

The UK Strategy for Rare Diseases

Second Progress Report from the UK Rare Diseases Policy Board

Covering the period 2016-2018

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Contents

The UK Strategy for Rare Diseases	1
Second Progress Report from the UK Rare Diseases Policy Board	1
Covering the period 2016-2018.....	1
Contents	3
Chapter 1: Foreword	5
Chapter 2: Introduction	6
Governance of the implementation of the UK Strategy for Rare Diseases	7
Implementing the UK Rare Disease Strategy in England.....	8
Implementing the UK Rare Disease Commitments in Scotland	9
Implementing the UK Rare Disease Commitments in Wales	9
Implementing the UK Rare Disease Commitments in Northern Ireland	10
Chapter 3: Empowering those affected by rare diseases	12
UK-wide implementation plan activities 2016-18	12
Key nation-specific implementation plan activities 2016-18	18
England.....	18
Scotland	21
Wales	23
Northern Ireland	25
Chapter 4: Identification, prevention, diagnosis and intervention	28
UK-wide implementation plan activities 2016-18	28
Key nation-specific implementation plan activities 2016-18	31
England.....	31
Scotland	32
Wales	33
Northern Ireland	34
Chapter 5: Coordination of care	38
UK-wide implementation plan activities 2016-18	38
Key nation-specific implementation plan activities 2016-18	39
England.....	39
Scotland	41
Wales	42
Northern Ireland	44
Chapter 6: Research	46

UK-wide implementation plan activities.....	46
Key nation-specific implementation plan activities 2016-18.....	48
England.....	48
Scotland.....	53
Wales.....	54
Northern Ireland.....	57
Chapter 7: Registries and data	58
UK-wide implementation plan activities.....	58
Key nation-specific implementation plan activities 2016-18.....	59
England.....	59
Scotland.....	61
Wales.....	61
Northern Ireland.....	62
Chapter 8: Key Challenges and Next Steps.....	64
Progress on Next Steps as of 2016 Report.....	64
Forward look to 2020	64
Next Steps	67
Annex 1 – Agenda of the Rare Diseases Forum conference 2017.....	68
Annex 2 – List of European Reference Networks	70

Chapter 1: Foreword

As co-chairs of the UK Rare Diseases Policy Board, we are delighted to present this second Progress Report on the UK Strategy for Rare Diseases which covers the period from February 2016 to February 2018. This is an excellent opportunity to celebrate successes, reflect on remaining challenges and look forward to the final two years of the timeline of the UK Strategy.

The Rare Disease Policy Board has met eight times since the publication of the last Progress Report, considering a range of issues and overseeing progress against the Strategy in the four UK nations. As co-chairs we appreciated the quality of conversation and openness from the various delivery partners represented on the Board, enhanced by the engagement and constructive input brought to the table by our two excellent patient representatives.

There have been many highlights since the publication of the last Progress Report. These have included the creation of the Policy Board, which has been an excellent platform for focussed discussion and increased collaboration between all four nations. We also thoroughly enjoyed the Rare Diseases Forum conference and welcomed the creation of opportunities for patient engagement through the Rare Disease Policy Forum and the new digital Forum platform. We also saw the establishment of a task and finish group to look at, and improve, the 'Diagnostic Odyssey' of rare disease patients.

Highlights from across the rare diseases landscape include the continuing success of the 100,000 Genomes Project and the increasing participation of all four UK nations in this. We also recognise the UK's involvement and leading role in the European Reference Networks as a great achievement, maintaining the UK's status as a world leader in the field of rare diseases and delivering tangible benefits to patients.

During this two-year period, the UK Rare Diseases Policy Board have also provided advice on, and welcomed, implementation plans from the Department of Health and Social Care and NHS England. We strongly believe that these represent an important milestone in providing greater transparency for all the good work that is being done across the sector in implementing the UK Strategy.

Finally, the UK Rare Disease Policy Board would like to express its thanks to all those who have contributed material for the report. We are also grateful to those who have agreed to share their individual experiences in the case studies, which reinforce the spirit of the Strategy and its goal of improving the lives of patients, and their families, living with a rare disease. As chairs, we look forward to the next two years of the current Strategy and continued sustained commitment to its goal by all those involved to deliver it by 2020.

Professor Gina Radford, Deputy Chief Medical Officer for England, and
Alastair Kent, OBE

Co-Chairs, UK Rare Diseases Policy Board

Chapter 2: Introduction

- 2.1 There are between 6,000 and 8,000 rare diseases ([Orphanet](#)) that affect the lives of around 3 million of the UK population and approximately [80% are of genetic origin](#).
- 2.2 Rare diseases are defined as affecting around 5 people or fewer in 10,000 and require special, combined efforts to enable patients to be treated effectively. 1 in 17 people will suffer from a rare disease at some point in their lives.
- 2.3 The publication of the [UK Strategy for Rare Diseases in 2013](#) (Strategy) represented a significant milestone for patients with rare diseases. The Strategy, a high-level framework containing 51 commitments, set out a vision to 2020 for improving the lives of all those affected with a rare disease, covering five areas:
- Empowering those affected by rare diseases
 - Identifying and preventing rare diseases
 - Diagnosis and early intervention
 - Coordination of care
 - The role of research
- 2.4 Meeting the aims of the Strategy involves a collaborative approach across multiple stakeholders. This includes the four UK health departments: the Department of Health and Social Care for England (DHSC), the Directorate for Healthcare Quality & Improvement at the Scottish Government, the Health and Social Services Group at the Wales Government and the Department of Health in Northern Ireland.
- 2.5 In addition to the four UK health departments, stakeholders also include but are not limited to:
- healthcare providers and commissioners in the NHS;
 - regulators such as the National Institute for Health and Care Excellence (NICE), the Medicines and Healthcare products Regulatory Agency (MHRA) and the Health Research Authority (HRA);
 - research funders such as the National Institute for Health Research (NIHR) and the Medical Research Council (MRC);
 - as well as key partners such as NHS Digital, Public Health England (PHE), Genomics England, Health Education England (HEE), the UK National Screening Committee (UKNSC), industry and patient groups.
- 2.6 The first Progress Report titled '[Delivering for patients with rare diseases: Implementing a strategy](#)' was published by the Rare Disease Policy Forum in 2016 and described progress made on a UK-wide basis over the first 2 years of the UK Strategy. It recognised the significant progress in its implementation across the UK but also recognised that much remained to be done to meet the needs of those affected by rare diseases.

- 2.7 We are now over half-way through the Strategy's timeline and two years on from the publication of the first Progress Report. This presents us with an excellent opportunity for further reflection on progress made across the UK in addressing the needs of patients with rare diseases. This report therefore serves to highlight and celebrate initiatives and achievements across the four nations over 2016-2018, as well as looking at UK-wide developments and challenges in the rare diseases landscape that will be important in the forward look to 2020.
- 2.8 Since the Strategy's publication in 2013, the rare disease landscape has undergone a large transformation, especially with regards to the success and evolving legacy of the 100,000 Genomes Project and new emerging technologies such as genome editing. Many seminal publications such as the independent annual report '[Generation Genome](#)' by England's Chief Medical Officer, the '[Life Sciences Industrial Strategy](#)' and '[Life Sciences: Sector Deal](#)', have been published in 2017, all of which focus on the importance of genomics for health care, including rare diseases. Alongside this will be the impact of leaving the European Union, something we know is of particular significance to the rare diseases community. These developments have resulted in new opportunities and new challenges alike, none of which could have been anticipated in 2013.
- 2.9 In this report we look at progress achieved under the five themes of the Strategy, an additional theme of registries and data, and dedicate a final chapter to outlining the remaining challenges and next steps. The chapters of this report therefore cover:
- Empowering those affected by rare diseases
 - Identification, prevention, diagnosis and intervention
 - Coordination of care
 - Research
 - Registries and data
 - Key challenges and next steps
- 2.10 This Progress Report should be read alongside the most recent implementation plans published in each of the UK nations. Links to all implementation plans for England, Scotland, Wales and Northern Ireland can be found [here](#).

Governance of the implementation of the UK Strategy for Rare Diseases

- 2.11 The Strategy provides the foundation to improve services and support for patients and to promote the role of research in increasing our understanding of rare diseases and how they might be treated across the four UK countries.
- 2.12 In response to the Strategy, DHSC established the **UK Rare Disease Forum** to oversee and coordinate how the Strategy is delivered across the UK after its publication in 2013. The Forum's membership included representation from the rare diseases community, industry, academics and researchers.
- 2.13 In October 2016, revised governance arrangements were introduced. The [UK Rare Disease Policy Board](#) was established as a new UK-wide body with responsibility for facilitating the coordination of policy development in meeting the 51 commitments set out

in the Strategy. As well as supporting policy development and implementation, the Board also considers how the Strategy could be improved by harnessing the outputs from across the broader genomics and rare diseases landscape. The primary focus of the [UK Rare Disease Forum](#) is now to provide stakeholder insight and advice on key issues, challenges and risks to delivery of the 51 commitments in the Strategy to the Policy Board. This is discussed in more detail in paragraph 3.16.

- 2.14 The Policy Board aims to work collaboratively with the wider UK Rare Disease Forum. The Board publishes its membership and minutes of [Board meetings](#). Furthermore, a platform to facilitate collaborative working between the Board and the Forum was launched in November 2017 at the annual Rare Diseases Forum conference.
- 2.15 As we go forward, the Policy Board will consider each nation's progress against the Strategy, particularly where there is UK-wide impact. It will also work where appropriate with the new National Genomics Board in meeting its vision to make sure that the UK remains the world's leading centre for genomic medical research, and to leverage this position to deliver quantifiable benefits for NHS patients and for the life sciences sector.
- 2.16 The commitments in the Strategy are jointly shared by the four UK health departments and the NHS. The **Rare Diseases Advisory Group** (RDAG) makes recommendations to NHS England and the devolved administrations of NHS Scotland, NHS Wales and NHS Northern Ireland on developing and implementing relevant commitments in the Strategy. The RDAG also makes recommendations to these bodies regarding highly specialised services (those used by usually no more than 500 patients per year).
- 2.17 The membership of RDAG is broad and includes representatives from Royal Colleges, commissioners, patient and public voice representation and professionals such as a geneticist and an ethicist.

Implementing the UK Rare Disease Strategy in England

- 2.18 Although much progress in implementing the Strategy had been made behind the scenes, until recently, no formal implementation plan for England had been published.
- 2.19 In March 2017, Philip Dunne MP, Minister of State for Health announced that NHS England would develop an implementation plan for the commitments outlined in the Strategy for which it has lead responsibility. For those commitments that are outside of the scope of NHS England, DHSC would support its arm's length bodies to coordinate the publication of an implementation plan for the remaining commitments.
- 2.20 Both implementation plans by [NHSE](#) and [DHSC](#) were published jointly in January 2018 and describe the actions and framework in place to deliver the Government's commitment to improve the lives of those affected by rare disease as defined in the Strategy.
- 2.21 To ensure continued relevance of the implementation plan, DHSC will convene an annual review meeting with representatives from key delivery partners, including NHS England, NIHR, PHE, HEE, UKGTN, NICE, Genomics England and patient representatives.

Implementing the UK Rare Disease Commitments in Scotland

- 2.22 Following the publication of the UK Strategy the Scottish Government worked with a wide range of stakeholders to develop an implementation plan for Scotland. '[It's Not Rare to Have a Rare Disease](#)' was published in June 2014 and seeks to ensure that the needs of people with rare diseases are reflected in health and social care service planning and delivery across Scotland.
- 2.23 The plan aims to provide appropriate healthcare support to people with rare diseases through primary care, community, acute and specialist services, within existing service arrangements.

The Rare Disease Oversight Implementation Group

- 2.24 The role of the Rare Disease Implementation Oversight Group (RDIOG) is to monitor the implementation of the Scottish Rare Disease Plan 'It's Not Rare to Have a Rare Disease' and to ensure that the 51 commitments in the Strategy are being met.
- 2.25 The group is made up of clinicians, geneticists, biochemists, as well as representatives from NHS National Services Scotland, patient groups, NHS National Education Scotland, the Farr Institute and the Scottish Government.
- 2.26 The work of the RDIOG is underpinned by a workplan to ensure that action is being progressed across 5 key rare disease themes.
- 2.27 A full Progress Report of actions taken since publication of the implementation plan will be published in early 2018.

Implementing the UK Rare Disease Commitments in Wales

- 2.28 The '[Welsh Implementation plan for Rare Diseases](#)' was first published in February 2015. The implementation of the plan is supported by a national Implementation Group which has representatives from every health board in Wales and other key stakeholder organisations.
- 2.29 On Rare Disease Day, 29 February 2016, the Rare Diseases Implementation Group (RDIG) held an event to heighten awareness of rare diseases, the Welsh implementation plan and the need for better co-ordination across Wales.
- 2.30 An update on the progress made by the Welsh Government and NHS Wales was published in February 2016. The [report](#) sets out the successes in recognising the importance of rare diseases and actions put in place to improve the care of and support for patients, their families and carers.
- 2.31 The [implementation plan](#) was updated and republished in July 2017. The Implementation Group has agreed a number of priorities for 2017/18 to help achieve this:
- identifying the support pathway for patients with an unknown diagnosis (the so-called Diagnostic Odyssey);
 - creating and ensuring better use of best practice and evidence in primary and secondary care as well as improving pathways for accessing specialist services;

- undertaking significant event analysis including delayed diagnosis of a rare disease and shared evidence learning; and
- ensuring feedback from patients is utilised to enhance rare disease pathways within health boards.

A further progress update for Wales will be published in Spring 2018.

Implementing the UK Rare Disease Commitments in Northern Ireland

- 2.32 Working closely with local stakeholders following the publication of the UK Strategy, the Department of Health in Northern Ireland developed and published '[Providing High Quality Care for people affected by Rare Diseases](#)' - The Northern Ireland Implementation plan for Rare Diseases' in October 2015.
- 2.33 This paper provides an integrated framework, aligned with the Northern Ireland Executive's Programme for Government, for continuing action by the Department and other Executive Departments, the Health and Social Care (HSC) sector, the voluntary sector, and education and research stakeholders to improve services and address the needs of people living with a rare disease regardless of their age, where they live and whatever their circumstances. The 51 commitments across the five strategic themes are therefore an integral part of the Health and Social Care Board's approach to health commissioning, particularly with regard to specialist services and including treatments that are not routinely provided by local HSC Trusts.
- 2.34 The planning process also identified four priority actions as key drivers of the implementation of the overall strategy in Northern Ireland:
- to enhance methods of communication between patients and health services (under the 'patient empowerment' theme);
 - to enhance training and education in relation to rare diseases amongst healthcare professionals;
 - to plan for the introduction of Northern Ireland's register for rare diseases (both under the 'diagnosis and early intervention' theme); and
 - to secure funding to establish a Northern Ireland Genomics Medicine Centre through participation in the 100,000 Genomes Project (under the 'role of research' theme).
- 2.35 Recognising the UK Strategy's key commitment to continuing international collaboration to tackle rare diseases wherever possible, the Northern Ireland implementation plan contains a sixth theme which focuses on identifying opportunities for collaboration with the Republic of Ireland (RoI) in cross-jurisdictional initiatives to support people with rare diseases. The RoI Plan, published in 2014, similarly included a commitment to cross-border collaboration.
- 2.36 The Northern Ireland Rare Disease Stakeholder Group, led by the Department and comprising health commissioners, clinicians, academic expertise and patient representatives from the Northern Ireland Rare Disease Partnership (NIRDP), oversees the delivery against the UK Strategy commitments, including the additional all-Ireland theme, and the priority actions agreed for the region. Further detail and examples of

progress are provided throughout this report. A full progress report of action taken in Northern Ireland since publication of the implementation plan will be published in 2018.

