Health Information and Quality Authority

An tÚdarás Um Fhaisnéis agus Cáilíocht Sláinte

Review of national rare disease strategies in selected countries

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About the Health Information and Quality Authority (HIQA)

The Health Information and Quality Authority (HIQA) is an independent statutory authority established to promote safety and quality in the provision of health and social care services for the benefit of the health and welfare of the public.

HIQA's mandate to date extends across a wide range of public, private and voluntary sector services. Reporting to the Minister for Health and engaging with the Minister for Children, Equality, Disability, Integration and Youth, HIQA has responsibility for the following:

- **Setting standards for health and social care services** — Developing person-centred standards and guidance, based on evidence and international best practice, for health and social care services in Ireland.

- **Regulating social care services** — The Chief Inspector within HIQA is responsible for registering and inspecting residential services for older people and people with a disability, and children's special care units.

- **Regulating health services —** Regulating medical exposure to ionising radiation.

- **Monitoring services** — Monitoring the safety and quality of health services and children's social services, and investigating as necessary serious concerns about the health and welfare of people who use these services.

- **Health technology assessment** — Evaluating the clinical and cost-effectiveness of health programmes, policies, medicines, medical equipment, diagnostic and surgical techniques, health promotion and protection activities, and providing advice to enable the best use of resources and the best outcomes for people who use our health service.

- **Health information** — Advising on the efficient and secure collection and sharing of health information, setting standards, evaluating information resources and publishing information on the delivery and performance of Ireland's health and social care services.

- **National Care Experience Programme** — Carrying out national service-user experience surveys across a range of health services, in conjunction with the Department of Health and the HSE.

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Foreword

A national rare disease strategy sets out a country's plan to support people with rare diseases or disorders to ensure that they receive the best possible care and support throughout their lives. While individual rare diseases or disorders vary greatly, there are common clinical challenges, in that they are difficult to diagnose, they often require highly specialised care, and optimal treatment and care pathways are often not achieved. National rare disease strategies therefore aim to provide a unified approach to reducing the burden of rare diseases, and improving the quality of care for people with rare diseases.

Ireland's first national rare disease strategy was the *National Rare Disease Plan for Ireland 2014 – 2018*. In February 2023, the Minister for Health announced a commitment to developing a new National Rare Disease Plan, in line with the Programme for Government. An understanding of the issues of importance identified in other countries' national rare disease strategies, the structures used to support strategy implementation, and how these compare to Ireland's previous national strategy, may help to inform the development of a new national rare disease strategy in Ireland. This report contains an international review of national rare disease strategies in selected countries, conducted at the request of the Department of Health.

Work on this review was undertaken by an Evaluation Team from the Health Technology Assessment Directorate in HIQA. An Expert Advisory Group was convened to advise the Evaluation Team during the course of the review. HIQA would like to thank its Evaluation Team, the members of the Expert Advisory Group and all who contributed to the preparation of this report.

Dr Máirín Ryan

Deputy Chief Executive & Director of Health Technology Assessment

Acknowledgements

HIQA would like to thank the representatives from within the selected countries approached during data verification and all members of the Expert Advisory Group (EAG) listed below who provided their time, advice and information in support of this work.

HIQA notes that membership of the EAG involves review of evidence synthesis documents; it does not necessarily imply agreement with all aspects of the evidence synthesis report.

The membership of the EAG was as follows:

Dr Ayesha Ali	Medical Advisor for Highly Specialised Services, NHS England.
Dr Mark Bale	Interim Director, National Genetics and Genomics Office, Health Service Executive.
Ms Vicky McGrath	Chief Executive Officer, Rare Diseases Ireland.
Mr Ciarán Murphy	Assistant Principal Officer, Rare Disease & Long Covid Policy, Department of Health.
Prof Eileen Treacy	Clinical Lead, National Rare Diseases Office, Health Service Executive.

The following members of the HTA directorate contributed to the management, technical writing or dissemination of this report:

Valerie Power, Louise Larkin, Michelle Norris, Michelle O'Neill, Michelle O'Shea, Ellen Reidy, Máirín Ryan, Debra Spillane, Susan Spillane, Dana Swanton.

Conflicts of interest

Dr Mark Bale works as an external consultant for IQVIA. IQVIA conducts clinical trials and investigations around cell and gene therapy, and analyses real world and health data sets related to rare disease.

List of abbreviations used in this report

COVID-19	coronavirus disease 2019
ERN	European Reference Network
EU	European Union
EUCERD	the European Union Committee of Experts on Rare Diseases
EUROPLAN	the European Project for Rare Diseases National Plan Development
EURORDIS	EURORDIS-Rare Diseases Europe
HSE	Health Service Executive (Ireland)
NAMSE	National Action League for People with Rare Diseases (Germany)
NAP	National Action Plan (Austria)
NCPRD	National Clinical Programme for Rare Diseases
NKSE	National Coordination Centre for Rare Diseases (Austria)
NRDO	National Rare Diseases Office (Ireland)
SWAN	Syndrome Without A Name
UK	United Kingdom
UN	United Nations
WHO	World Health Organization

Key points

- This report provides a review of national rare disease strategies in selected countries. The findings of this review will support the work of the Department of Health in developing an updated national rare disease strategy in Ireland.
- National rare disease strategies were identified from 12 selected countries: Austria, Australia, Denmark, England, Finland, France, Germany, the Netherlands, Northern Ireland, Portugal, Scotland and Wales. The *National Rare Disease Plan for Ireland 2014 – 2018* was also included for comparison.
- A descriptive analysis of strategy contents, including aims, themes and priorities, implementation, governance, and funding models, was undertaken.

Strategy contents:

- Improving treatment and coordination of care was identified as an overall aim in the majority of national rare disease strategies. Aims relating to improving the diagnosis of rare diseases, increasing awareness and or communication in the area of rare diseases, and educating and involving patients, were also identified.
- Strategy themes and priorities identified in all 12 selected countries included: screening and diagnosis; access to healthcare and coordination of services; rare disease research; and patient representation and empowerment. Further themes or priorities which were frequently identified included: access to orphan medicines and innovative health technologies; health information systems and patient registries; and health workforce education and training.
- Strategy implementation details included:
  - descriptions of actions planned or in progress
  - implementation agencies
  - outcomes or measures for monitoring and evaluating strategy implementation.
- Implementation actions were related to strategy themes and priorities. The level of detail reported for actions varied between countries; ten countries described detailed implementation actions and two countries outlined high-level strategic actions in their national strategies.
- Six countries outlined implementation agencies that were responsible for leading or collaborating on the implementation of all actions in their national

strategies. A further five countries outlined implementation agencies for some, but not all, actions. One country, Australia, did not specify which particular agencies would implement the actions.

- Outcomes or measures related to strategy evaluation or monitoring were outlined in four countries' strategies. Three countries also outlined that strategy implementation indicators were to be developed. However, these were not identified at the time of data extraction.

- Strategy governance was ultimately the responsibility of national ministries for health, or equivalent, with collaboration in some countries from ministries with responsibilities for sectors such as education, research, and social security.

- The governance and or organisational structures through which strategies were developed, implemented, monitored and evaluated varied between countries. These structures involved existing health authorities, newly-established bodies, or a combination of both. Eight countries established dedicated bodies to oversee and coordinate national rare disease strategy implementation.

- Seven countries outlined that funding was allocated to either overall strategy implementation, individual strategy priorities and or individual strategy actions. Funding sources included European Commission funding, government funding and delivery partners' budgets. Five countries outlined that lack of funding was a challenge to, and constraint of, strategy implementation.

Comparison with National Rare Disease Plan for Ireland 2014 – 2018:

- The *National Rare Disease Plan for Ireland 2014 – 2018* shared similar aims, themes and priorities to the reviewed national rare disease strategies. However, unlike Ireland, a number of the selected countries also prioritised themes of health workforce education and training, and access to mental health and psychology services.

- Ireland, Denmark and the Netherlands outlined 'recommendations' in their national strategies. Six other countries described more definitive 'actions' in their strategies. The remaining four countries outlined 'proposed actions', 'planned activities' or 'measures'.

- Unlike Ireland, three of the 12 countries published annual action plans to accompany their national strategies. These plans included details of the tasks or outputs planned for that year, and the entities responsible for their delivery.

- Implementation actions varied, reflecting the national context of each country and the time of strategy development. For example, unlike Ireland, five strategies published since 2020 included actions related to advances in genetics and genomics.

- The governance and organisational model outlined in the *National Rare Disease Plan for Ireland 2014 – 2018* shared a number of similar features to the models outlined in the strategies of the selected countries. Examples included the use of a combination of existing and newly-established structures within the health service to implement and monitor strategy recommendations, and the establishment of an Oversight Group that reports to the Department of Health.

- Like Ireland, five countries did not specify a funding model in their strategies.

Overall:

- The rare disease policy landscape is complex and spans multiple sectors such as health, social care, education, and disability. A national rare disease strategy aims to provide a unified approach to reducing the burden of rare diseases, and improving the quality of care for people with rare diseases.

- The current review describes national rare disease strategies in 12 selected countries, and outlines insights into what countries identified as issues of importance, actions undertaken, and the governance and funding structures used to support the implementation of rare disease strategies. This will inform the development of an updated national rare disease strategy in Ireland.

Plain language summary

A rare disease or disorder is a condition which affects very small numbers of people. However, there are many different kinds of rare diseases or disorders. For example, in the European Union (EU), there are more than 6,000 known rare diseases or disorders. These conditions commonly require very specialised health services, often termed as 'highly specialised care'. People with rare diseases or disorders may find it hard to access the care they need. This can be because experts and other healthcare staff who understand the condition may not be available locally, or even in the patient's own country.

A national rare disease strategy is a document that lays out a country's plan to support people with rare diseases or disorders, and address the important issues they face. National rare disease strategies aim to make sure people with rare diseases or disorders can access the care they need.

This review describes national rare disease strategies in 12 countries: Austria, Australia, Denmark, England, Finland, France, Germany, the Netherlands, Northern Ireland, Portugal, Scotland and Wales. These countries were chosen mainly because they had published their national strategies after or at the same time as Ireland's strategy, the *National Rare Disease Plan for Ireland 2014 – 2018*.

For each country, the report describes the following:

- what the strategy set out to do and over which years
- the main topics in the strategy (for example, exploring access to health services or how to make it easier for patients to get a diagnosis)
- the actions suggested in the strategy (for example, an action to make it easier for patients to get access to a new treatment)
- who was responsible for the actions suggested and how the countries would check that the actions are carried out
- how the countries plan to pay for these actions.

The report also compares the strategies from these countries to the *National Rare Disease Plan for Ireland 2014 – 2018*.

The strategies from all of the selected countries focused on screening and diagnosis, access to healthcare, research, and how to make sure that patients are included in rare disease or disorder decision-making. Most of the selected countries also focused on access to new treatments, setting up and improving systems for recording how many people have different types of rare diseases or disorders, and educating and training healthcare staff.

Ten countries described in detail how they would carry out their strategy, with three countries having yearly action plans for their national strategies. These yearly action plans included the tasks for each year and who would be responsible for them. Strategy actions differed by country and by when the strategy was developed. For example, five strategies published since 2020 referred to genetic testing, that is, testing a person's DNA to look for changes that can cause health problems.

In most countries, the department or ministry of health was responsible for the strategy. In some countries, the responsibility was shared with other government departments, like the department of education or social security.

Eight of the countries set up specific groups or organisations to be in charge of putting the national rare disease strategy into action. The Irish *National Rare Disease Plan* set out to use both existing organisations and new groups within the health service. Ireland also set up an Oversight Group – this group reported back to the Department of Health on progress.

Seven countries described how they paid for their national rare disease strategies to be carried out. The money came from sources including the European Commission, the national government, and the existing budgets of organisations involved in carrying out the strategy. Like Ireland, five countries did not mention a specific funding source for their strategies. A lack of funding was described as a challenge to carrying out the strategy actions.

This report describes the national rare disease strategies of 12 selected countries. The findings of this report will help the Department of Health when developing an updated national rare disease strategy for Ireland.

