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England Rare Diseases Action Plan 2023: main report

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Applies to England

Contents

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Ministerial foreword

In January 2021, we published the UK Rare Diseases Framework (https://www.gov.uk/government/publications/uk-rare-diseases-framework/the-uk-rare-diseases-framework), a national vision to improve the lives of the approximately 3.5 million people in the UK living with a rare disease. England's first Rare Diseases Action Plan (https://www.gov.uk/government/publications/england-rare-diseases-action-plan-2022/england-rare-diseases-action-plan-2022) followed in 2022, transforming the priorities of the framework into concrete actions.

One year on, we report on progress in delivering our commitments. Through dedicated work across the healthcare system, and in partnership with the rare diseases community, we have made significant progress. Improvements to newborn screening are laying the groundwork for early diagnosis. Genomics England's clinical research interface is helping provide people with new diagnoses, explain symptoms and support onward care. Healthcare professionals have access to new digital educational resources. A new toolkit for virtual consultations facilitates access to coordinated care of multiple specialists. Transformative new treatments have been approved, including a life-saving gene therapy for metachromatic leukodystrophy. Work is ongoing to map access to these drugs, to ensure equity across the country.

There is still more to do. Many living with rare diseases still encounter poorer than average access, experience or outcomes in healthcare services. This second action plan includes 13 new actions to ensure that everyone living with a rare disease gets the treatment, care and support they need. We will work to reduce health inequalities faced by people living with rare diseases, lower barriers to participation in clinical research and improve the way services are commissioned in NHS England.

These commitments are supported by funding for ground-breaking research, including investments of nearly £790 million into Biomedical Research Centres, and a £12 million UK Rare Disease Research Platform. This research is essential in furthering the understanding, diagnosis and treatment of rare diseases, consolidating the UK's position as a science superpower and innovation nation.

Over the year ahead, we will continue to work with delivery partners and the rare disease community to monitor progress and drive change. Thank you to all those involved in the ongoing work to support the development and delivery of our action plans. In particular, thank you to the members and representatives of the rare disease community, who have so generously shared their time and personal experience to inform, shape and improve this action plan. This continued partnership enables us to strive to better address the needs of this community every single day.

Helen Whately MP

Minister of State (Minister for Social Care), Department for Health and Social Care

Executive summary

The 2021 UK Rare Diseases Framework set out a shared vision for improving the lives of people living with rare diseases across the UK. During 2022, each of the 4 UK nations published an action plan, detailing how these priorities would be addressed. England's first action plan was published in February 2022, outlining 16 actions.

Over the past year we have made significant progress. Here, in England's second action plan, we update on key achievements in 2022, including:

- changes to the UK National Screening Committee to support robust decision-making within the constraints of limited evidence bases, to help improve how decisions are made on newborn screening for rare diseases
- extensive public engagement to support design of a whole genome sequencing (WGS) research study in the NHS to screen for up to 200 rare genetic conditions in newborns where early intervention could transform outcomes
- identification and return of over 1,000 new, complex diagnoses for people with rare diseases to the NHS, through the Genomics England Clinical Research Interface, to inform the most appropriate clinical care
- development and expansion of innovative digital educational resources on rare diseases, which have had strong uptake by healthcare professionals
- creation and rollout of a toolkit for virtual healthcare consultations, to improve care coordination for patients with complex, multi-system rare diseases
- recruitment of over 2,500 new volunteers to the National Institute for Health and Care Research (NIHR) BioResource, to increase scientific understanding of rare diseases and facilitate improved diagnostics and treatments
- completion of innovative research studies, such as the MELODY (https://www.imperial.ac.uk/medicine/research-and-impact/groups/melody-study/) COVID-19 study, to inform targeted treatment policies for the rare diseases community

This second action plan also sets out 13 new specific, measurable actions to drive further improvements, and address areas of outstanding need. Actions have been developed together with delivery partners across the health system, and in close consultation with the rare disease community.

Key commitments in this action plan include:

- increasing data sharing between NHS England, NCARDRS and Genomics England, benefitting patients by improving our understanding of equity of access to genomic testing and supporting interpretation of genomic test results

- improving the way in which services for rare diseases are commissioned, through ensuring service specifications support coordinated access to specialist care, treatment, drugs, social care, mental health and special educational support
- improving the Be Part of Research platform, to make it easier for people living with rare diseases to participate in research, should they choose to do so
- addressing health inequalities for people living with rare diseases by gathering the evidence needed to include rare diseases in NHS England's Core20PLUS5 (https://www.england.nhs.uk/about/equality/equality-hub/national-healthcare-inequalities-improvement-programme/core20plus5/) framework, and enabling ICSs to develop targeted actions to reduce these inequalities
- evaluating the effectiveness of the UK Rare Diseases Framework and England's Action Plans in making a difference to people living with rare diseases

These commitments are supported by recently announced funding for ground-breaking research initiatives, fostering collaborations which accelerate the understanding, diagnosis and therapy of rare diseases. These include the MRC-NIHR UK Rare Disease Research Platform and NIHR Biomedical Research Centres, at least 17 of which will include a focus on rare disease research.

To further our understanding of the needs of the rare diseases community, we have also committed to holding a series of workshops, on topics including non-genetic rare conditions, the transition from paediatric to adult services, and registries (see focus area: registries, below), ensuring our policy remains relevant and fit for purpose.

In the coming year we will focus on progressing these actions, seeking input from the rare diseases community to ensure we are measuring the outcomes that matter most. We will look to learn from areas of best practice, and continue working with the community and wider stakeholders to define remaining priority gaps.

In so doing we will continue to make progress towards achieving our overarching vision – delivering improvements in diagnosis, awareness, treatment and care, and creating lasting positive change for those living with rare diseases.

Introduction

The 2021 UK Rare Diseases Framework (https://www.gov.uk/government/publications/uk-rare-diseases-framework) set out a national vision for improving the lives of the 3.5 million people in the UK living with a rare disease under 4 priority areas:

- helping patients get a final diagnosis faster
- increasing awareness of rare diseases among healthcare professionals
- better coordination of care

- improving access to specialist care, treatments and drugs

These priorities are supported by 5 underpinning themes:

- patient voice
- national and international collaboration
- pioneering research
- digital, data and technology
- wider policy alignment

Since its publication, all 4 UK nations have published action plans, outlining their commitments to deliver on this collective framework.

England's first action plan, published on 28 February 2022, included 16 specific, measurable actions under each of the framework's priorities. Based on extensive engagement with the rare disease community, it also set out key challenges, and identified focus areas for future work.

This is England's second action plan, developed with delivery partners across the health system and in collaboration with people living with rare conditions. It contains a progress report on actions from the first action plan, and details of new actions for the year ahead. Background on governance underpinning the development of England's action plans is covered in the first action plan and is not revisited here. Publication of this action plan follows our commitment to publish action plans annually during the lifetime of the UK Rare Diseases Framework.

Box 1: what are rare diseases?

A rare disease affects fewer than 1 in 2,000 people within the general population. It is estimated that there are over 7,000 rare diseases, with new conditions continually being identified as research advances.

While around 80% of rare diseases have an identified genetic origin, they can also be caused by other factors such as disordered immunity or infections. Although rare diseases are individually rare, they are collectively common, with 1 in 17 people being affected by a rare disease at some point in their lifetime.

Rare diseases can be both life-limiting and life-threatening, and disproportionately affect children. 75% of rare diseases affect children and more than 30% of children with a rare disease die before their fifth birthday. People living with rare diseases, and their families, often face a lifetime of complex care leading to a profound impact on their education, financial stability, physical mobility and mental health.

Community engagement

People living with rare diseases are at the centre of the development of England's action plans. The rare diseases patient and clinician communities are represented on all our governance boards (https://www.gov.uk/government/groups/uk-rare-disease-forum), and we engage with a broad range of stakeholders through the UK Rare Diseases Forum and online platform, providing opportunities for discussion and feedback. Each of our delivery partners also have their own programmes of stakeholder engagement. Input from the rare diseases community forms an integral part of all the actions listed below.

In response to feedback, this year we have also undertaken a review of the forum, to ensure it remains fit for purpose, including increasing the diversity of membership and amplifying patient voice. We have partnered with Genetic Alliance UK to establish a standing, England Rare Diseases Action Plan Patient Advisory Group, which has been consulted throughout the drafting of this action plan.

We have also hosted a focus group session with Breaking Down Barriers (https://breaking-down-barriers.org.uk/) (a network of over 60 organisations working together to improve the lives of families from diverse and marginalised communities) to explore how health inequalities experienced by people from diverse and marginalised communities affected by rare conditions are being addressed in England's action plans.

Further details of our engagement activities and those of our delivery partners can be found in the patient voice section below.

Section 1: progress report on actions in England's 2022 Rare Diseases Action Plan

Over the course of 2022, the England Rare Diseases Framework Delivery Group has continued to meet regularly to coordinate delivery of England's action plans. The group brings together publicly funded delivery partners and representatives of the rare disease patient and clinician communities, to monitor the delivery of existing commitments, and agree on the content of future action plans.