Chapter 3: Empowering those affected by rare diseases

3.1 This chapter explores progress under the first theme of the Strategy – *empowering those affected by rare diseases*.

UK-wide implementation plan activities 2016-18

Empowering patients through the 100,000 Genomes Project

- 3.2 The 100,000 Genomes Project has been one of the key vehicles for delivering progress against many of the 51 commitments in the Strategy, including commitments under the theme of empowering those affected by rare diseases. As such, aspects of the Project are discussed both here and in chapters 4 and 6.
- 3.3 In April 2003 the first complete genetic code of a human being, their genome, was sequenced. This was the result of a collaborative effort by thousands of scientists across the world over 13 years, costing approximately £1.4 billion. Just 15 years on, the entire genome can be sequenced in under a day, for less than £1000. This leap in the speed and reduction in the cost of sequencing has opened up the potential of genomics for mainstream healthcare – and the UK is at the forefront of this vision.
- 3.4 To fulfil this ambition, former Prime Minister David Cameron launched the 100,000 Genomes Project in late 2012. [Genomics England](#), a company wholly owned and funded by DHSC, was set up to deliver this flagship project in collaboration with a number of key partners such as NHSE, HEE, PHE and 85 NHS Trusts and hospitals across England.
- 3.5 The project is focused on patients with a rare disease and their families, as well as patients with cancer and has four main aims:
- to create an ethical and transparent programme based on consent;
 - to bring benefit to patients and set up a genomic medicine service for the NHS;
 - to enable new scientific discovery and medical insights; and
 - to kick start the development of a UK genomics industry.
- 3.6 To deliver the project NHSE has setup a world leading nationwide network of 13 NHS Genomic Medicine Centres (GMCs) which are providing equitable access to populations of ~3-5 million. They are responsible for the clinical care and consent process of patients along with providing clinical data and appropriate samples from participants.
- 3.7 One of the aims of the project is to accelerate the uptake of advanced genomic medicine practice into the NHS. To support genomics in being embedded into routine clinical care, NHSE is continuing to develop genomic medicine infrastructure, including:

- Procuring a national genomic laboratory network underpinned by a genomic testing directory, which will have a focus on facilitating and supporting academic and industry collaboration;
 - Working in partnership with Genomics England to secure whole genome sequencing (WGS) provision for routine care, and the supporting informatics infrastructure;
 - Developing the underpinning clinical service (through development of the existing clinical genetics service and evolving the role of GMCs established through the project).
- 3.8 Since its establishment, the devolved administrations have joined the Project. The Northern Ireland Genomic Medicine Centre, through engagement with clinicians in multiple specialties, is recruiting rare disease and cancer patients who will receive WGS as part of the Project, and are planning for the continuing legacy of the service beyond its lifetime. Scotland has also established its own sequencing capability with links to Genomics England, and Wales is in the process of recruiting rare disease patients for WGS via Genomics England as part of their recently published [Genomics for Precision Medicine Strategy](#).
- 3.9 The 100,000 Genomes Project has made a significant contribution to meeting the Strategy's commitments to empower patients with a rare disease. Since 2015, participants in the 100,000 Genomes Project and their carers have been invited to join a national 100,000 Genomes Project Participant Panel. Today there are over 25 members involved from across the country and counting. The Panel acts as an advisory committee to the Genomics England Board, and their aim is to ensure that the interests of participants are at the heart of the Project.
- 3.10 Members of the panel have worked on a number of projects during 2017, including developing a leaflet on what happens next after families have joined the Project, providing feedback and guidance on new activities including the new Management Information System, sharing 100,000 Genomes Project stories with the media, and raising awareness for the Project through local events and support networks.
- 3.11 Several panel members are also members of other Genomics England committees including Genomics England's independent [Ethics Advisory Committee](#) which identifies, defines, examines and responds to ethical issues in the 100,000 Genomes Project. It also helps to ensure the Project is delivered in the interests of the public and of participants.
- 3.12 Genomics England also set up an engagement programme – known as the 'Genomics Conversation' – with key stakeholders including the public, NHS staff and industry. The Conversation harnessed new and existing networks to: stimulate the debate around genomics; engage relevant audiences efficiently and discover the issues that are meaningful to audiences; and measure outcomes to inform future communications.
- 3.13 The results of this '[Genomics Conversation](#)' were published in a report in November 2016 and ran in parallel to many other complementary activities such as the 'Socialising the Genome' project. This project, co-funded by the Wellcome Trust and Sanger Centre,

aims to bridge the gap between how professionals speak about genomics and how the public talk about it, encouraging informed debate.

- 3.14 Genomics England is now expanding its Genomics Conversation into a wider Public Dialogue. This Dialogue will run initially for two years and will encompass UK-wide public events, debates, roundtables, insight research, analysis and other activities in partnership with NHS England and key stakeholders.
- 3.15 The Project also launched a [‘Track my sample’](#) capability in 2017. This means that by filling out an online form, patients can request where their sample is in the Genomics England pipeline – if it has been sent for sequencing, if it’s being quality checked or if it’s reached the analysis and interpretation stages.

Rare Disease Forum

- 3.16 Following the proposal for the restructure of the governance to the Strategy, a smaller focussed UK Rare Disease Policy Board, concentrating on high-level policy development and implementation of the 51 commitments in the Strategy, and a larger UK Rare Disease Stakeholder Forum, were established in October 2016.
- 3.17 As part of supporting continued communication and partnership between the Board and the Forum, the Policy Board is committed to hosting an annual Rare Disease Forum conference. It also launched in November 2017 an online communication platform for Forum members to interact with and inform the work of the Policy Board.

2017 Rare Disease Forum Conference – Birmingham Children’s Hospital

- 3.18 The first Rare Disease Forum conference was held on the 24th November 2017 at Birmingham Children’s Hospital. The conference agenda is provided in **Annex 1**. It was attended by more than 50 participants including members of the UK Rare Disease Forum, UK Rare Disease Policy Board, clinicians, professionals, patient representatives and industry. The day was co-chaired by Professor Gina Radford and Alastair Kent, OBE, the co-chairs of the Policy Board.
- 3.19 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.
- 3.20 It began with a series of short talks given by representatives from devolved administrations, the European Reference Networks (ERNs), Genomics England, and NHS England followed by a panel Q&A involving the speakers and representatives from all four UK nations.
- 3.21 This was followed by two participant-led breakout sessions in which attendees reflected on the highlights and challenges experienced by the rare diseases community over the past two years, along with discussing a forward view for 2018 and what they felt should be a focus for the work of the Policy Board during this period.
- 3.22 Participants discussed as highlights since the publication of the last Progress Report the work of the 100,000 Genomes Project and advances in genomic medicine in general. They also discussed the continuing efforts made to upskill the current and future

workforce and gave overall recognition to the UK as leading the way for improving the lives of those living with a rare disease.

- 3.23 Participants also recognised that quality of care for rare diseases patients was still variable geographically; they recognised the need for better co-ordination of care in order to support patient's families and improve the patient experience; the continued relevance of the themes of the Strategy in light of recent political and technological advances; and participants highlighted that they wanted to ensure that current momentum would be maintained once the Strategy ends in 2020.
- 3.24 As a forward look for 2018, key themes included increasing collaboration at all levels of involvement, from the individual up to the national level and finding opportunities for sharing and learning from the many examples of good practice seen throughout the four nations. Effective capture and sharing of valuable data was also highlighted, along with raising the awareness of rare diseases and the fact that, though they are rare, collectively they are common.
- 3.25 The participant discussions at the conference have informed the final section of this report, in which we look forward to the next two years of the Strategy, and were discussed at the January 2018 Policy Board meeting. Overall, the conference helped to reinforce the sense that, though there are many different voices in the rare disease community, the message is the same - to improve the lives of those, and their families, living with a rare disease.

Case Study: Feedback from the Annual Rare Diseases Forum conference 2017

Attendees were asked for their feedback after the conference, covering the following points:

- which sector they represented;
- how they rated the event; and
- if they felt they had an opportunity to contribute their views to the discussion (if attendees answered no, they were given an opportunity to share their views on the feedback form).

Of those that attended the conference, 20 out of 52 attendees returned feedback. Of these 20, 19 rated the event as either 'excellent' or 'good' and felt that they were given an opportunity to contribute their views.

General comments written on the forms spoke of the conference as being an excellent opportunity to both interact with others from the rare diseases landscape and to contribute to the overall discussion. One attendee commented that they would have liked more time to discuss the topics on the agenda, and that the theme of the day could have been communicated more clearly before the event.

The majority of written feedback highlighted that the conference had been an excellent catalyst for increasing awareness of the need for greater collaboration.

Launch of the Rare Disease Forum Exchange Platform

- 3.26 In 2016, DHSC committed to support the Rare Diseases Forum by providing an online networking and communication platform. Following development of its functionality, the Rare Disease Forum Platform was formally launched at the 2017 annual Rare Disease Forum conference.
- 3.27 Key functionalities of the platform, which is hosted by DHSC, include:
- a means to submit questions/discussion points for standing item at Rare Disease Policy Board meetings;
 - a platform for reporting back on these questions/discussion points to the Forum; and
 - a place to keep up with the work of the Policy Board, including the agendas and minutes of their meetings.
- 3.28 The platform's purpose is to facilitate discussion between the Board and the Forum and as such, its design and mode of operation will be an evolving concept, based on feedback from its users.

Rare Diseases UK Patient Empowerment Group (PEG)

- 3.29 The [Patient Empowerment Group](#) (PEG) was established by the [Rare Disease UK](#) campaign to help monitor the implementation of the Strategy. The purpose of the group is to ensure that the patient voice is properly informed and effectively represented in the implementation of the Strategy.
- 3.30 PEG's membership is taken from patient group supporters of the Rare Disease UK campaign. The membership is carefully chosen to ensure there is a broad range of rare diseases represented, including variations in age of onset and body system affected. The membership includes both genetic and non-genetic forms of rare disease and has representation from all four nations, including from the implementation oversight groups in Scotland and Wales.
- 3.31 PEG offers the opportunity for any group working to implement the Strategy to have advice from patients or for materials to be reviewed. Groups that have accepted this invitation include the PHE, NHS England, and DHSC. The group has met with both Deputy Chief Medical Officers in England that have had oversight of the implementation of the Strategy. PEG has also provided evidence to the All Party Parliamentary Group on Rare, Genetic and Undiagnosed Conditions in its investigations into the implementation of the Strategy.
- 3.32 There has been a long-standing relationship with PHE who have brought many aspects of their work to deliver the [National Congenital Anomaly and Rare Disease Registration Service](#) (NCARDRS) to PEG for discussion and consultation. These topics have included the testing of communication tools, discussions on how to integrate patient organisation held registry data and a discussion of the team's business plan. These regular meetings have also been an opportunity for PEG members to ask the NCARDRS team questions about the service and have been a valuable two-way dialogue for both sides.

Case Study – UK: Rare Disease UK's patient survey

The 'Rate your rare disease care' survey run by Rare Disease UK, the national campaign for people with rare diseases and all who support them, managed by the charity Genetic Alliance UK received responses from a large number of individuals which were collected and analysed. The survey was conducted in two phases, with the first covering overall care and general feedback and the second collecting further responses on care satisfaction according to factors such as type of care and region in which the care was received.

The first phase of the survey involved 573 respondents who were asked to rate the overall care received by themselves or their loved one affected by a rare disease, along with an opportunity to write an unstructured comment. 62% of all participants responded to the initial question by rating their overall care as somewhere across the spectrum from excellent to satisfactory, compared to 38% who rated their overall care as poor.

For the second phase of the survey, 125 participants responded to more detailed questions about the care they had experienced. For this subset of participants, 67% rated their overall quality somewhere between excellent to satisfactory but with a different distribution within this range compared to the first cohort of correspondents. The responses to the survey highlighted a clear correlation between the overall rating of the care experienced and degree of specialism of their main provider of care (care was on average rated better where the degree specialism of their main provider increased). Also clear was the regional variation in the overall care rating.

The results of the two-phase survey, along with a full analysis carried out by Rare Disease UK was published on the same day as this report and can be found at the following link: <https://www.raredisease.org.uk/our-work/rate-your-rare-disease-care/>. The results of this survey will be used to inform the future work of the Rare Disease Policy Board and inform the future implementation of the Strategy.

The Rare Diseases Advisory Group (RDAG)

- 3.33 As outlined in chapter 2, in which the governance of the implementation of the Strategy was discussed, RDAG is a UK-wide group that makes recommendations to NHS England and the three devolved administrations on the commissioning of highly specialised services.
- 3.34 In order to bring important views and perspectives to the group, and to champion the service user, patient and carer/family viewpoint, there are four patient and public voice members on the RDAG.

Key nation-specific implementation plan activities 2016-18

England

NHS England's 'Framework for patient and public participation in specialised commissioning'

- 3.35 In January 2017, NHS England published a '[Framework for patient and public participation in specialised commissioning](#)'. This sets out how 163 patient and public members are involved in NHS England's governance structures. In particular, there are two patient representatives and one voluntary sector/community representative on each of the 42 Clinical Reference Groups.
- 3.36 In addition, NHS England involves patients on the working groups that develop 'products' such as clinical commissioning policies and service specifications. As well as involving patients through these mechanisms, NHS England has developed processes for engaging patients and the public when developing commissioning products (through its registered stakeholder structure) and for public consultation.

NICE - Highly Specialised Technologies (HST)

- 3.37 The [National Institute for Health and Care Excellence](#) (NICE) formally took responsibility for the development of guidance for highly specialised technologies (HST) in April 2013. NICE's HST programme determines whether selected very rare disease treatments should be recommended for NHS-wide commissioning in England. NHS England is required to fund treatments recommended in NICE HST guidance, normally within three months of publication of final guidance.
- 3.38 Since April 2013 NICE has published 6 pieces of guidance for technologies through the HST programme, 3 of which have incorporated managed access agreements (MAA). An MAA is a process through which patients can receive new treatments while long-term data on the treatment is still being gathered, at a lower cost.
- 3.39 NICE recognises the need to consider treatments for ultra-rare conditions differently and undertook a review of the methods of evaluation for such treatments in 2016-17.
- 3.40 Following a public consultation, NICE introduced changes to its methods for the evaluation of HST topics in April 2017. Under the revised methodology, products that are evaluated through the HST program will be assessed against a sliding scale, so that the more additional quality-adjusted life years (QALYs) a treatment offers, the greater the cost per QALY level it will attract, starting at £100,000 per QALY, rising to a maximum of £300,000 per QALY.
- 3.41 The new approach provides a more explicit framework for decision-making than NICE have had before and provides greater clarity for patients and companies about the point at which treatments for very rare conditions evaluated by NICE can be recommended for

routine commissioning. It shows that what matters most, and what will attract the highest premium, is therapeutic benefit. This change was introduced alongside other changes to NICE's technology appraisal and HST programmes that are intended to address concerns about the affordability of new treatments.

Case Study – England: Managed Access Agreements

Children and adults with a rare inherited bone disease will be able to access a potentially life-enhancing drug, thanks to an innovative deal between NHS England, NICE and manufacturer Alexion.

