Welsh Implementation Plan for Rare Diseases
Annual Update 2017
1. Overview:

A rare disease is a life-threatening or chronically debilitating disease that affects five people or fewer in 10,000. There are between 5,000 and 8,000 rare diseases and, while each one affects relatively few people, together they affect the lives of three million people across the UK, which would imply some 150,000 people affected in Wales. Rare diseases can take many and varied forms, including physical and psychiatric disorders. Some 80% are genetic in origin, but that means many are not. Most appear at an early age but again, that means many do not and so services must be alert to the signs at many different stages in people’s lives. It is estimated some 350 diseases account for 80% of cases, but it is also estimated over 200 new diseases are identified each year.¹

The Welsh Implementation Plan for Rare Diseases² was updated in July 2017 and re-affirms the Welsh Government’s commitment to both empowering those with a rare disease and ensuring those affected by any kind of rare disease have timely access to high quality pathways of care. The Rare Disease Implementation Plan puts in place a framework to deliver the Welsh Government’s commitment to the vision in the UK Strategy for Rare Diseases.³

To support the implementation of the plan, the Welsh Rare Diseases Implementation Group (RDIG) was established. The RDIG includes broad representation from each health board in Wales, Welsh Health Specialised Services Committee (WHSSC), the Rare Disease and Genetics Alliance and, crucially a patient representative. The Group is chaired by Dr Graham Shortland, Medical Director, Cardiff and Vale University Health Board.

This annual update details the work undertaken for rare diseases and is aligned against the five themes from the Implementation Plan, which are:

- Theme 1 - Empowering those affected by rare diseases;
- Theme 2 - Identifying and preventing rare diseases;
- Theme 3 - Diagnosis and early intervention;
- Theme 4 - Co-ordination of care;
- Theme 5 - The role of research.

The report provides narrative on the actions outlined in the Implementation Plan and work undertaken by Welsh Government (including Health Care Research Wales), Health Boards, Welsh Health Specialised Services Committee, the Wales Screening Programme, All-Wales Medicines Strategy Group, the All-Wales Medical Genetics Service, the Welsh Rare Diseases Implementation Group and the Wales Gene Park.

This report also identifies areas where further work is needed and the actions being taken to address these gaps.

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¹ What is a rare disease?  
² Welsh Rare Diseases Implementation Plan (July 2017)  
³ UK Strategy for Rare Diseases
2. The Challenge

By their very nature rare diseases offer specific challenges to the NHS. There are many such diseases and in any given area there may be very few people affected by any one disease. Our vision is for fully integrated primary, secondary and specialist pathways of care, designed around the needs of the patient, to provide the support needed for patients to do what they can to manage their condition.

The diagnosis of a rare disease or condition generally marks the beginning of profound changes in the life of the individual and the lives of their family and friends. It may affect relationships, career prospects, income and expectations for the future. Everyone’s experience of living with a rare disease will be different, but there will be lots of issues and challenges that are shared by many people living with the condition.

Whilst many rare diseases will be identified at or before birth through specialist services, others first appear later, presenting primary and community care services with the challenge of identification and management.

There is a lack of awareness and identification of rare diseases amongst healthcare professionals outside of the specialist services, often resulting in a delayed diagnosis or misdiagnosis in patients.

There are a number of specific challenges which health boards are facing, including:

- **Aneurin Bevan University Health Board (ABUHB)** report that given the range of rare diseases, there is a challenge both in coding and recording of the epidemiological data on these and also in ensuring that clinicians in all areas have an awareness and understanding of the ABUHB rare diseases strategic approach.

- **Betsi Cadwaladr University Health Board (BCUHB)** report common all Wales challenges, including difficulty and/or delay in diagnosis, often limited information and variable or limited treatment options. Within rare diseases, there are many conditions that qualify under the broad heading, each will have different facets to presentation, investigation and diagnosis, with individual clinicians unlikely to see many (if any) similar cases in the future. There is, therefore, a general need for awareness as to possible diagnoses beyond the more common. Coding is a challenge, computer systems within the hospitals do not lend themselves to searching for rare diseases, access to Primary Care systems is limited, and much of the care is provided by tertiary centres in England.

- **Cardiff & Vale University Health Board (C&VUHB)** report there are a large number of specialist services, with many catering for rare diseases individually. The challenge for the health board is to join them together in a coherent way and combine the different rare disease themes. As with the national Implementation

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Epidemiology is the study of how often diseases occur in different groups of people and why. Epidemiological information is used to plan and evaluate strategies to prevent illness and as a guide to the management of patients in whom disease has already developed (http://www.bmj.com/about-bmj/resources-readers/publications/epidemiology-uninitiated/1-what-epidemiology).
Plan, there are many other competing interests for formal programme support and there is the need to facilitate better working across the organisation.