Here we summarise key achievements over the past year against the 16 actions in England's first action plan. Significant progress has been made, with a number of actions either concluded, or extended to include new milestones for the coming year. However, delivery has taken place against the backdrop of a challenging environment, and within a wider context of priorities shaped by our recovery from the impacts of the COVID-19 pandemic. As a result, some actions have not met all their milestones within the expected timeframe, and will continue this year. More details on the status and progress of each action can be found in annex A.

Priority 1: helping patients get a final diagnosis faster

The UK Rare Diseases Framework outlined the importance of getting a rapid and accurate diagnosis. This can ensure timely access to treatment and care, provide a possible prognosis, and offer options for family planning.

Newborn screening plays an important role in diagnosing rare diseases early. We are committed to improving the evidence base to support the UK National Screening Committee (UK NSC) make rapid and robust decisions about newborn screening for rare diseases.

In the past year, the UK NSC has established a new remit and terms of reference. It now covers both population and targeted screening, and will be developing a more effective horizon scanning function, as well as a mechanism by which it can provide advice to researchers on evidence development.

The UK NSC Bloodspot Task Group has been established and is pursuing an important programme of work, including a comparison of key principles for newborn screening between the UK and those of the European Organisation for Rare Diseases (EURORDIS) – an alliance of patient organisations and individuals active in the field of rare diseases across Europe. This work will enable the UK NSC to build its evidence base for recommendations on screening for rare diseases.

The UK NSC has recently recommended newborn screening for tyrosinaemia (https://nationalscreening.blog.gov.uk/2023/02/02/uk-nsc-recommends-introduction-of-screening-for-tyrosinaemia-in-newborns/), a rare genetic disease. Evaluation is ongoing for severe combined immunodeficiency (SCID). The evaluation will determine if screening for SCID will work as well in England as it has in countries with different populations and health systems. This will allow the UK NSC to make a recommendation about whether newborn screening for SCID should become part of the NHS Newborn Blood Spot Screening Programme.

We also committed to exploring the feasibility of implementing whole genome sequencing (WGS) to screen for a defined set of genetic conditions in newborns. Recruitment to the research study is due to begin as scheduled in 2023, following completion of a host of supporting activities that finalise necessary systems, clinical pathways, processes, education and training to enable implementation. Public and patient engagement has been key. With oversight for the programme provided by an NHS Steering Group, Genomics England has led and attended over 200 stakeholder meetings, held over 20 working groups and interviewed over 100 parents to inform the design and implementation of the study.

Over 150 clinicians have also been engaged in preparation for mapping of results and healthcare pathways, which will be completed in 2023, before the study begins recruiting. To support the programme, an NHS England (NHSE) Newborns Genomes Programme Clinical Assurance Group was established in 2022, bringing together commissioning teams across NHSE and professional bodies to review the evidence for the conditions and treatment pathways and the impact of follow-on clinical care pathways.

Four principles for gene selection for the research study (https://www.genomicsengland.co.uk/initiatives/newborns/choosing-conditions) have been finalised, following an extensive engagement process. Assessment of genes which could be tested for against these principles is due to be completed in early 2023. Genomics England is working closely with Health Education England (HEE) to develop education and training resources to support healthcare professionals involved in the research study.

More broadly, NHSE regularly reviews the genomic testing available for individuals with a suspected rare genetic condition available through the NHS Genomic Medicine Service, and makes updates to the National Genomic Test Directory (Test Directory). These updates are based on the latest evidence, following review by experts and patient and public representatives.

The Test Directory specifies which genomic tests are commissioned by NHSE, and which patients are eligible to access a test. The Test Directory currently covers testing for over 3,200 rare diseases and over 200 cancers. During the most recent update in October 2022, 150 changes were made to the Test Directory, including the addition of testing for the rare lung condition Pulmonary Alveolar Microlithiasis.

Thirty-one rare conditions are now included within the eligibility criteria for WGS, meaning more patients can access comprehensive sequencing technologies within the NHS. NHSE is also working on expanding other types of genomic testing for rare diseases, such as transcriptomics, in a series of pilot studies.

Case study: Genomics England Clinical Research Interface

In our first action plan, Genomics England committed to further developing its clinical research interface. This means that when researchers find information of potential relevance to an individual's health in whole genome sequences in the trusted research environment (the National Genomic Research Library), it can be passed back to the NHS Genomic Medicine Service (GMS). The GMS is then able to review, validate and report this information, if it is important in the diagnosis and management of the individual. This benefits patients by increasing the potential number of diagnoses from whole genome data and identifying new genomic findings that can be fed back into the NHS to inform clinical care.

Work on this has progressed well. The original target was to return 100 diagnoses in a year, but this has been far exceeded (more than 1000 diagnoses were returned to the NHS during 2022). Here, our specific case study illustrates the impact this activity has had for just one group of people who were previously undiagnosed.

Rett syndrome is a rare, genetic neurological and development disorder that affects the way the brain develops, causing toddlers to experience seizures,

movement problems and loss of speech. These symptoms can make diagnosis particularly difficult. Variations in the MECP2 gene, which causes Rett syndrome, can be difficult to pick up through genomic sequencing owing to complexity of a particular region of the gene (exon 3). During 2022, through an in-depth focus on this particular genetic region from an expert in genomics, 19 new diagnoses of Rett syndrome were found and returned to the NHS through the clinical research interface. Having this diagnosis will help to explain the children's symptoms and allow for more appropriate onward care for these children and their families.

During 2022, NHSE developed a proposal for a syndrome without a name (SWAN) pilot for people whose conditions remain undiagnosed. The model brings together multidisciplinary teams, covers all ages and aims to provide good geographical coverage across England. The model is being discussed through NHSE governance and finance structures. If relevant funding is agreed the SWAN pilot will be implemented in 2023.

Priority 2: increasing awareness of rare diseases among healthcare professionals

As part of its Genomics Education Programme (GEP), Health Education England (HEE) has developed GeNotes, to increase the awareness of genetic and rare diseases amongst healthcare professionals.

GeNotes has been developed with established working groups across a wide variety of medical specialties. It provides resources for healthcare professionals that support with genomic testing and feedback of results for rare diseases aligned to the National Genomic Test Directory, and an extended learning journey in genetic and non-genetic rare disease.

GeNotes has successfully completed its private beta phase for oncology, paediatrics and general practice, and published a public beta platform with oncology as the first specialty. In the coming months, oncology will be joined by women's and foetal health, cardiology, pharmacogenomics, general practice and paediatrics.

Alongside this, HEE has committed to extending its remit on rare disease to include non-genetic rare disease. This new programme of work has involved the creation of a rare disease education hub, which includes information for healthcare professionals, and links to education and training opportunities. To support this broadening of its remit, HEE is working with Medics 4 Rare Diseases to enhance the development of the hub and associated learning resources.

The GEP is now supported by a newly established patient advisory group – Patient Advisors for Genomics Education (PAGE). This ensures that the patient voice is central to decision-making, and patient views are invited, gathered and acted on as part of the GEP's education, training and workforce planning

process. The group will ensure the programme's education resources are informed by the experiences of people and families living with rare diseases, as well as clinicians. Alongside this, HEE is collaborating with the Academy of Medical Royal Colleges to evaluate medical curricula to ensure information on rare diseases is appropriately integrated.

The National Congenital Anomaly and Rare Disease Registration Service (NCARDRS) has worked in partnership on 10 academic papers on rare diseases in 2022 that have been published, accepted for publication or are under peer review. Findings have been presented at national and international conferences and events, and conveyed to relevant patient groups.

Priority 3: better coordination of care

Due to the complex nature of their conditions, many people living with rare diseases will need support from many different parts of the health and social care system throughout their lives. Over the last year, to improve coordination of care, NHSE England has been developing a toolkit for virtual consultations – improving the use of videoconference and telephone clinic calls for patients with complex, multi-system rare diseases. This toolkit was made available in 2022 across highly specialised services (HSS). Uptake will be monitored through annual clinical meetings, and a feedback survey has been developed.

Priority 4: improved access to specialist care, treatment and drugs

Many rare diseases do not have established treatments, but where they do exist, they can be life-changing and lifesaving.

During 2022, NHSE developed a map of programmes that promote access to drugs and are actively using a 'preparedness template' with industry to develop a shared understanding of the service implications for new drugs, approved by the National Institute for Health and Care Excellence (NICE), so patients benefit as early as possible. An analytical approach has been developed to measure both the overall and geographical uptake of drugs for patients with rare diseases. This combines data from several sources, such as Blueteq and locally held NHSE systems.

In June 2022, NHSE and NICE launched the Innovative Medicines Fund (IMF), which will fast-track the most promising, cutting-edge medicines to NHS patients. Together with the Cancer Drugs Fund it represents a £680 million investment. The IMF provides faster patient access for non-cancer drugs while further data is collected. The IMF will build on recent positive NICE appraisals for, and NHS adoption of, cutting-edge treatments secured for patients by the NHS Commercial Medicines Directorate, including gene therapies for metachromatic leukodystrophy (Libmeldy®), spinal muscular atrophy (Zolgensma®) and inherited retinal dystrophies (Luxturna®).