Hypophosphatasia (HPP) is a rare inherited bone condition that can appear any time from before birth to adulthood. In babies it is often fatal, and in older children and adults it can be debilitating, leading to bone deformities that may result in delayed walking, limb weaknesses, skeletal pain and fractures. The disease is more common in older children and adults, affecting 1 in 6,370. The drug asfotase alfa was previously only recommended for use in babies by NICE in draft guidance, as evidence showed it could be life-saving.

A new 'managed access agreement', between NHS England and manufacturer Alexion, will broaden access of asfotase alfa to infants, children and adult patients with paediatric-onset HPP, who experience the most disabling symptoms and are expected to benefit most from therapy. It is a novel deal because it is a value-based risk sharing agreement to provide wider cost-effective access for patients, informed by their first-hand experience of the ongoing impact that treatment is having on their health and quality of life.

Because of the small numbers of patients with rare diseases it can be challenging to get sufficient numbers treated in research trials to have certainty about the level of health benefits. The agreement helps address this lack of certainty and allows for a five year period to gather real-world data about how well the treatment benefits these patients before longer term commissioning decisions are taken.

Case Study – England: Atypical haemolytic uraemic syndrome (aHUS)

aHUS is a condition that results in clots in small blood vessels and can affect the brain, gut, kidney and other organs. In January 2015, NICE recommended the drug eculizumab for the treatment of aHUS through its Highly Specialised Technology (HST) Programme and included a requirement that the drug should be initiated through an expert centre. Eculizumab halts the disease process in aHUS and greatly improves the patient's quality of life. NICE had worked closely with the national patient group, aHUS UK, in considering the HST.

In response to this advice, NHS England agreed that a formal procurement process was needed to select the expert centre as a number of Trusts expressed an interest in providing the service.

The HSS team therefore continued to work with aHUS UK, and the expert clinicians who had been involved in the HST programme, to agree a service specification to be used to support selection of the expert centre. This service specification was developed in accordance with the principles set out in the NICE HST and which are common to a number of Highly Specialised Services. These comprise an expert centre that confirms the patient's diagnosis and has oversight of the patient's management but which works with more local renal centres to deliver the drug as close as possible to the patient's home.

aHUS UK were particularly interested in the way in which the expert centre would work with renal centres across the country as most patient management continues to be delivered locally to the patient. They were also interested about the support for early diagnosis and engagement with GP training; this is a key role for the national centre in ensuring awareness of the condition.

A Patient and Public Voice member of RDAG sat as a member of NHS England's procurement project team to secure the expert aHUS centre. They contributed to all aspects of the procurement process including scoring of proposals and involvement in clarification meetings with providers to discuss the proposals.

NHS England announced in May 2016 that a collaboration between Newcastle Upon Tyne Hospitals NHS Foundation Trust and Newcastle University has been awarded the contract to oversee the treatment of patients with aHUS.

Subsequent to the service being established, NHS England has been in touch with the patient group (recently reformed as Answers for aHUS) to ask for feedback on the performance of the national service. There is already collaboration between the patient group and the national expert centre on a number of fronts including an NIHR trial which is starting to look at a safe care pathway for the withdrawal of eculizumab when it is no longer indicated.

Case Study – England: Strimvelis for the treatment of severe combined immunodeficiency

Around 3 babies a year in England are born with severe combined immunodeficiency due to adenosine deaminase deficiency, ADA-SCID. The disease leaves children extremely vulnerable to infection and severely impacts on their quality of life, usually resulting in the need for them to live as sheltered from possible sources of infection as possible. If left untreated, infants with ADA-SCID die before school age.

Until recently the only treatment offered for ADA-SCID was a stem cell transplant. However, only 20-25% of infants have a suitable matched related donor (MRD) and remaining options present a high risk of graft versus host disease which can be life threatening.

Strimvelis treatment is an alternative option for those without a suitable MRD, and offers the

potential to cure the immune aspects of the condition as well as avoiding some of the disadvantages of current therapies. Costing €594,000 (£530,000), the treatment usually has to be administered only once and the effects are thought to be life-long.

Strimvelis is the second gene therapy for an inherited disease to be licensed anywhere in the world and represents an important development both in the treatment of ADA-SCID and in the treatment of rare diseases as a whole.

Strimvelis has recently been considered as part of NICE's HST programme. The resulting draft guidance, which is the first time NICE has applied its new, higher cost effectiveness limits for treatments for very rare conditions, has recommended Strimvelis when no suitable MRD is available. This recommendation means that children born with ADA-SCID in England will now have a better chance of survival and of being able to live as near to a normal life as possible, without the constant threat of contracting a potentially life-threatening infection.

Scotland

3.42 The Scottish Government is fully committed to empowering people in terms of their health and social care. A number of plans, policies and recommendations have been made since the last biennial report that are being driven and delivered across Scotland. These will also directly impact on people who are affected by rare diseases.

- [‘The Health & Social Care Delivery Plan’](#) is the Scottish Government’s plans for enhancing health and social care services by 2021.
- [‘Realistic Medicine’](#) is the CMO’s annual report which addresses variation in care; management of clinical risk; reduction in harm and waste; and innovating to improve, in order to provide a sustainable NHS. It puts the individual at the centre of their treatment.
- [‘Making it Easy: A Health Literacy Plan for Scotland’](#) is an action plan that seeks to “make Scotland a health literate society that enables all of us to live (and die) well on our own terms and with any health condition we may have”.
- [House of Care](#) provides a simple visual model of a house built around collaborative care planning conversations between individuals and their health care professionals. The approach has been implemented in 55 GP practices across Scotland.
- [What Matters to You](#) aims to encourage and support meaningful conversations between people who provide health and social care and the people, families and carers who receive health and social care and is being tested in secondary care diabetes services.
- [Care Opinion](#) is an online feedback service that enables people to give real-time feedback and engage in constructive dialogue with healthcare service providers about the services they, their families and people they care for have received.
- [Health & Social Care Standards](#) will come into effect from April 2018. These will set out the standards that people should expect when using health and social care services. They aim to ensure people are fully involved in all decisions about their care and support.

- Provision of [Communication Equipment & Support](#) gives children and adults across all age ranges and care groups, who have lost their voice, or are at risk of losing their voice or who have difficulty speaking a statutory right to access the communication equipment and support they need.

Case Study – Scotland: Care Opinion

Care Opinion (previously Patient Opinion) is a not-for-profit social enterprise that provides an online feedback service enabling people in Scotland to give real-time feedback, and engage in constructive dialogue with healthcare service providers about the services they, their families, or the people they care for, have received.

The Scottish Government has supported the roll out of Care Opinion across Scotland since 2013. A contract was awarded in April 2015, which provides for every territorial NHS Board in Scotland and relevant special boards to be fully registered with the service.

All Boards subscribe to Care Opinion and are reading and responding to issues directly. There are now around 780 NHS Scotland staff reading stories and we continue to see a higher distribution of staff responding as time goes on. This allows people posting stories to receive a targeted response and provides assurance that their concerns, or messages of thanks, have reached the appropriate staff member(s).

Care Opinion held an event in Glasgow on 17th May 2017 for clinicians wishing to explore how they and their teams can use Care Opinion to support their local learning and improvement work. Some clinicians at this event reported barriers to testing ways of supporting clinicians to respond to postings on Care Opinion. This was subject to social media discussion, which involved some Scottish Government officials emphasising support to empower more clinicians to use Care Opinion if they wish to do so.

There have been 13 changes to services, made or planned, because of stories on Care Opinion. These include:

- NHS Ayrshire and Arran is providing weekly waiting time updates for CT/MRI scans to avoid giving people unrealistic expectations.
- The Royal Hospital for Sick Children (Glasgow) is looking at ways to improve the condolence letters they issue to bereaved parents.

Care Opinion intends to focus on development in the following areas:

- Creating case studies and further exemplar videos to demonstrate the impact of using Care Opinion to encourage feedback.
- Continuing to raise public awareness through partnerships with third sector patient-led organisations, social and conventional media.
- Supporting Care Opinion and NHS Board clinical leaders to explore effective ways to empower and support clinicians as responders to postings and use information

to further refine and develop clinical involvement that is linked to local learning and quality improvement work.

Care Opinion want people to share their experiences of the care they have received from NHS Scotland. These can be either positive or negative experiences which are directly accessed by the relevant staff in the relevant health board. It gives staff the opportunity to hear and address first-hand experiences of care. This can help open a dialogue between the person and staff member(s), or allow staff member(s) to consider making changes to service provisions and/or share good practice with other health boards.

The site shows that a number of people who have a rare disease or a member of their family have used the site and received a very quick response from their NHS Scotland board. They have been able to provide feedback on the level of awareness about their condition amongst healthcare professionals, to thank staff for their treatment and care, or provide feedback on how it could have been improved – both of these are important as they can help inform pathways in the future.

You can search Care Opinion for stories that relate to your condition or your health board:
<https://www.careopinion.org.uk/>

Wales

3.43 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, derived from good quality research.

Rare Disease UK and the Welsh Rare Disease Patient Network: Empowering patients to take part in the policy process

3.44 [Rare Disease UK](#) (RDUK) is a national campaign for people with rare diseases and all those who support them. In Wales, the RDUK aims to influence the development and implementation of the Strategy for in Wales, ensure rare diseases are viewed as a public health priority by the Welsh Government and the NHS, and brings together and mobilises the rare disease community.

3.45 In collaboration with the Wales Gene Park, RDUK established the Welsh Rare Disease Patient Network to engage patients, families and patient organisations to ensure the patient voice is properly informed, and effectively represented in the discussion and development of the implementation of the Strategy.

3.46 The network also supports the recruitment of rare disease patients to research studies and helps to identify patients with specific rare diseases for which no support group exists in Wales. Genetic Alliance UK (the charity leading this campaign) has secured funding to work with rare disease patients and families locally to help them to establish

and develop responsive and dynamic peer support networks or patient groups, in addition to sitting on the Welsh Rare Diseases Implementation Group.

Improved access to health technologies and orphan medicines for rare disease patients in Wales

- 3.47 The magnified impact of rare diseases raises the significance of innovative treatments arriving on the horizon. It is imperative that these are made available in Wales, for the benefit of patients, their families and wider society. Health technology appraisal (HTA) is vital in ensuring patient access to treatments. The nature of rare diseases presents a number of challenges that must be met to ensure an effective appraisal process can be carried out. 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.
- 3.48 In addition, the All Wales Medicines Strategy Group (AWMSG) has an established process for appraising orphan and ultra-orphan medicines developed specifically for rare diseases to enable even greater involvement of patients and clinicians in Wales. In recognition of the clinical needs of patients with rare diseases, and acknowledging the potentially high costs of treatment, broader considerations are taken into account when appraising ultra-orphan medicines than those for orphan medicines, or for other medicines.
- 3.49 The evaluation process ensures that clinical and patient experts are consulted on the value they place on the impact of a medicine for the individual and caregivers. Evaluating societal preferences as well as the benefits to caregivers, the rarity and severity of the condition and clinical evidence provides an approach that is centred on the needs of the patient and their family.
- 3.50 In July 2017, the new treatment fund opened to deliver swift access to innovative new medicines to support people with life-threatening conditions in Wales. An additional £16 million annually 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).

Case Study – Wales: Betsi Cadwaladr University Health Board (BCUHB):

As part of their partnership work, 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.

BCUHB has developed exceptionally strong partnership arrangements with third sector organisations in North Wales who help provide the knowledge and guidance patients need to

secure access to health and social care services and to manage and improve their condition. The Health Board is looking at ways to strengthen the mechanisms for patient involvement in service provision and research. 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; and
- be a single point of contact for patients, their carers and professionals as a resource for information advice and signposting.

Northern Ireland

- 3.51 In October 2016 the Department of Health (NI) launched '[Health and Wellbeing 2026: Delivering Together](#)', a 10-year strategic approach (2016-2026) to transforming health and social care in Northern Ireland, with a commitment to co-production of new and reconfigured services as one of its central premises.
- 3.52 This is a key element of the Department's statutory duty under Personal and Public Involvement (PPI) to involve both users of health and social care and carers in the policy making process. This duty extends to commissioners and providers of health and social care services in Northern Ireland. This is demonstrated in the approach to rare diseases, with the Northern Ireland Rare Disease Partnership (NIRDP) playing a lead role in partnership with the Department, HSC organisations, clinicians and academics, and as representatives of the range of specific rare disease patient groups, in both the development and delivery of Northern Ireland's implementation plan.
- 3.53 Patient and service user experience is recognised as a key element in the commissioning and delivery of quality healthcare in Northern Ireland. In line with this, the Public Health Agency's '[10,000 Voices](#)' initiative gives people an opportunity to provide feedback on their experiences of accessing health and social care services. It encourages members of the public to tell their story with a view to shaping future healthcare services to deliver better outcomes for patients, their families and carers. All surveys carried out as part of this initiative include a rare disease identifier, which will help to enhance understanding of

how this particular group of patients and carers experience the health service.

- 3.54 The needs of rare disease patients, and relevant Strategy commitments, are therefore part of the commissioning process for specialist and highly specialist services in Northern Ireland, further supported by the Health and Social Care Board and Public Health Agency membership of RDAG.
- 3.55 Specifically, a series of patient engagement workshops were held across the region in 2017 as part of a rare diseases information and communications review. The findings of these workshops will be used to inform appropriate actions across all themes of the Strategy and have been factored into wider reconfiguration workstreams, for example in the modernisation of neurology services. NIRDP also represents the Northern Ireland patient and public voice at UK level as a member of RDAG.
- 3.56 As a direct result of the engagement workshops, NIRDP recently appointed two care coordinators, whose geographic remit will cover all of Northern Ireland's five Health and Social Care Trusts, and whose role will involve working to bridge the gaps which rare disease patients identified in the availability of information relating to their conditions, health and other public services, and community support at local, regional and national level. It is envisaged that the two year project will serve as a pilot to inform how these needs can best be met in the longer term.
- 3.57 Work is continuing, as part of the '[Encompass](#)' project to deliver a digital platform for Health and Social Care in Northern Ireland, to develop an Electronic Healthcare Record (EHCR) for all patients accessing health and social care services. Its phased development from 2020/21-2023/24 will transform the way in which healthcare professionals communicate with each across the system and throughout the patient journey. In particular for rare disease patients this will provide a better experience as their information relating to often-detailed medical history will become more easily accessible both to themselves and to those providing their care. The development process for the EHCR has involved close consultation and collaboration both with HSC staff at all levels and with patients and carers.

Case Study - Northern Ireland: Project Echo and Vasculitis Ireland

Vasculitis Ireland, an all-Ireland patient representative group with close links to clinicians and researchers in Northern Ireland, England, and in the Republic of Ireland, has worked with NIRDP and health commissioners to find ways to streamline and improve the patient journey for those suffering from this debilitating and life threatening condition.

Delayed diagnosis, complex care pathways and lack of easy access to highly specialist expertise were identified as key issues. Working together, clinicians from the Northern Ireland Regional Nephrology Service, and representatives from NIRDP, Vasculitis Ireland, the Public Health Agency and the Health and Social Care Board agreed to pilot the use of Project Echo

methodology with this patient cohort, initially connecting the regional specialists with GPs and local hospital clinicians. In the second phase it is intended to extend the network to include participation by tertiary care specialists from Addenbrookes and Tallaght Hospitals.

Project ECHO is a lifelong learning and guided practice model that revolutionises medical education and exponentially increases workforce capacity to provide best-practice specialty care and reduce health disparities. The heart of the ECHO model™ is its hub-and-spoke knowledge-sharing networks, led by expert teams who use multi-point videoconferencing to conduct virtual clinics with community providers. In this way, primary care doctors, nurses, and other clinicians learn to provide excellent specialty care to patients in their own communities.