1 Background

According to Rare Diseases International and the World Health Organization (WHO), a rare disease is defined as "a medical condition with a specific pattern of clinical signs, symptoms, and findings that affects fewer than or equal to 1 in 2,000 persons living in any WHO-defined region of the world."[1] Similarly, the European Commission considers a disease to be rare if it affects fewer than 5 in 10,000 people in the European population.[2] Within the European Union (EU), there are more than 6,000 known rare diseases or disorders affecting up to 6% of the population.[3] While rare diseases or disorders vary greatly, there are common clinical challenges, in that they are difficult to diagnose, they often require highly specialised care, and optimal treatment and care pathways are often not achieved.[4] Due to their complexity, rare diseases or disorders have been considered a policy priority at both national and European level since the 1990s.[5]

Across the EU, rare disease policy and strategy development progressed rapidly following the European Commission's Communication on Rare Diseases in 2008,[2] and the subsequent Council of the European Union's *Recommendation on an action in the field of rare diseases* in 2009.[6] This is supported at a global level with the United Nations (UN) resolution on *Addressing the Challenges of Persons Living with a Rare Disease and their Families*.[7] Initiatives such as the European Project for Rare Diseases National Plan Development (EUROPLAN),[8] the European Union Committee of Experts on Rare Diseases (EUCERD) Joint Action,[9] the EU joint action on Data and Policies for Rare Diseases (RD-ACTION),[10] the EU-funded Rare 2030 project on foresight in rare disease policy,[11] and the Global Network for Rare Disease[12] have contributed to this progress. These initiatives have supported the development and implementation of national rare disease strategies, the sharing of expertise and experiences, and the linkage of national efforts with a common strategy, particularly at European level. Despite this, opportunities for further progress with respect to policy and strategy were outlined in the Rare 2030 recommendations. These recommendations were developed from a two-year study with over 200 thought leaders in the field of rare diseases and with thousands of people living with rare diseases. It aimed to set out a roadmap for rare disease policy in Europe from 2020 to 2030. The recommendations included calls for a European policy framework for rare diseases, and for all European countries to implement a renewed national rare disease plan or strategy by 2025.[13]

The benefits to implementing national rare disease strategies include visibility and transparency around national activities and programmes.[5] Their implementation is supported by the WHO[14] and EURORDIS-Rare Diseases Europe (EURORDIS).[15] While EURORDIS recommend guaranteeing rare disease patients' access to timely and adequate medical and social care as an overall national strategy goal, a wide

variation of approaches to national rare disease strategies development and implementation has been reported at both European level and internationally.[5, 16] For example, while some countries adopt high-level, broad national rare disease strategies, others adopt national rare disease plans, which may be composed of more specific, measureable actions.[5] Additionally, the level to which government policy or legislation underpins a national rare disease strategy can vary considerably between countries.[16]

This observed variation in national strategies may have been further increased by the COVID-19 pandemic, during which the care of people with rare and undiagnosed diseases was impacted.[17] Dependent on an individual country's level of disruption to care services during the pandemic, their national priorities and actions for tackling rare diseases or disorders may have altered. In light of this disproportionate impact on people with rare diseases, in 2021, the UN General Assembly called on member states to strengthen their health systems and adopt national strategies that promote universal health coverage and protect the human rights of people living with a rare disease and their families.[7] This resolution was revised in 2023, with Ireland as a co-sponsor.[18]

The first National Rare Disease Plan for Ireland covered the period from 2014 to 2018.[19] It set out a vision where people with rare diseases receive timely access to the best possible evidence-based, patient- and family-centred care throughout their lives, and have their needs and experiences recognised, understood and addressed within all aspects of the Irish health system. In February 2023, the Minister for Health announced a commitment to developing a new National Rare Disease Plan, in line with the Programme for Government.[20] This was followed in December 2023 by the establishment of Ireland's National Rare Disease Steering Group, tasked with developing this new plan.[21] This report aims to gain an updated understanding of national rare disease strategies in other selected countries, and to describe the key aims, priorities, and actions relevant to rare disease strategies. This review was conducted at the request of the Department of Health and will inform the development of an updated national rare disease strategy in Ireland.

2 Methods

A detailed summary of the methods used for this review is provided in the *Protocol for review of national rare disease strategies in selected countries* (available at www.hiqa.ie). In brief, this review presents a synthesis of national rare disease strategies in 12 countries (excluding Ireland). The countries included were selected on the basis of having published a national rare disease strategy after or at a similar time to the publication of the *National Rare Disease Plan for Ireland 2014 – 2018*,[19] combined with other factors such as geographical proximity to Ireland, population

size, organisation of health services, European Union membership and or the availability of documents in English.

Seven EU/EEA countries were included (Austria, Denmark, Finland, France, Germany, the Netherlands, and Portugal), as well as the UK (England, Northern Ireland, Scotland, and Wales) and Australia. Additionally, information from the *National Rare Disease Plan for Ireland 2014 – 2018* was extracted for comparison with the selected countries.[19]

National rare disease strategies included, but were not limited to:

- broad overview strategies (which may include themes, priorities and actions, for example)
- strategy implementation plans and or frameworks
- strategy evaluation plans and or frameworks
- legislation, rules, regulations and mandates
- policies.

Within these documents, relevant information included, but was not limited to, the following elements:

- strategy timelines
- aims
- themes and priorities (for example, improving access to treatment, promoting research into rare diseases or disorders)
- targets (if identified)
- implementation actions (for example, information about the types of actions and with whom responsibility for implementation lies)
- governance and organisational structures
- funding model(s) (for example, government funding, EU funding and research specific funding).

When identifying relevant documents, local, territorial or provincial, and global-focused rare disease strategies were considered out of scope.

Information on national rare disease strategies was primarily sought from government resources (websites, reports and press releases), with representatives from key national-level organisations contacted for confirmation and additional resources as appropriate. Information identified up until 30 November 2023 was included for analysis within this review.

Throughout this report, the term 'rare diseases' is used as a general term to refer to rare diseases and disorders that may or may not be symptomatic or diagnosed.

3 Findings

The findings of the review are presented in three main sections, as follows:

- **Section 3.1 Identified information:** presents a descriptive summary of the relevant identified information.
- **Section 3.2 Strategy contents:** presents a summary of strategy contents including aims, themes, actions to be implemented, governance structures, and funding models.
- **Section 3.3 Comparison with the National Rare Disease Plan for Ireland 2014 – 2018:** presents a summary of the similarities and differences between the included strategies and the *National Rare Disease Plan for Ireland 2014 – 2018*.[19]

3.1 Identified information

Relevant national rare disease strategies were identified for all 12 of the selected countries and also for Ireland (see Table 3.1). Multiple documents and or resources were identified for ten of the selected countries and for Ireland (Australia,[22, 23] Austria,[24-26] Denmark,[27-30] England,[27-30] Germany,[31, 32] Ireland,[19] the Netherlands,[29, 33, 34] Northern Ireland,[33, 34] Portugal,[35-41] Scotland[42] and Wales[43]). These documents and or resources included main strategies and or actions plans; strategy evaluation and or recommendation documents; and supporting documents.

To confirm the identified information, and to identify any additional relevant resources, key representatives for all 12 selected countries were contacted by email. Contact was made with key representatives in ten countries (Australia, Austria, Denmark, England, Finland, Germany, Northern Ireland, Portugal, Scotland and Wales). All of these countries confirmed the documents identified, with only Australia outlining a further resource that was relevant to include in the review. A key representative from Germany provided details of a research report.[44] However, this report was not included in the review as it did not meet the definition of a national rare disease strategy, as outlined in the protocol. Contact was attempted, but could not be made with representatives for France and the Netherlands.

Table 3.1 National rare disease strategy documents or resources identified for Ireland and the selected countries.

Country	Main strategy and or action plan document(s)	Strategy evaluation and or recommendation document(s)	Supporting document(s) (for main strategy or evaluation)
Ireland	National Rare Disease Plan for Ireland 2014 – 2018[19]	National Rare Disease Plan for Ireland: An Interim Report on Implementation[45] and Summary of Recommendations[46]	N/A
Australia	National Strategic Action Plan for Rare Diseases 2020[22]	Implementing the National Strategic Action Plan for Rare Diseases: May 2023 Status Report[23]	N/A
Austria	National Action Plan for Rare Diseases 2014-2018[47]	Evaluation of the National Action Plan for Rare Diseases 2020[48]	National Action Plan for Rare Diseases 2014-2018 Executive Summary[49]
Denmark	National Strategy for Rare Diseases 2014[24]	1. National Strategy for Rare Diseases: Status Evaluation and Recommendations for Future Efforts 2018[25] 2. Evaluation of National Strategy for Rare Diseases 2022[26]	N/A
England	1. England Rare Diseases Action Plan 2022[27] 2. England Rare Diseases Action Plan 2023: Main report[28] and Annexes[30]	N/A	The UK Rare Diseases Framework 2021*[29]
Finland	National Programme for Rare Disease 2019-2023[50]	N/A	N/A
France	French National Plan for Rare Diseases 2018-2022[51]	N/A	N/A
Germany	National Plan of Action for People with Rare Diseases 2013[32]	Interim report on the implementation of the National Action Plan 2017[31]	N/A
The Netherlands	National Plan for Rare Diseases 2013[52]	Coordination Consultation for Rare Diseases: Final Advice 2017[53] and Appendix[54]	N/A
Northern Ireland	Northern Ireland Rare Diseases Action Plan 2022/23[34]	Northern Ireland's Rare Diseases Action Plan Progress Report Year 1 (March 2022-March 2023)[33]	The UK Rare Diseases Framework 2021*[29]
Portugal	1. Integrated Strategy for Rare Diseases 2015-2020[35] 2. Annual Plan 2016[36] 3. Annual Plan 2017[37] 4. Annual Plan 2018[38]	1. Interim Report on the Implementation of the Integrated Strategy for Rare Diseases 2015-2020 – Year 2017[39]	N/A

Country	Main strategy and or action plan document(s)	Strategy evaluation and or recommendation document(s)	Supporting document(s) (for main strategy or evaluation)
	5. Annual Plan 2019[40]	2. Annual Report Integrated Strategy for Rare Diseases 2015-2020 – Year 2018[41]	
Scotland	Rare Disease Action Plan 2022[42]	N/A	The UK Rare Diseases Framework 2021*[29]
Wales	Wales Rare Diseases Action Plan 2022-2026[43]	N/A	The UK Rare Diseases Framework 2021*[29]

Key: N/A: Not available; UK: United Kingdom.
Note: *The UK Rare Diseases Framework 2021[29] provides a framework for the strategies relating to England, Northern Ireland, Scotland and Wales and is therefore provided as a supporting document.

3.2 Strategy contents

Following review of the included national rare disease strategies, the information identified was segmented into the following sections for analysis:

- timeline and aims
- themes and priorities
- implementation
- governance and or organisational structures
- funding model.

While strategy targets were outlined in the protocol for this review as possible information of interest, no distinct targets were identified within the national rare disease strategies of the selected countries. Similar information related to strategy outputs and or outcomes is described in section 3.2.3, under 'Outcomes or measures for monitoring and evaluation'.

Each section provides a descriptive summary of the relevant information extracted from the national rare disease strategies of the 12 selected countries. Information relating to Ireland is included in summary tables within each section. However, for clarity, descriptions of and comparisons to Ireland are presented separately in section 3.3.

3.2.1 Timeline and aims

Timeline

Of the 12 selected countries (excluding Ireland):

- The strategies for England,[27, 28] Northern Ireland,[34] Scotland,[42] and Wales[43] were underpinned by the UK Rare Diseases Framework[29] which has a specific timeline, 2021-2026.
- Eight countries (Austria,[47] England,[27, 28] Finland,[50] France,[51] Portugal,[35-38, 40] Scotland,[42] Wales[43] and Northern Ireland[34]) published a national rare disease strategy or strategies with defined timelines (beginning and end dates for implementation).
- Of the strategies with a defined timeline, all were ongoing at the time of writing this report, except the National Action Plan for Rare Diseases 2014-2018 (Austria),[47] the French National Plan for Rare Diseases 2018-2022,[51] the Integrated Strategy for Rare Diseases 2015-2020 (Portugal)[35] and the Rare Diseases Action Plan April 2022-March 2023 (Northern Ireland).[34]
- The durations of national rare disease strategies with a defined timeline ranged from one year (England[27]) to five years (Portugal[35] and the UK Rare Diseases Framework[29]).