Additionally, NHSE is developing a strategic approach for advanced therapy medicinal products (ATMPs) in the NHS. NHSE remains actively involved with ATMP Engage, the patient collaboration co-chaired by Genetic Alliance UK and the Cell and Gene Therapy (CGT) Catapult. In establishing a structured approach to ATMP commissioning, NHSE has engaged with a range of stakeholders across industry, as well as individual patient groups and providers.

Using horizon scanning, NHSE has also instigated structured proactive engagement with individual ATMP manufacturers 12 to 24 months prior to marketing authorisation. This activity continues to iterate over time; as such, there is no planned strategic publication that will accompany this work.

Further advances have also been made with the Early Access to Medicines Scheme (EAMS), which promotes access to medicines that patients with life-threatening or debilitating conditions would be otherwise unable to access, and the Innovative Licensing and Access Pathway (ILAP), which supports the path to market of innovative and novel treatments.

In July 2022, the Innovation Accelerator (IA) (https://www.gov.uk/government/publications/innovation-accelerator/innovation-accelerator) was announced and provides innovators and developers of innovative products access to MHRA scientific expertise, regulatory guidance and enhanced advice and signposting. Further information on all of these initiatives is provided in annex C.

Case study: Medicines Repurposing Programme

The multi-agency Medicines Repurposing Programme (https://www.england.nhs.uk/medicines-2/medicines-repurposing-programme/) identifies and progresses opportunities to use existing medicines in new ways, outside their current marketing authorisation.

Potential candidate medicines are assessed against eligibility criteria (https://www.england.nhs.uk/publication/medicines-repurposing-programme-candidate-proposal/) and prioritised for inclusion in the programme. Upon formally entering the programme, tailored support is provided for each medicine, which might include building further clinical evidence, facilitating licensing and/or promoting other actions that enable more equitable access.

The second medicine to enter the programme is metformin, a licensed diabetes drug that could potentially also be used to treat tuberous sclerosis complex (TSC). TSC is a rare genetic condition that causes (mainly non-cancerous) tumours to develop throughout the body. Following a request from the Medicines Repurposing Programme, the NIHR released a call for applications for research funding (https://www.nihr.ac.uk/funding/22564-evaluating-the-efficacy-of-metformin-in-tuberous-sclerosis-complex/32319) to determine whether metformin is safe and effective for treating TSC.

NICE's new methods for health technology evaluation were published in 2022. From 2023 onward, most topics using the previous methods will conclude and the impact of introducing the new methods on rare diseases will emerge. In 2022, NICE introduced the use of the Summary of Information for Patients (SIP) to help support individual patient experts participate in NICE technology appraisals.

Actions under underpinning themes

In the 2022 action plan we announced £40 million of funding for the NIHR BioResource (https://bioresource.nihr.ac.uk/), which works in over 50 rare disease areas to link genetic information to clinical characteristics to increase understanding of disease mechanisms for diagnostic and treatment development.

In 2022, NIHR BioResource continued to recruit people with rare diseases from 60 NHS trusts in England, adding more than 2,500 new volunteers across 40 disease areas. The funding has also supported several new research studies, including an industry partnership to generate induced pluripotent stem cells to test novel compounds for rare diseases treatments. The NIHR BioResource also expanded the RNA Phenotyping Project to include participants from 17 rare disease areas (see case study in annex C).

In 2022, we committed to mapping the rare disease research landscape, in collaboration with the Medical Research Council (MRC) and the National Institute for Health and Care Research (NIHR). Whilst good progress has been made, the data analysis phase, using the Orphanet definitions of rare diseases, has proved more challenging than anticipated.

Analysis has now been completed for MRC and NIHR data, and a report describing the research landscape is being prepared. Wider funders sit on the project's steering group, providing insight into rare disease research across the devolved administrations, and research funded by charities and industry. Stakeholder workshops to seek feedback on gaps and priorities for future funding are planned for after publication.

Case study: MELODY

The MELODY (Mass Evaluation of Lateral flow immunOassays for the Detection of SARS-CoV-2 antibody responses in immunosuppressed people) study shows the power of national disease registration to enable pioneering rare diseases research. The study assessed antibody status after 3 or more COVID-19 vaccines in people with a rare autoimmune rheumatic disease (RAIRD), a solid organ transplant or a lymphoid malignancy. Immuno-suppressed people are more severely affected by COVID-19 than the general population. However, there was little evidence to inform targeted booster and treatment policies for this community.

One reason why MELODY is such a powerful study is that population register data was used from NHS Blood and Transplant (NHSBT), alongside cancer and rare disease data from the National Disease Registration Service (NDRS). Over 100,000 people were invited to take part in the study, which could be undertaken in their own home, overcoming many of the traditional barriers to rare disease research.

Over 23,000 people returned lateral flow test results, including over 6,500 with RAIRD. Building on previous partnership with the RECORDER collaboration (https://digital.nhs.uk/ndrs/data/data-stories/recorder), people with RAIRD were identified by applying an algorithm to routinely collected data.

Data was also collected on anxiety and depression, and information on shielding, which can be analysed alongside antibody status. The MELODY study represents the largest mental health study performed in this population, at this time. The majority of the cancer and RAIRD participants consented to have their study data linked to their NDRS record and other relevant datasets. Therefore, the study brings together both real-world and patient self-reported data to deliver meaningful, actionable output that includes the patient voice and minimises the data collection burden.

Because the participants came from population-based registers, differences between those that took part in the study and those that did not can be analysed, giving a better understanding of the potential biases in the results, and enabling the study to inform how to improve COVID-19 outcomes for the whole community. Most participants consented to be re-contacted for research purposes, creating future research opportunities. The MELODY study data will become a national data asset within the NDRS.

NHS England (NHSE) has progressed work to reduce health inequalities across highly specialised services (HSS). Health inequalities is now on the agenda for all annual clinical meetings for HSS, focussing on access, experience and outcomes, logging how health inequalities have been addressed in procurements, and drafting a framework to help teams understand and address health inequalities when commissioning, that will be piloted in 2023.

Following a paper on geographical access to HSS, presented at the Rare Diseases Advisory Group, a standard operating procedure for undertaking this exercise has been developed. This exercise will be repeated every 3 to 4 years. Additionally, NHSE is considering the development of an equalities and health impact assessment by bidders as part of the standard procurement process.

Section 2: addressing the priorities of the UK Rare Diseases Framework in 2023

Building on the actions listed above, this second action plan also outlines our commitments for the coming year, including the outcomes that we aim to

achieve to continue to make progress against the 4 priorities of the framework. Each action is described below with further information provided in annex B.

The new actions are numbered from 17 onwards, to provide continuity with England's 2022 action plan. This will allow for continued reporting against actions from the first action plan that are due to continue into 2023 and 2024. As well as specific numbered actions, additional supporting activities that will also contribute to making progress on the aims of the framework can be found in annex D.

Focus areas

Recognising that not all concerns of people living with rare conditions could be addressed in England's 2022 action plan, we committed to considering how best to take forward outstanding areas of priority for the community. Informed by stakeholder engagement, we identified 6 focus areas for 2022:

- support for people with non-genetic and undiagnosed conditions
- coordination of care
- mental health and psychological support
- clinical research delivery
- registries
- monitoring and evaluation (development of high-level metrics)

These topics have been considered in meetings of the England Rare Diseases Framework Delivery Group, formed the focus of engagement activities over the past year, and have shaped the development of actions. They are discussed in more detail under the relevant priorities and themes below.

> The new actions below are numbered from 17 onwards, to provide continuity with the first 16 actions outlined in England's 2022 action plan.

Priority 1: helping patients get a final diagnosis faster

Diagnostic delays can have a profound impact on people living with rare conditions and their families, affecting both mental and physical health, as well as having significant cost implications for the NHS.

Action 17: commission research on how best to measure the diagnostic odyssey

There are currently no robust and routinely used methods for measuring the diagnostic odyssey – the time between symptoms first presenting and people receiving a definitive diagnosis – for rare diseases across the NHS.

Developing metrics to accurately determine the time it takes for people living with rare diseases to receive a final diagnosis is a crucial step in establishing a baseline time to diagnosis. This baseline will enable us to better understand the impact of interventions designed to help patients get a final diagnosis faster. For example, metrics could be used to assess variation amongst different cohorts of patients with the same disease, location at diagnosis (to assess geographical equity) and place of NHS care (to identify variations between NHS providers).

In the coming year, DHSC will commission policy research through an NIHR open call (https://www.nihr.ac.uk/funding/policy-research-programme-prp-35-01-14-research-to-support-evidence-building-and-the-evaluation-of-the-uk-rare-diseases-framework-2021-2026/32379), inviting researchers to develop an effective method for measuring the time to diagnosis for both genetic and non-genetic rare conditions, with input from the rare diseases community. Outcomes of the 2-stage application process are expected by autumn 2023, with research commencing after contracting. The outcome of the call, the successful research proposal, and progress made will be reported in the 2024 action plan.