- Cwm Taf University Health Board (CTUHB) reports given the nature of rare diseases, they are currently unaware of how many patients within their resident population that are affected by a rare disease and what exactly their experiences and patient journey has been.

- Hywel Dda University Health Board (HDUHB) report, while being a semi-rural health board they are not able to provide many of the services other health boards are able to provide. Therefore, the challenge for the health board is to diagnose and refer as appropriate, and to support the patients whilst they are undergoing their treatment. In addition, ensure that there is enough coverage provided to allow those clinicians involved in rare diseases to undertake Continuing Professional Development (CPD).
3. Progress/Key Achievements:

The Rare Diseases Implementation Group (RDIG) identified the following priorities for 2017-18:

- Identifying the support pathway for patients with unknown diagnosis (The Diagnostic Odyssey);
- Creating and ensuring better use of best practice and evidence in primary and secondary care and improve pathways for accessing specialist services;
- Undertaking significant event analysis including delayed diagnosis of a rare disease and shared evidence learning;
- Ensuring feedback from patients is utilised to enhance rare disease pathways within health boards.

The progress made against these is highlighted in the themes below.

Theme 1: Empowering those affected by rare diseases
Following the proposal for a restructuring of the UK Rare Disease Strategy governance configuration in 2016; this led to the creation of a smaller focussed UK Rare Disease Policy Board, concentrating on high-level policy development and implementation of the 51 commitments in the Strategy. A larger UK Rare Disease Stakeholder Forum was implemented in October 2016. As part of supporting continued communication and partnership between the Board and the Forum, the UK Policy Board hosts an annual Rare Disease Forum conference. The first Rare Disease Forum conference was held on 24 November 2017 at Birmingham Children’s Hospital. The conference provided an opportunity for feedback, discussion and development of ideas concerning the implementation of the Strategy and therefore had a participant-led focus. In November 2017 an online communication platform was launched, allowing for Forum members to interact with and inform the work of the Policy Board.

There are a number of policies and reports which reinforce the Welsh Government’s commitment to person-centred care such as the Health and Care Standards. If people receive the right care and support they will be empowered to improve or manage their own health and wellbeing. Interventions to improve people’s health must be based on best practice and derived from good quality research.

Health Technology Wales (HTW) has been established to deliver a strategic, national approach to the identification, appraisal and adoption of new health technologies into health and care settings across NHS Wales.

In January 2017, Welsh Government’s new treatment fund was initiated to deliver swift access to innovative new medicines to support people with life-threatening conditions in Wales. An additional £16 million annually for five years has been provided to help health boards in Wales speed up access to medicines recommended by the National Institute for Health and Care Excellence (NICE) and the All Wales Medicines Strategy Group (AWMSG). After the first year, the average time for recommended new medicines to be made available to patients was only 10 days, ahead of the 60 day deadline. Patients can now access 82 new medicines, much more quickly than they would have, had the fund not been in place. Of these, 42 have been recommended and are now available to treat rare diseases. This
includes migalastat to treat Fabry disease, Eliglustat to treat Gaucher disease, Olaratatumab to treat Sarcoma, Levatinib to treat thyroid cancer and stripentol to treat a form of epilepsy called Dravet syndrome.

**Case study – New Treatment Fund**

Migalastat is a medicine used to treat patients aged 16 years or over with Fabry disease. This is a rare genetic disorder of the Lysosomal Storage function. It results in a specific enzyme not working correctly or in some cases the enzyme is missing. It usually affects males mostly and is difficult to diagnose. It causes life-limiting severe pain, cardiac and renal problems. Diagnosis usually occurs in adolescence and life expectancy is between 40 – 50 years of age where the disease has progressed. The disease has a significant impact on both quality and length of life.

Migalastat offers a new treatment option for Fabry disease sufferers. Currently, patients receive fortnightly treatment which requires them to spend up to four hours receiving intravenous infusion Enzyme Replacement Therapy. As a daily oral therapy, migalastat negates the need for patients to travel for treatment and spend significant amounts of time in clinic whilst the infusion is administered. Migalastat was appraised and positively recommended by NICE for routine use in March 2017. The new treatment fund has allowed quicker access to the medicine giving people with Fabry disease freedom from the frequent hospital visits required and long treatments, improving their quality of life.