- Four countries did not provide an end year for their strategies: Australia,[22] Denmark,[24] Germany,[30] and the Netherlands.[31]
- The earliest rare disease strategies included were the National Plan for Rare Diseases (the Netherlands)[31] and the National Plan of Action for People with Rare Disease (Germany)[30] which both began in 2013. The most recently published strategy included was England's Rare Disease Action Plan 2023.[28]

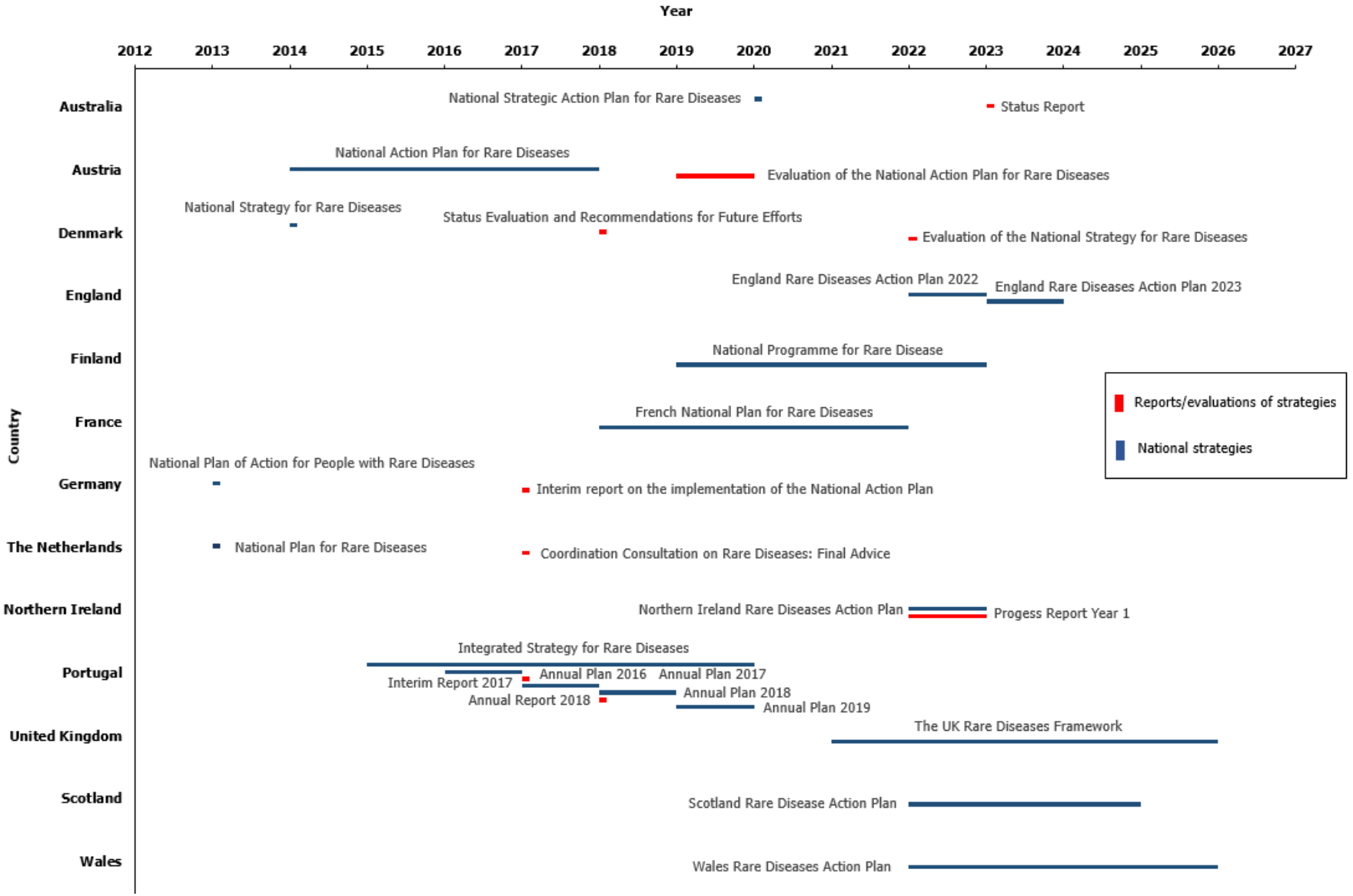
To accompany their main strategy, Portugal published four annual plans for the years 2016,[36] 2017,[37] 2018[38] and 2019.[40] England also published annual action plans for the years 2022[27] and 2023.[28]

Austria conducted an evaluation of the National Action Plan,[48] which took place between December 2019 and March 2020. Denmark undertook two evaluations of their strategy,[24] the first published in 2018[25] and the second published in 2022.[26]

Germany published an interim report on the implementation of the National Plan of Action for People with Rare Diseases[31] in March 2017. Portugal also published an interim report on the Integrated Strategy for Rare Diseases[39] in 2017, and a further annual report for the year 2018.[41] Australia completed a status report on their National Action Plan[23] which was published in May 2023 and Northern Ireland published a report on the progress made in relation to the Rare Diseases Action Plan[33] between March 2022 and March 2023.

See Figure 3.1 for a summary of the timelines of the included national rare disease strategies and associated documents.

Figure 3.1 Timeline of national rare disease strategies, strategy evaluations, and status reports identified.



Aims

Within the included rare disease strategies the following terms were identified:

- aims
- visions
- pillars
- objectives
- principles
- purposes
- actions
- themes
- ambitions and levers (see Table 3.2).

For clarity, the term 'aim' was used as a representative term within this review to refer to overarching aims. More specific strategy themes and priorities are described in section 3.2.2.

The UK Rare Diseases Framework[29] outlines unique aims separate to those listed in the strategies from Northern Ireland,[34] England,[27, 28] Wales[43] and Scotland[42] and therefore will be referred to separately in this section.

All of the included rare disease strategies, except those from Denmark and Germany, focused on improving treatment and coordination of care, with this being an underpinning general aim.[22, 27, 28, 34, 35, 43, 47, 50-52] This would be achieved through a number of strategic aims including:

- Improvements in the diagnosis of rare diseases; a strategic aim for France,[51] Northern Ireland,[34] Portugal (Annual Plans for 2016[36] and 2017[37]), the Netherlands[52] and the UK.[29] Only France[51] outlined a specific diagnostic intervention as a strategic aim, namely reinforcing and potentially expanding their neonatal screening programmes.
- Increasing awareness and or communication in the area of rare diseases; a strategic aim for Australia,[22] England (Action Plan 2022[27]), Finland[50] and France.[51]
- Educating and involving patients with respect to their rare disease; a strategic aim for Australia[22] and Finland.[50] Similarly, greater health literacy for patients, families and caregivers was a strategic aim for Portugal (Annual Plans for 2016[36] and 2017[37]).

Denmark[24] and Germany[32] did not refer to the concepts of treatment and care within the aims of their respective strategies. However, both countries addressed these concepts in the themes and priorities of their strategies (see section 3.2.2).

Another key aim identified within a number of strategies, for example, in Australia,[22] France[51], and the Netherlands[52], was the potential for further research into rare diseases.[52]

The general concept of greater involvement and engagement between stakeholders and national coordination was identified within the aims of strategies for Australia,[22] Austria,[47] and Finland.[50] The French National Plan for Rare Diseases[51] specifically stated aims to increase research potential and encourage innovation in the area of rare diseases.

Table 3.2 Aims and timeline identified in the national rare disease strategies of Ireland and the selected countries.

Country Information source Timeline	Aims
Ireland ▪ National Rare Disease Plan for Ireland[19] 2014-2018	▪ **Vision** An Ireland where: People with rare disease receive timely access to the best possible evidence-based, patient-centred and family-centred screening (as appropriate), diagnosis, treatment and care through all stages of their lives. The needs and experiences of people with rare disease are recognised, understood and addressed within all aspects of the Irish health system, including policy, services and research/information systems.
▪ Interim Report on National Rare Disease Plan for Ireland (Interim Report on Implementation[45] and Summary Recommendations[46])	▪ See *National Rare Disease Plan for Ireland 2014 – 2018*.
Australia ▪ National Strategic Action Plan for Rare Diseases[22] Published February 2020	▪ **Vision** The best possible health and wellbeing outcomes for Australians living with a rare disease. **Critical Enablers** (of effective rare diseases policy) ▪ Multi-stakeholder involvement and engagement ▪ Collaborative governance and leadership ▪ State, national and international partnerships ▪ High quality, comprehensive collection, and effective use, of rare disease data **Pillars:** 1. Awareness and Education 2. Care and Support 3. Research and Data These **Principles** are the foundation for this Action Plan: ▪ Person-centred ▪ Equity of access ▪ Sustainable systems and workforce
▪ Implementing the National Strategic Action Plan for Rare Diseases: May 2023 Status Report[23] Scan in September 2022, October 2022 and February 2023. Published May 2023	▪ **Objectives** 1. Track implementation of the Action Plan since its launch in 2020. 2. Identify projects, initiatives and achievements of various stakeholders and, where relevant, align these against the Pillars, Priorities and Themes in the Action Plan and map these to 5 key elements of progress in a logic model. 3. Identify gaps and strengths in Action Plan implementation to guide the sector towards the more effective and efficient use of time, expertise and resources. 4. Set a baseline for future monitoring and evaluation of Action Plan progress.

Country Information source Timeline	Aims
Austria ▪ National Action Plan (NAP) for Rare Diseases[47] 2014-2018	▪ To improve the lives of Austrian patients affected by rare diseases regardless of gender, age, degree of disability or socio-economic status, as well as their families and extended social and professional environment. The NAP intended to define appropriate measures and incentives to overcome existing fragmentation, improve the flow of information, optimise and coordinate processes and eliminate points of weakness. The NAP combines plan and strategy.
▪ Evaluation of the NAP for Rare Diseases[48] December 2019-March 2020	▪ The aim of the evaluation of the NAP is to examine to what extent it was and is suitable, through increased networking of involved stakeholders in the area diseases to improve the processes and information for those affected by them. The primary users of the evaluation are its clients, as well as actors in connection with the NAP, and representatives of people with rare diseases.
▪ Austrian National Action Plan (NAP) for Rare Diseases (Executive Summary)[49] 2014-2018	▪ To improve the lives of all patients with rare diseases – involving their families as well as their professional and social environment – irrespective of age, gender, extent of disability or socio-economic status.
Denmark ▪ National Strategy for Rare Diseases[24] Published in 2014	▪ The national strategy's deliberations and recommendations must be seen as benchmarks for a unified and coherent development of efforts for the benefit of people with rare diseases in both the short and long term. The strategy is not an action plan, but it contains recommendations and focus areas that can be translated into concrete initiatives.
▪ National Strategy for Rare Diseases: Status Evaluation and Recommendations for Future Efforts[25] Published in 2018	▪ The purpose of the status evaluation was to take stock of the National Strategy for Rare Diseases in Denmark,[24] and in the basis of uncovering the challenges, to come up with recommendations that can help to remedy them and support the quality of future efforts. Three to five years after initial strategy publication this report provided the status of the implementation of the strategy's approximate 100 recommendations, and results in an action-orientated status report that focuses on selected topics and recommendations. In the preparation for the status evaluation, based on the strategy's chapters, it was found to be appropriate to condense the 100 recommendations into 6 selected themes, which together cover the majority of the strategy's recommendations.
▪ Evaluation of the National Strategy for Rare Diseases[26] Published December 2022	▪ This report conveys an evaluation of the national strategy from 2014 as well as the Status evaluation of the National Strategy for Rare Diseases. The purpose was to collect and disseminate results and experiences from the work with the national strategy with a view to providing a renewed overview of the area and with a particular focus on increasing the quality of the organisation around rare diseases going forward.
England ▪ England Rare Diseases Action Plan 2022[27] 2021-2022	▪ Delivering improvements in diagnosis, awareness, treatment and care, and creating lasting positive change for those living with rare diseases.

Country Information source Timeline	Aims
▪ England Rare Diseases Action Plan 2023: Main report and annexes[28] 2023	▪ 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.
Finland National Programme for Rare Diseases[50] 2019-2023	Three main themes have been highlighted in the revised National Programme for Rare Diseases: ▪ Increase expertise and its communication. ▪ Build up involvement of patients with are disease in decision-making concerning them. ▪ To establish national coordination firmly.
France French National Plan for Rare Diseases[51] 2018-2022	The aim is to drive a national momentum, underpinned by key measures that should lead to important improvements in terms of diagnosis, care provision, our understanding of these diseases and the development of effective treatments. More specifically, the strategy states that it aims to: ▪ Make sure each patient receives a faster diagnosis and reduce diagnostic delay ▪ Reinforce the structuring of databases in order to increase research potential ▪ Boost the role of clinical networks to coordinate the actions of the multiple players concerned and support certain key phases, such as delivery of the diagnosis ▪ Ensure greater clarity of the care pathway for both patients and their families ▪ Encourage innovation and make it accessible ▪ Put in place new neonatal screening programmes ▪ Reinforce France's role as a driving force in Europe. The strategy is hinged around three ambitions: ▪ to enable a rapid diagnosis for all in order to reduce diagnostic delays and undiagnosed diseases ▪ to innovate in order to treat ▪ to improve the quality of life and care pathway of patients. And two levers: ▪ communication and training ▪ modernisation of organisations and national funding mechanisms. The main quantitative objective is: to ensure all people living with a rare disease receive an accurate diagnosis, care, and available therapy within one year of their first specialised medical consultation.
Germany ▪ National Plan of Action for People with Rare Diseases[32] Published in 2013	▪ The National Action Plan has two main goals: to prepare policy suggestions and proposed actions. It then names a number of action fields (see Themes and priorities) and a number of goals associated with each.