This pilot project exemplifies how patients can work constructively with clinicians, health service administrators and service managers, to produce (and rapidly move to testing) innovative solutions to complex multi-faceted issues.

Case Study – Northern Ireland: 22Q11 and Working Together to Tackle the Gaps in Service Provision

22Q11 deletion syndrome is a spectrum of disorders, resulting from a sub microscopic deletion of part of a chromosome. Typical physical effects include heart defects; characteristic facial features; and problems with the immune system. Research also shows that behavioural and psychiatric effects are important, too. Multi-disciplinary support is therefore essential for those living with 22Q11DS.

The improved networks and dialogue between clinicians, patient groups and commissioners developed during the extensive consultation processes on the UK Rare Disease Strategy, and the subsequent coproduction of the NI implementation plan led to identification of a gap in service provision: whilst physical manifestations of 22Q11DS were managed within existing generic services, nothing was in place to help with the behavioural/psychiatric issues.

Clinicians, health commissioners, and the 22Q11DS Patient Support Group worked closely with the Belfast Trust worked together to develop and subsequently deliver a 22Q11DS Support Clinic, led by the Regional Medical Genetics Service which focussed on behavioural and psychiatric impacts and was supported by volunteers from the Patient Group. This unique service, developed in close collaboration between families, clinicians and service managers with support from commissioners, has been recognised as a ground breaking early intervention in the care of those living with this complex condition

Chapter 4: Identification, prevention, diagnosis and intervention

- 4.1 This chapter explores progress under the second and third themes of the Strategy – *identifying and preventing rare diseases and diagnosis and early intervention*.

UK-wide implementation plan activities 2016-18

The 100,000 Genomes Project

- 4.2 The 100,000 Genomes Project is helping to address unmet diagnostic need. [Existing testing in the NHS](#) is focussing on at most 1.5% of the total human genome. In many cases, testing is only available to look at common “troublemaker” genes and if those specific changes are not present, the cause can remain a mystery. A lack of diagnosis often leads patients with a rare disease finding themselves on a “Diagnostic Odyssey” involving serial referrals to several specialists and many different, often invasive, tests. Over half wait for more than one year after first symptoms and some have waited over 20 years. These “Diagnostic Odysseys” cause uncertainty and distress for those affected as well as considerable costs for health and social care budgets.
- 4.3 Genomic medicine is part of the move from a ‘one size fits all’ approach to treatments and interventions to more personalised medicine. Advances in genomic medicine can particularly aid identification, prevention, diagnosis and intervention for patients with a rare disease as approximately 80% are of genetic origin. By combining and analysing information about our genome with other clinical and diagnostic information, patterns can be identified that can help to determine our individual risk of developing disease; detect illness earlier; and, determine the most effective interventions to help improve our health.
- 4.4 The 100,000 Genomes Project is helping to drive advances in genomic medicine and is already providing diagnoses to patients with a rare disease. The Project uses whole genome sequencing which delivers a view of the entire genome and detects a broader range of class of genomic variants than other technologies, giving substantially greater power to understanding the role of genes in health and disease.

Case Study – UK: Providing diagnosis through the 100,000 Genomes Project

The 100,000 Genomes Project is already changing the lives of patients with a rare disease. Jessica, aged 4, had shown developmental delay since the age of four months, and developed intractable fits. The medication received previously had little impact, and as a result she underwent many tests, including exome sequencing, without arriving at a diagnosis.

Jessica was enrolled on to the 100,000 Genomes Project. As a result, her entire genome was

sequenced and compared to a reference sequence. The reference sequence is used by scientists world-wide and is a representative example of a human genome sequence. Through comparing to the reference sequence, 6.4 million differences, or variants, were identified. Because Jessica's condition is rare, those interpreting the sequence knew that the variant they were looking for was rare too. The next step in this case was therefore to look for rare variants. Almost 700,000 were rare.

Using information from scientific studies and research papers, 700,000 variants were then narrowed down to almost 3,000. Jessica's parents also did not have the condition, so these variants were then compared to those of her parents. As a result, possible variants were further reduced from 3,000 to just 67.

These remaining variants were then checked against a knowledge base curated by Genomics England – PanelApp. This tool has information on thousands of genes that may be linked to rare diseases, as reported by expert doctors and researchers. Out of the 67 variants, one was located in a gene listed in PanelApp as being linked to symptoms similar to Jessica's, giving Jessica a much needed diagnosis.

As a result, an effective non-pharmacological intervention - a high fat diet – was identified which helps glucose to be made in the patient's brain and can reduce seizures in the patient.

Diagnostic Odyssey Task and Finish Group

- 4.5 One of the commitments in the 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.
- 4.6 The PIRU published a report of its findings in April 2015; '[Diagnostic Odyssey for Rare Diseases: exploration of potential indicators](#)'. The report concludes that automated data collection captured on a nationwide basis is not possible at this time based on current NHS data collections and systems. Therefore the Rare Diseases Policy Board established a Task and Finish group in early 2017, chaired by Dr Trevor Cole (Consultant Clinical Geneticist at Birmingham Women's and Children's NHS Foundation Trust) with an 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 diseases.
- 4.7 Three specified conditions are being used as exemplars to consider the options available. Developing an automated method to measure time to diagnosis for patients with rare diseases on a national basis will provide information about where and when delays are occurring. This knowledge will allow policy developers and clinical professionals to consider interventions to reduce the delays.

- 4.8 The Task and Finish group met twice in 2017 with further smaller satellite meetings taking place with the clinical representatives and NHS Digital in order to work through a small number of patient examples. The first piece of work is to determine the specific data points available in secondary care from NHS Digital for individual patient journeys going back up to five years.
- 4.9 This initial collection of anonymised and aggregated data concluded in December 2017 and the first review of the outputs with all clinical representatives took place at the end of January 2018. The full group will then reconvene later in 2018 and a report on findings and recommendations will be published in the coming year.

Case Study – UK: The Deciphering Developmental Disorders Study

The Deciphering Developmental Disorders (DDD) study was launched with the aim of finding out if using new genetic technologies (such as exome sequencing) can help doctors understand why patients develop certain developmental disorders.

The study was launched in April 2011 with joint funding from the Health Innovation Challenge Fund - a partnership between Wellcome and the Department of Health - and the Wellcome Sanger Institute, supported by the National Institute for Health Research. Following the launch of the scheme, patients were recruited over four years, resulting in the collection of DNA and clinical information of nearly 14,000 undiagnosed children and adults in the UK with developmental disorders, and their parents.

The study has brought together doctors in 24 Regional Genetics Services, throughout the UK and Republic of Ireland, with scientists at the Wellcome Sanger Institute. The DDD study involves experts in clinical, molecular and statistical genetics, as well as ethics and social science. It has a Scientific Advisory Board consisting of scientists, doctors, a lawyer and patient representative, and has received National ethical approval in the UK

As of January 2018, the study has completed the initial processing of the large amounts of data collected throughout the project. As a result of their work so far, the DDD study team has identified 30 more genes not previously associated with developmental disorders and estimate that these account for ~5% of diagnoses in DDD.

Most notably, as a result of their work in linking and analysing genomic and clinical data, diagnoses for ~35-40% of previously undiagnosed patients recruited onto the study have been found, significantly shortening their diagnostic odyssey.

The DDD study will continue to run until 2021 and the team are committed to keep re-analysing data to try to find diagnoses for as many children who remain undiagnosed as possible.

Key nation-specific implementation plan activities 2016-18

England

Move to routine commissioning of WGS for rare diseases

- 4.10 WGS is currently being used as part of the 100,000 Genomes Project. In rare diseases, the results returned so far indicate there is an increased diagnostic yield of at least 20-25%, signifying new diagnostic findings and information about the underlying cause for a person's disease where existing tests have failed. Furthermore, the results are demonstrating the importance of collecting detailed medical information regarding patients to help better understand the findings that are being obtained from a WGS.
- 4.11 Since the inception of the 100,000 Genomes Project the expectation has been that by the end of the project NHS England, working in partnership with Genomics England, will commission WGS and embed genomic medicine into routine care pathways where it is clinically and cost effective to do so, in line with NHS constitution to continue to operate at the limit of science.
- 4.12 WGS will be introduced as part of a comprehensive national genomic testing repertoire for the NHS – initially for rare and inherited disease and some cancers. The testing repertoire will include tests from the level of WGS to tests for single genes, molecular markers and other functional genomic tests that are important to fully determine the patients predicted response to treatment. The NHS will require a single directory of tests, informed by evidence and based on the latest technological advances, to ensure that the tests that are no longer clinically or cost effective are decommissioned or replaced.

Genomics Education Programme

- 4.13 [The Genomics Education Programme](#) (GEP) was launched in 2014 and is a three-year, £20 million programme in which HEE is working in partnership with key stakeholders to lead the education contribution of the 100,000 Genomes Project, driving the development of a genomics-literate workforce.
- 4.14 The aims of the GEP are to:
- Raise awareness across the NHS of the 100,000 Genomes Project, its ambitions and achievements;
 - Underpin workforce development in critical areas e.g. genomics, bioinformatics, molecular pathology and genomic counselling;
 - Ensure that workforce transformation in genomic medicine is sustainable beyond 2018
 - Promote the understanding and use of genomic data amongst staff;
 - Identify, in consultation with NHS England and Genomics England, opportunities to support the UK Rare Diseases Strategy and Life Sciences Industrial Strategy and meet the commitments in the CMO annual report 2016, 'Generation Genome';
 - Make available world class masters, doctoral and post-doctoral training programmes in genomics, epidemiology and bioinformatics.

- 4.15 Since the launch of the GEP, the programme has made substantial progress in each of these aims. Notable achievements include:
- The funding and delivery of more than 550 Master's places in Genomic Medicine (which includes a module focusing on the genetics of common and rare diseases) across 10 Higher Education Institutes in England, both successfully and ahead of schedule;
 - The delivery of more than 60,000 CPD sessions to date (formal, online or face-to-face education or training, informal, self-directed study), which exceeds the 2018 Mandate target of 52,000 educational episodes;
 - Funding for 27 extra [Higher Specialist Scientist Training](#) (HSST) places for Genetics and 11 places in Molecular Pathology of Acquired Disease. The first cohort of HSST bioinformaticians are now in training and the first round of registrations have been achieved through [Health and Care Professionals Council](#) (HCPC);
 - Development of a scientist training programme in Genomic Counselling which has been approved by the HCPC and has full recruitment to the first cohort of 15. This has been incorporated into HEE business as usual with subsequent recruitment to a second cohort of 10 in 2017;
 - Launch of the first Whole Genome Sequencing [Massive Open Online Course](#) (MOOC), achieving more than 14,000 learner registrations in its first year.
- 4.16 The GEP recognises that the next steps and key priorities for 2018 and beyond include continuing to support the improvement of services for patients with a rare disease and the preparation of the NHS workforce for mainstreaming personalised medicine.

Scotland

Introduction of new screening tests in Scotland

- 4.17 Following a review conducted by the UK National Screening Committee, the Scottish Government extended the Newborn Blood Spot Screening programme to test for Homocystinuria (HCU), Maple Syrup Urine Disease (MSUD), Glutaric Aciduria type 1 (GA1), and Isovaleric Aciduria (IVA) to all newborn babies up to one year old, extended from 6 months old.
- 4.18 The four additional conditions are very rare. They typically occur in between 1 in 100,000 and 1 in 200,000 births. In general, early dietary-based treatment for these conditions is effective. If untreated, babies with MSUD, IVA and GA1 can become suddenly and seriously ill, while symptoms of HCU can take up to one or two years to emerge.
- 4.19 Prior to the introduction of the four new tests, babies in Scotland were screened for Phenylketonuria (PKU), Congenital hypothyroidism (CHT), Sickle cell disease (SCD), Cystic Fibrosis (CF) and medium-chain acyl-CoA dehydrogenase deficiency (MCADD).
- 4.20 Since the new screening programme began on 20 March 2017, 20,748 babies have been tested, with 24 samples referred for either further testing or clinical referral.

Wales

- 4.21 The National Newborn Blood Spot Screening programme offers all eligible babies screening for rare but serious diseases. Babies who test positive can then be treated early, improving their health and, in some cases, preventing severe disability or even death. The programme offers screening for nine conditions that need to be identified early to prevent serious complications Congenital hypothyroidism (CHT), Cystic fibrosis (CF), Glutaric aciduria type 1 (GA1), Homocystinuria (HCU), Isovaleric acidaemia (IVA), Maple syrup urine disease (MSUD), Medium-chain acyl-CoA dehydrogenase deficiency (MCADD), Phenylketonuria (PKU) and Sickle cell disorders (SCD).
- 4.22 Additional funding was secured in the 2016-17 financial year from Welsh Health Specialised Services Committee (WHSSC) for very rare genetic tests that are not available in Wales but available via the UK Genetic Testing Network (UKGTN).
- 4.23 Welsh Government's Genomics for Precision Medicine Strategy 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.
- 4.24 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.
- 4.25 The Rare Disease Implementation Group in Wales has set up a Task and Finish group looking at the investigation of children with delayed development.

Case Study - Wales: A Diagnostic Odyssey - Two siblings presented with learning difficulties, behavioural problems and generalised epilepsy

Patient A was initially referred to the All Wales Medical Genetics Service by the health board Learning Disability Directorate for Fragile X testing in 1985 (cytogenetics) and in 1993 (molecular genetics).

They were then referred from Psychological Medicine and Neurology to cytogenetics to carry out Fluorescence In Situ Hybridisation (FISH) for the analysis of 22Q11.2 deletion syndrome (1996) and Smith-Magenis syndrome (2002); no abnormality was detected.

Further referrals were received from Clinical Genetics and Neurology for the molecular genetic analysis of Angelman, Rett and ARX syndromes (2004), as well as GLUT1-deficiency syndrome (2013); no pathogenic mutation was detected.

Finally, in 2015 they were referred for gene panel testing from Clinical Genetics to be included on the Severe Early Infantile Epilepsy 36 Gene Panel where a mutation was detected in the UBE3A gene confirmed a diagnosis of Angelman syndrome for patient A.

Cascade screening was carried out for other family members, which showed that the mutation detected was maternally inherited and had also been inherited by the other affected sibling.

Gene panel testing was able to confirm a diagnosis that had remained elusive for 30 years in this family at a fraction of the combined total costs of all previous tests. In addition to the reduction in the cost of diagnosis, a quicker diagnosis removes uncertainty about the nature of the child's condition. Additionally, in some instances, a definitive diagnosis can inform treatment selection as some genetic forms of epilepsy require specific drugs for treatment and early treatment can result in an improved prognosis.

In the absence of a diagnosis, patients may receive the wrong drug and experience unnecessary side effects, not to mention the unknown recurrence risk that would affect reproductive choices.

Gene panel testing often reduces the number of specialist appointments that are required before a diagnosis is achieved and results in earlier referral to Clinical Genetics for family follow-up; both of these benefits also save costs for the NHS.

Northern Ireland

- 4.26 One of the priority actions for the NI Department of Health, linked to the findings of patient engagement workshops (see paragraph 3.55) conducted in 2017 under theme 1 of the Strategy, is to improve understanding and awareness of rare disease issues amongst healthcare professionals.
- 4.27 Working with Queen's University Belfast, the Northern Ireland Rare Disease Partnership has provided awareness training sessions to first and final year medical undergraduate students since 2014.
- 4.28 The sessions to first year students form part of the sociology component of the medical curriculum and focus on raising awareness of students to the prevalence and impact of rare conditions, using speakers who are themselves directly impacted by a rare condition. The sessions to fifth year students take place immediately before they graduate as doctors and are aimed at providing an overview of the prevalence and impact of rare conditions. The sessions are also aimed at reinforcing the importance of professional curiosity in detecting and diagnosing rare diseases as well as highlighting the benefits of collaborative working across specialisms and with patients, especially those who are experts in their own conditions. As a result of being directly impacted by a rare condition, those giving the sessions speak from lived experience. Both sessions have been very well received and anecdotally are influencing awareness of rare disease issues in the medical profession.