Action 18: increased data sharing for patient benefit to improve our understanding of equity of access to genomic testing and support interpretation of genomic test results

To ensure more people are receiving an accurate, timely diagnosis, it is important to understand what testing is being undertaken across the country. The NHS Genomics Strategy committed to developing an interoperable informatic and data infrastructure that enables the NHS to use and share genomic data appropriately to improve patient care, and drive health improvements for individuals and populations. NHSE, NCARDRS and Genomics England each hold large amounts of data on rare disease patients' diagnoses and genomic variants. In the coming year, they will explore how to share this data more consistently between them for patient benefit, including technical, information governance and data protection considerations, in consultation with patient organisations.

This increased data sharing will enable comparisons of data on patients who have had rare disease tests in the NHS GMS, with national registry data from patients who have not had testing but with conditions which may be eligible for testing. This will also form part of work that NHS England is taking forward to monitor equity of access to genomic testing.

The diagnostic variant data NCARDRS receives from NHS Genomic Medicine Service Labs will also be combined with similar data held by Genomics England. This facilitates a unified ecosystem for variant frequencies, for conditions tested through different technologies across the NHS in England.

Combining these data will involve establishing mechanisms for data transfers and scoping their feasibility, and developing an analysis strategy to compare the coverage of eligible patients with the coverage of diagnostic genomic testing for exemplar conditions. The agreements, first data transfer and preliminary analysis will be completed by February 2024. Publication of dashboards

showing data on equity of access to testing will follow, building on models developed by the National Disease Registration Service for cancer. Outcomes of the analysis will be shared with DHSC, and could be used to prioritise future NHSE service development.

Focus area: support for people with undiagnosed conditions

For some people living with extremely rare diseases, the complex and rare nature of their conditions may mean that they never receive a diagnosis. We are committed to ensuring that these people and their families also receive the support and care they need.

Building on a commitment in the 2022 action plan to pilot new approaches for patients with undiagnosed rare conditions (action 5), a proposal for a pilot syndrome without a name (SWAN) programme has now been developed to reduce the time to diagnosis for patients with undiagnosed rare diseases through multidisciplinary review, enhanced testing and structured follow-up (see annex A).

Over the course of 2022, we have met with SWAN UK to understand the challenges facing people and families with undiagnosed rare conditions. England's Rare Diseases Framework Delivery Group has invited NHS Wales to present on progress on the Welsh SWAN clinic. During the coming year we will continue to draw on experiences from this clinic to inform our policy. We are also committed to engaging with the findings of SWAN UK's 2022 survey (https://www.undiagnosed.org.uk/swanuk-news/do-you-have-a-child-affected-by-an-undiagnosed-condition/) to better understand lived experiences.

Focus area: support for people with non-genetic rare conditions

People with non-genetic rare conditions continue to face barriers in receiving accurate diagnosis and appropriate care. This includes a lack of epidemiological data. Of the 10 epidemiological papers published and submitted by NCARDRS under action 9 during 2022 (see annex A), all addressed non-genetic conditions.

In the coming year, NCARDRS will continue to work on developing ways to identify people with non-genetic rare conditions. This will include leveraging the findings of studies like RECORDER (https://www.nottingham.ac.uk/research/groups/recorder/index.aspx) and MELODY (https://www.imperial.ac.uk/medicine/research-and-impact/groups/melody-study/).

HEE will continue its work to extend the remit of the Genomics Education Programme to include non-genetic rare diseases (action 8), through a partnership with Medics 4 Rare Diseases (see annex D). DHSC will hold a workshop to better understand the challenges faced by people living with non-genetic rare conditions. We will also further explore the recommendations of reports such as 'Resetting the balance' (https://rairda.org/resetting-the-balance-report/), which outlines the needs and challenges facing people living with non-genetic and late-onset rare conditions.

Priority 2: increasing awareness of rare diseases among healthcare professionals

Raising awareness of rare diseases within the health system is crucial to improving the diagnostic experience for people living with rare conditions, as well as ensuring the best possible standards of clinical care.

Action 19: publishing and implementing specific strategies for increasing awareness of rare diseases in the nursing and midwifery, pharmacy and primary care workforce

It is vital that training on how to engage, inform, involve and support the diverse rare disease population is accessible to all healthcare professionals involved in their care. In addition to ongoing work with clinicians across a range of specialties, including collaborations with the Academy of Medical Royal Colleges and other individual Royal Colleges, HEE is currently working with subject matter experts in nursing and midwifery, pharmacy and primary care to ensure rare diseases are incorporated and specified in the strategies being developed and updated.

Following engagement through a series of roundtables, the strategies are due to be published in early 2023. HEE will collaborate with the 3 workforce groups to implement the outcomes of these strategies and evaluate their efficacy.

While the focus of this action is on 3 specific professional groups initially, it enhances and adds to HEE's wider work to ensure all healthcare professionals are aware of rare diseases. It is also supported by the work of the Genomic Laboratory Hubs and Genomic Medicine Service (GMS) Alliance regions to increase awareness of genomics across different professional groups, as outlined in the NHS GMS Strategy, Accelerating Genomic Medicine in the NHS (https://www.england.nhs.uk/long-read/accelerating-genomic-medicine-in-the-nhs/#:~:text=The%20NHS%20GMS%20will%20aim,in%20access%20to%20genomic%20testing.) (see annex D).

Priority 3: better coordination of care

Because of the chronic and complex nature of their conditions, many people living with rare diseases will require support from across the health and social care system. Recognising that care coordination is a central concern for the rare diseases community, we identified priority 3 as a key focus area for 2022 to 2023.

Action 20: commission research to provide the evidence needed to operationalise better coordination of care in the NHS

To improve coordination of care it is vital to understand how proposed models of care coordination could be best implemented within the NHS. The NIHR-funded CoOrdinated Care Of Rare Diseases (CONCORD) study

(https://fundingawards.nihr.ac.uk/award/16/116/82) sought to investigate how services for people with rare diseases are coordinated in the UK, and how people living with rare diseases, and healthcare professionals who treat rare diseases, would like them to be coordinated.

The study published a landmark definition of coordination of care in rare diseases (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7319081/) and a taxonomy of care coordination (https://www.medrxiv.org/content/10.1101/2021.11.16.21266387v1), as well as developing hypothetical models of care coordination (https://www.medrxiv.org/content/10.1101/2021.11.16.21266395v1).

In England's 2022 action plan, we committed to partnering with NHSE "to explore how the economic case for different care coordination models proposed in the CONCORD study could best be evaluated".

In the coming year, DHSC will commission policy research through an NIHR open call to fill the remaining evidence gaps. Developed in consultation with the rare diseases community, this research will improve our understanding of the most cost-effective, tractable and impactful approaches to improving coordination of care for people living with rare disease, taking into account recent changes to how some NHS services are commissioned (see annex E).

Outcomes of the 2-stage application process are expected by autumn 2023, with research commencing as soon as possible after contracting. The outcome of the call, the successful research proposal, and progress made in the interim will be reported in the 2024 action plan. However, immediate interventions to improve care coordination are also needed, and actions to address this are below.

Action 21: include the definition of coordination of care in all new and revised services specifications for patients with rare diseases, and ensure the priorities of the UK Rare Diseases Framework are embedded across NHSE highly specialised services

Building on the findings of CONCORD, NHSE will ensure all new and revised service specifications for patients with rare diseases are mapped against the definition of care coordination as set out in Defining Coordinated Care for People with Rare Conditions: A Scoping Review (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7319081/). This will include providing co-ordinated pathways for access to specialist care, treatment, drugs, social care, mental health and special educational support. Service specifications will include a requirement to report data to NCARDRS where appropriate. This will apply to all service specifications for patients with rare diseases, not just those falling under highly specialised services.

In addition, discussions will be held at each of the 80 HSS annual clinical meetings about what the service is doing in respect to the 4 priorities of the UK Rare Disease Framework, with reference to: transition from paediatric to adult care; clinical outcomes; ongoing research and opportunities for patients to take part in research.

Service specifications define the standards of care expected from organisations funded by NHS England. They set out details specific to the service, including the intended outcomes, applicable service standards, and how compliance will be measured. NHSE is responsible for implementing commissioning plans, including how services will be monitored. Regular monitoring of quality metrics by commissioners and the metrics definitions can be found on the NHSE website. To ensure the voice of the rare diseases community is heard, there are patient and public voice representatives on all specification working groups, and patient groups may attend annual clinical meetings where appropriate.

Focus area: coordination of care, including transition from paediatric to adult care

Improving the experience of transition from paediatric to adult services for young people living with rare conditions remains a high priority, and we will take steps to address this in the year ahead.

In recognition of the importance of this timepoint in the patient journey, NICE (https://www.nice.org.uk/guidance/ng43), NHS Wales (https://gov.wales/transition-and-handover-childrens-adult-health-services) and NHS Scotland (https://www.gov.scot/publications/supporting-disabled-children-young-people-and-their-families/pages/adult-health-and-social-care/) have all published guidance on the transition from children's to adult services.

However, we know that this transition remains a challenge for many young people and families living with rare conditions, as highlighted in a 2022 report on improving transition from paediatric to adult care for young people living with a rare disease (https://www.camraredisease.org/collaboration-transitions/). To address this, in the coming year we will partner with NICE to host a workshop to better understand how the NICE quality standard on transition (https://www.nice.org.uk/guidance/qs140) could be adapted to ensure it is relevant to the needs of the rare diseases community.