We have made some specific progress in empowering those affected by rare diseases in Wales, including:

Within Aneurin Bevan University Health Board (ABUHB) they are moving away from departmental condition-specific information to online, national resources, recognising that these resources tend to be of a higher standard and are kept more up to date than some local resources. This is being led by ABUHB’s paediatric department. These new web resources will be accessible by patients and their families; containing not just up to date condition information but information on local support groups and signposting for further support. In addition, easy read information for individuals with a learning disability and a rare condition is being developed to ensure information is available in a format that is accessible to them.

As part of their partnership work, Betsi Cadwaladr University Health Board (BCUHB) aims to ensure improvements across the whole ‘patient journey’, from the first contact with their GP through diagnosis to ongoing management of a rare condition. Patients and their family/carers are actively involved in joint partnership groups emphasising the commitment by BCUHB to the fundamental role that the patient, supported by their family/carer and/or patient organisation will play during this journey. Those affected are an important source of information to the Health Board, sharing their understanding both on the condition and the service response, which can help develop their teams and the service more widely to perform better. By setting up Service Advisory Groups, BCUHB is taking positive steps to improve patient involvement in the planning of services for patients with rare conditions.
It is recognised by BCUHB that individuals with complex problems, their family and carers, greatly value a single point of contact with a professional who is responsible for overseeing and co-ordinating the delivery of their agreed formal care and support. The Board has recently appointed a number of disease specific care co-ordinator posts in North Wales to deliver local support to patients as a key worker. These posts will:

- Track patients along their disease pathway;
- Co-ordinate the local multidisciplinary care of patients across North Wales in primary, secondary and Third Sector care ensuring patients can access high quality care;
- Liaise with the consultant for specialist input;
- Be a single point of contact for patients, their carers and professionals as a resource for information advice and signposting.

In addition, patient concerns have been taken under the remit of BCUHB’s Executive Nurse Director, resulting in both a greater clinical focus and faster response times. This will allow a more timely understanding of some of the key issues, and facilitate meaningful interaction with the patients.

Hywel Dda University Health Board (HDUHB) are seeking sponsorship for a ‘Rare Diseases Day’ with the aim of creating a forum for patients and their carers. This is to include a Facebook page; the intention to organise a yearly meeting to bring together interested groups under an umbrella.

HDUHB have undertaken work to improve access to services across the Health Board for patients with neuro-endocrine tumours, also improving their Multidisciplinary team (MDT) work with the University Hospital of Wales, and extending their Lead Endocrine consultants service into their hospitals with the aim of providing a better service for those patients with rarer endocrine disorders. In addition, they have started a new service centred on pulmonary fibrosis; this will centre on waiting list initiatives; access to new drugs and the provision of a new clinic at Prince Philip Hospital.

**Theme 2: Identifying and preventing rare diseases and Theme 3: Diagnosis and early intervention**

One of the commitments in the UK Strategy is to “work to achieve reduced times for diagnosis of rare diseases”. In 2014, the UK Rare Disease Forum commissioned the Policy Innovation Research Unit (PIRU), based at the London School of Hygiene and Tropical Medicine, to explore whether an accurate, effective and cost-effective method could be developed for the routine measurement of the time from initial presentation of symptoms of a rare disease to a definite clinical diagnosis. A report of its findings was published in April 2015; ‘Diagnostic Odyssey for Rare Diseases: exploration of potential indicators’.

The Rare Diseases Policy Board established a Task and Finish group in early 2017, with the aim to further explore and propose a mechanism to automate the collection of data to measure the time travelled in the diagnostic pathway for patients with rare

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5 Diagnostic Odyssey for Rare Diseases: exploration of potential indicators (April 2015)
diseases. Three specified conditions are being used as exemplars to consider the options available. The first piece of work is to determine the specific data points available in secondary care for individual patient journeys going back up to five years. This initial collection of anonymised and aggregated data concluded in December 2017 and a report on findings and recommendations will be published in 2018.

Welsh Government’s Genomics for Precision Medicine Strategy\(^6\) was published in July 2017. It sets out the Welsh Government’s plan to create a sustainable, internationally competitive environment for genetics and genomics to improve health and healthcare provision for the people of Wales.

In September 2016, Genomic Medicine Centre was awarded Medical Research Council (MRC) and Welsh Government funding of £1m and £2.4m respectively to support Wales’ involvement in the Genomics England 100,000 Genomes Project. The Genomic Medicine Centre will work closely with the Wales Gene Park, All Wales Medical Genetics Service and health boards and trusts across Wales to facilitate the development of genomic medicine in Wales. The 100,000 Genomes Project in Wales will be used as an exemplar towards the integration of genomic medicine into clinical care pathways in Wales and aligns with the Welsh Government Genomics for Precision Medicine Strategy. The project is due to begin in Wales in January 2018.