- 4.29 Through the Northern Ireland Rare Disease Stakeholder Group, work has commenced on a training needs analysis through surveys and workshops with the aim of producing a Training Action Plan. The Department will work with the Northern Ireland Medical and Dental Training Agency (NIMDTA), universities, Royal Colleges and patient groups to deliver appropriate training.
- 4.30 The Group has also commenced planning for the introduction of a Northern Ireland Rare Disease and Congenital Abnormalities Registry. This will be further progressed as a priority through 2018, together with work on the necessary enabling secondary legislation.
- 4.31 The Regional Genetics Service at the Belfast Health and Social Care Trust provides genetic testing services for all of Northern Ireland. Around 80% of rare diseases are genetic, with the majority of these affecting children, and Northern Ireland patients continue to have equitable access to appropriate and emerging diagnostic modalities by highly skilled clinicians. Patients and their families have been enabled through this service to participate in ground-breaking research at local, UK, European and international levels, helping them to benefit from Next Generation Sequencing, whether for individual genes, gene panels, whole exomes or whole genomes. The real difference this has made to people's lives is highlighted through a number of case studies below.
- 4.32 Recognising the pace of development of diagnostic testing, additional funding has been made available since 2016 to ensure that Northern Ireland patients continue to have access to new and emerging genetic tests. For example, £190,000 of additional investment in 2016 ensured routine access to 11 new tests introduced by UKGTN for conditions in hepatology, neurology, ophthalmology and metabolic disorders.
- 4.33 Furthermore, Northern Ireland's participation in the 100,000 Genomes Project will enable the development of the Health and Social Care system's capabilities in respect of genomic and personalised medicine, as well as contributing to the overall UK research programme. It is envisaged that many of the 1200 rare disease patients participating in the Project will also receive a faster accurate diagnosis of their condition, leading to better care pathways suitable to their needs.
- 4.34 The NIRDP, in conjunction with the Patient and Client Council, conducted a survey in 2012 to gauge rare disease patient experience of the diagnostic pathway. This survey provides an initial benchmark; and a follow-up survey will be carried out to assess the impact of the activity around the production of the UK Rare Disease Strategy and the actions above on the patient experience of diagnosis.

Case Study - Northern Ireland: Exome sequencing and helping patients and families through accurate diagnosis 1

Making a genetic diagnosis can be extremely important for families, even if we can't change the outcome. It is therefore vital that patients within Northern Ireland have access to the clinical expertise and molecular diagnostics and analytics facilities that make this possible.

Polly (not her real name) is the first child of healthy parents, but soon after she was born, it was clear there was something wrong. Her muscle tone was extremely stiff and she was unable to move properly. She would lie with her back arched and as time went on it was clear that her development was significantly delayed. Her head remained small (microcephaly) and it seemed that she was unable to control her muscle movements, making her unable to perform tasks independently, or to achieve mobility.

The underlying cause of her condition was not clear, but initially her clinicians felt that this disorder probably had a low risk of recurrence. She was enrolled in the DDD Study, which is a research project centred in Cambridge that analysed the exomes (the protein encoding part of the genome) of almost 14,000 children across the UK. She was one of over 700 children recruited in Northern Ireland before recruitment closed in 2015 (data analysis is ongoing).

Mutations were found in a specific gene, which had not previously been linked with genetic disorders. Several other children were also found with mutations in the same gene. In all cases the child had two faulty copies of the gene, and the parents were healthy carriers. This was extremely important for a number of reasons.

Firstly, we now had a firm diagnosis for Polly, which was of great help to her parents. Secondly, we were able to compare Polly to the other children with the condition, and alert the clinical community to this "new" disorder. Thirdly, by understanding the mechanism, we could start to look at potential therapies. Polly is now being considered for Deep Brain Stimulation (DBS) at Great Ormond St Hospital, which we hope will help with her management. Perhaps most importantly, Polly's parents wanted to think about the possibility of having another child. Although the risk is 25%, we can in principle offer prenatal diagnosis or pre-implantation genetic diagnosis (PGD) to greatly lessen the risk of this happening again.

The family are now deciding how they wish to proceed, but they now have options that were not previously available, and our studies of other children with the same disorder are giving us new information to help us better manage their care.

Case Study - Northern Ireland: Exome sequencing helping patients and families through accurate diagnosis 2

Shortly after delivery, a little baby boy developed prolonged epileptic seizures, and was admitted to the Neonatal Intensive Care Unit. The pregnancy had been normal, and there was no family history to suggest any potential problems. A number of older siblings were healthy and developing normally.

Over the subsequent weeks his seizures could not be controlled despite significant doses of anti-epileptic medication. He had an MRI scan, which was normal, and EEGs (electroencephalograms) which showed extensive epileptic encephalopathy, indicating severe

brain dysfunction.

There were no external physical features that would point towards a specific genetic diagnosis. He was extensively investigated - DNA microarray and testing for specific genetic causes of epilepsy were normal. He also had a number of metabolic investigations, including a skin and muscle biopsy and a lumbar puncture, all of which came back normal.

Unfortunately his clinical condition continued to deteriorate, and in close consultation with his parents, the decision was taken to withdraw care, and he died at 14 weeks of age, having spent nearly all this time in NICU. This was devastating for his parents, and that distress was compounded by the fact that we could not give them a diagnosis or a recurrence risk if they decided to have another child.

Clinicians in the Belfast Health and Social Care Trust recruited him into the DDD Study, and sent DNA samples on the baby and his parents to Cambridge. Exome analysis showed a mutation in a gene that had only very recently been linked to severe epilepsy in newborns. This confirmed the diagnosis, and since the gene mutation was not found in his parents, we were able to advise them that the risk of recurrence was very low.

Since then they have gone on to have a healthy new baby who is doing very well. Without the availability of exome sequencing, and the research that identified this gene, we would not have been able to provide an answer for this family. As it is, this has allowed them to extend their family, and achieve closure from this sad episode. It has also allowed us to provide more information for other families in a similar position, and the gene is now part of the standard Next Generation Panels for early infantile epilepsy.

Chapter 5: Coordination of care

5.1 This chapter explores progress under the fourth theme of the Strategy – *coordination of care*.

UK-wide implementation plan activities 2016-18

European Reference Networks (ERNs)

5.2 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.

5.3 [European Reference Networks](#) (ERNs) are centres of knowledge, skills and expertise in the field of rare diseases and complex conditions. They function as virtual networks that provide a platform to create partnerships between healthcare providers. They enable the principles of improved access for patients to highly specialised services and support European co-operation on highly specialised healthcare, knowledge sharing and improved diagnosis and care in medical domains where expertise is limited.

5.4 ERNs can also be focal points for medical training and research. The diagnosis, treatment and management of rare diseases require the highest level of partnership working to remove unnecessary barriers and facilitate access to high quality care and treatment.

5.5 There are currently 24 ERNs across the European Economic Area, with 26 Member States participating, creating a large network of over 300 highly specialised healthcare providers.

5.6 The UK is heavily involved by:

- Participating in 23 of 24 networks (see ERN networks in **Annex 2**) involving 113 separate UK groups in this initiative of pan-European action on rare diseases; and
- Leading 6 networks (more than any other Member State).

ERNs were created through the EU cross-border healthcare directive and are awarded through an independent and competitive assessment process managed by the European Commission. The first 24 ERNs were set-up in March 2017 and are formalised by a 5-year Framework Partnership Agreement.

Case Study – Europe: Rare and Complex Epilepsies

[EpiCARE](#), a European Reference Network, aims to improve the understanding and management of rare and complex epilepsies through the use of e-tools and expert discussion. This enables complex diagnostic and therapeutic interventions in a wider number of patients across Europe.

It is a network of 28 centres across 13 countries, with active participation of individuals representing disease specific organisations. EpiCARE is currently led and coordinated by Professor Helen Cross at Great Ormond Street Hospital, with the participation of a further three UK centres (National Hospital for Neurology and Neurosurgery Queen Square, Oxford, and Glasgow).

Such a network will give patients access to new treatments as they develop. An example is seen in Dravet syndrome, a rare early onset epilepsy (prevalence 0.4/10000) with poor prognosis for seizure control and neurodevelopmental outcome.

A European registry has been initiated and new cohort-relevant outcomes measures are in development. Trials of new treatments have been completed, but the registry will enable knowledge of the positioning of these patients around Europe and give them access to participate in natural history and outcome studies.

Key nation-specific implementation plan activities 2016-18

England

Rare Disease Insert

- 5.7 NHS England is in the process of developing a 'rare disease insert'; this will form part of its contract documentation with providers that deliver specialised services to patients with rare diseases. The 'insert' will, in practice, be a set of criteria that will allow NHS England to hold providers to account for the way in which they treat patients with rare diseases.
- 5.8 Work with stakeholders identified the highest priorities for inclusion in the insert. There will therefore be up to three criteria in the insert (depending on the nature of the service):
- The provider must ensure that there is a person responsible for coordinating the care of any patient with a rare disease;
 - The provider must give every patient with a rare disease an 'alert card' (including information about: the patient's rare disease; any particular aspects of the treatment of that rare disease that needs to be taken into account in providing care to that patient; and how to contact an individual expert in that patient's care); and

- The provider must ensure that every paediatric patient with a rare disease has an active transition to an appropriate adult service.

Case Study – England: Care Coordination

Multiple sclerosis (MS) is a condition that affects the brain and spinal cord. There is currently no cure for MS but treatments and specialist help can: help to control disease activity; decrease disability from the condition; and reduce ongoing symptoms. Although MS overall is not a rare disease, it is rare when the onset is in childhood, with only about 5-10% of individuals experiencing symptoms before the age of 16.

In August 2017, NHS England published a service specification entitled '[Multiple Sclerosis Management service for Children](#)'. The service will:

- Provide advice to/receive referrals from local paediatric neurologists;
- Undertake expert multi-disciplinary team assessment and care planning;
- Provide bespoke care plans to ensure that follow up appointments with local clinicians can be informed by a bespoke care plan; and
- Provide ongoing treatment and review for patients with more complex conditions.

The service will aim to:

- Improve outcomes and reduce time to diagnosis;
- Ensure expert assessment, individualised care planning and management;
- Provide access to innovative therapeutic medications; and
- Reduce the rate of avoidable relapses and therefore result in fewer emergency admissions.

Case Study – England: First Children’s Rare Disease Centre in the world at Birmingham Children’s Hospital

Birmingham Children’s Hospital are very proud to be developing the first Rare Disease Centre for children in the world. The centre will open in late 2017/early 2018 and it has been designed by children, young people, and their families, as well as the Patient Support Organisations, at every step of the way. The Rare Disease Centre has been generously funded by donations to the Birmingham Children’s Hospital Charity’s Star Appeal which raised £3.65 million in the record time of 18 months - <https://www.youtube.com/watch?v=99EpYxYc-7w>

At BCH, we treat approximately 9000 patients with over 500 different rare diseases from all over the UK. We have 11 highly specialised services for which there is funding for multidisciplinary care. However, we wanted to ensure that patients with other conditions also had the best care available arising from highly coordinated multidisciplinary and multispecialty clinics together with peer support and consistent access to research, information and treatment. We are proud to be redefining best care from a ‘one-size fits all’ to a patient-centred approach in which we help the children under our care and their families have the best quality of life possible.

Over 70 different MDT clinics will be held in the new centre, and our facilities include:

- A family area as a waiting room where Patient Support Organisations can provide support
- Play areas within the waiting room (including soft play, and arts and crafts)
- A kitchen for refreshments as well as dedicated storage for special feeds
- A sensory room for children who have multiple sensory deficits, learning difficulties and/or may have autistic spectrum features
- A “chillout room” for those who would like to be in a quieter area
- Disabled toilets including the first adult changing facilities at BCH
- Wider doors for easy wheelchair access
- Braille and Induction Loop Hearing
- Quiet, non-clinical, room for sensitive conversations.
- Nine consulting rooms – all with large windows including one double room for Physiotherapy and Occupational Therapy assessments
- Research room where research projects can be discussed confidentially.
- Seminar Room equipped with audio visual facilities to allow for multidisciplinary meetings between professionals, including experts in other institutions, before and/or after clinics as well as use by Patient Support Groups and Educational Meetings for families.

Publications in Rare Disease Supplement, Guardian 28 February 2017:

<http://www.healthawareness.co.uk/rare-diseases/praise-for-the-first-rare-disease-centre-in-the-uk>

<http://www.healthawareness.co.uk/rare-diseases/raising-the-bar-in-rare-disease-patient-care>

Scotland

Specialist Care in the UK

- 5.9 Through the National Service Division (NSD) and the National Specialist Services Committee, NHS Scotland receives and considers applications for new specialist services and networks. NSD currently scans for:
- The impact of new medical technologies for existing specialist services;
 - The need to develop pathways for access to new specialist services in England;
 - The need to commission new specialist services or Nationally Managed Clinical Networks in Scotland.
- 5.10 Of particular relevance to the rare disease agenda is the proposed development of an Inherited Metabolic Disease Service in Scotland. The term Inherited Metabolic Diseases (IMD) covers a group of over 650 individual conditions, each caused by a defective single enzyme or transport protein. Individually each condition is rare; collectively IMDs are a significant cause of morbidity and mortality. Early identification and introduction of specialist diet or drug treatments is crucial as patients otherwise face severe health complications. Without treatment many IMDs can lead to severe learning or physical disability and death at an early age.

- 5.11 Around 1000 people in Scotland attend services for people with IMD and over half of this group is 16 years of age or older. Due to the rarity of individual metabolic conditions and their complex nature, treating IMDs requires an integrated specialised clinical and laboratory service to provide satisfactory care and management.
- 5.12 Over 2016, a review of the IMD National Managed Clinical Network highlighted the need to assess the sustainability of the current provision of services in Scotland on account of:
- The greater number of IMD patients surviving into adulthood;
 - The impact of orphan drugs and the potentially significant increases in patients who meet clinical criteria for use of these drugs;
 - The implementation of the Strategy.

The Expert Review Group recommended the national designation of an integrated IMD Service for Scotland as outlined in the service specification developed by the group. The application is expected to be considered in December 2017.

Wales

- 5.13 The Welsh Health Specialised Services Committee (WHSSC) commission specialised and highly specialised services for the people of Wales. They are responsible for ensuring there are appropriate service standards and specifications for the commissioning of highly specialist care.
- 5.14 'Informed health and care – A digital health and social care strategy for Wales' 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.
- 5.15 The Welsh Rare Disease implementation plan highlights the importance of individuals, and those important to them, to be given the opportunity to have open 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

Case Study 10: A Welsh Case Study – A patient care plan

Linda has had Wegeners 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 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 email 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.

More information on care plans can be found here:

<http://gov.wales/topics/health/nhswales/healthservice/chronic-conditions/?lang=en>

Northern Ireland

- 5.16 As members of RDAG, Northern Ireland commissioners participate in the process of confirming the service standards and commissioning specifications for highly specialist care as well as agreeing the accreditation of individual units across the UK as providers of those services. Close collaboration through these structures and processes facilitates the development by commissioners of referral pathways for the care of Northern Ireland rare disease patients to appropriate services, whether they are provided locally or elsewhere.
- 5.17 The phased introduction of the Electronic Healthcare Record (see paragraph 3.57) will further facilitate coordination of care of rare disease patients by providing patient history to all parts of the service to which a patient is referred.