Covering transition more broadly, the Children and Young People Transformation Team at NHSE (https://www.england.nhs.uk/get-involved/cyp/), in conjunction with the Burdett Trust for Nursing (https://www.btfn.org.uk/), have developed a National Framework for Transition, which will be published in 2023. It will encompass a comprehensive offer for 0- to 25-year-olds that reaches across mental and physical health services, delivering an integrated approach that will reduce health inequalities across the health, social care, education and voluntary sectors. The framework has been developed in close consultation with parents, young people and clinicians, including a 6-week consultation which attracted more than 1,200 responses.

Over the coming year, we will work with NHSE to ensure that the needs of young people living with rare conditions, and their families and carers, are considered in the implementation of the framework. We will also continue to work with the rare diseases community to learn from wide-ranging existing work to understand and improve the transition from paediatric to adult services.

Focus area: mental health support

The challenges of living with a rare condition – whether diagnosed or undiagnosed – can have a profound impact on an individual's mental health and that of their family or carers. It is important that psychological support is considered when developing services for people living with rare conditions, and that this is coordinated with wider health and social care needs.

This is echoed by the findings of a number of recent publications, including recommendations from a quantitative survey and multi-stakeholder workshop on mental health support for rare disease in the UK (https://bmchealthservres.biomedcentral.com/articles/10.1186/s12913-022-08060-9), and the Emotional Odyssey systematic review and statement of good practice (https://rd-rp.com/a-consensus-statement-psychological-support-at-diagnosis/). These emphasise the importance of a well-supported diagnosis and access to psychological support as part of onward care. They also highlight the need for healthcare professionals to be aware of mental health needs, and for increased signposting to trusted sources of support.

The NHS Long Term Plan (https://www.longtermplan.nhs.uk/) commits an additional £2.3 billion a year for mental health services in England by the 2023 to 2024 financial year – supporting an additional £2 million people to get the NHS-funded mental health support they need. To support the mental health commitments in the NHS Long Term Plan, we aim to grow the mental health workforce by an additional 27,000 staff by financial year 2023 to 2024.

We provided an extra £500 million in the 2021 to 2022 financial year to accelerate expansion plans and address waiting times for mental health services, give more people the mental health support they need and invest in the NHS workforce.

In addition, on 24 January 2023 we announced plans to publish a Major Conditions Strategy, tackling conditions that contribute most to morbidity and mortality across the population in England, including mental ill health. The strategy will set out a strong and coherent policy agenda, including a shift to integrated, whole-person care. It will cover the patient pathway from prevention to treatment and outline the standards patients should expect in the short-term and over a 5-year timeframe. An interim report will be published in the summer.

More specifically, for people diagnosed with rare genetic conditions, proposed updates to the NHS Clinical Genomic Services specification emphasise the importance of access to clinical psychology to provide essential care to people affected by genetic conditions. The updated service specification underwent public consultation in 2022 and is due to be published in 2023.

Although this is primarily relevant to people living with rare genetic conditions, it serves as a template for wider services. Under action 21 in this plan, all new and revised service specifications for patients with rare diseases will be required to consider user's psychosocial needs and ensure coordinated pathways for access to mental health support as part of mapping services against a broader definition of coordination of care.

Mental health support was identified as a focus area for this year's action plan. To better understand the needs of the community, over this year we have met with key stakeholders including RareMinds (https://www.rareminds.org/), Genetic Alliance UK (https://geneticalliance.org.uk/) and Rare Disease Research Partners (https://rd-rp.com/), and have held focused meetings on the topic with our delivery partners.

As a result, mental health support is considered within many of the actions contained in this plan, including action 21 (as mentioned above) and action 20 (commissioning research to provide the evidence needed to operationalise better coordination of care in the NHS). These are further supported by action 19 (publishing and implementing specific strategies for increasing awareness of rare diseases in the nursing and midwifery, pharmacy and primary care workforce), as supporting the healthcare workforce to ensure patients are well informed and well cared for during their diagnostic and management journey will in turn have a positive impact on mental and psychological health.

Improving rare disease knowledge and awareness among mental health professionals is also key to improving the provision of psychological support. The ongoing work of HEE on GeNotes (action 6) will help ensure that all healthcare professionals are alert to the challenges of living with a rare condition, and able to signpost to sources of additional support. In collaboration with Medics 4 Rare Diseases, HEE will also look at developing further educational content as part of their Genomics Education Programme, to support mental and psychological health for those living with rare disease and their families.

Particularly following the COVID-19 pandemic, many patient organisations have played an important role in funding projects to provide mental health support to their communities. In the coming year, we will continue to engage with areas of best practice (including patient organisations and the third sector) to learn from their approaches to providing mental health support to the rare diseases community. Mental health was also a key focus of the MELODY study (see case study above), and work is ongoing to analyse the study's findings.

Priority 4: improved access to specialist care, treatment and drugs

Action 22: improved 'findability' of people living with rare diseases using NCARDRS

Without an accurate understanding of the number of people living with rare diseases, it is difficult to organise specialist services in the places that make the most sense, or to accurately assess equity of access to testing, treatments and services. People may also miss out on being invited to clinical trials or being offered new treatments.

To improve understanding of rare disease in England, the National Congenital Anomaly and Rare Disease Registration Service (NCARDRS) has committed to

improve the quality, coverage, completeness and transparency of national rare disease registration data. This includes increasing data submissions for people with rare disease to NCARDRS through reporting requirements in NHSE service specifications; beginning to apply techniques developed to date to multiple rare diseases; and exploring how NCARDRS and NHS DigiTrials can work together to improve findability of rare disease patients for suitable clinical studies.

A new web-based self-reporting system (https://digital.nhs.uk/ndrs/about/rare-diseases) has been made available for public testing. The aim is to enable patients to register themselves with the national register to ensure they are included in the national data for their disease. Records based on self-reporting can be validated through linkage to pre-existing routine datasets or by contacting the clinician nominated by the person registering. Support is available for people living with rare conditions who would prefer to self-register by post or telephone, to ensure that this system reduces, rather than exacerbates, health inequalities. NCARDRS will work with stakeholders to ensure that the self-reporting system is fit for purpose.

A new NCARDRS rare disease data dictionary will make clear to external stakeholders which data items are available for different rare diseases. A public dashboard will be developed, which will include information such as which rare diseases NCARDRS collects data on, how the data is collected, and prevalence and incidence figures, where available. This is due to be published for public testing by February 2024.

NCARDRS will continue to work with delivery partners and others to ensure that the registration data is made available where appropriate and to provide subject matter expertise to support improvements in patient care and outcomes. All 4 nations of the UK have also committed to working together to make sure that registry activities align so that we can begin to achieve truly national disease registration.

Action 23: continue to improve the understanding of the impact of NHS England's specialised services commissioning activities on rare disease patients, and act on this information

NHS England (NHSE) is responsible for developing nationally mandated clinical commissioning policies and selecting providers to deliver specialised services for people living with rare diseases (see annex E). Recognising the importance of patient voice in shaping these services, NHSE specialised commissioning has piloted and implemented the use of patient impact assessments (PIAs) in the development of clinical commissioning policies.

PIAs involve clinical policy working groups (including patient and public voice representatives) in completing a brief factual summary of what the impact of living with a particular rare condition is like on patients and their carers. These summaries are tested with a variety of stakeholders for accuracy. To date, 30 PIAs have been used by members of the Clinical Priorities Advisory Group (CPAG) as part of their consideration of clinical commissioning policies, to improve their understanding of the lived experience of the condition. The use of

PIAs is currently being evaluated to ensure they continue to be a valuable source of information, alongside the clinical and commissioning information considered by members.

From spring 2023, NHSE has also committed to routinely requesting equality health impact assessments from bidders, which will be considered when undertaking provider selection exercises for services for patients with rare diseases. NHSE will also amend the terms of reference of the Rare Diseases Advisory Group, enabling it to consider all clinical policy propositions for patients with rare diseases (not just those treated in highly specialised services) and to feedback to the CPAG with a particular focus on the likely impact of the policy on those patients. It will also be expanding its use of Patient Reported Outcome Measures (PROMs) in services for patients with rare diseases.

Action 24: establish a highly specialised services programme board and strengthen the role of NHS England in commissioning wider services for patients with rare diseases

Following the Health and Care Act 2022 (https://www.legislation.gov.uk/ukpga/2022/31/contents/enacted), NHSE will build on its existing governance framework to continue to strengthen its role in commissioning of high quality highly specialised services (HSS) and other services for patients with rare diseases.

The act permits NHSE, by direction, to allow for the commissioning of specialised services to be exercised by integrated care boards (ICBs). NHSE has published its intention to delegate responsibility for commissioning over 60 services to ICBs from April 2023 and around a further 25 services over time. All 80 HSS (and some other services) will remain nationally commissioned.

To provide continued assurance of the high-quality of services for patients with rare diseases, NHSE will establish, from April 2023, a Highly Specialised Services Programme Board (HSSPB), which will meet quarterly. The terms of reference of the NHSE Rare Diseases Advisory Group (RDAG), will also be revised to strengthen its clinical advice and clinical leadership role by June 2023.