The All Wales Genetic Laboratory received additional funding in the 2016-17 financial year from Welsh Health Specialised Services Committee (WHSSC) for very rare genetic tests. The All Wales Genetic Laboratory has introduced genomic analysis using Next Generation Sequencing (NGS). As a result, more patients with rare diseases are able to access genomic sequencing results, and therefore receive a diagnosis, appropriate treatment and management.

The Newborn Bloodspot Screening programme in Wales offers all eligible babies, at day five of life, a quality assured screening test for serious diseases that would benefit from early intervention and reduce mortality and/or morbidity from the disease. The test offers screening for Congenital hypothyroidism (CHT); Cystic fibrosis (CF); Inherited metabolic disorders (IMDs) including Medium-chain acyl-CoA dehydrogenase deficiency (MCADD); Phenylketonuria (PKU); Maple syrup urine disease (MSUD); Isovaleric acidaemia (IVA); Glutaric aciduria type 1 (GA1); Homocystinuria (HCU); and Sickle cell disorders (SCD).

In the period 1 April 2016 to 31 March 2017, 33,505 babies were tested and the programme identified 39 serious conditions including: Congenital hypothyroidism; cystic fibrosis; medium-chain acyl-CoA dehydrogenase deficiency; Phenylketonuria and sickle cell disorders.

A network of paediatricians exists across health boards in Wales to ensure rapid, informed and appropriate clinical responses, both locally and in the specialist centre when a positive baby is identified. Specific additional work has been to concentrate on the delivery of high quality blood spot analysis and the quality of samples.

\(^6\) Genomics for Precision Medicine Strategy (July 2017)
delivered across health boards including midwife sampling. The service had 99.6 per cent test rate of newborn babies in Wales in 2016/17.

The Rare Disease Implementation Group in Wales has set up a Task and Finish group looking at the investigation of children with delayed development.

In addition, we have made some specific progress identifying, preventing, diagnosis and early intervention of rare diseases in Wales, including:

Cardiff & Vale University Health Board (C&VUHB) continues to provide all Wales leadership in a number of specific disease areas, including the Newborn Bloodspot Screening Wales and the All Wales Genetic Laboratory; along with regular audit meetings with Clinical Services, to ensure that there is uptake of National Guidelines and strengthening of pathways for patients across Wales; e.g. European pathway for the treatment of PKU and Galactosaemia pathways.

Cwm Taf University Health Board (CTUHB) has identified a patient group and considered the timeline of events starting from referral made by the GP to secondary care, the impact the illness had on the patient and family; where are the gaps in service and establish lessons learnt. The paediatric medical case studies have highlighted initial learning.

Hywel Dda University Health Board (HDUHB) in conjunction with WHSSC report that they are supporting the inclusion of rare diseases care and treatment within existing patient reported experience measures (PREMs) and patient reported outcome measures (PROMs). In addition, HDUHB have adopted the TONIC7 (Trajectories of Outcome in Neurological Conditions) study (The Walton Centre, Liverpool) to look at the quality of life and diagnostic odyssey of patients with Motor Neurone Disease and their carers.

Theme 4: Coordination of Care
In any given country the number of patients who suffer from a specific rare disease may be small. This scarcity of rare disease patients, and often as a result expertise, means that diagnosis, treatment and management of rare diseases can strongly benefit from cross-border collaboration.

"Informed health and care – A digital health and social care strategy for Wales"8 sets out the Welsh Government’s ambition to build on the progress already made and transform how the people of Wales, citizens and staff, embrace modern information technology and digital tools to deliver safer, more efficient and joined-up health and social care services to improve outcomes and experiences of patients and service users. Linkages of health records is being considered through wider programmes within the NHS Wales Information Service, and progress has been made developing integrated individual healthcare records and establishing a Welsh Clinical Portal.

The Welsh Rare Disease Implementation Plan highlights the importance of individuals, and those important to them to be given the opportunity to have open

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7 More information on the TONiC can be found here.
8 Informed health and care – A digital health and social care strategy for Wales
and transparent discussions about personalised plans that enable a holistic approach to promoting their choices of treatment, care and support. This philosophy of care is important to individuals, and the health care system, as it promotes: partnership between all agencies which may be able to help; a reduction of unplanned hospital admissions; the enabling of more people to die in their preferred place and the supporting of care wishes by anticipatory care planning.

We have made some specific progress in the co-ordination of care for those affected by rare diseases in Wales, including:

Betsi Cadwaladr University Health Board (BCUHB) is establishing a rare disease planning group to support the local implementation of the Welsh Rare Disease Implementation Plan. Tackling uncoordinated and silo based working. The purpose of the group will be to support BCUHB deliver on the national priorities for our patients.