Case Study - Northern Ireland: Multiple Systems Atrophy, A New Approach

Multiple System Atrophy is a rare, progressive, aggressive neurological disorder. Until recently, those with MSA in Northern Ireland were seen in movement disorder clinic, where the neurologist may only have one or two people with this condition.

As a result of the improved networks of communication between patient groups and clinicians developed in the consultation processes on the UK Rare Disease Strategy and subsequently the Northern Ireland implementation plan, a regular (3-4 times a year) “MSA” Neurology Clinic has been established, supported by the MSA Trust’s Clinical Nurse Specialist who has responsibility for Northern Ireland, the Republic of Ireland, Scotland and the “Northern” part of England, and by volunteers from the MSA Trust in Northern Ireland.

This brings together into one scheduled Neurology Outpatients Clinic people who would otherwise be seen at random in Neurology Outpatients Clinics across Northern Ireland. An essentially “administrative” innovation led by the Consultant is providing better support and care for patients. The designated clinics enable commitment and support from specialist neurotherapy services and the MSA Nurse Specialist, facilitating patient access to the available expertise in one appointment, and enabling the development of specialist expertise. As the travelling Nurse Specialist shares experience across the UK and Ireland, knowledge is exchanged and capacity and networks built.

This demonstrates how, when communication barriers have been lowered and a clear policy intent has been set, there is eagerness at working level to innovate and work in partnership:

between clinicians, managers and patient groups, and across boundaries. A similar initiative is underway in the Republic of Ireland, demonstrating how patients and their organisations can transcend jurisdictional boundaries to bring innovation and services to people in need.

Chapter 6: Research

6.1 This chapter explores progress under the fifth, and final, theme of the Strategy – the *role of research*.

UK-wide implementation plan activities

European Reference Networks

6.2 In addition to their contribution to co-ordination of care (see Chapter 5), ERNs also provide a valuable platform for stimulating and conducting research. This is through their own research activities but also through the sharing and consolidation of expertise, their support in generating evidence-based clinical practice and by increasing the pool of patients with a given rare disease, thereby providing invaluable data in a research field that can be data-poor.

Case Study – Europe: Rare Urogenital Disease

[eUROGEN](#) is the European Reference Network for rare urogenital diseases and complex conditions, which is made up of 29 specialist healthcare providers in 11 Member States. The network offers virtual review of rare and very complex cases, including the diagnosis and treatment of people with highly complex urogenital disorders, those who have rare urogenital cancers and children who have suffered with urogenital disorders from birth.

Though they are still in set-up phase, there are already examples of cross-border benefits for patients. Professor Chris Chapple who is Consultant Urological Surgeon at Sheffield Teaching Hospitals NHS Foundation Trust and Secretary General of the European Association of Urology (EAU) leads eUROGEN. He recently had a case referred to them where there had been three previous attempted repairs of a vesico-vaginal fistula from a major teaching centre in another member state.

They successfully carried out the repair without any difficulty, as they are a subspecialist unit in Sheffield Teaching Hospitals NHS Foundation Trust, which carries out approximately 20 of these procedures per year. The referring department saw one such procedure every 18 months. Prior to this surgery, the patient had been unable to work for 18 months and had suffered with incontinence and other functional problems that severely affected her quality of life. She is now fully recovered and back at work.

eUROGEN will use high-cost research facilities within our healthcare providers more efficiently, reducing costs and stimulating research: etiological, reconstructive and regenerative medicine techniques, laboratory, animal models, translation and Advanced Therapy Medicinal Products.

One of our first research activities will be to address one of the gaps in current effective treatments for patients by developing a new safer tissue engineered material for use in urogenital surgery. Clinical trials can be run in our hospitals. Networking our knowledge and expertise together will create a European supra-hub of expertise to foster learning and generate research and innovation more attuned to the needs of our patients.

100,000 Genomes Project

6.3 The 100,000 Genomes Project is enabling pioneering research, in part through its creation of a unique dataset which links phenotypic (medical) and genomic data. This will enable development of new and more effective treatments for patients as well as contributing to UK growth.

6.4 As of late 2017, over 2,000 researchers in 342 UK and international institutions were part of Genomics England's [Clinical Interpretation Partnership](#) (GeCIP). GeCIPs have been set up as part of Genomics England to work on improving the clinical application and interpretation of data from the 100,000 Genomes Project. The GeCIPs work within specific domains (for example rare cardiovascular diseases) and carry out research to:

- Improve understanding of genomic medicine and its application to healthcare;
- Improve understanding of diseases; and
- Lead the way to developing new diagnostics and treatments.

There are currently 14 GeCIPs covering rare disease domains, several covering rare cancers and GeCIPs in cross cutting domains such as 'Enabling Rare Disease Translational Genomics via Advanced Analytics and International Interoperability'.

6.5 Genomics England works with industry via the [Discovery Forum](#) which was launched in July 2017 and builds on the work of the previous [GENE consortium](#). The Discovery Forum provides a platform for collaboration and engagement between Genomics England, industry partners, academia, the NHS and the wider UK genomics landscape. Genomics England also works with companies that specialise in data analysis, so that the 100,000 Genomes Project can benefit from cutting edge advances in handling Big Data.

6.6 Companies who are members of the Discovery Forum work with the researchers, clinicians and analysts who have been successful in joining a GeCIP within a managed framework. This partnership between industry, the academic research community and clinicians will help to accelerate the development of new diagnostics and treatments for NHS patients as all findings will have to be shared.

6.7 Maintaining public confidence around the use of patient data is a key aim of the project. As such, Genomics England maintains high security standards around storage and access of data.

- 6.8 Both academic and industry researchers access de-identified subsets of the data for approved research purposes and through a secured online platform only. In this way, the dataset is used as a 'reference library' rather than a 'lending library' - patient data is never sold but only ever accessed under approved conditions. In addition, any profits generated by charging for access to the 'reference library' are reinvested back into health care and health research. Genomics England uses an explicit consent model for the 100,000 Genomes Project, meaning that participants are made aware of, and agree, to having their de-identified data used for research purposes.

Case Study – UK: Endocrine and Metabolism GeCIP

There are hundreds of rare inherited metabolic and endocrine diseases that have serious effects on health and quality of life. Many are diagnosed late and there are few highly effective treatments. 8,000 families with rare inherited metabolic and endocrine diseases will be included in the 100,000 Genomes Project.

As part of the Endocrine and Metabolism GeCIP, researchers will use the data from WGS to improve understanding of what causes inherited metabolic and endocrine syndromes. This work will form the basis of future studies to develop new treatments.

Specific aims of this GeCIP are to:

- Develop bioinformatics algorithms to classify inherited metabolic and endocrine disorders into groups;
- Identify new genes that cause disorders. Establish clinically useful risk scores to allow NHS diagnostic testing, prediction of disease and severity;
- Study disease mechanism;
- Invite affected individuals for further metabolic and endocrine testing. This will help the researchers better understand how disease impacts on physiology;
- Use collaborations with the biotech and pharma industry to develop new approaches to treatment; and
- Work together with other GeCIP domains and NHS Genomic Medicine Centres to train the next generation of scientists, technologists and clinicians in genomic medicine.

Key nation-specific implementation plan activities 2016-18

England

NIHR Biomedical Research Centres

- 6.9 In 2016 the Secretary of State for Health announced a record £816 million investment in the [NIHR Biomedical Research Centres](#), over 5 years from 1 April 2017, which has been awarded to 20 leading NHS and university partnerships across England. Each of the 20

NIHR Biomedical Research Centres hosts the development of new, ground-breaking treatments, diagnostics, prevention and care for patients in a wide range of diseases and has considerable expertise, capacity and activity in research for rare diseases.

NIHR BioResource and NIHR Rare Diseases Translational Research Collaboration (RD-TRC)

- 6.10 The NIHR BioResource provides a national cohort of healthy volunteers, patients and their relatives who are willing to provide clinical information and samples that will enable them to be recalled to participate in early translational (experimental medicine) research studies and early phase clinical trials.
- 6.11 [The NIHR BioResource – Rare Diseases](#) was established specifically to:
- identify the genetic causes of rare diseases;
 - improve rates of diagnosis and to enable studies to develop and validate treatments; and
 - improve care for sufferers and their families.
- 6.12 The NIHR BioResource – Rare Diseases is enrolling rare disease patients to the BioResource using a national consent model across 60 NHS Trusts. In partnership with Genomics England, this programme led the pilot for the rare diseases element of the 100,000 Genomes Project, and has delivered the sequencing of whole genomes of over 12,000 NIHR BioResource rare disease participants.
- 6.13 The NIHR Rare Diseases Translational Research Collaboration (RD-TRC) was established in 2013, in parallel to the launch of the UK Rare Diseases Strategy, and is formed from the NIHR Biomedical Research Centres and Clinical Research Facilities, all with world-leading research expertise into rare diseases. The RD-TRC provides:
- research infrastructure to support fundamental discoveries and translational research on rare diseases;
 - support for increasing research collaborations which lead to improved diagnosis; treatment and care; and
 - support for deep phenotyping (defined as the precise and comprehensive analysis of phenotypic abnormalities) of people with rare diseases.
- 6.14 A number of patients consented to the NIHR BioResource – Rare Diseases have undergone in-depth phenotyping through the NIHR RD-TRC, which has recruited 16,324 patients, to support 61 projects across 14 themes. Each theme is focussed on specific groupings of acquired and inherited rare disorders. In parallel, detailed clinical and laboratory phenotype data have been captured using Human Phenotype Ontology (HPO) terms, including rare diseases where deep phenotypic data was collected through the NIHR RD-TRC.

6.15 The RD-TRC has also been actively engaging with industry partners. The RD-TRC has consulted with industry on the selection of acquired and inherited rare disorders that are included in the work of the programme. The RD-TRC also launched an open call in 2014 for applications to establish industry-collaborative research projects in rare diseases, specifically those that generated in-depth phenotypic information to develop new treatments and speed up diagnosis. The open call received 29 expressions of interest, 9 of which were funded between 2015 and 2017.

NIHR Bioresource for Translational Research in Common and Rare Diseases

6.16 In considering the future direction of the NIHR support for rare diseases, DHSC wanted to build on the success of the NIHR BioResource, NIHR BioResource - Rare Diseases, and NIHR RD-TRC. Future support would therefore aim to provide a world-leading, national accessible resource that will enable the identification of phenotyped and genotyped volunteers and facilitate a seamless, one-stage central recall for early translational research.

6.17 During the 2017 to 2018 period, the NIHR BioResource, NIHR BioResource - Rare Diseases and the NIHR RD-TRC, which share common aims and infrastructure, are being integrated.

6.18 This will result in a newly formed NIHR BioResource for Translational Research for Common and Rare Diseases. This BioResource will provide a nationally accessible resource of volunteers from the general population as well as patients with common and rare diseases. These volunteers will have consented to being recalled for non-commercial and commercial early translational (experimental medicine) research studies.

6.19 It will be founded on the principles of:

- A national consent process that facilitates: central recall of participants for early translational (experimental medicine) research studies based on genotype and/or phenotype; collection of health and lifestyle information, including from health and social care records (now and in the future), and collection of biosamples.
- A national repository for biosamples at the NIHR National Biosample Centre.
- A secure national database with connectivity to the NHS N3 network containing personal and health data on all participants.

6.20 This will create a unique resource that significantly improves the national capability to undertake and support studies that require access to national patient cohorts. It will continue to support in-depth phenotyping for rare diseases, and facilitate its linkage to genomic data, to provide greater understanding of the mechanisms underlying rare and common diseases, and to support the development of new treatments and diagnostics.

6.21 It will facilitate recall by investing in genomic and phenotypic characterisation of participants, providing investigators with unprecedented access to highly characterised patients with common and rare diseases, and volunteers from the general population. In

addition, it will provide rare disease patients and their families with increased opportunities to become involved in research, and shape how it evolves within the framework of rapid technological advances.

Research Permissions for Rare Disease Research (HRA)

- 6.22 In January 2011 an independent review of health research regulation by the Academy of Medical Sciences '[A new pathway for the regulation and governance of health research](#)' stated that: "A complex and bureaucratic regulatory environment is stifling health research in the UK".
- 6.23 [Health Research Authority](#) (HRA) Approval is for all project-based research that involves NHS organisations in England. It brings together two processes – the assessment of governance and legal compliance ethics review – into one streamlined and simplified system. HRA Approval replaces the need for local checks by each participating organisation, enabling NHS trusts to focus on delivering research. Researchers will benefit from HRA Approval through the elimination of duplicate application routes and paperwork.
- 6.24 The HRA Approval process for setting up health research in the NHS was fully rolled out in March 2016. The process, which is now fully embedded, focusses on providing standard and consistent approaches across the NHS, with standard information requirements and processes by NHS organisations. The assessment provides an opportunity for tailored instructions to be given to NHS organisations to address the specific considerations of a study, including proportionate study set-up. This includes handling of arrangements for identification and/or referral of patients with rare diseases.
- 6.25 The HRA continues to engage with NHS research and development as well as sponsors to support consistent implementation of streamlined processes. The Department of Health and Social Care and HRA are currently considering how the bureaucratic impact on researchers of reporting after commencement of projects can be reduced further.
- 6.26 The HRA publishes online guidance on preparation of participant information sheets and consent forms for clinical trials which is continually reviewed and revised as necessary. The guidance has been updated to incorporate more emphasis on proportionate approaches after stakeholder engagement. The HRA is currently in the process of updating its website, with input from stakeholders, to ensure its content is clear and user friendly. It is also working with the Human Tissue Authority to explore the public's understanding and preferences around consent as well as working with MHRA on a statement on the use of e-consent.

Patient and Public Involvement in Research

- 6.27 The NIHR is a world-leader in promoting and advancing active patient and public involvement resulting in high quality health and social care research. The NIHR is the only Government research funder in the world to support an initiative dedicated to promoting and advancing public involvement in research, [INVOLVE](#). This initiative has

been focusing on strengthening the NIHR's approach to public involvement in the following areas: diversity and inclusion, learning and development, and community and co-production.

- 6.28 As part of this the NIHR, together with Health and Care Research Wales, the Public Health Agency in Northern Ireland and the Chief Scientist Office in Scotland, is developing a set of core standards to improve the quality and consistency of public involvement in research. The standards will help research organisations, researchers and the public to get better at delivering public involvement wherever they are.
- 6.29 In December 2016, the NIHR hosted a workshop to build on recommendations of the ['Going the Extra Mile'](#) report, a strategic review of public involvement in NIHR which was published in 2015. The aim of the workshop was to explore how the NIHR might broaden and deepen its partnership with the public over the next 10 years and considered how the NIHR might develop an approach to assessing the impact of public involvement on research, using routine data to develop and share intelligence and knowledge of this impact.
- 6.30 In 2017, the NIHR also launched the national ['I Am Research'](#) campaign, which followed from the previous success of the ['OK to ask'](#) campaign, to help raise awareness of research. Through local events, radio coverage and social media activity 'I Am Research' has given health and social care professionals, patients and the public the opportunity to learn about the importance of research in everyday care. The statistics indicate that there has been increased traffic to a range of opportunities to get involved in research. The campaign highlights included:
- 186 events held in NHS trusts, GP surgeries and community settings across England;
 - 20 pieces of radio coverage, with a 34 million audience reach;
 - 46,220 general leaflets ordered;
 - 7,321 campaign page views;
 - Over 1.5 million social reach for the NIHRs first ever Thunderclap;
 - 5,032 engagements and 26,921 reach on Facebook;
 - 12,997 #IAmResearch tweets (data from Symplor); and
 - 1,015 views for the Facebook Live broadcast

UK Clinical Trials Gateway

- 6.31 [The UK Clinical Trials Gateway](#) (UKCTG) contains all experimental medicine trials registered on ISRCTN (the UK clinical trials registry) and ClinicalTrials.gov, including those trials focussed on rare diseases. The UKCTG has been exploring ways to maximise its potential to be used by patients to identify opportunities to participate in clinical trials.
- 6.32 The NIHR Clinical Research Network Coordinating Centre (NIHR CRNCC) has recently taken responsibility for managing the UKCTG and is in the process of introducing a series of updates to the system in order to improve the usability and flexibility of the

Gateway for both volunteers and researchers. As part of this they will be exploring how the Gateway could be used to enable researchers to make direct contact with volunteers and as an appropriate recruitment source for future studies.