Patient and public voice representatives play an active role on RDAG, and the chair of RDAG will be a member of the HSSPB. Decisions made at the HSSPB will be ratified by the National Commissioning Group, which includes in its membership the chair of the Patient and Public Voice Advisory Group. To ensure UK-wide alignment, both groups will include membership from the devolved administrations.

Action 25: review the effectiveness of EAMS, ILAP and the IMF in improving access to treatments for people living with rare diseases

The 2022 action plan listed several schemes which facilitate early access to novel, high-cost treatments, including the Innovative Medicines Fund (IMF),

Early Access to Medicines Scheme (EAMS) and Innovative Licensing and Access Pathway (ILAP).

Over the coming year, NHS England, MHRA and NICE will review the impact of these initiatives, including their effectiveness in improving access to treatments for people living with rare diseases. This will aid in transparency, provide an understanding of how the schemes are working for rare diseases medicines, and identify any potential gaps or improvements.

As part of this monitoring, the MHRA will determine the proportion of applications to EAMS and ILAP that are medicines being developed to treat rare diseases. Similar monitoring will be undertaken by NHSE for the IMF, supported by NICE. Data on the number of rare disease medicines progressing through the schemes will be collected and reported in England's 2024 action plan. The rare diseases community will be consulted throughout the process, to ensure the results are relevant to stakeholders.

Action 26: registration of national data for rare genetic conditions which cause an inherited predisposition to cancer

Population-based disease registration offers the opportunity to develop an unbiased and inclusive understanding of the experience of people living with rare conditions. The National Disease Registration Service (NDRS) has previously worked with stakeholders to improve the understanding and management of more common inherited cancer syndromes, such as Lynch syndrome, using national cancer registration and genomic test data. Infrastructure and expertise from this is available to NCARDRS to support similar efforts for rarer inherited cancer predisposition conditions.

This year, NCARDRS will improve registration of some rare genetic conditions that cause an inherited predisposition to cancer. NCARDRS is uniquely placed to link to the national cancer data held by the National Cancer Registration and Analysis Service and will work with the UK Cancer Genetics Group to consider which conditions have the greatest unmet need and potential for immediate benefit.

Aggregate variant level data will be shared securely with relevant stakeholders, and will be used to inform research and contribute to the public dashboard described under action 22 above. Through inclusion on the national rare disease register, linked rare disease and cancer data will be available to improve our understanding of these diseases (including cancer risk) and to support better coordination of care, access to new treatments, and outcomes.

This approach could be used as an exemplar, with the possibility of scaling-up to understand the cancer risk of multiple rare diseases, or describing non-cancer morbidities in people with genetic conditions.

To better understand the needs of this community, we have also invited the UK Cancer Genetics Group (https://www.ukcgg.org/) to submit a paper outlining the most pressing needs for families living with rare genetic conditions that cause an

inherited predisposition to cancer. This will be considered at a meeting of the England Rare Diseases Framework Delivery Group in the year ahead.

Focus area: improving clinical research delivery for rare diseases

Clinical research is an important part of the pipeline in the development and approval of new treatments and drugs. The UK Clinical Research Recovery Resilience and Growth (RRG) programme is delivering the government's ambition for clinical research (see annex D).

Rare disease clinical research requires innovative approaches to address challenges such as low patient numbers and difficulties accessing specialist centres. These were highlighted in a 2022 workshop run by the Academy of Medical Sciences (https://acmedsci.ac.uk/more/events/forum-clinical-trials-for-rare-and-ultra-rare-diseases), which identified 3 key areas of opportunity to improve clinical research delivery: improving recruitment of trial participants, reducing the burden of trial participation, and making the best use of trial data, including real-world data. This year we will continue to explore the recommendations from this workshop to determine what more can be done to make it easier for people living with both genetic and non-genetic rare conditions to participate in clinical research where they wish to do so.

Improving recruitment of trial participants

The use of population-based data, as described in action 22 (improving 'findability' of people with rare diseases using NCARDRS), will make it easier for people living with rare conditions to be identified and invited to take part in clinical research. It will also improve equity of access, as relevant demographics and potential biases that may affect uptake can be identified and addressed at the planning stage.

Building on digital platforms such as NCARDRS, NHS DigiTrials and other key infrastructure, we are developing a data-enabled 'find, recruit and follow up' approach to improve our ability to identify and approach people who may be eligible for specific studies, and monitor the progress of participants. This will increase access to research for people across all areas of the country, ensuring more people living with a rare disease can access research of relevance to them. Another tool that can support people living with rare diseases to participate in research, is Be Part of Research (https://bepartofresearch.nihr.ac.uk/). This is an online service that helps members of the public understand what clinical research is and what it might mean to take part, as well as showing what clinical research is currently happening across the UK.

The Be Part of Research platform includes all phases of clinical trials. It draws studies from the International Standard Registered Clinical/soCial sTudy Number (ISRCTN) (https://www.isrctn.com/) and ClinicalTrials.gov registry (https://www.clinicaltrials.gov/), as well as the NIHR Clinical Research Network portfolio. It is of upmost importance that researchers list their studies on one of these public registers. The Be Part of Research website is searchable by condition and provides details of active studies, information about what the

study involves, location, eligibility criteria and contact details for the researchers conducting the study.

Action 27: improving the Be Part of Research platform for people living with rare diseases

The Be Part of Research platform is undergoing active development to enable members of the public to register to be contacted about areas of health research they may be interested in. Over the coming year, we will seek feedback from the rare diseases community as part of the development process, through beta testing of the Be Part of Research user interface, and involvement in Be Part of Research's stakeholder engagement group. Through this group, consultations will take place on the most user-friendly way to categorise rare disease studies on the platform. Further input will be gathered to ensure that the searchable criteria listed above appropriately meet the needs of those with lived experience.

Over the coming year, the visibility of Be Part of Research will also be increased, for example through increased signposting from the NHS. Collectively, increased awareness and effective use of the Be Part of Research platform among the rare disease community will facilitate increased opportunities for research participation.

Reducing the burden of trial participation

The UK Clinical Research RRG programme has set up a collaborative project, led by the Health Research Authority (HRA), between members of the public and the research community to explore people-centred clinical research. This will consider the barriers and enablers of participation and involvement in clinical research from a diverse range of perspectives.

The HRA is also leading work to improve the information provided by researchers to potential participants in research, ensuring that information is relevant, meaningful and enables informed decision-making about participation. Guidance will be published in 2023 to 2024, including recommendations on how people with lived experience should be involved in the co-creation of accessible participant-facing information.

The HRA has also published guidance for the research community on responsibilities of organisations and investigator oversight when participants take part in research across a number of settings, include home care. This is particularly relevant to participants with rare diseases, who would benefit from being able to take part in research in the care settings that are most appropriate for them.

Making the best use of trial data, including real-world data

For many rare diseases, it may not be feasible to recruit enough participants into a traditional randomised clinical trial to gain conclusive results. One possible solution to this is to make use of real-world data (see box 2).

Box 2: real-world data and evidence

There are vast amounts of data being collected on patients, which are securely stored, for example, in electronic health records and disease and patient registries. Such data is commonly called real-world data (RWD), reflecting the fact they it is collected while patients go about their regular lives, as opposed to being specifically collected in a clinical study. When such data is analysed, the information produced may be referred to as real-world evidence (RWE).

When sponsors plan to conduct clinical trials or research using RWD, the Medicines & Healthcare Products Regulatory Agency (MHRA) supports them through guidance and scientific advice. Through their guidelines and engagement with sponsors, the MHRA assists in improving the design of studies, ensuring the quality of the source data is acceptable, and learning how to gain approval for studies to be run in the UK.

MHRA has recently published 2 guidelines (https://www.gov.uk/government/publications/mhra-guidance-on-the-use-of-real-world-data-in-clinical-studies-to-support-regulatory-decisions) for sponsors planning to conduct clinical research using RWD to support regulatory decision-making. Guideline development work is ongoing to produce additional advice, including on use of RWD as an external control arm (cohort of patients which can provide potential comparator information to contextualise the results from single arm non-randomised clinical trials), which would be particularly applicable to rare diseases. These guidelines are due to be published in 2023.

In addition, NICE published its real-world evidence (RWE) framework (https://www.nice.org.uk/about/what-we-do/real-world-evidence-framework) in June 2022. The framework describes best practices for planning, conducting and reporting real-world evidence studies. The aim is to improve the quality and transparency of evidence submissions, to ensure that real-world data can be used to fill evidence gaps and speed up patient access to innovative and effective treatments.

This year, NICE will focus on the operationalisation of the RWE framework, including running training sessions, providing early advice to evidence-developers on the use of RWD, and feeding back to evidence-developers on how to improve the quality and transparency of the evidence presented, to support committee decision-making.

Underpinning themes

Patient voice

It is vital that our policy continues to be shaped by the needs and experiences of those living with rare conditions. With this in mind we, and our delivery partners, have consulted with the community throughout action plan development.