Cardiff & Vale University Health Board (C&VUHB) have worked to improve the use of best practice in services, across primary, secondary and tertiary services, with an increase in local outreach clinics for children with inherited metabolic disease in West Wales (increase in clinic capacity) and also in 2018 the setting up of a clinic in the South East (ABUHB). In addition the previously commenced service for patients in North Wales with Inherited Metabolic Disease is now well embedded.

Cwm Taf University Health Board (CTUHB) has made progress firstly establishing a Local Planning and Delivery group, with group members including: an executive lead, a clinical lead, commissioning and planning leads. This local group meets quarterly and uses the health board action plan as a live document throughout the year to monitor progress.

Case Study – A patient care plan

Linda has had Wegener’s granulomatosis, a form of vasculitis, for over 12 years now and it has caused her many additional health issues. Vasculitis was diagnosed when Linda’s windpipe closed, that means she has a tracheostomy tube to breathe through and no way of talking, other than with an electro-larynx. She also has recurrent pulmonary emboli, peripheral neuropathy, hearing loss, and steroid induced type 2 diabetes. The illness and the medication have made Linda suffer a loss of concentration, and she is not as able to stand up and speak up for herself as she used to be. Being unable to speak unaided and requiring time to process information and to formulate an answer; means that Linda is often “railroaded” by people who do not have the patience to wait for her, or who feel she needs help when she is just thinking. Sadly this includes medical professionals.

Having heard about the care plan we felt it would be a good way for Linda’s feelings and needs to be documented and explained. As we live in one health board area, but are treated in another neighbouring health board, we wanted to ensure as best as possible that Linda’s condition is noted should she be admitted to hospital, and should I not be there to help her, there is a plan to follow that lays out Linda’s feelings and needs. Emma Hughes of Genetic Alliance UK originally offered us some guidance on what sort of things the care plan could include. We went away and
approached the Interstitial lung diseases (ILD) Specialist nurse attached to Linda’s Vasculitis consultant, and happily, she agreed to organise the care plan. This was a new thing for her too. She met with us to go over the basics, and then arranged a meeting with us; herself, our GP, and her colleagues from our health board - all professionals helping Linda were invited and informed of the meeting.

The care plan included such things as: diagnoses, medication, access to treatment, resuscitation wishes, communication, and care needs. It is reviewed annually. The meeting agreed the care plan and the lead professional sent copies to all concerned. That means that Linda’s details are now on Cardiff and Vale, Aneurin Bevan university health boards, and the GP computer systems. This gives peace of mind should Linda be admitted to a local hospital. It is key to us that Linda’s medication is understood by all who come into contact with her as it has taken years to get a working regime, and many people do not understand the nature of her rare disease. We also emailed a copy of all correspondence from the consultant to the community respiratory nurse for our area and she ensures that they are updated onto the Aneurin Bevan University Health Board computer system. This has given us a great deal of peace of mind, but to be honest we did wonder if it would prove to be of any practical use.

We are delighted to say that it did prove very positive when Linda had to be admitted to hospital earlier this year for planned mastectomy surgery. This was carried out at University Hospital Llandough and the staff were given a copy of the care plan. As a result they invited me to stay with Linda whilst she was in hospital, and this meant that Linda was completely relaxed and not at all on edge. It was great for me too as husband and carer to know that she was safe.

I would recommend anyone in a similar situation to consider doing this, as it means that if ever you are admitted to hospital, and perhaps it is an emergency situation, there is a primary document that lists your underlying rare health problems, which may not be evident from your admission. It has provided us with a great deal of peace of mind.9

Hywel Dda University Health Board (HDUHB) for some diseases, including; Cystic Fibrosis and Muscular Dystrophy have set up and improved transition services for young people transitioning to adult services.

Theme 5: Role of Research
Health and Care Research Wales Strategic Plan sets out the vision for Wales to be internationally recognised for its excellent health and social care research that has a positive impact on the health, wellbeing and prosperity of the people in Wales. The updated Welsh Rare Diseases implementation plan sets out the Welsh Government’s commitment to research for people with rare diseases and sets out a number of actions for health boards.