NHS England Rare Disease Collaborative Networks

- 6.33 NHS England will develop and implement a process for recognising Rare Disease Collaborative Networks (RDCNs), with NHS England defining a RDCN as a 'recognised network of member centres, each of which has a demonstrable research-active interest in a rare/very rare disease, the aim of the network being to improve patient outcomes'.
- 6.34 The RDCNs will build on the enthusiasm shown by providers in the UK to be members of ERNs and will compliment ERN activity in a national context. The key criteria for RDCNs are as follows:
- They focus on rare diseases where expertise is likely to be scarce and where there is no existing formal commissioning arrangement; this focus is likely to be more restricted than the 24 broader disease groups covered by the ERNs;
 - They build on research-active establishments and use their research activity as a marker of a high quality service that is likely to mean good outcomes for patients;
 - They complement other key partners in rare disease care including genetic specialist rare disease centres, Genomics Medicine Centres and the NIHR BioResource;
 - They will be UK-wide where feasible;
 - They will involve recognised patient groups, where these exist; and
 - Their recognition will allow patients to make an informed choice about their care and provide a focus for referring clinicians.

Scotland

The Scottish Genomes Partnership

- 6.35 The Scottish Genomes Partnership (SGP) was established in January 2015, with a £15m investment from the Universities of Edinburgh and Glasgow. Ten state-of-the-art Illumina HiSeq X genome sequencing instruments were installed at their sequencing hubs. These are Edinburgh Genomics and the Translational Research Centre at the Wolfson Wohl Cancer Research Centre.
- 6.36 In February 2016, the SGP received £6m in research funding from Scotland's Chief Scientist Office (£4m) and the UK's Medical Research Council (£2m). This created a Scotland-wide research partnership to pioneer precision medicine and human genome discovery through academic, NHS clinical and industrial collaborations. The aims of the partnership are to:
- Test the utility of WGS for (a) diagnosis of rare diseases and (b) clinical trial stratification for cancers;
 - Add value to Scotland's strengths in genomic medicine and science, building a strong foundation for health and wealth creation;

- Expand Scotland's capacity to lead national and international collaborations in human genomics; and
 - Provide a supportive environment for Scottish academics, small and medium-sized enterprises (SMEs) and industry to engage in genomics and bioinformatics research.
- 6.37 In March 2017, the SGP Rare Disease collaboration with Genomics England's 100,000 Genomes Project opened for recruitment. 1,000 participants will be recruited through the nationally designated NHS Scotland genetic clinics in Aberdeen, Dundee, Edinburgh and Glasgow by the end of March 2018.
- 6.38 A Scientific Advisory Board to the SGP has been established. Members have commended the exceptional high quality of the ongoing work, and noted the cohesive nature of cross-Scotland working on cutting edge issues of clinical and biological relevance.
- 6.39 NHS Scotland have recognised that this is a fast moving area and that staff will need to be trained in this new area of work. As a result, the local delivery plan for NHS Education Scotland (NES) includes a commitment to provide support for the provision of genetic workforce development programmes through the National Genetic Education and Training website.

Wales

100,000 Genomes Project

- 6.40 In September 2016, Professor Julian Sampson was awarded MRC and Welsh Government funding to support Wales' involvement in Genomics England's 100,000 Genomes Project. The award provides £1m MRC funding, allied to a £2.4m Welsh Government investment, to support the establishment of an inter-institutional Genomic Medicine Centre in Cardiff.
- 6.41 The Genomic Medicine Centre is working 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.
- 6.42 Patients who take part have the potential to benefit from quicker and more accurate diagnosis and improved services through research and its translation to clinical application. The funding will enable 420 NHS patients with suspected rare inherited diseases, who fulfil Genomics England's eligibility criteria and their biological parents to take part in the 100,000 Genomes Project due to begin in January 2018. Research-based whole genome sequencing will be provided by Genomics England and genetic variants that appear likely to be causative will be interpreted by the General Medical Council Wales and confirmed for NHS Wales by AWMGS. Laboratory, clinical, bioinformatics and health informatics staff from the NHS and higher education institutions across Wales will work to achieve wide integration of genomic data from the project in patient care.

- 6.43 Welsh researchers will also contribute to and exploit the project's resource of UK genomic and linked clinical data for research through membership of GeCIPs (Genomics England Clinical Interpretation Partnerships).
- 6.44 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.

Case Study – Wales: Cardiff and Vale University Health Board (CVUHB)

Research and development is an important component of the metabolic service with CVUHB. The Service has several projects:

- Sanoffi Genzyme Grant of the “Development and validation of biomarkers to monitor patients with Fabry Disease”;
- Lysosomal;
- Porphyria Registries;
- Acute Porphyria Natural History Study (Alnylam pharmaceuticals).

Case Study – Wales: Hywel Dda University Health Board (H DUHB)

Despite the largely rural nature of the H DUHB, research and development at a local level still undertakes biomarker discovery and some commercial trials, for example the Zambon study which is a randomised controlled trial of an inhaled antipseudomonal for idiopathic bronchiectasis.

Contributions are made to national and international registries, such as the European Bronchiectasis Registry (EMBARC) and portfolio projects (porphyrias, rarer dementias and rarer epilepsies etc).

Case Study – Wales: 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 project (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 performed in Wales were previously 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 WGS– through cost savings we have been able 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; and
- 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 monthly genomic multi-disciplinary teams.

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 also 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 a rare disease.

Northern Ireland

- 6.45 The Regional Genetic Service at the Belfast Health and Social Care Trust enables the participation of Northern Ireland patients in ground-breaking research at local, UK, European and international levels. Further information is provided in chapter 4.
- 6.46 Joint funding of £3.3m awarded in 2015 by Northern Ireland Department of Health and MRC has supported the establishment of the Northern Ireland Genomic Medicine Centre. This investment in infrastructure, services and skills will ensure delivery of the core aims of the 100,000 Genomes Project, and accelerate the mainstream adoption of genomic medicine in the Health and Social Care system in Northern Ireland. It will also enable Northern Ireland's participation in GeCIPS and the future development of genomic and stratified medicine programmes based on areas of proven clinical trial capability, delivery and leadership.
- 6.47 It is envisaged that patients who take part will have the potential to benefit from quicker and more accurate diagnosis and improved services through research and its translation to clinical application.
- 6.48 Specifically, the funding will enable over 400 Northern Ireland patients with suspected rare inherited diseases, who fulfil Genomic England's eligibility criteria, and their biological parents (i.e. over 1200 samples in total) to take part in the 100,000 Genomes Project and avail of whole genome sequencing to be provided by Genomics England.

Chapter 7: Registries and data

- 7.1 Since the publication of the Strategy in 2013, it is clear that the landscape in which we are now working has changed significantly. The increasing interconnectivity of our world has improved our ability to identify and link with rare diseases patients. Driven by technological advancements, the collection and storage of comprehensive and structured health data for these patients has also increased in scale.
- 7.2 In light of this, registries and data have become invaluable tools for improving the treatment, care and research for rare diseases. The importance of this was highlighted in the 2016 Progress Report and this continues to be the case in 2018 onwards. As a result, we thought it would be helpful to dedicate a standalone chapter to progress in this area.

UK-wide implementation plan activities

The Life Sciences Industrial Strategy

- 7.3 The '[Life Sciences: industrial strategy](#)' was published on the 30th August 2017. The report, written by Life Science's Champion Professor Sir John Bell, provides recommendations to Government on the long term success of the life sciences sector. It was written in collaboration with industry, academia, charity, and research organisations.
- 7.4 The report highlighted that significant opportunities remain to create greatly improved data infrastructure around the UK that has the potential in the first instance to improve the quality of care provided to NHS patients, and to support better planning and delivery, allowing NHS managers to run their services more effectively.
- 7.5 To help realise this, the life sciences sector proposed in their report that Government establish two to five Digital Innovation Hubs providing data across regions of three to five million people.
- 7.6 The Government published the '[Life Sciences: Sector Deal](#)' on 6th December 2017 in response to the Life Sciences Industrial Strategy. In this, the Government committed to working to develop a number of regional, interoperable Digital Innovation Hubs which support the use of data for research purposes within the legal framework, and meet the strict parameters for sharing data and the security standards set out by the National Data Guardian.
- 7.7 They will create controlled environments for real world clinical studies, the application of novel clinical trial methodology, and the comprehensive evaluation of new innovations so that patients can benefit from scientific breakthroughs much faster. NHS England, NHS

Digital and Health Data Research UK in partnership with others will lead the delivery of this programme, drawing on input from multiple stakeholders including the academic sector, the life sciences industry, the charity sector and patients.

- 7.8 The Life Sciences Industrial Strategy also recommended that national registries of therapy-area-specific data across the whole of the NHS in England should be created and aligned with the relevant charity. The Government is currently considering these proposals, along with other recommendations, as part of the on-going Sector Deal process.

Key nation-specific implementation plan activities 2016-18

England

The National Congenital Anomaly and Rare Disease Registration Service

- 7.9 Public Health England launched the National Congenital Anomaly and Rare Disease Registration Service (NCARDRS) on the 1 April 2015, in response to the Strategy and the Chief Medical Officer's recommendation to ensure nationwide coverage of congenital anomalies (also known as birth defects). Before this less than half the country collected data on congenital anomalies. We simply did not know how many children or adults were living with these rare conditions.
- 7.10 NCARDRS supports the request from patients, identified through public consultation, for a national registration service, and continues to work closely with patients and patient groups including Rare Disease UK's Patient Empowerment Group.

Question without answers

- 7.11 For many rare disease conditions we still do not have answers to some of the simplest questions: How many people have the disease? Where do they live? What is their life expectancy? How often do they require hospital care? What was their treatment and did those treatments work? The information required to answer these questions is out there and it is the role of NCARDRS to collect the data we have available so that we can start to answer some of these questions.
- 7.12 To do so, high quality, accurate data on every child born with a congenital anomaly and every person living with a rare disease must be collected. Without this basic information we cannot hope to understand the causes and risks or the services that are needed to support patients and their families.
- 7.13 Improving information has the potential to improve treatment and outcomes for people with rare diseases and ensure patients and their families are involved in decisions about their care. Using register data we are able to give information to parents that often really helps them in coming to terms with the diagnosis.

Data Collection

- 7.14 For the first time there is national coverage of congenital anomaly registration. This past year, NCARDRS opened three new regional offices in London, the East of England and the North West, all areas where there had previously been no registration. This means there are now a total of eight offices across England, a single data management system and a team of around 35 dedicated registration officers and analysts. NCARDRS currently takes data from 567 NHS providers across the country.
- 7.15 Much of the focus to date on data has been in ensuring there is high ascertainment and completeness, as well as consistency and standardisation across the country. This is complex information and NCARDRS might receive partial bits of information from multiple data sources. Staff are highly trained to piece this together and they work very closely with the hospitals, laboratories and specialist centres in their patch.
- 7.16 The information NCARDRS collects is not a mandatory data set. They have to demonstrate their benefit to clinicians so that clinicians continue to notify them, and they do this by providing information back to clinicians for service improvement and audit. NCARDRS provide benchmarking data and monitoring information, together with information on detection rates and outcomes for screening programmes and will be doing more of this routinely over the next year. For many clinicians working in rare diseases the most pressing need is to identify prevalence – to establish how many people have the disease. For this it is crucial to have national data. It has taken some time to achieve this, but NCARDRS now have the systems and processes in place and are working hard on this as they expand out from congenital anomalies to other rare diseases.

The Need for Quality Data

- 7.17 Data out is only as good as the data you put in. There is still a long way to go but the goal of NCARDRS is to ensure that by 2020 every clinician has access to information about rare diseases, their prevalence and trends in a clear, accessible and useful format. We also want to ensure that more information is available to patients and the public. This year NCARDRS will be exploring the feasibility of a patient portal to enable patients to self register.
- 7.18 We might not be free from rare disease at any point in our lifetimes, but understanding their causes and effective treatment begins with understanding the factors that cause them. And as any good researcher or clinician will tell you - that begins with accurate high quality data.

Data Already Provided by NCARDRS

- 7.19 In 2015, there were a total of 2,905 cases with one or more congenital anomaly notified to the four NCARDRS reporting regions, covering 141,474 total births. This gives an estimated overall birth prevalence of 205 per 10,000 total births or 1 in 49 births.

- 7.20 The most common congenital anomaly subgroups were those that were chromosomal in origin (e.g. Down's, Edward's, Patau's syndrome) with a prevalence of 50.2 per 10,000 total births, congenital heart defects with 49.9 per 10,000 total births and limb anomalies, 29.8 per 10,000 total births. Just over a quarter of congenital anomalies were known to be associated with genetic conditions.
- 7.21 In terms of the timing of diagnosis and outcome, of the 2,905 cases with one or more congenital anomalies, the timing of diagnosis was known for 95% of cases. Just over two Congenital Anomaly Statistics 2014/15 10 thirds of these were diagnosed prenatally (at any gestation) and nearly a third were diagnosed postnatally in 2015.
- 7.22 NCARDS are in the process of migrating over 71,000 records going back as far as 1985 from the old regional congenital registers.

Scotland

- 7.23 In July 2016, a Short Life Working Group was established by the Rare Disease Implementation Oversight Group to consider how information on rare diseases can be captured in Scotland to enable monitoring and reporting. During its first year the group scoped current data sources within NHS Scotland.
- 7.24 It found that there are numerous data sources that exist within NSS that may capture information on rare diseases but that the data sources may be of minimal use due to the limitations of the coding systems used. For example, coding systems do not allow the level of details required to capture many rare diseases. Additionally, the very nature of a rare disease being rare also means that it may never be possible to capture such data.
- 7.25 Following the review of data carried out by the Short Life Working Group it was agreed as a first priority to start scoping work on a Congenital Anomalies Register. This was catalysed by the findings from the group that one did not already exist and there was a large amount of support from clinicians and patients to have one.
- 7.26 Congenital anomalies comprise a wide range of abnormalities of body structure or function that are present at birth and are of prenatal origin. Congenital anomalies account for approximately 80% of all rare diseases and affect approximately 2-4% of pregnancies in Scotland.
- 7.27 Initial scoping is being carried out and a full business case will be written towards the end of 2017, beginning of 2018.

Wales

Congenital Anomaly Register and Information Service (CARIS)

- 7.28 [CARIS](#) was established in 1998 with the objective of assessing patterns of anomalies in Wales, including possible clusters and their causes. Information from CARIS informs planning of wider health services, including screening services.