The UK Rare Diseases Forum is essential in putting forward constructive and collective stakeholder views, reflecting experiences across the 4 nations. In response to feedback from members, this year we have changed the forum's operations to amplify patient voice. We have also invited forum members and the rare diseases community to form Independent Advisory Groups (IAGs) to formulate recommendations relevant to all 4 nations of the UK. The first IAG will focus on development of quality standards (see below) for rare diseases, and the call for proposals remains open. All 4 UK nations have committed to formally recognising IAGs, considering their outputs and reporting back how their feedback has been used.

In partnership with Genetic Alliance UK, we have established the England Rare Diseases Action Plan Patient Advisory Group to facilitate greater input into rare diseases action plans from the perspective of people with lived experience. Their input was shared with the England Rare Diseases Framework Delivery Group, and has been central to shaping the action plan.

All actions for the coming year place patient voice centrally, drawing on their wealth of knowledge and experience to shape services, design meaningful research and ensure we measure what matters most to people living with rare diseases. There is still more to do and we will continue to consult with stakeholders as we monitor progress of current actions and develop England's next Rare Diseases Action Plan.

Delivery partners' engagement activities

HEE's Genomics Education Programme (GEP) has established a patient advisory group called Patient Advisors for Genomics Education (PAGE). This ensures that the voice of patients with cancer and rare disease, as well as that of the general public, is embedded across the work of the GEP.

Patient and public voice representatives are included in the membership of the UK National Screening Committee (UK NSC) Bloodspot Task Group to help the UK NSC make recommendations about new or modified screening programmes.

NICE has engaged with stakeholder groups or nominated experts for over 10 different ultra-rare disease areas where it was undertaking evaluations in 2022.

Genomics England's Participant Panel continues to meet regularly on a wide variety of topics. Genomics England has also carried out regular structured engagement work related to the Newborn Genomes Programme, as detailed in section 1.

National and international collaboration

The small numbers of people with individual rare diseases make collaboration essential. The UK is committed to building national and international connectivity so that data and expertise can be shared for the benefit of people living with rare diseases. We continue to engage with the World Health Organisation (WHO) and Rare Diseases International on development of the important Global Network for Rare Diseases initiative, which will pool resources and connect centres of excellence around the world, to improve diagnosis and care for people living with a rare disease.

We also engage with the Horizon Europe Partnership on Rare Diseases (https://ec.europa.eu/info/research-and-innovation/funding/funding-opportunities/funding-programmes-and-open-calls/horizon-europe/european-partnerships-horizon-europe/candidates-european-partnerships-health_en), due to begin in autumn 2024. To support UK input into the proposal for the partnership, we have worked with Newcastle University to establish an International Mirror and Action Group, bringing together UK researchers working on rare diseases.

Pioneering research

We are committed to supporting ground-breaking, innovative research. The 2022 autumn statement (https://www.gov.uk/government/publications/autumn-statement-2022-documents) confirmed an increase in public spending on research and development (R&D) to £20 billion a year by the 2024 to 2025 financial year, enabling the government to strengthen our world-leading R&D and cement the UK's position as a science superpower and innovation nation.

Many of the actions outlined in this action plan either support, or are supported by, research. Examples include commissioning research to provide the evidence needed to operationalise better coordination of care in the NHS (action 17), and improving the findability of people living with rare diseases using NCARDRS (action 22). We will also publish an initial report on the UK rare diseases research landscape in 2023, based on mapping in partnership with MRC and NIHR (action 15).

The NIHR Biomedical Research Centres

In October 2022, the NIHR announced a new investment of nearly £790 million in 20 Biomedical Research Centres (BRCs) across the country. The NIHR BRCs enable effective collaboration between world-leading universities and the NHS, bringing together academics and clinicians to translate scientific breakthroughs into potential new treatments, diagnostics and medical technologies. Out of the 20 NIHR BRCs, at least 17 will support research into rare conditions (see examples in box 3).

Box 3: rare diseases research at NIHR Biomedical Research Centres (BRCs)

Great Ormond Street Hospital (GOSH) BRC

Severe combined immunodeficiency due to adenosine deaminase deficiency, also known as ADA-SCID, is a rare, life-threatening disease that prevents children from living a normal life. Children with ADA-SCID have no immune system and, if left untreated, the condition can be fatal within the first 2 years of life.

To tackle ADA-SCID, GOSH BRC is developing a new gene therapy that has shown promising results in initial clinical trials (https://www.gosh.nhs.uk/news/gene-therapy-offers-a-potential-cure-to-children-born-without-an-immune-system/). Two to 3 years after the treatment, all of the 50 children treated with the new gene therapy are alive and well, with no serious side effects reported. Of these, 48 are no longer showing symptoms of ADA-SCID. In the 2 cases in which treatment wasn't successful, both children were able to return to current standard treatments.

If approved, gene therapy would be a welcome new treatment option for ADA-SCID as it is a one-time procedure that has the potential to provide life-long results.

University College London Hospital (UCLH) BRC – novel gene therapy for haemophilia A

Research supported by NIHR UCLH BRC has led to a ground-breaking therapy that could lead to a cure for haemophilia (https://www.uclhospitals.brc.nihr.ac.uk/news/groundbreaking-therapy-could-cure-haemophilia). Patients with haemophilia have a genetic defect that affects their body's ability to stop bleeding. After a single dose of this novel gene therapy, patients with haemophilia A experienced an increase in the missing protein that helps their blood clot and fewer bleeding events.

Newcastle BRC - UK gene therapy first for Duchenne muscular dystrophy

Biomedical Research Centre researchers in Newcastle have launched the UK arm of a global gene therapy study in Duchenne muscular dystrophy (https://www.newcastlebrc.nihr.ac.uk/key-milestone-first-uk-patient-enrolled-in-dmd-gene-therapy-trial-at-dmd-hub-site/). This is the first time gene therapy has been given in the UK to a patient with Duchenne muscular dystrophy, for which there is currently no approved disease-modifying treatment.

The MRC NIHR Rare Diseases Research Platform

One of the major challenges in rare diseases research is being able to bring the right expertise, people and technology together for impactful research. To address this, MRC and NIHR launched a joint funding call in September 2022, to form a new UK Rare Disease Research Platform

(https://www.ukri.org/opportunity/establish-an-integrated-uk-rare-disease-research-platform-nodes/).

The platform will facilitate greater collaboration between academic, clinical and industry research, and people living with rare diseases, research charities and other stakeholders, to accelerate the understanding, diagnosis and therapy of rare diseases. The platform brings together challenge-led thematic nodes, with a central hub to support networking and activities that enable research. A total of £12 million is available to fund up to 10 nodes over 5 years. Outcomes of the call are expected in April 2023.

Digital, data and technology

Secure, linked datasets containing standardised, interoperable data can be used to improve diagnosis, locate consenting individuals for research, improve coordination of care, and obtain information on the prevalence and distribution of rare diseases.

England's 2022 data strategy, Data saves lives: reshaping health and social care with data (https://www.gov.uk/government/publications/data-saves-lives-reshaping-health-and-social-care-with-data/data-saves-lives-reshaping-health-and-social-care-with-data#improving-trust-in-the-health-and-care-systems-use-of-data), outlines how data will be used to benefit all parts of health and social care. Commitments include:

- investing in secure data environments to power life-saving research and treatments
- using technology to allow staff to spend more quality time with patients
- giving people better access to their own data through shared care records and the NHS app

Underpinning work aims to increase public trust and improve transparency in how the health and care system uses data.

A joint funding package of up to £200 million (https://www.gov.uk/government/news/260-million-to-boost-healthcare-research-and-manufacturing) between NHSE, DHSC and the Department for Business, Energy & Industrial Strategy (BEIS) was announced in March 2022. Funding will support NHS research data infrastructure and data enabled clinical trials, including in genomics, and national and sub-national secure data environments (SDEs).

These investments, designed to make health data more securely accessible and linkable for research and development, have direct implications for people living with rare conditions. An England-wide ecosystem will enable research access to secure, high-quality, linked datasets at national and subnational levels. Clinical trials capacity will be increased by embedding clinical trial operations within NHS health data, improving the efficiency of trial set up, and increasing the volume of people recruited.

Following a competitive process, £13.5 million of funding for development of subnational secure data environments was awarded to NHS organisations in November 2022. Two genomics driver projects will develop and test approaches to data linkage and federation, sharing learning to inform design of subnational SDEs.

Focus area: registries

Rare disease registries play an important role in increasing understanding of rare diseases. All 4 national registries in the UK[footnote 1] continue to meet regularly to share best practice and agree consistent approaches. All registries are committed to maximising their ability to access and share data to facilitate collaborative research. National registries provide a central repository for rare diseases data and have strategic importance in delivery of the UK Rare Diseases Framework. Data needs to be reported to such registries in a standardised way to enable efficient, effective and equitable use and re-use of securely-held data, to support population-level clinical research.

Over the coming year, we will explore the possibility of NIHR and UKRI-MRC, as the major government funders of rare disease research, requiring researchers to report relevant rare disease data to NCARDRS (or other national registry) as a condition of funding.

In December 2022 we partnered with NCARDRS to host a stakeholder workshop to discuss the challenges and opportunities for population-based rare disease registration. This enabled us to better understand stakeholder data-related needs. We will hold a second workshop to build on this initial discussion and to start to identify solutions, building on existing services. A report and recording of this workshop will be made available on the NDRS website.