We have made some specific progress in Wales, including:

9 More information on care plans can be found here
Researchers at Cardiff & Vale University Health Board (C&VUHB) and Cardiff University have developed a more reliable method of screening for Duchenne muscular dystrophy (DMD) in newborn babies. In collaboration with biotechnology company PerkinElmer, they have developed a diagnostic kit that can accurately screen for the disorder by analysing neonatal dried blood spots. DMD is the most fatal common genetic disorder diagnosed in childhood. The disorder gradually causes muscles to weaken, leading to an increasing level of disability and eventually premature death. DMD almost always affects boys, with around 100 boys born in the UK with the condition each year, and about 2,500 living with the condition in the UK at any one time. The new screening test originated from research by Dr Stuart Moat of C&VUHB and Professor Ian Weeks from Cardiff University. When PerkinElmer joined the collaboration, the research was successfully adapted to an existing PerkinElmer analyser, allowing it to be translated into a routine test that could be used globally.

Hywel Dda University Health Board (HDUHB) is setting up a rare disease database. They are working in collaboration with researchers in Dublin, Utrecht, London, Sheffield and European patient support groups, for a Horizon 2020 Bid (H2020-MSCA-ITN-2018); for nEURO a consortium looking at redesign of drug trial for rare diseases. The project will start with Amyotrophic lateral sclerosis (ALS) (also known as motor neurone disease (MND) and Lou Gehrig's disease) and fronto-temporal dementia. HDUHB have secured that the clinical lead in the Wales’ team, will be based in the health board, working to secure partnerships with Fujitsu, Pfizer and Siemens through Swansea University, School of Management.

**Case Study: Evaluating clinical exome sequencing for the benefit of the management of patients with rare diseases (aka SIGNAL) - Principal Investigator, Rachel Butler, All Wales Genetics Laboratory**

Health and Care Research Wales (HCRW) funded a Research for Patient and Public Benefit (RfPPB) in 2015 for the evaluation of Clinical Exome sequencing (CES) in rare disease patients in Wales. The project is nearing completion within the All Wales Medical Genetics Service, which aspires to be at the forefront of improving genetic testing for NHS patients.

The detection of the genetic reason for a rare disease early in a patient’s clinical pathway avoids the need for many other needless investigations, and enables the appropriate treatment and care to be given to the patient and their family. It is therefore a clear example of Prudent Healthcare.

The project piloted the use of CES as a diagnostic genetic test in Wales. Most NHS gene tests then performed in Wales were based on conventional Sanger sequencing technology. Sanger sequencing is relatively expensive and typically only tests one gene at a time. In contrast, CES uses massively parallel ‘next-generation’ sequencing technology to read many or all of the exons (protein-coding sections) of the genome. CES targets only genes of known disease relevance (e.g. genes listed in the Online Mendelian Inheritance in Man database). CES generates less data than whole exome sequencing (only ~5000 genes are sequenced). This reduces costs, increases sequencing depth/coverage of important genes, and aids clinical interpretation of the mutations detected.
The aims of the project were to assess the clinical, practical and financial impact of using CES as a routine DNA sequencing method for diagnostic genetic testing for patients with rare diseases. We wanted to determine:

a) if we could replace hundreds of the single- and multi-gene tests currently used by the NHS in Wales, with CES followed by targeted bioinformatic analysis?

b) the cost-benefit of CES for patients with rare disease? What is the understanding and acceptability of genomic sequencing to patients? How will patients respond to the potential availability of genetic results (incidental findings) unrelated to their rare disease?

The project is nearing completion and is due to report at the end of November 2017.

To date:

- 139 (from 60 Intellectual Disability families) Clinical Exome Sequences (of consented patient samples) have been completed and are currently being analysed through our bioinformatic pipeline;
- 21 samples (from 7 families) have been selected for additional Whole Genome Sequencing (WGS) – through cost savings we have been able to compare the results of CES and WGS within the project;
- Previous clinical investigations for all index patients have been catalogued and are being analysed by our Health Economist for comparison with the CES approach;
- 55 patient pre-testing questionnaires were received and 14 face to face interviews (with members of 8 families) have been completed;
- Of particular significance, protocols and operational pathways have been established within the All Wales Medical Genetics Service (AWMGS) for the routine use of CES for rare disease patients, including a monthly Genomic Multidisciplinary team.

It is acknowledged that genomic technologies change rapidly and therefore that their application to clinical practice also changes. Whilst CES is now becoming embedded within the AWMGS, staff should now look to the next technologies such as whole exome and whole genome sequencing to determine the right time (or perhaps the right clinical indications) for their introduction into clinical practice. The increasing use of genomic technologies also raises the fundamental issues of data-sharing and the importance of good phenotypic (clinical) information to support clinical services for patients with rare disease.
4. Areas of Focus/Future Priorities:

As we have already identified by their very nature rare diseases offer specific challenges to the NHS and in particular individual health boards. There are many such diseases and in any given area there may be very few people affected by any one disease.

