increased knowledge and understanding this gives society as to why and how diseases occur, and the consequences for the individual will change the way we view and treat disease. It will give us opportunities to radically transform the lives of those with rare diseases in many ways. Seizing the opportunity presented by genomic tests will help transform the care of those people with rare diseases.

8.2. To get the best results and benefits for people with a rare disease, their families and those who support them, it is important for patients, health and social care providers, research and industry to work together. This is essential if the UK is to achieve the main aim of this Strategy: we want to put the patients' needs first, bringing together the talent, skills and professionalism of all relevant sectors. This will bring real, positive change in how we deal with rare diseases and how we help people with complex conditions.

8.3. This Strategy's vision has to become a reality by 2020. To achieve this, all 4 UK countries will produce individual implementation plans that set out how they will put the Strategy into action, in line with their national policies and priorities. However, it will be essential that, wherever possible, we work together in drawing up these plans to ensure that they complement each other and reflect the need to work together for better patient benefit.

8.4. Finally, this Strategy commits all 4 UK countries to continue with international collaboration to tackle rare diseases wherever possible. Reaching out to our international partners is essential if we are really going to make a difference to the lives of those affected by rare diseases.



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