Wider policy alignment

While the framework and action plan represent the government's primary commitments to the rare disease community, they are also closely aligned with wider initiatives, including the recently published 2022 to 2025 implementation plans for both The Future of UK Clinical Research Delivery (https://www.gov.uk/government/publications/the-future-of-uk-clinical-research-delivery-2022-to-2025-implementation-plan) and Genome UK (https://www.gov.uk/government/publications/genome-uk-2022-to-2025-implementation-plan-for-england).

Improving the lives of those living with rare diseases goes beyond healthcare, encompassing a range of public services, including support for physical and learning disabilities. It is important these needs are considered holistically. A number of policy initiatives supporting people with disabilities have either recently been announced or are expected in the coming months (see annex D). Importantly for people living with rare conditions and their families, provision of support is based on an assessment of need, removing barriers associated with disease or diagnostic status.

UK-wide alignment of rare diseases policy

All 4 UK nations have now published their rare diseases action plans. We continue to work closely with the devolved administrations to ensure policy is aligned across the UK, and that we learn from progress made by all nations. As part of this, we will consider Rare Disease UK's 'Recommendations for the Rare Disease Action Plans' report (https://geneticalliance.org.uk/gauk-news/news/rare-voice-in-policy-2/), which identifies areas of potential learning and collaboration.

We will also adopt a UK-wide approach wherever possible, for example through the inclusion of research from Northern Ireland, Scotland and Wales under action 15 ('map the rare disease research landscape to identify gaps and priorities for future funding').

Health equity

People living with rare conditions and their families can face significant barriers to accessing the care and support that they need. Equity is a key theme of the Rare Disease Day campaign (https://www.rarediseaseday.org/what-is-rare-disease-day/), and a central tenet of the 2021 UN General Assembly resolution on persons living with a rare disease (https://www.rarediseasesinternational.org/un-resolution/).

Steps to reduce health inequalities are embedded across the actions in this plan. We remain committed to considering the additional challenges faced by people from diverse and marginalised communities who are affected by a rare condition. In December 2022, we partnered with Breaking Down Barriers to run a focus group on health equity, looking at progress over the past year, and identifying opportunities for further improvements. A report of this focus group meeting will be available on the Breaking Down Barriers website (https://breaking-down-barriers.org.uk/). In the coming year, we will continue to explore how to build on the group's findings.

Our delivery partners are also actively engaged in promoting health equity and working to reduce health inequalities. All NCARDRS outputs include analysis by domains of deprivation, where appropriate, enabling these to be measured and acted on. The Diverse Data initiative at Genomics England has been established with the aim of reducing health inequalities and improving outcomes for all communities in genomic medicine.

Case study: insights from the Sickle Cell Whole Pathway Review

Over the past year, NHS England has carried out a comprehensive programme of work investigating health inequalities faced by individuals living with sickle cell diseases, which is a rare disease in the UK. This work involved gathering evidence from a range of sources, including people living with sickle cell disease, clinicians, service providers and policy makers. Key

findings from this work included the need for developing a clinical care pathway that enables prompt access to specialist care, access to electronic care plans and the need to educate and train healthcare practitioners and the public about the condition.

As a result of this work, the ‘Can you tell it’s Sickle Cell?’ campaign was launched, as part of a bigger drive to improve sickle cell care across the NHS. This campaign included the development of new resources, including an e-learning module, which aims to improve understanding of health inequalities related to sickle cell. These resources will be made available in June 2023. Additionally, as a result of this work, a specific programme of work has been stepped up to improve the delivery of clinical services to the patient group.

It is likely health inequalities faced by people living with other rare diseases echo those of people living with sickle cell disorders. Therefore, this programme of work around sickle cell can serve as an exemplar case study for future initiatives examining the health inequalities faced by the rare disease community.

Action 28: develop a plan to include rare diseases in NHS England’s Core20PLUS5 framework

NHS England has developed an approach called Core20PLUS5 (https://www.england.nhs.uk/about/equality/equality-hub/national-healthcare-inequalities-improvement-programme/core20plus5/) to support NHS integrated care systems (ICSs) reduce health inequalities at both national and local levels. The approach defines a target population that would benefit from a tailored healthcare approach to improve healthcare inequalities, and identifies 5 focus clinical areas requiring accelerated improvement.

‘Core20’ refers to the most deprived 20% of the national population as identified by the national Index of Multiple Deprivation (IMD). ‘PLUS’ refers to population groups that are likely to experience poorer than average health access, experience and/or outcomes, but are not identified by the IMD. ‘PLUS’ population groups are determined locally by ICSs based upon national NHSE recommendations and evidence from ICS population health data. Together, ‘Core20PLUS5’ provides a prioritisation framework to inform the work of ICSs in improving health equity from 2021 to 2024.

Over the coming year, we will work in partnership with NHS England to gather evidence to support the inclusion of rare diseases as an example of a ‘PLUS’ population group. The rare diseases community will be consulted throughout the process, to ensure that the evidence gathered appropriately reflects the lived experience of people living with rare diseases. Progress will be reported in the 2024 England Rare Diseases Action Plan. Recognising rare diseases within the Core20PLUS5 framework would raise the profile of health inequalities faced by people living with rare diseases at both national and system levels. This would

enable ICSs to prioritise these conditions and develop targeted actions to reduce health inequalities associated with rare diseases.

Focus area: monitoring and evaluation

All actions in England's action plans are underpinned by a logic model, describing the outputs and outcomes that will be delivered, and the metrics used to measure progress. The England Rare Diseases Framework Delivery Group will continue to meet regularly to monitor ongoing actions and identify any barriers to implementation.

We will also continue to work across the 4 UK nations to align policy and share best practice. Stakeholder feedback will be sought through the UK Rare Diseases Forum, with regular progress reports available through the online platform. England's third action plan will be published in 2024, and will report on progress against the actions set out here as well as proposing updated and new actions.

Action 29: commission portfolio level evaluation of England's Rare Diseases Action Plans with input from the rare disease community on design of metrics

In addition to progress against individual actions, we committed in the 2022 action plan to determining whether the actions are collectively achieving meaningful progress against the 4 priorities of the UK Rare Diseases Framework, and bringing about real change for people living with rare diseases.

In the coming year, DHSC will commission policy research through an NIHR open call, inviting researchers to work with the rare diseases community and wider stakeholders (including industry and the third sector) to develop metrics and methodology to measure improvement of the lives of people living with rare diseases in the UK across the 4 priority areas; and to apply these metrics to assess the outcomes of the framework as delivered through England's action plans.

Evaluating the influence of the framework will tell us whether the interventions over this 5-year period have been effective in making a difference to what matters most to the rare diseases community, and will help shape future rare diseases policy. The outcomes of this research will help identify areas of potential inequality, enabling us to focus efforts towards outstanding areas of need.

Outcomes of the 2-stage application process are expected by autumn 2023, with research commencing as soon as possible after contracting. The outcome of the call, the successful research proposal, and progress made in the interim, will be reported in the 2024 action plan. We envisage that the first phase (developing metrics) could begin in 2023, with the actual evaluation to take place between 2024 and 2025. Interim findings will be used to develop the next phase of rare diseases policy, and a final report will be published following the end of the framework in 2026.

Future directions

This action plan provides an update on progress against the 16 actions outlined in England's first action plan, as well as setting out 13 new actions for 2023 and 2024. As outlined in section 1, we continue to take significant steps towards achieving the priorities of the UK Rare Diseases Framework. We will work closely with the community to continue to deliver on these priorities in the year ahead.

While we remain committed to improving the lives of those living with rare conditions, this commitment is set against the backdrop of a challenging delivery environment. This includes challenges across the health and care system following the COVID-19 pandemic, and organisational changes, including the transition of NHS Digital and Health Education England into NHS England in 2023. These organisational moves will inevitably impact on how quickly progress can be made over the next year. However, the creation of a single organisation responsible for data, digital technology and workforce for the NHS will ultimately translate into patient benefit, and ensure the health and care sector is fully equipped to face the future and deliver for patients.

In the coming year, therefore, we will focus on progressing and completing existing actions, including ongoing actions from the 2022 action plan. Progress will be reported in minutes of meetings of the England Rare Diseases Framework Delivery Group, with a more detailed report in the 2024 England Rare Diseases Action Plan. At the same time, we will continue to engage with stakeholders through the UK Rare Diseases Forum and online platform to gather feedback on implementation of actions. Recognising that there is always more to do, we will also continue to work with the England Rare Diseases Action Plan Patient Advisory Group to define remaining priority gaps.

Most importantly, we will ensure, through ongoing dialogue, that people living with rare conditions remain at the heart of the decision-making process, and that this policy continues to be shaped by the views of those whose lives it will impact the most.

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1. The National Congenital Anomaly and Rare Disease Registration Service in England, the Congenital Anomaly Register and Information Service (CARIS) in Wales, the Congenital Anomaly and Rare Disease Registration and Information System Scotland (CARDRISS), and the Northern Ireland RAre Disease and Congenital Anomalies Register (NIRADCAR).

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