We need to make best use of the scarce resources available within NHS Wales and work collectively to plan and deliver services for people with rare diseases.

Whilst, the last 12 months has seen some progress in improving care for people with a rare disease in Wales, there are a number of areas where we have not made as much progress as we would have liked, and further work is required. Work is still required to ensure there are clear referral/treatment pathways, improve awareness and education to aid early diagnosis/improved management and strengthen collaborative working with national groups/work programmes.

Patient reported outcome measures (PROMs) and patient reported experience measures (PREMs) are a challenge in that they are generic, rather than specific to a condition.

Within individual health boards there will be some specific areas of focus for work over the coming year. This includes:

Aneurin Bevan University Health Board (ABUHB) have identified a range of areas in need of improvement and focus, these include access to timely and up to date information, better use of patient feedback and best practice to improve pathways for primary and secondary care services. In addition to identify ways of including rare disease treatment within patient reported experience measures (PREMs) and patient reported outcome measures (PROMs) within specific clinical areas.

Betsi Cadwaladr University Health Board (BCUHB) recognises difficulties in identifying the right support to develop the local rare diseases group. The result is that this area of work is often in addition to other activity, rather than a specific focus; consequently, urgent work often overwhelms this important area. There is a need to better use patient feedback, compare actions with best practice, and to review pathways across care services where indicated. Third sector should be utilised more effectively as a potentially valuable resource and support.

Cardiff & Vale University Health Board (C&VUHB) has a unique opportunity to work with Cardiff University to strengthen their joint working. C&VUHB is committed to strengthening its joint working in 2018 with Cardiff University with a refreshed Memorandum of Understanding and opportunity to influence in the area of Rare Diseases.

A team of researchers, clinical scientists, and clinicians from C&VUHB and Cardiff University have attracted funding from Genzyme to develop a rapid, reliable, robust, reproducible and standardised assay to measure the Fabry disease biomarker in urine. Currently they do not have good tests to monitor patients with this disease, and are unable to tailor treatment to patient needs. There is therefore a need to
develop assays in order that response to therapy can be better assessed, likely clinical events can be better anticipated, and treatment plans personalised.

C&VUHB continue to undertake the national leadership role for rare diseases, a significant amount of this work will be in partnership with WHSSC. Previously there has been an audit day for patients with Lysosomal storage disease. This will be expanded in February 2018 to include non-lysosomal metabolic disorders with clinicians from South Wales and North Wales working together with WHSSC to facilitate an audit workshop to look at equity of services and service outcomes. This will include scoping the requirement of future service development. The outcome from that work will be taken forward as part of an ongoing business case discussion with WHSSC.

Cwm Taf University Health Board (CTUHB) will use the medical case studies and patient stories that will be completed by the end of 2017/18 to further improve the care for patients with a rare disease.

The key priorities identified for 2018-19 Welsh Implementation Group include:
- Identify and improve the pathway for patients with unknown or delayed diagnosis;
- Ensure better use of patient feedback, best practice and evidence to improve pathways for primary, secondary and specialist services;
- Improve reporting of rare disease information including epidemiology, significant event analysis and shared learning.
5. Summary and Conclusion:

Due to the nature of rare diseases, cross border working is essential, within Wales, the United Kingdom and often, Europe. Representatives from Wales will continue to attend regular meetings of the UK Rare Diseases Advisory Group, the Rare Diseases Policy Board and participate in the Forum.

We have made some progress in improving the care of people with a rare disease in Wales as highlighted in this update, yet there is still more to do. All stakeholders must continue to work together to build on the progress to date and deliver improved care.

The implementation of the rare disease implementation plan has gained momentum during 2017 and building blocks have been developed to help address a number of the priorities. Continued exposure and the raising awareness of the Rare Disease Implementation Plan and the Implementation Group with senior management within health boards continues to bring positive returns, however there is ample room to build on this.

The Rare Disease Implementation Group and its Chair, Dr Graham Shortland is grateful to everyone who has participated in the implementation of the plan so far and will be working closely with colleagues across Wales over the next 12 months to drive forward this agenda.
## Appendix 1 – Links to helpful resources