Country Information source Timeline	Aims
▪ Interim report on the implementation of the National Action Plan for People with Rare Diseases[31] Published March 2017	▪ This document is intended to provide an overview of the current implementation status and the achievement of the objectives of the measures and projects formulated in the national action plan.
Northern Ireland ▪ Northern Ireland Rare Diseases Action Plan[34] April 2022 to March 2023	▪ Through this action plan, we will take the first steps in Northern Ireland towards achieving our overarching vision – delivering improvements in diagnosis, awareness, treatment and care, and creating lasting positive change for those living with rare diseases
▪ Northern Ireland's Rare Diseases Action Plan: Progress Report Year 1[33] March 2022-March 2023	▪ This report details the progress made by the Northern Ireland Rare Disease Implementation Group in the first year of the *Rare Diseases Action Plan for Northern Ireland* published in March 2022.
Portugal ▪ Integrated Strategy for Rare Diseases 2015-2020[35] 2015-2020	▪ The Integrated Strategy for Rare Diseases, based on an inter-ministerial, inter-sectoral and inter-institutional cooperation, which makes a complementary use of medical, social, scientific and technological resources, has a mission to develop and improve [*the strategic priorities listed in Table 3.4*].
▪ Annual Plan 2016[36] 2016	▪ For the year 2016, all activities will have as their main objective the combating of the vulnerability of this population group, through reducing the dispersion of information about these diseases, increased access to diagnostic and therapeutic interventions, better referral in the health system and greater health literacy for patients, families and caregivers.
▪ Annual Plan 2017[37] 2017	▪ For the year 2017, all activities will have as their main objective the combating of the vulnerability of this population group, through reducing the dispersion of information about these diseases, increased across to diagnostic and therapeutic interventions, better referral in the health system and greater health literacy for patients, families and caregivers.
▪ Annual Plan 2018[38] 2018	▪ The objective of this Strategy is to ensure that people with a rare disease have better access and quality of healthcare and treatment, based on the scientific evidence and greater speed and variety of social responses adapted to each case.
▪ Annual Plan 2019[40]	▪ For the year 2019, all activities will have as their main objective the combating of the vulnerability of this population group, through reducing the dispersion of information about these diseases, increased access to diagnostic and therapeutic interventions, better referral in the health system and greater health literacy for patients, families and caregivers
▪ Interim Report on the Implementation of the Integrated Strategy for Rare Diseases 2015-2020 – Year 2017[39] 2017	▪ Within the scope of the powers attributed to this Interministerial Commission, the annual report on the implementation of the 2017 annual plan of the Strategy is presented.

Country Information source Timeline	Aims
▪ Annual Report Integrated Strategy for Rare Diseases 2015-2020 – Year 2018[41] 2018	▪ In this annual report, the activities developed by the Interministerial Commission in the year 2018 were presented, in accordance with the strategic priorities defined in the Strategy.
Scotland Rare Disease Action Plan[42] 2022-2025 approximately	This Action Plan, and the further iterations that will follow, set out the measures the Scottish Government will take to put into action the priorities of the UK Rare Diseases Framework. We will achieve this by working with partners across the National Health Service Scotland, third sector organisations and beyond, and continue to strive to ensure that all people living with a rare disease are able to access the best possible care and support.
The Netherlands ▪ National Plan for Rare Diseases[52] Published in 2013 ▪ Coordination Consultation for Rare Diseases: Final Advice[53] Published 28 February 2017	▪ To make recommendations for activities that can improve the position of people with a rare disease in the broad field of diagnostics, treatment, care, research and information provision. The strategy aims to designate various field parties as primarily responsible for such activities. ▪ The aim of the coordination consultation was to discuss: ▪ implementation of recommendations from the National Plan for Rare Diseases. ▪ bottlenecks regarding implementation. ▪ making an inventory of new developments or identifying white spots. ▪ coordination between the various parties that carry out activities or projects in the field of rare diseases and orphan drugs. ▪ bundling "loose" recommendations into coherent action points. ▪ the final advice from the Rare Diseases Coordination Consultation was drawn up on behalf of the Ministry of Health, Welfare and Sport. The basis for the coordination consultation is the National Plan for Rare Diseases from 2013. The final advice provides an update of the state of affairs of the National Plan for Rare Diseases. In addition, it offers a look at future policy in the field of rare diseases and orphan drugs.
United Kingdom The UK Rare Diseases Framework[29] 2021-2026	The UK Rare Diseases Framework aims to ensure that the lives of people living with rare diseases continue to improve. We will work across the 4 nations of the UK to ensure that rare disease patients receive the best possible care, building on the commitments in the UK Strategy for Rare Diseases and major advances in the diagnosis and treatment of rare diseases. This framework will develop positive change in how we diagnose, treat and care for patients with a rare disease.
Wales Wales Rare Diseases Action Plan[43] 2022-2026	The UK Rare Diseases Framework identifies the key priorities for rare diseases going forward and creates a vision for the future, which is shared by all four UK nations to address health inequalities, improve the quality and availability of care, and improve the lives of people living with rare diseases. To implement the UK Rare Diseases Framework, Wales developed their own action plan, outlining commitments to meet the priorities of the Framework.

Key: NAP: National Action Plan (Austria); UK: United Kingdom.

3.2.2 Themes and priorities

Within the reviewed national rare disease strategies, the following related terms were identified: themes, priorities, pillars, fields of action, action fields, focuses, focus areas, pivotal objectives, and principles (see Table 3.4). For clarity, the term 'themes and priorities' was used as a representative term within this review. It refers to the domains described in the strategies reviewed using the terms listed above. Some domains may be addressed in other areas of the strategies reviewed, for example, under implementation or descriptions of governance and organisational structures. In such cases, those domains are addressed in the relevant section or sections of this report.

The main themes and priorities identified in the national rare disease strategies of the selected countries are presented in Table 3.3. These themes and priorities are summarised under the following domains:

- screening and diagnosis
- access to and coordination of healthcare services
- rare disease research
- patient representation and empowerment
- access to orphan medicines and innovative health technologies
- health information systems and patient registries
- health workforce education and training
- cross-sectoral collaboration to support community participation
- international cooperation, including ERNs
- awareness and information for patients and the public
- monitoring and evaluating strategy progress and outcomes
- governance structures
- access to mental health and psychology services.

The subsections below summarise the findings in relation to these themes and priorities for the selected countries. The themes and priorities are addressed in order of the frequency with which they were identified in the reviewed national rare disease strategies, from most frequently to least frequently identified, as presented in Table 3.3.

Table 3.3 Overview of themes and priorities identified in the national rare disease strategies of Ireland and the selected countries.

Theme or priority domain	AU	AT	DK	Eng	FI	FR	DE	NL	NI	PT	Scot	Wales	IE	Number of Selected Countries**
Screening and diagnosis	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	**12/12**
Access to and coordination of healthcare services	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	**12/12**
Rare disease research	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	**12/12**
Patient representation and empowerment	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	**12/12**
Access to orphan medicines and innovative health technologies	✓	✓	✓	✓		✓	✓	✓	✓	✓	✓	✓	✓	**11/12**
Health information systems and patient registries	✓	✓	✓	✓		✓	✓		✓	✓	✓	✓	✓	**10/12**
Health workforce education and training	✓	✓	✓	✓		✓		✓	✓		✓	✓		**9/12**
Cross-sectoral collaboration to support community participation	✓		✓	✓	✓	✓			✓	✓	✓	✓	✓	**9/12**
International cooperation, including ERNs	✓		✓	✓	✓	✓	✓		✓		✓	✓	✓	**9/12**
Awareness and information for patients and the public	✓	✓	✓		✓	✓	✓	✓					✓	**7/12**
Monitoring and evaluating strategy progress and outcomes	✓		✓	✓			✓	✓					✓	**5/12**
Governance structures	✓	✓			✓		✓						✓	**4/12**
Access to mental health and psychology services	✓		✓	✓*							✓			**4/12**

Key: AU = Australia; AT = Austria; DK = Denmark; Eng = England; ERN = European Reference Network; FI = Finland; FR = France; DE = Germany; NL = the Netherlands; NI = Northern Ireland; PT = Portugal; Scot = Scotland; IE = Ireland.
Note: *2023 only. **Ireland is not included in the total amount of selected countries (12).

Screening and diagnosis

All 12 countries included screening for and or diagnosis of rare diseases as a theme or priority in their national rare disease strategies. This primarily related to ensuring timely and accurate diagnosis of rare diseases, as seen in the national strategies of Australia,[22] Austria,[47] England,[27, 28] France,[51] Germany,[32] the Netherlands,[53] Northern Ireland,[34] Portugal,[35] Scotland,[42] and Wales.[43] Three countries specifically prioritised advances in diagnostics and providing access to new diagnostic technologies: Germany,[31, 32] the Netherlands,[53] and Scotland.[42]

In terms of screening and diagnosis, genetics was noted as a broad theme or priority for four countries: Denmark,[24] France,[51] the Netherlands,[53] and Scotland.[42] Specific themes and priorities observed in relation to this were pre-conception care (that is, care provided before pregnancy),[53] peri-conception genetic testing and counselling (that is, testing and counselling carried out during the period from before conception to early pregnancy),[22] and antenatal and preimplantation diagnostics (that is, diagnostics carried out during pregnancy, or prior to the implantation of an embryo during in vitro fertilisation).[51] Newborn screening was distinctly noted as a theme or priority in four countries: Australia,[22] Denmark,[24] France,[51] and Scotland.[42]

People with undiagnosed diseases were identified as a priority population in the national rare disease strategies of five countries: Australia,[22] England,[28] France,[51] Germany,[32] and Wales.[43] In addition, people with non-genetic conditions were highlighted as a priority population in England's Rare Diseases Action Plan 2023.[28]

Access to healthcare and coordination of services

Themes or priorities related to access to healthcare and coordination of services were included in the national rare disease strategies of all 12 selected countries. The Australian national rare disease strategy provides an example of the overall nature of the themes or priorities included in this domain, as it prioritises the provision of care and support that is integrated and appropriate for people with rare diseases, as well as being both person- and family-centred.[22]

Improving access to care was identified as a broad priority in five countries (Austria,[47] Australia,[22] France,[51] the Netherlands,[52] and Portugal[35]), while improving access to specialist care was identified as a more specific priority in the UK Rare Diseases Framework,[29] and subsequently across the national strategies of England,[27, 28] Northern Ireland,[34] Scotland[42] and Wales.[43]

Coordination of care was a broad theme or priority across eight countries' national rare disease strategies (Denmark,[24] England,[27, 28] Finland,[50] the Netherlands,[52] Northern Ireland,[34] Portugal,[35] Scotland[42] and Wales[43]). A particular emphasis

on planning and coordination of specialised services was observed for Denmark.[24] Improving care pathways was a general theme or priority for France[51] and Austria.[47] A specific focus on transitions between services, particularly from paediatric to adult services, was observed for Denmark,[25, 26] France,[51] and Scotland.[42] Access to and coordination of rehabilitation services was a theme or priority for Austria[47] and Denmark.[24]

Healthcare settings highlighted across themes or priorities included specialised centres for rare diseases (Denmark,[24] Finland,[50] and Germany[31, 32]), hospitals, and community settings (Denmark[24-26]). Strengthening networks of specialist centres was a particular priority for France[51] and Germany.[31, 32]

Finally, a facilitator of better care coordination noted as a priority was improved communication. This included communication both between healthcare professionals and between patients and healthcare professionals (France[51] and Scotland[42]).

Rare disease research

All 12 countries included themes or priorities relating to rare disease research in their national strategies. These were primarily broad themes or priorities that focused on promoting research in the field of rare diseases.

Specific themes or priorities relating to clinical research and the translation of research and innovation into clinical practice were included in the national strategies of Australia,[22] England,[28] and France.[51] In Germany,[31, 32] a broad theme relating to research highlighted a number of focus areas, including pathophysiology, diagnostics, clinical trials, health services research, ethical, legal and social aspects, cooperation between academia and industry, and international cooperation. The Australian national rare disease strategy also included as a priority the development of a national research strategy for rare diseases.[22] The stated purposes of this research strategy were to support all types of research for rare diseases, contribute to agreed priorities and systematically address research gaps.