7.29 Key patterns of anomalies detected by CARIS to date are:

- 31,123 cases of congenital anomaly between 1998 and 2015. There were a total of 602,972 (live and still) births in Wales during this time. This gives a gross rate of 5.2%, unchanged from the previous year.
- Between 1998 and 2014, 26,816 babies with anomalies were born (86.2%), of whom 96.9% survived until their first birthday. Survival was reduced where very complex anomalies were observed.
- Between 1998 and 2015, most (59.9%) of the cases on the register had a single anomaly, and 11.6% had an underlying chromosomal disorder. The rate of chromosomal disorders is increasing each year. This may relate to increased maternal age and the availability of genetic screening.
- 40% of those babies affected were female, 58% were male; and 14 were described as intersex and the gender of the remainder was unknown or not recorded often because the pregnancies ended in termination or miscarriage.
- The five most common groups of anomaly, in descending order, were circulatory, limb, musculoskeletal, urinary and digestive.

Northern Ireland

7.30 The need for a coordinated and cohesive approach to information on rare diseases was identified as a priority in the consultation process leading to the development of Northern Ireland's implementation plan. This was therefore reflected in the Priority Action "To complete a database review and produce a costed action plan to implement a Northern Ireland register of Rare Disease".

7.31 Work to identify existing data sources, and ways in which a Rare Disease and Congenital Abnormalities Registry for Northern Ireland can be progressed, in line with NI's unique legislation and health and social care information systems, is nearing completion. Key principles are:

- For information governance and confidence reasons the Registry must be based within NI's HSC system;
- The Registry must be based where appropriate (e.g. use for research purposes) on a fully consented model in order to comply with NI legislative requirements;
- The Registry must include both rare disease and congenital abnormalities, as in the English NCARDS proposal;
- The Registry must align with and link to the developing NI patient and service user information infrastructure;
- The Registry must be capable of sharing information (subject to information governance requirements) with Registries elsewhere in the UK, in the Republic of Ireland, and internationally.

7.32 Further work to take forward the establishment of the Registry, with full support from the community in Northern Ireland, and on the basis of Northern Ireland's legislation and integrated health and social care system has been initiated.

Chapter 8: Key Challenges and Next Steps

Progress on Next Steps as of 2016 Report

- 8.1 The first Progress Report was published in 2016. This report highlighted three key issues to address over the 2016-2018 period which were:
- Consolidation - building and transforming the best of existing provision to fully realise the potential of relevant initiatives;
 - Collaboration - working across the rare diseases community at all levels; and
 - Evaluation - the development of metrics for the implementation of the Strategy.
- 8.2 Throughout this report we have described a range of activities which illustrate progress against these three key issues. Highlights under 'consolidation' include the work of the 100,000 Genomes Project and the commitment to evolve this into a National Genomics Service. Successful consolidation has also been demonstrated in the development of the NHS England 'rare disease insert', the work conducted by the Welsh Rare Disease Patient Network, the extension of the new-born screening tests in Scotland and in Northern Ireland the continuing partnership approach involving the Department, the HSC system, academics, clinicians, patients and carers and their representatives, across the whole range of rare disease related activities.
- 8.3 The use of effective collaboration has also been demonstrated in the UK's high levels of involvement in many European Reference Networks, the successful work of the Genomics England Clinical Interpretation Partnerships (GeCIPs), Discovery Forum and the work done to embed a UK-wide approach to the 100,000 Genomes Project. Finally, 'evaluation' is now being addressed through each of the 4 national implementation plans.

Forward look to 2020

- 8.4 Reflecting on recent changes in the rare diseases landscape, the wider political context in which rare diseases play a part, and the discussions and insights from the Rare Diseases Forum annual conference, several topics are highlighted below as key opportunities and challenges facing the implementation of the Strategy between now and 2020.

The National Genomics Board

- 8.5 Dame Sally Davies, England's Chief Medical Officer, published her annual report entitled 'Generation Genome' on the 4th of July 2017. It outlined a clear vision for genomic medicine and the opportunities to build on initiatives like the 100,000 Genomes Project. As part of this report, she made a series of recommendations aimed at those able to bring about change, to guide how the UK's genomic potential can be realised to both improve patients' outcomes and maintain a leadership role in genomics.

- 8.6 Her first recommendation was for a National Genomics Board (NGB), chaired by a Minister, to facilitate collaboration and effective delivery of key actions. This recommendation was accepted by Ministers in July and the establishment of the NGB was announced in November 2017 under the chairmanship of Lord O'Shaughnessy, Parliamentary Under-Secretary of State for the Department of Health and Social Care.
- 8.7 The NGB's vision is to make sure that the UK remains the world's leading centre for genomic medical research, and to leverage this position to deliver quantifiable benefits for NHS patients and for the life sciences sector.
- 8.8 The Policy Board believes this marks a significant step forward for the community, bringing the profile of rare diseases ever higher up the agenda of policy makers. The establishment of the NGB reinforces the work of the Rare Disease Policy Board in championing rare disease patients during the two years before the end of the Strategy and will augment the UK approach to improving the lives of those with rare diseases now and going forward.

European Union (EU) Exit

- 8.9 Some of the changes in the rare diseases landscape over the past years could not have been accounted for when the Strategy was published in 2013. Of particular note is the UK's intention to leave the EU.
- 8.10 Challenges arise for the rare diseases community as clinical and research expertise in this field can be scarce in any one country. Of particular note is the UK's involvement in the European Reference Networks, which are, as set out in this report, a key vehicle for delivering a number of the Strategy's commitments.
- 8.11 The Government's policy paper, '[Collaboration on Science and Innovation: A Future Partnership Paper](#)' stresses the importance of continued collaboration with European partners to ensure that the UK remains one of the best places in the world for science and innovation. ERNs for rare diseases patients were cited in the paper as an example of collaboration that the UK and EU need to discuss in the negotiations, given the mutual benefits.
- 8.12 The Government has also stated that there are three principles which will help us rise to the challenge of developing a new regulatory system post Brexit: patients should not be disadvantaged; innovators should be able to get their products into the UK market as quickly and simply as possible; and we continue to play a leading role promoting public health.
- 8.13 We should also recognise that genetics and genomics are areas where the UK is recognised internationally as world-leading.

- 8.14 The recent publication of the '[Industrial Strategy](#)' white paper, and the agreement between Government and the life sciences sector of a multi-billion pound Sector Deal, further demonstrate that the Government is committed to ensuring that the UK remains at the forefront of innovation. The Sector Deal will help ensure new pioneering treatments and medical technologies are produced in the UK, improving patient lives and driving economic growth. An initial collaboration under the Sector Deal will include the 'Data to early diagnostics and precision medicine' programme, in which genomics will play a key role.
- 8.15 Through such times of change, the Rare Diseases Policy Board will continue to champion the voice of the rare diseases community, ensuring that we do not lose sight of what is important – improving the lives of patients and their families living with a rare disease.

Collaboration between the Four Nations

- 8.16 In light of the UK's exit from the EU, now more than ever is an important time for all four UK nations to continue to work together in the rare diseases landscape, where scale is a key driving factor for progress. The 2017 annual Rare Diseases Forum conference, where a great number of different sectors and interests were represented, was an excellent opportunity for us to be reminded that collaboration is key and that we can work more effectively, and positively, if we work together.
- 8.17 Health policy is a devolved matter and each of the four nations will continue to drive their own strategic priorities in line with national implementation plans, with a collaborative approach and overview being afforded through the Rare Diseases Policy Board. This report has served to highlight many examples of best practice in each of the four nations. Through the leadership of the Rare Diseases Policy Board, we will continue to draw on these examples and share the successes and lessons learnt as a result. This will ensure that we continue to grow and strengthen collaboration between the 4 nations, with the aim of improving equity of access and quality of treatment for rare diseases patients across the UK.

The Value of Data

- 8.18 Data is becoming increasingly prevalent in the digital age and, if used effectively, can be an invaluable resource. In the rare diseases field, on a patient by patient basis, this data can include phenotypic and genotypic information, longitudinal healthcare records and information on a patient's care experience.
- 8.19 Such data is key to our understanding of rare diseases and how they affect people's lives, but it is the pooling of standardised, high-quality data under strict information governance rules that adds real value. This allows it to become one of the most important tools for connecting and empowering patients, increasing the molecular understanding of rare diseases and ultimately, improving the lives of those living with rare disease

- 8.20 Some of the successes in this field over the past two years are highlighted in Chapter 7. In addition, the 100,000 Genomes Project has already accumulated a large number of relevant genomic variants, and the subsequent development of a National Genomic Service in England will lead to the production of one of the richest datasets for rare diseases research in the world.
- 8.21 We recognise still that more needs to be done to improve the collection, sharing and analysis of rare diseases data. The NGB will provide leadership where the use of genomic data for improving diagnoses and treatments for rare diseases is concerned. As the Rare Disease Policy Board we will continue our work to provide context for the role of data within the original formulation of the Strategy and champion its importance in helping to meet the 51 commitments.

Next Steps

- 8.22 As we approach the last two years of the Strategy, the Policy Board will develop channels of communication such as the online Platform, and build participation by a wide range of stakeholders, as a means of continuous engagement that will guide the priorities of the Board going forward. Our next and final Progress Report is due in 2020 where we will reflect on the overall progress made since the publication of the Strategy in 2013.
- 8.23 The Rare Diseases Policy Board would like to thank everyone involved in this report, and the wider rare diseases community, for their ongoing hard work and dedication in helping to make progress towards implementing the 51 commitments of the Strategy. We hope this report serves as both an accurate reflection and a celebration of the tremendous efforts made by so many individuals and organisations. We also hope that this report acts as a reminder to us all that there is still work to be done and that what should remain at the heart of this is the goal of improving the lives of those, and their families, suffering from a rare disease.

Annex 1 – Agenda of the Rare Diseases Forum conference 2017

<p>Introduction – Professor Gina Radford, Deputy CMO for England and co-chair of the UK Rare Diseases Policy Board</p> <ul style="list-style-type: none"> • "What are the roles of the Policy Board and the Forum" • Overview of actions to date 	<p>10:30 – 10:45</p>
<p>Developments from the DAs/ALBs (Chair: Professor Gina Radford)</p> <p>Four 5 min presentations, emphasising the (UK) nature of progress and highlighting significant achievements and challenges:</p> <ul style="list-style-type: none"> • Mark Walker - Vice-chair Rare Disease Implementation Group, Wales • Tom Fowler – Genomics England • Victoria Hedley – European Reference Networks • Fiona Marley – NHS implementation plan for England <p>Panel Q&A including the above speakers and officials from Scotland and Northern Ireland (30-40min)</p>	<p>10:45 - 11:45</p>
<p>Three breakout discussion groups on progress, limitations and challenges</p> <p>Three 45min attendee-led discussions on highlights, limitations and key challenges to date from previous presentations or from member experiences</p> <p>Facilitators: Larissa Kerecuk, Jayne Spink, Nick Meade Chairs: Beverly Searle, Kerry Leeson-Beevers, Natalie Frankish (Facilitators to provide feedback in the afternoon session)</p>	<p>11:45 – 12. 30</p>
<p style="text-align: center;">Lunch</p> <p>Attendees are free to explore stands / presentations covering:</p> <ul style="list-style-type: none"> ▪ Genomics England on 100,000 genomes project (Tom Fowler) 	<p>12:30 – 13:15</p>

<ul style="list-style-type: none"> ▪ European Reference Networks (Victoria Hedley) ▪ Forum platform walkthrough (Katie Spencer, Bettina Mavrommatis) 	
<p>Three breakout sessions on forward view and outstanding issues</p> <p>Three 60min attendee-led discussions on the forward view, e.g. what are the issues for 2018 that could be a focus for the work of the policy board?</p> <p>Facilitators: Larissa Kerecuk, Jayne Spink, Nick Meade</p> <p>Chairs: Beverly Searle, Kerry Leeson-Beevers, Natalie Frankish</p>	13:15 – 14:00
<p>Break for coffee</p>	14:00 – 14:15
<p>Feedback by facilitators (supported by the chairs) of the morning and afternoon breakout sessions and discussion</p>	14:15 – 15:30
<p>Summary and conclusions – Alastair Kent, OBE</p>	15:30 – 15:40
<p>Close of Meeting</p>	15. 45

Annex 2 – List of European Reference Networks

Acronym	Full Title	Coordinator Name	Country of coordinator
ERN PaedCan	European Reference Network on Paediatric Cancer (Haemato-Oncology)	St. Anna Kinderspital and St. Anna Kinderkrebsforschung	AT
ERN LUNG	European Reference Network on Respiratory Diseases	Universitätsklinikum Frankfurt	DE
ERN-RND	European Reference Network on Neurological Diseases	Universitaetsklinikum Tuebingen	DE
ERKNet	European Reference Network on Kidney Diseases	Universitätsklinikum Heidelberg	DE
MetabERN	European Reference Network on Hereditary Metabolic Disorders	Helios Dr Horst Schmidt Kliniken	DE
ERN TRANSPLANT-CHILD	European Reference Network on Transplantation in Children	Hospital Universitario La Paz	ES
ERN EYE	European Reference Network on Eye Diseases	Hôpitaux Universitaires de Strasbourg	FR
ERN Skin	European Reference Network on Skin Disorders	Assistance Publique-Hôpitaux de Paris, Hôpital Necker-Enfants Malades	FR
EuroBloodNet	European Reference Network on Haematological Diseases	Assistance Publique-Hôpitaux de Paris, Hôpital Saint-Louis	FR
VASCern	European Reference Network on Rare Multisystemic Vascular Diseases	Assistance Publique-Hôpitaux de Paris, Hôpital Bichat	FR

ERN EURACAN	European Reference Network on Adult Cancers (Solid Tumours)	Centre Léon Bérard	FR
ERN BOND	European Reference Network on Bone Disorders	Rizzoli Orthopaedic Institute	IT
ERN ReCONNET	European Reference Network on Connective Tissue and Musculoskeletal Diseases	Azienda Ospedaliera Universitaria Pisana	IT
ERN GENTURIS	European Reference Network on Genetic Tumour Risk Syndromes	Radboud University Medical Center Nijmegen	NL
ERN GUARD-HEART	European Reference Network on Diseases of the Heart	Academisch Medisch Centrum bij de Universiteit van Amsterdam	NL
ERNICA	European Reference Network on Inherited and Congenital anomalies	Erasmus Medical Center Rotterdam	NL
Endo-ERN	European Reference Network on Endocrine Conditions	Leiden University Medical Center	NL
ERN CRANIO	European Reference Network on Craniofacial Anomalies and ENT Disorders	Erasmus MC: University Medical Center	NL
EpiCARE	European Reference Network on Epilepsies	Great Ormond Street Hospital for Children NHS Foundation Trust	UK
ERN eUROGEN	European Reference Network on Urogenital Diseases and Conditions	Sheffield Teaching Hospitals NHS Foundation Trust	UK
ERN EURO-NMD	European Reference Network on Neuromuscular Diseases	The Newcastle upon Tyne Hospitals NHS Foundation Trust	UK
ERN ITHACA	European Reference Network on Congenital Malformations and Rare Intellectual Disability	Central Manchester University Hospitals NHS Foundation Trust	UK

ERN RARE-LIVER	European Reference Network on Hepatological Diseases	The Newcastle upon Tyne Hospitals NHS Foundation Trust	UK
ERN RITA	European Reference Network on Immunodeficiency, Autoinflammatory and Autoimmune Diseases	The Newcastle upon Tyne Hospitals NHS Foundation Trust	UK