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<td>Congenital Anomaly Register and Information Service:</td>
<td><a href="http://www.caris.wales.nhs.uk">http://www.caris.wales.nhs.uk</a></td>
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<tr>
<td>EURORDIS:</td>
<td><a href="http://www.eurordis.org/about-eurordis">http://www.eurordis.org/about-eurordis</a></td>
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<tr>
<td>Health and Care Research Wales:</td>
<td><a href="https://www.healthandcarereresearch.gov.wales">https://www.healthandcarereresearch.gov.wales</a></td>
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<td>InterNational Anaplastic Thyroid Cancer Tissue Bank:</td>
<td><a href="http://www.inatt.org">www.inatt.org</a></td>
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<td>MediWales - the Life Science Network for Wales:</td>
<td><a href="http://www.mediwales.com">http://www.mediwales.com</a></td>
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<tr>
<td>Orphanet - The portal for rare diseases and orphan drugs:</td>
<td><a href="http://www.orpha.net/">http://www.orpha.net/</a></td>
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<tr>
<td>Policy Innovation Research Unit report - <em>Diagnostic odyssey for rare diseases: exploration of potential indicators:</em></td>
<td><a href="http://www.piru.ac.uk/assets/files/Rare%20diseases%20Final%20report.pdf">http://www.piru.ac.uk/assets/files/Rare%20diseases%20Final%20report.pdf</a></td>
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<td>Rare Disease UK:</td>
<td><a href="https://www.raredisease.org.uk/">https://www.raredisease.org.uk/</a></td>
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<td>Rare diseases list:</td>
<td><a href="https://globalgenes.org/rarelist/">https://globalgenes.org/rarelist/</a></td>
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<td>The All Wales Medicines Strategy Group:</td>
<td><a href="http://www.awmsg.org">www.awmsg.org</a></td>
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<td>The Genetic Alliance:</td>
<td><a href="https://www.geneticalliance.org.uk">https://www.geneticalliance.org.uk</a></td>
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<td>UK Rare Disease UK:</td>
<td><a href="https://www.england.nhs.uk/commissioning/rdag">https://www.england.nhs.uk/commissioning/rdag</a></td>
</tr>
<tr>
<td>UK Rare Diseases Forum:</td>
<td><a href="https://www.gov.uk/government/groups/uk-rare-disease-forum">https://www.gov.uk/government/groups/uk-rare-disease-forum</a></td>
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<tr>
<td>Welsh Rare Disease Implementation Plan (to be refreshed during 2017):</td>
<td><a href="http://gov.wales/topics/health/nhswales/plans/rare/?lang=en">http://gov.wales/topics/health/nhswales/plans/rare/?lang=en</a></td>
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### Other Welsh NHS Delivery Plans:

<table>
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<tr>
<th>Plan Model</th>
<th>Link</th>
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<tbody>
<tr>
<td>Neurological Conditions Delivery Plan (to be refreshed during 2017)</td>
<td><a href="http://gov.wales/topics/health/nhswnes/plans/neurological/?lang=en">http://gov.wales/topics/health/nhswnes/plans/neurological/?lang=en</a></td>
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<tr>
<td>Respiratory Conditions Delivery Plan (to be refreshed during 2017)</td>
<td><a href="http://gov.wales/topics/health/nhswnes/plans/respiratory/?lang=en">http://gov.wales/topics/health/nhswnes/plans/respiratory/?lang=en</a></td>
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### Other resources:

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<tr>
<td>Improving general hospital care of patients who have a learning disability:</td>
<td><a href="http://www.1000livesplus.wales.nhs.uk/sitesplus/documents/1011/How%20to%2020%202822%2029%20Learning%20Disabilities%20Care%20Bundle%20web.pdf">http://www.1000livesplus.wales.nhs.uk/sitesplus/documents/1011/How%20to%2020%202822%2029%20Learning%20Disabilities%20Care%20Bundle%20web.pdf</a></td>
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<td>Informed health and care – A digital health and social care strategy for Wales:</td>
<td><a href="http://gov.wales/topics/health/nhswales/about/e-health/?lang=en">http://gov.wales/topics/health/nhswales/about/e-health/?lang=en</a></td>
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<td>NHS Wales Planning Framework:</td>
<td><a href="http://gov.wales/topics/health/nhswales/organisations/planning/">http://gov.wales/topics/health/nhswales/organisations/planning/</a></td>
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<tr>
<td>Primary Care Services Plan:</td>
<td><a href="http://gov.wales/topics/health/nhswales/plans/care/?lang=en">http://gov.wales/topics/health/nhswales/plans/care/?lang=en</a></td>
</tr>
<tr>
<td><strong>Safe Care, Compassionate Care:</strong> National Governance Framework to enable high quality care in NHS Wales:</td>
<td><a href="http://www.wales.nhs.uk/sitesplus/documents/888/Appendix%20Item%206%20Safe%20Care%20C%20Compassionate%20Care.pdf">http://www.wales.nhs.uk/sitesplus/documents/888/Appendix%20Item%206%20Safe%20Care%20C%20Compassionate%20Care.pdf</a></td>
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