Patient representation and empowerment

Patient representation and empowerment was included as a theme or priority in the national rare disease strategies of all 12 countries. For example, in the Netherlands,[52] 'amplifying the voice of the patient with a rare disease' was an identified theme. Similarly, 'patient voice' was a theme across the national rare disease strategies of England,[27, 28] Northern Ireland,[34] Scotland[42] and Wales,[43] as an underpinning theme of the UK Rare Diseases Framework.[29] For Scotland,[42] the inclusion of the 'patient voice' was also demonstrated in the priorities of the national strategy, since each included descriptions of what the priority meant from the perspective of the rare diseases community.

Strengthening the involvement of people with rare diseases in their own care and support was highlighted as a theme or priority in the national strategies of Australia[22] and Finland.[50] In Finland,[50] this also included involvement in developing health and social care services in their local areas. Broader themes and priorities relating to the empowerment, involvement and integration of people with rare diseases in healthcare and society were included in the national rare disease strategies of Denmark,[24-26] Finland,[50] France,[51] and Portugal.[35]

The roles of patient representative organisations were addressed in themes and priorities of national rare disease strategies from Austria,[47] Denmark,[24-26] France,[51] and Germany.[32] These roles included: patient advocacy (Germany[32]); patient education and empowerment (Denmark[24-26]); international cooperation (Denmark[24]); contributing to improvements in medical care, particularly where there are deficits or where research is lacking (Germany[32]); and improving quality of life and contributing to the general care of people with rare diseases (Austria[47]). The involvement of patient representative organisations was a cross-cutting theme within the German national rare disease strategy, to be included across all other themes and priorities.[32] Similarly, the French national rare disease strategy prioritised mapping the positions and missions of patient representative organisations, among other stakeholders, to better integrate them into the rare disease sector and optimise their impact.[51] In the Danish national rare disease strategy,[24] people with rare diseases without representative organisations were also highlighted as a priority population.

Access to orphan medicines and innovative health technologies

Eleven of the 12 selected countries included themes or priorities in their national strategies that related to innovative health technologies, including orphan medicines. Finland was the only country that did not explicitly address this theme or priority.

Broad themes or priorities related to improving the availability of, and access to, treatment or therapies for people with rare diseases were included in the national strategies of five countries: Austria,[47] Denmark,[26] France,[51] the Netherlands,[52] and Portugal.[35] In seven countries, themes or priorities focused more specifically on access to innovation (France[51]), best available health technologies (Australia[22]), specialist care, treatments and drugs (England,[27, 28] Northern Ireland,[34] Scotland[42] and Wales[43]), or orphan medicines (Germany[32]). Off-label use of medicines for the care of people with rare diseases was also included as a theme or priority in two countries: Germany[32] and the Netherlands.[52]

Financing and reimbursement of therapies for rare diseases, including orphan medicines, were highlighted as themes or priorities in the national rare disease strategies of Austria[47] and the Netherlands.[52] Promoting the development of evidence and innovation were themes or priorities in the national strategies of

Germany[32] and France,[51] respectively. In Denmark,[24] EU support for the development of orphan medicines was also noted as a theme or priority.

Health information systems and patient registries

Ten of the 12 selected countries included themes or priorities in their national rare disease strategies that related to health information systems, including rare disease patient registries. Finland's national strategy did not explicitly address this as a theme or priority, although activities relating to health information systems were included under the broader theme of 'coordination of activities related to rare diseases'.[50] Similarly, the Netherlands included activities relating to rare disease coding, specifically ORPHAcode implementation, and patient registries under themes linked to research and organisation of care,[52] which were subsequently highlighted as examples of positive initiatives in their coordination consultation.[53]

Broad themes or priorities that included the use of health information systems in the field of rare diseases were observed for Denmark[24-26] and Germany.[31, 32] Similarly, national strategies for England,[27, 28] Northern Ireland,[34] Scotland[42] and Wales[43] all included the broad underpinning theme of 'digital, data and technology'.

Specific themes or priorities relating to patient registries were also included in the national rare disease strategies of Denmark[24-26] and Germany,[32] and in England's Rare Diseases Action Plan 2023.[28] Patient registries were addressed extensively in the French national rare disease strategy under the theme of data sharing. France also included as priorities the development of FAIR (findable, accessible, interoperable, and reusable) data warehouses, and conditions for the reuse of data collected using e-health tools for research.[51]

The stated purposes of these themes or priorities included improving epidemiological knowledge of rare diseases (Australia,[22] Austria[47] and Portugal[35]), informing care management and health system planning (Australia[22]), aiding diagnosis (France[51]), facilitating research and the development of new treatments (Australia[22] and France[51]) and ensuring adequate compensation for the treatment of rare diseases (Austria[47]).

Health workforce education and training

Themes or priorities relating to health workforce education and training were included in the strategies of nine of the 12 selected countries: Australia,[22] Austria,[47] Denmark,[24] England,[27, 28] France,[51] Northern Ireland,[34] Scotland,[42] the Netherlands,[52] and Wales.[43] Where included, this was a consistent theme or priority, for example, in Denmark, education and skills development was consistently included as a theme across the national strategy and both evaluations.[24-26]

The stated purpose of education and training for healthcare professionals was primarily to improve their awareness of how to recognise and manage rare diseases, as seen in the national strategies of Australia,[22] Austria,[47] England,[27, 28] France,[51] the Netherlands,[52] Northern Ireland,[34] Scotland,[42] and Wales.[43] This included awareness of advancing technologies that may be of particular benefit to people with rare diseases, such as genomic testing (Wales[43] and Australia[22]) and digital tools (Wales).[43] However, the prioritisation of education and training was not limited to healthcare professionals specialising in the care of people with rare diseases. For example, in the Netherlands,[53] an area identified as not having received sufficient attention in the National Rare Diseases Strategy 2013[52] was the development of medical expertise outside the specialist centres, particularly the need for greater knowledge and skills among general practitioners and paediatricians to enable early identification of rare diseases.

In Australia,[22] the development of a national rare disease workforce strategy was also stated as a priority. This was linked to the need for sustainable systems and a workforce that can respond to current and future demands.

Cross-sectoral collaboration to support community participation

Themes and priorities related to cross-sectoral collaboration to support community participation among people with rare diseases were included in the national strategies of nine of the selected countries: Australia,[22] Denmark,[24] England,[27, 28] Finland,[50] France,[51] Northern Ireland,[34] Portugal,[35] Scotland,[42] and Wales.[43] For example, social integration and citizenship was highlighted a strategic priority in Portugal,[35] while the Finnish national rare disease strategy prioritised involvement of people with rare diseases in society and their communities.[50] In France,[51] facilitating the integration of carers of people with rare diseases was also included as part of this priority. In Denmark,[24] social supports at municipality level were highlighted as a theme or priority, particularly with reference to education and employment for people with rare diseases.

This theme or priority was addressed across the national rare disease strategies of England,[27, 28] Northern Ireland,[34] Scotland,[42] and Wales,[43] through the underpinning theme of 'wider policy alignment'. For example, in England's Rare Diseases Action Plan 2022,[27] this theme was taken to encompass a broad range of initiatives beyond healthcare, including social care, housing, financial aid, and supports for special educational needs. Similarly, cross-sectoral coordination was also identified as a theme or priority for Australia[22] and Denmark.[24-26]

In addition, the Dutch coordination consultation highlighted the relative lack of attention paid to the social aspects of rare diseases in their national strategy.[53] Areas noted as requiring greater attention included education, employment,

finances, social integration, and transport, as well as impacts on families and informal caregivers of people with rare diseases.

International cooperation, including European Reference Networks

Nine of the 12 selected countries included themes or priorities relating to international cooperation: Australia,[22] Denmark,[24] England,[27, 28] Finland,[50] France,[51] Germany,[31, 32] Northern Ireland,[34] Scotland,[42] and Wales.[43] Broad themes or priorities relating to international cooperation were included for Australia,[22] Denmark,[25, 26] England,[27, 28] Northern Ireland,[34] Scotland,[42] and Wales.[43] Participation in EU initiatives relating to rare diseases was noted as a priority for Denmark,[24] while Finland included European Reference Networks (ERN) as a specific theme or priority.[50]

Both France[51] and Germany[32] included European and international cooperation under themes or priorities relating to research, data sharing (France[51]) and patient representative organisations (Germany[32]). In addition, although international cooperation was not cited as a distinct theme or priority for the Netherlands,[52] the importance of European and international cooperation was noted under the theme of research. Furthermore, while Austria[47] also did not include international cooperation as a distinct theme or priority, all of the themes or priorities in their national rare disease strategy aimed to take account of both national requirements and European recommendations.

Awareness and information for patients and the public

Raising awareness of rare diseases and making information available to patients and the public was a theme or priority in the national rare disease strategies of seven of the 12 selected countries: Australia,[22] Austria,[47] Denmark,[24] Finland,[50] France,[51] Germany,[32] and the Netherlands.[52]

General themes and priorities related to increasing knowledge and awareness of rare diseases were observed for Australia,[22] Austria,[47] Finland,[50] and Germany.[32] Providing access to information and education for people with rare diseases was a distinct theme or priority in Australia,[22] Denmark,[24-26] and the Netherlands,[52] with a focus on enabling patients to be active participants in their care.[22, 24] The Dutch coordination consultation,[53] cited provision of information for patients and families as an area where positive initiatives had been noted. In France,[51] although not explicitly stated as a theme or priority, the overall priority of improving care pathways included incorporating patient education programmes into the pathways.

Monitoring and evaluating strategy progress and outcomes

Five countries included themes or priorities relating to monitoring and or evaluating the implementation of the national rare disease strategy: Australia,[22, 23]

Denmark,[24, 26] England,[28] Germany,[31, 32] and the Netherlands.[52] Monitoring and evaluation was included as an additional focus area in England's Rare Diseases Action Plan 2023,[28] based on stakeholder engagement. Similarly, in Australia,[22] 'the need for national leadership, coordination and consistency' was identified as a theme based on consultation with stakeholders in the rare disease sector. As part of this theme, stakeholders called for an annual implementation plan to accompany the national strategy, with regular monitoring and review of implementation. In Denmark, implementation, evaluation, follow-up and monitoring were prioritised in the national strategy in 2014,[24] with implementation listed as a distinct theme in the 2022 evaluation.[26]

Governance structures

Themes or priorities relating to governance were included in the national rare disease strategies of four countries: Australia,[22, 23] Austria,[47] Finland[50] and Germany.[31, 32] These priorities primarily related to establishing and or maintaining organisational structures to coordinate activities relating to rare diseases at national level. For example, in Austria,[47] the establishment of two permanent advisory committees for rare diseases at the Federal Ministry of Health was identified as a priority. In Germany,[31, 32] priorities related to governance referred to maintaining ongoing collaboration among partners involved in developing the national rare disease strategy, as well as establishing structures to monitor and evaluate strategy implementation.

Access to mental health and psychology services

Four of the selected countries included themes or priorities relating to access to mental health and or psychology services: Australia,[22] Denmark,[25, 26] England,[28] and Scotland.[42] For England,[28] 'mental health and psychological support' was identified as a focus area for 2023, in addition to the priorities and themes shared with the UK Framework.[29] For Scotland,[42] mental health was not explicitly listed a priority, as per the UK Framework. However, Scotland's Rare Disease Action Plan[42] included additional points outlining issues of importance to the rare disease community for each priority, based on feedback from the rare disease community. This feedback identified that embedding counselling and mental health support as part of the diagnostic journey was importance to 'Priority 1: Ensuring patients get the right diagnosis faster', and making mental health support available at all stages of the patient journey was relevant to 'Priority 3: Better coordination of care' (see Appendix B, Table B28).

Other themes or priorities

Themes or priorities not covered by the listed domains included health equity, which was included as a distinct theme in England's Rare Diseases Action Plan 2022.[27]

Equity was also addressed as part of the Australian strategy's priority of providing equitable access to the best available health technology.[22] 'Facilitating increased reproductive confidence', which referred to pre-conception genetic testing and counselling, was only explicitly stated as a priority for Australia.[22] Furthermore, Australia highlighted a list of priority populations in their national rare disease strategy,[22] which included Australians living with a rare disease (diagnosed or undiagnosed), Australians with an increased chance of developing a rare disease or of having a child with a rare disease, Aboriginal and Torres Strait Islander people; people living in regional, rural and remote areas; people from culturally and linguistically diverse backgrounds; people experiencing socio-economic disadvantage; and a wide range of other partners, such as carers and families, government, and industry. Finally, Denmark[24] included a priority relating to the need for new structures following an evaluation of municipal reforms. This priority was specifically relevant in the Danish national context at the time of the publication of their national strategy in 2014,[24] and was not a distinct theme or priority in the subsequent strategy evaluations.

Table 3.4 Themes or priorities identified in the national rare disease strategies of Ireland and the selected countries.

Country Information Source	Themes or priorities
Ireland ▪ National Rare Disease Plan for Ireland 2014 – 2018[19] ▪ Interim Report on National Rare Disease Plan for Ireland 2014-2018 (Interim Report on Implementation[45] and Summary of Recommendations)[46]	Themes or priorities not stated, but recommendations grouped under the following: ▪ Recognition of rare disease – Information and research ▪ Prevention, diagnosis and care ▪ Enhancing access to appropriate drugs and technologies ▪ Empowering, protecting and supporting rare disease patients and carers ▪ Implementation, monitoring and review of the National Rare Disease Plan. **Principles** ▪ Equity: Patients resident in Ireland should receive the best possible evidence-based diagnosis and care irrespective of the rarity of their condition and the location of optimal care services. Equality in accordance with prevailing health and other legislation should underpin the provision of care. ▪ Collaboration: Cross-sectoral, cross-border and international cooperation are integral for Ireland to deliver on the vision for rare disease patients and a core activity of all policy actions. ▪ Family-centredness: Implementation of policy actions should be built around the development of coordinated packages of care for patients and their carers. ▪ Sustainability: A strategic approach to improving the situation of rare disease patients and carers should be sustainable. Policy actions should be implemented in a way that planning, delivering and monitoring rare disease issues become core work of the health system. Transparency: Progress with the implementation of the policy actions should be transparent to all stakeholders.
Australia ▪ National Strategic Action Plan for Rare Diseases 2020[22] ▪ Implementing the National Strategic Action Plan for Rare Diseases: May 2023 Status Report[23]	Three pillars were identified, each with associated priorities. All were consistent across both the action plan and status report. ▪ Pillar 1: Awareness and Education o Priority 1.1: Increase every Australian's awareness of rare diseases including, where applicable, relevant prevention measures. o Priority 1.2: Ensure Australians living with a rare disease have access to information and education that enables them to be active participants in their rare disease journey. o Priority 1.3: Develop a national rare disease workforce strategy that responds to current and future demands, including the impact of genomics. ▪ Pillar 2: Care and Support o Priority 2.1: Provide rare disease care and support that is integrated and appropriate for all Australians living with a rare disease, while being both person and family-centred. o Priority 2.2: Ensure diagnosis of a rare disease is timely and accurate. o Priority 2.3: Facilitate increased reproductive confidence. o Priority 2.4: Enable all Australians to have equitable access to the best available health technology. o Priority 2.5: Integrate mental health, and social and emotional wellbeing, into rare disease care and support. ▪ Pillar 3: Research and Data

Country Information Source	Themes or priorities
	○ Priority 3.1: Enable coordinated and collaborative data collection to facilitate the monitoring and cumulative knowledge of rare diseases, informing care management, research and health system planning. ○ Priority 3.2: Develop a national research strategy for rare diseases to foster, support and drive all types of research for rare diseases, contributing to agreed priorities and systematically addressing gaps. ○ Priority 3.3: Ensure research into rare diseases is collaborative and person-centred. ○ Priority 3.4: Translate research and innovation into clinical care; clinical care informs research and innovation. Themes informed by stakeholder consultation with the rare disease sector and used as measures of progress over time: ▪ Theme 1: The need for national leadership, coordination and consistency ▪ Theme 2: The need to prioritise the systematic building of knowledge, evidence and expertise ▪ Theme 3: The need for a person-centred approach and ongoing collaboration ▪ Theme 4: The need to measure rare diseases ▪ Theme 5: The need for sustainable systems and workforce ▪ Theme 6: The need for stakeholder collaboration ▪ Theme 7: State, national and international partnerships as well as cross-sector (i.e. specifically, across government sectors) collaboration ▪ Theme 8: The need to progress early implementation wherever possible. Priority populations were also identified (see Appendix B, Table B1).
Austria ▪ National Action Plan (NAP) for Rare Diseases 2014- 2018[47]	Fields of action: 1. Mapping/illustrating rare diseases in the health and social system. 2. Improving medical-clinical care for those affected by rare diseases. 3. Improving the diagnosis of rare diseases. 4. Improving therapy and access to therapies for rare diseases. 5. Promoting research in the area of rare diseases. 6. Improving knowledge and awareness of rare diseases. 7. Improving epidemiological knowledge in the context of rare diseases. 8. Establishment of permanent advisory committees for rare diseases at the BMG (Federal Ministry of Health). 9. Acknowledgement of the merits of patient organisations for rare diseases.
▪ Evaluation of the NAP for Rare Diseases 2020[48]	The evaluation addressed the following questions: ▪ According to the assessment of the stakeholders involved, do the actions in NAP lead to an improved living situation for people with rare diseases in Austria? ▪ What is the degree of implementation of the actions? What are the reasons that some actions were implemented and others were not? ▪ What are the assessments regarding the creation process? Were the various relevant stakeholders sufficiently involved in the preparation and implementation of the NAP? ▪ Were the main challenges faced by people with rare diseases managed through appropriate actions? ▪ How should the further implementation of the actions be promoted?

Country Information Source	Themes or priorities
	▪ How was the financing of the actions secured? ▪ What learning experiences can be derived for the further implementation of the actions?
Denmark ▪ National Strategy for Rare Diseases 2014[24]	No themes or priorities specified. Recommendations grouped into the following chapters: ▪ Size and characteristics of the patient group ▪ Organisation of the health professional efforts ▪ Challenges for the hospital services ▪ New diagnostic and treatment opportunities ▪ Organising rehabilitation and other initiatives in the municipality ▪ New structure in the social area after evaluation of the municipal reform ▪ The need for coordination and coherence in the efforts ▪ Information and knowledge sharing ▪ Empowerment, patient education and patient organisations ▪ Registries, databases and research ▪ Education and competence development ▪ EU initiatives in the area of rare diseases ▪ Implementation, evaluation, follow-up and monitoring.
▪ National Strategy for Rare Diseases: Status Evaluation and Recommendations for Future Efforts 2018[25]	**Themes included in Evaluations:** ▪ Theme 1: Rare patients in the hospital system and the municipality ▪ Theme 2: Sector transitions, cooperation and coordination ▪ Theme 3: Patient education, coping and empowerment ▪ Theme 4: International cooperation ▪ Theme 5: Education and skills ▪ Theme 6: Registration, documentation and knowledge
▪ Evaluation of the National Strategy for Rare Diseases 2022[26]	**Additional themes included in 2022 Evaluation:** ▪ Theme 7: Availability of treatment ▪ Theme 8: Implementation
England ▪ England Rare Diseases Action Plan 2022[27]	Priorities and underpinning themes for both the 2022 and 2023 action plans, as per the UK Rare Diseases Framework. **Priorities:** ▪ Priority 1: helping patients get a final diagnosis faster ▪ Priority 2: increasing awareness among healthcare professionals ▪ Priority 3: better coordination of care ▪ Priority 4: improving access to specialist care, treatments and drugs. **Underpinning themes:** ▪ Patient voice ▪ National and international collaboration

Country Information Source	Themes or priorities
▪ England Rare Diseases Action Plan 2023[28]	▪ Pioneering research ▪ Digital, data and technology ▪ Wider policy alignment ▪ Health equity (included as a theme in the England Rare Diseases Action Plan 2022 only). **Focus areas** (included in the England Rare Diseases Action Plan 2023 only): ▪ 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).
Finland National Programme for Rare Diseases 2019–2023[50]	Three pivotal objectives and associated focus areas: 1. Increasing knowledge on rare diseases and strengthening expertise. ▪ Increasing knowledge and awareness ▪ Strengthening the status of Rare Diseases Units and allocation of resources to them. ▪ European Reference Networks (ERN) ▪ Promoting research 2. Strengthening of patient involvement in rare disease. ▪ Empowerment and involvement of people with rare diseases in society and their communities. ▪ Involvement of people with rare disease in developing healthcare and social welfare services in their own areas. ▪ Safeguarding the involvement of people with rare diseases in their care and services. 3. Coordination of activities related to rare diseases. ▪ National coordination. ▪ Regional coordination. ▪ Coordination of care and services of a person with rare diseases.
France French National Plan for Rare Diseases 2018-2022[51]	**Focuses** (for objectives associated with each focus, see Appendix B, Table B12): ▪ Focus 1: Reducing diagnostic delays and undiagnosed diseases ▪ Focus 2: Improving neonatal screening and antenatal and preimplantation diagnostics to enable earlier diagnoses ▪ Focus 3: Sharing data to aid diagnosis and the development of new treatments ▪ Focus 4: Promoting access to treatments in rare diseases ▪ Focus 5: Giving new momentum to research in the field of rare diseases ▪ Focus 6: Promoting the emergence of and access to innovation ▪ Focus 7: Improving care pathways ▪ Focus 8: Facilitating the integration of people with rare diseases and their carers ▪ Focus 9: Training health and welfare professionals to better identify and manage rare diseases ▪ Focus 10: Reinforcing the role of rare disease clinical networks in care and research issues

Country Information Source	Themes or priorities
	▪ Focus 11: Specifying the positioning and missions of other national players in the field of rare diseases.
Germany ▪ National Plan of Action for People with Rare Diseases 2013[32] ▪ Interim report on the implementation of the National Action Plan for People with Rare Diseases 2017[31]	**Action fields** (used across both documents; for associated areas, see Appendix B, Tables B13 and B14): ▪ Action Field 1: Care, centres, networks ▪ Action Field 2: Research ▪ Action Field 3: Diagnostics ▪ Action Field 4: Information management ▪ Action Field 5: Implementation and future development ▪ Cross-sectional Action Field: Patient orientation (patient organisations to improve the medical treatment of persons with rare diseases) ▪ Cross-sectional Action Field: Registries.
The Netherlands ▪ National Plan for Rare Diseases 2013[52] ▪ Coordination Consultation for Rare Diseases: Final Advice 2017[53]	**Themes** (for descriptions and details on 'what is already there' and 'what is missing', see Appendix B, Table B17): ▪ Theme 1: Unfamiliarity with rare diseases ▪ Theme 2: Information provision and communication ▪ Theme 3: Organisation of care and availability of therapy ▪ Theme 4: Scientific research in the field of rare diseases ▪ Theme 5: Amplifying the voice of the patient with a rare disease ▪ Theme 6: Direction and continuity. Positive examples of initiatives were noted in the following areas: ▪ Diagnostics o Preconception care o Next Generation Sequencing o Genetic disorders ▪ Information provision o Information for patients and families ▪ Early detection ▪ Registration of rare diseases. 'White spots' identified as not receiving enough attention in the National Plan for Rare Diseases 2013: ▪ Medical and social domain: Too little attention has been paid to the connection with daily life, such as the domain of living, working, learning or leisure. ▪ (Medical) expertise outside the centres of expertise: General practitioners and paediatricians have insufficient experience and expertise to identify rare diseases at an early stage. While this has been a focus area, the recognition of rare diseases still deserves attention and can be greatly improved.
Northern Ireland ▪ Northern Ireland Rare Diseases Action Plan 2022/23[34]	Priorities and underpinning themes as per the UK Rare Diseases Framework.

Country Information Source	Themes or priorities
▪ Northern Ireland's Rare Diseases Action Plan: Progress Report Year 1 (March 2022-March 2023)[33]	
Portugal ▪ Integrated Strategy for Rare Diseases 2015-2020[35] ▪ Annual Plans 2016,[36] 2017,[37] 2018[38] and 2019[40] ▪ Interim Report on the Implementation of the Integrated Strategy for Rare Diseases 2015-2020: Year 2017[39] ▪ 2018 Annual Report: Integrated Strategy for Rare Diseases 2015-2020[41]	**Strategic priorities** (used consistently across the strategy, and all annual plans and reports): 1. Coordination of care 2. Access to early diagnosis 3. Access to treatment 4. Clinical and epidemiological information 5. Research 6. Social integration and citizenship.
Scotland Scotland Rare Disease Action Plan[42]	Priorities and underpinning themes as per the UK Rare Diseases Framework, with an additional vision statement for each priority. **Priorities:** ▪ Priority 1: Ensuring patients get the right diagnosis faster. Our vision is for people living with a rare disease across the UK to get a final diagnosis faster and for research into previously unrecognised conditions to identify new rare diseases and provide new diagnoses. ▪ Priority 2: Increasing awareness of rare diseases among healthcare professionals. Our vision is for healthcare professionals to have an increased awareness of rare diseases and use of genomic testing and digital tools to support quicker diagnosis and better patient care. ▪ Priority 3: Better coordination of care. Our vision is for people living with a rare disease to experience better coordination of care throughout the patient journey. ▪ Priority 4: Improving access to specialist care, treatment and drugs. Our vision is for people living with a rare disease to have improved access to specialist care, treatments and drugs. Feedback on each priority received from the rare community ('What Matters to You?') is included in Appendix B, Table B28.
Wales Wales Rare Diseases Action Plan 2022-2026[43]	Four priorities as per the UK Rare Diseases Framework, each with an accompanying vision statement: ▪ Priority 1: helping patients get a final diagnosis faster. The vision is for rare disease patients across the UK to get a final diagnosis faster and for research into previously unrecognised conditions to identify new rare diseases and provide new diagnoses. ▪ Priority 2: increasing awareness of rare diseases among healthcare professionals. The vision is for healthcare professionals to have an increased awareness of rare diseases and use of genomic testing and digital tools to support quicker diagnosis and better patient care.

Country Information Source	Themes or priorities
	▪ Priority 3: better coordination of care. The vision is for rare disease patients to experience better coordination of care throughout the patient journey. ▪ Priority 4: improving access to specialist care, treatments and drugs. The vision is for rare disease patients to have improved access to specialist care, treatments, and drugs. The underpinning themes of the UK Rare Diseases Framework must be incorporated across each priority area of the Welsh Action Plan and are also addressed separately.

Key: BMG: Federal Ministry of Health (Austria); ERN: European Reference Network; EU: European Union; NAP: National Action Plan (Austria); UK: United Kingdom.

3.2.3 Implementation

Details on implementation were outlined to varying extents in all of the included national rare disease strategies. Specifically, these details included descriptions of the actions planned for strategy implementation, the agencies responsible for implementation, and outcomes or measures for monitoring and evaluating strategy implementation. A high-level overview of national rare disease strategy implementation is outlined in Table 3.5.

Actions

Within the included national rare diseases strategies, the following related terms were identified: actions; recommendations; activities and objectives (see Appendix A, Table A1). For clarity, the term 'actions' was used as a representative term within this review.

For all of the countries included, implementation actions, either planned or in progress, were outlined. Summaries and or samples of actions are outlined in Appendix A, Table A1, with further information on strategy implementation actions for each selected country outlined in Appendix B.

Ten of the countries included outlined specific actions for implementation (Australia,[22] Austria,[47] Denmark,[24-26] England,[27, 28] Germany,[32] the Netherlands,[52, 53] Northern Ireland,[34] Portugal,[36-38, 40] Scotland,[42] Wales[43]), with Finland[50] and France[51] outlining broad, high-level actions. Finland[50] stated they did not outline a detailed list of actions but described key principles and objectives to guide decision-making, while France[51] outlined that detailed action plans would be developed by key players for the broader actions outlined in the national strategy.

Seven countries outlined implementation actions within their main strategy, and the status of these actions in further evaluation or annual report documents: Australia,[22, 23] Austria,[47, 48] Denmark,[24-26] Germany,[31, 32] the Netherlands,[52, 53] Northern Ireland,[33, 34] and Portugal.[36-38, 40] However, Denmark reduced over 100 recommendations across 13 themes, outlined in their 2014 main strategy,[24] to 23 recommendations, across 6 themes, in their 2018 strategy evaluation.[25] This was to ensure all included recommendations were action oriented. While these 23 recommendations were then retained in the 2022 strategy evaluation,[26] two themes which had been omitted from the 2018 evaluation (Availability of Treatment, and Implementation), containing five recommendations in total, were reintroduced (see Appendix A, Table A1 and Appendix B).

For Portugal, while broad high-level actions were provided in their main strategy covering the period from 2015 to 2020, more specific activities were provided within their annual plans presented for 2016 to 2019. For example the Integrated Strategy

for Rare Diseases 2015-2020 outlined *"Improve the access to early treatment by means of surgery, drugs or nutrition of serious rare diseases"* as an action for the theme of Access to Treatment,[35] while the 2019 Annual Plan outlined *"Development of informative material on nutrition care in the area of Rare Diseases"* as an activity planned for 2019, for the same theme.[40]

Lastly, the UK Rare Diseases Framework 2021[29] provided guidance to the UK nations around the development of their national rare disease strategies, within which they included specific actions which each nation should undertake, such as *"ensure any impacts on health inequalities are considered when developing action plans"*.

Implementation agencies

Leads or lead organisations, responsible bodies or entities; owners; collaborators; first points of contact; delivery partners; stakeholders; or other parties were outlined for all included actions in the national rare disease strategies of Austria,[47] England,[27, 28] France,[51] Germany,[32] the Netherlands[52] and Wales[43] (see Table 3.5 and Appendix A, Table A1):

- Austria[47] and Germany[32] outlined the entities or bodies responsible for action implementation. Examples for Austria included the Federal Ministry of Health and the National Centre for Coordination of Rare Diseases; and for Germany, examples included the Federal Ministry of Health and the German Hospital Federation.

- England[27, 28] outlined lead organisations or owners of actions, while France[51] outlined leaders and collaborators associated with their actions. Examples included: the Department of Health and Social Care, and Genomics England for England; and the Directorate General for Care Provision for France.

- The Netherlands[52] outlined first points of contact and other relevant parties for all included recommendations. For example, for the recommendation to increase general awareness of rare diseases, the first point of contact was the Association of Collaborating Parent and Patient Organisations for Rare and Genetic Disorders, with the Dutch Patient Federation listed as another relevant party.

- Wales[43] outlined delivery partners and stakeholders for all included actions, with examples including: the All Wales Therapeutics and Toxicology Centre and the Congenital Anomaly Register and Information Service.

While Portugal did not outline implementation agencies for their main strategy, the Integrated Strategy for Rare Diseases 2015-2020,[35] they outlined responsible entities in the 2018[38] and 2019 Annual Plans.[40] Denmark,[24-26] Finland,[50] Northern Ireland,[34] and Scotland[42] outlined implementation agencies for some, but not all actions. Lastly, Australia[22] outlined that a number of stakeholders, such as government agencies and the public, should consider implementation of actions, dependent on their area of responsibility, while Finland[50] outlined that strategy implementation requires commitment by all parties.

Outcomes or measures for monitoring and evaluation

Outcomes or measures for the monitoring and evaluation of strategy implementation were outlined for England,[27, 28] Northern Ireland,[34] Portugal[36, 37] and Wales[43] (see Table 3.5 and Appendix A, Table A1):

- England[27, 28] outlined outputs and outcomes against which strategic actions could be evaluated. For example, with the Action *"commission research on how best to measure the diagnostic odyssey"*[1][55] establishing a baseline time to diagnosis is outlined as an associated outcome, and the launch of a funding call for this research is outlined as an associated output.

- Northern Ireland[34] outlined key milestones and measures associated with strategy actions, while Wales[43] outlined measures or outcomes. For example, in Northern Ireland for the action *"develop a Northern Ireland Rare Diseases Registry"*, meetings would be held quarterly with registry colleagues, in all UK nations, to work towards a UK-wide national rare disease registration facility.[34] In Wales, for the action *"increase Whole Genome Sequencing testing for rare diseases",* success would be indicated by an increased number of tests performed.[43]

- While Portugal did not outline outcomes or measures for their main strategy, the Integrated Strategy for Rare Diseases 2015-2020,[35] they included products associated with actions for the 2016[36] and 2017[37] Annual Plans. For example, for the planned activity *"monitor the status of the provision of*

[1] The diagnostic odyssey is a term used to describe the time between first symptoms and receiving a diagnosis. This may involve various tests and procedures and delays in receiving effective care, and may have a significant impact on a person's quality of life and wellbeing.

diagnostic, therapeutic, rehabilitation and social inclusion interventions", the product was a report mapping the provision of care.

While the remaining main strategies did not outline outcomes or measures for monitoring and evaluation, a number of evaluation documents outlined methods of monitoring strategy implementation. Australia[22, 23] outlined that progress was monitored using a logic model, which captured activities carried out as part of the strategy according to the following elements: Inputs, Activities and Processes, Outputs, Outcomes and Impact. Demark[25, 26] outlined that the Danish Health Authority holds an annual status meeting to ensure implementation of strategy recommendations. The Netherlands' Final Advice from the Coordination Consultation[53] maps the status of each original recommendation to a particular colour, as follows: red ('has priority, needs action'), white ('a missing theme or topic in the strategy'), orange ('ongoing, monitor progress'), green ('ongoing, has been completed, or does not require action'). Austria,[47] France[51] and Scotland[42] also outlined that indicators were to be developed, however these were not identified at the time of data extraction.

Table 3.5 High-level overview of national rare disease strategy implementation in Ireland and the selected countries.

Country Information Source	Are actions outlined? (Yes or No and further information)	Are implementation agencies outlined? (Yes or No and further information)	Are outcomes or measures for monitoring and evaluation outlined? (Yes or No and further information)
Ireland			
▪ National Rare Disease Plan for Ireland 2014 – 2018[19]	▪ Yes, however called recommendations.	▪ Specific bodies and agencies are named for certain recommendations but not for all.	▪ Yes, a number of key outputs are listed within the recommendations and the EU EUCERD Indicators are used to monitor strategy implementation. The strategy also notes that "The HSE will report to the Department of Health using key performance indicator on a periodic basis in accordance with reporting requirements under the National Service Plan" although the KPIs are not listed.
▪ Interim Report on National Rare Disease Plan for Ireland 2014-2018 (Interim Report on Implementation and Summary of Recommendations)[45, 46]	▪ No, evaluation of main strategy recommendations.	▪ No, evaluation of main strategy recommendations.	▪ No, evaluation of main strategy recommendations.
Australia			
▪ National Strategic Action Plan for Rare Diseases 2020[22]	▪ Yes, specific actions.	▪ No, however document states that a number of stakeholders, such as government agencies and the public, should consider implementation of actions, dependent on their area of responsibility.	▪ No.
▪ Implementing the National Strategic Action Plan for Rare Diseases: May 2023 Status Report[23]	▪ No, evaluation of main strategy actions.	▪ No, however the evaluation outlines that the vast majority of activities were those undertaken by RVA Partner organisations (individual rare disease organisations).	▪ No, however the evaluation outlines that activities are outlined from Activities and Processes, to Outputs, Outcomes and measurable Impact.
Austria			
▪ National Action Plan (NAP) for Rare Diseases 2014-2018[47]	▪ Yes, specific actions.	▪ Yes, responsible entities outlined.	▪ No. Indicators were to be developed by 2015, however none identified presently.
▪ Evaluation of the NAP for Rare Diseases 2020[48]	▪ No, evaluation of main strategy actions.	▪ No, however recommendations for leads to be more specified.	▪ No.

Country Information Source	Are actions outlined? (Yes or No and further information)	Are implementation agencies outlined? (Yes or No and further information)	Are outcomes or measures for monitoring and evaluation outlined? (Yes or No and further information)
▪ National Action Plan for Rare Diseases 2014-2018 Executive Summary[49]	▪ No, summary of main strategy.	▪ No, summary of main strategy.	▪ No, summary of main strategy.
Denmark ▪ National Strategy for Rare Diseases 2014[24]	▪ Yes, however called recommendations.	▪ Specific bodies and agencies are named for certain recommendations but not for all.	▪ No.
▪ Evaluation of the National Strategy for Rare Diseases 2018[25]	▪ Yes, however is an evaluation which condenses down main strategy recommendations.	▪ Specific bodies and agencies are named for certain recommendations but not for all.	▪ No, however the Danish Health Authority holds an annual status meeting to ensure implementation of the recommendations.
▪ Evaluation of the National Strategy for Rare Diseases 2022[26]	▪ Yes, number of recommendations increases from 2014 evaluation.	▪ Specific bodies and agencies are named for certain recommendations but not for all.	▪ No, however the Danish Health Authority holds an annual status meeting to ensure implementation of the recommendations.
England ▪ Rare Diseases Action Plan 2022[27]	▪ Yes, specific actions.	▪ Yes, owners outlined.	▪ Yes, metrics and milestones associated with each action outlined.
▪ Rare Diseases Action Plan 2023[28]	▪ Yes, specific actions.	▪ Yes, lead organisations outlined.	▪ Yes, action specific monitoring and evaluation outlined along with outputs and outcomes.
▪ The UK Rare Diseases Framework 2021[29]	▪ No, framework for nations to develop action plans.	▪ No, framework for nations to develop action plans.	▪ No, framework for nations to develop action plans.
Finland National Programme for Rare Diseases 2019-2023[50]	Yes, however these are proposed actions and objectives not a detailed list of actions.	Specific bodies and agencies are named for certain recommendations but not for all. The current or proposed role of different actors in the development and coordination related to rare diseases are also outlined, but these are not action specific. The strategy also outlines that implementation requires commitment by all parties.	No.
France French National Plan for Rare Diseases 2018-2022[51]	Yes, quite specific. Further detailed action sheets are also to be developed by action leads.	Yes, leaders and collaborators outlined.	No, however action leads are to "develop detailed action sheets defining the schedule for roll-out of actions and follow-up, and results indicators".

Country Information Source	Are actions outlined? (Yes or No and further information)	Are implementation agencies outlined? (Yes or No and further information)	Are outcomes or measures for monitoring and evaluation outlined? (Yes or No and further information)
Germany			
▪ National Plan of Action for People with Rare Diseases[32]	▪ Yes, proposed actions.	▪ Yes, responsible bodies outlined.	▪ No.
▪ Interim report on the implementation of the National Action Plan 2017[31]	▪ No, evaluation of main strategy actions.	▪ No, evaluation of main strategy.	▪ No.
The Netherlands			
▪ National Plan for Rare Diseases 2013[52]	▪ Yes, however called recommendations.	▪ Yes, first point of contact and other relevant parties outlined for each recommendation.	▪ No, however there is a recommendation for a government advisory body that monitors and evaluates plan activities.
▪ Coordination Consultation for Rare Diseases: Final Advice 2017[53]	▪ Yes, further recommendations on strategy implementation.	▪ No, main strategy implementation agencies remain.	▪ No, however the document maps the status of each original recommendation to either red: has priority needs action; white: a missing theme or topic in the strategy; orange: ongoing, monitor progress; and green: ongoing, has been completed, or does not require action.
Northern Ireland			
▪ Northern Ireland Rare Diseases Action Plan 2022/23[34]	▪ Yes, specific actions.	▪ Specific bodies and agencies are named for certain recommendations but not for all.	▪ Yes, key milestones and measures for Year 1.
▪ Northern Ireland's Rare Diseases Action Plan Progress Report Year 1 (March 2022-March 2023)[33]	▪ No, evaluation of main strategy actions.	▪ No, evaluation of main strategy.	▪ No.
▪ The UK Rare Diseases Framework 2021[29]	▪ No, framework for nations to develop action plans.	▪ No, framework for nations to develop action plans.	▪ No, framework for nations to develop action plans.
Portugal			
▪ Integrated Strategy for Rare Diseases 2015-2020[35]	▪ Yes, however very high level.	▪ No.	▪ No.
▪ Annual Plan 2016[36]	▪ Yes, specific activities.	▪ No.	▪ Products associated with actions are outlined.

Country Information Source	Are actions outlined? (Yes or No and further information)	Are implementation agencies outlined? (Yes or No and further information)	Are outcomes or measures for monitoring and evaluation outlined? (Yes or No and further information)
▪ Annual Plan 2017[37]	▪ Yes, specific activities.	▪ No.	▪ Products associated with actions are outlined.
▪ Annual Plan 2018[38]	▪ Yes, specific activities.	▪ Yes, responsible entities outlined.	▪ No.
▪ Annual Plan 2019[40]	▪ Yes, specific activities.	▪ Yes, responsible entities outlined	▪ No.
▪ Interim Report on the Implementation of the Integrated Strategy for Rare Diseases 2015-2020 – Year 2017[39]	▪ No, evaluation of main strategy actions.	▪ No, evaluation of main strategy.	▪ No.
▪ Annual Report Integrated Strategy for Rare Diseases 2015-2020 – Year 2018[41]	▪ No, evaluation of main strategy actions.	▪ No, evaluation of main strategy.	▪ No.
Scotland ▪ Rare Disease Action Plan 2022[42]	▪ Yes, specific actions.	▪ Specific bodies and agencies are named for certain recommendations but not for all.	▪ No, however the strategy outlines they will look to develop metrics to measure strategy success.
▪ The UK Rare Diseases Framework 2021[29]	▪ No, framework for nations to develop action plans.	▪ No, framework for nations to develop action plans.	▪ No, framework for nations to develop action plans.
Wales ▪ Wales Rare Diseases Action Plan 2022-2026[43]	▪ Yes, specific actions.	▪ Yes, delivery partners and or stakeholders outlined.	▪ Yes, measures or outcomes for each action are outlined.
▪ The UK Rare Diseases Framework 2021[29]	▪ No, framework for nations to develop action plans.	▪ No, framework for nations to develop action plans.	▪ No, framework for nations to develop action plans.

Key: EU: European Union; EUCERD: European Union Committee of Experts on Rare Diseases; NAP: National Action Plan (Austria); RVA: Rare Voices Australia; UK: United Kingdom.

3.2.4 Governance and or organisational structures

Across the selected countries, national governments, and specifically ministries and departments with responsibilities for sectors such as health, social security and education, played leading roles in national rare disease strategy governance. However, there was also variation between countries in the governance and or organisational structures through which strategies were developed, implemented, monitored and evaluated (see Table 3.6 for summaries of information on governance identified in the national strategies and supporting documents for each selected country).

In Australia,[22] Austria[47] and Germany,[32] national governments assigned responsibility to specific rare disease organisations to lead the development of their national rare disease strategies, in line with international exemplars or recommendations. For example, the Australian strategy referred to the Genetic and Rare Diseases Information Center in the US, Centres of Excellence in the UK, and ERNs in Europe as positive international examples of implementation,[22] while the Austrian strategy noted that their actions were developed in line with the EUCERD recommendations.[47] In Australia, this responsibility was given to an existing umbrella patient representative organisation: Rare Voices Australia.[23] In Austria, the National Coordination Centre for Rare Diseases was established by the Federal Ministry of Health in 2011 to lead strategy development, in collaboration with two expert advisory bodies.[47] In Germany,[32] the approach was similar to Austria, the National Action League for People with Rare Diseases was founded in 2010 by the Federal Ministry of Health, the Federal Ministry of Education and Research and the Alliance of Chronic Rare Diseases to develop and coordinate the National Action Plan.[32] Each action in the plan was implemented by a responsible body, as outlined in section 3.2.3.

Denmark,[24] Finland[50] and Portugal[35] had similar approaches to governance, where established health authorities had strategic responsibility regarding their national rare disease strategies, and where a wider working group of organisations implemented the actions:

- In Denmark,[24] the national health authority led on the implementation of the Action Plan, providing a secretariat and organisational role for institutions and organisations which were part of a working group.
- In Finland,[50] the Ministry of Social Affairs and Health and the National Institute for Health and Welfare provided oversight, guidance and coordination in conjunction with a working group.
- In Portugal,[35] the Integrated Strategy for Rare Diseases was coordinated by an inter-ministerial commission chaired by the Director General of Health. The operationalisation of the strategy was also facilitated by representatives and

organisations such as members of the medical professions and patient representative organisations.

In France,[51] distinct strategic and operational governance structures were established: a strategic committee that guided the implementation of the national strategy, and an operational committee that ensured the implementation of actions. Each of these committees was chaired by representatives from the relevant government ministries (the Ministry of Solidarity and Health and the Ministry of Higher Education, Research and Innovation), and included representatives from other bodies within the rare diseases sector. For example, the strategic committee included representatives from the rare disease clinical networks, the project leader of the France Genomic Medicine 2025 plan, and representatives of patient associations. There was also a clear reporting structure between the committees and national government: the operational committee proposed an annual report, which the strategic committee validated and submitted to the Prime Minister.

In the Netherlands,[52] the Ministry for Health, Welfare and Sport guided policy in relation to centres of expertise, and the government was also responsible for funding orphan drugs and initiatives to promote early detection of rare diseases, such as newborn screening. The national plan outlined a requirement to appoint a coordinator to prevent fragmentation and unnecessary duplication, and to promote coherence. Additionally, each of the plan's recommendations had a designated party who was responsible for implementing the action.

In the UK,[29] a UK-wide governance model was established, which provided ongoing high-level coordination, support and engagement across England, Northern Ireland, Scotland and Wales. However, in addition, each of these four countries established its own implementation or delivery group with responsibility for drafting and monitoring national action plans:

- the Rare Diseases Framework Delivery Group (England),[27, 28]
- the Rare Diseases Implementation Group (Northern Ireland),[34]
- the Rare Disease Implementation Board (Scotland)[42]
- the Rare Disease Implementation Group (Wales).[43]

These groups worked with partner organisations in their respective countries to oversee the implementation of actions. For example, England's Rare Diseases Framework Delivery Group was responsible for development, oversight and coordination of the action plan.[27, 28] The group brought together publicly funded delivery partners across the health system and, as part of the wider system, organisations such as patient representative groups and independent policy institutes were also included. They also collaborated with the rare disease community in order to develop an approach to monitoring and evaluation.

Table 3.6 Governance identified in the national rare disease strategies of Ireland and the selected countries.

Country Information Source	Governance
Ireland	
▪ National Rare Disease Plan for Ireland 2014 – 2018[19]	▪ The Department of Health established a Steering Group to oversee the development of the National Rare Disease Plan. Five subgroups were convened to support the Steering Group, each chaired by a member of the Steering Group. The subgroups related to: o Research and information o Centres of expertise o Patient empowerment o Orphan drugs and technologies o Communication. Membership of the Steering Group included representatives from the Department of Health, the Health Service Executive (HSE), the Health Research Board and patient organisations (see Appendix B, Table B15 for full list of members). Implementation of rare disease management programmes should be specified within the HSE Service Plan mechanism, which provides an accountability framework with respect to the delivery of health services.
▪ Interim Report on National Rare Disease Plan for Ireland 2014-2018 (Interim Report on Implementation[45] and Summary of Recommendations[46])	▪ An Oversight Group to monitor the implementation of the National Rare Disease Plan was established by the Department of Health in 2015, largely comprised of members from the original Steering Group. A National Clinical Programme for Rare Diseases was established in 2013 under the National Clinical Strategy and Programmes Division of the HSE, as a joint initiative between the HSE and the Royal College of Physicians of Ireland. The programme acted as a channel for implementation of a specified number of the 48 recommendations from the national plan, for example, those relating to national centres of expertise and promoting participation in ERNs. A National Rare Diseases Office was also established by the HSE, as a core recommendation of the national plan.
Australia	
▪ National Strategic Action Plan for Rare Diseases 2020[22]	▪ The Australian Government commissioned Rare Voices Australia (RVA) to develop the Action Plan. The actions are for consideration by a wide range of stakeholders, including governments at all levels, non-government organisations, the public and private health sectors, industry, researchers and academics, rare disease organisations and the wider community. An implementation mechanism was proposed in the Action Plan, to be led by a 'national peak organisation' that builds capacity in the rare disease sector in line with international exemplars such as: The Genetic and Rare Diseases Information Centre (US), Rare Disease Centres of Excellence (UK) and European Reference Networks (ERNs). The 'national peak organisation' would also facilitate and provide secretariat support to Centres of Excellence (for example: research groups, clinics, rare disease organisations and hospitals) located throughout Australia.
▪ Implementing the National Strategic Action Plan for Rare Diseases: May 2023 Status Report[23]	▪ Implementation of the Action Plan is the ongoing responsibility of all stakeholders, including all levels of government, the public and private health sectors, rare disease organisations, industry, researchers and the wider community. RVA remains committed to leading the collaborative implementation of the Action Plan and will continue to monitor and evaluate progress and steer the sector to the realisation of the collective vision for the best possible health and wellbeing outcomes for Australians living with a rare disease.

Country Information Source	Governance
Austria	
▪ National Action Plan (NAP) for Rare Diseases 2014-2018[47]	▪ The NAP for Rare Diseases 2014-2018 was developed on behalf of the Federal Ministry of Health (BMG) by the National Coordination Centre for Rare Diseases (NKSE) in collaboration with two advisory bodies: o the Expert Group for Rare Diseases and o the Strategic Platform for Rare Diseases. The NAP sets nine central thematic priorities that take into account both the European recommendations and national requirements in the area of rare diseases and provides for monitoring and evaluation of its implementation. By setting up two advisory bodies, the BMG pursued the goal of incorporating knowledge and expertise on rare diseases from research and lived practice into the work of the NKSE.
▪ Evaluation of the NAP for Rare Diseases 2020[48]	▪ The Advisory Board for Rare Diseases was established as a permanent committee to replace the temporary Expert Group. The Advisory Board was tasked with supporting the NKSE through critical reflection and discussion, as well as through providing advisory support. The Strategic Platform was maintained as a permanent committee with a strategic support and feedback function between the BMG, the federal states and the social insurance providers. The Strategic Platform has extensive decision-making authority on the content developed by the NKSE, which is only limited by the decision-making authority of the institutions, committees and specialist groups in the healthcare system that are separately and ultimately responsible for a specific topic. The National Office for the Implementation of NAP was established in 2019 and took on the coordinating tasks previously undertaken by the NKSE. The evaluation recommended that improvements were needed in relation to role clarity and communication structures between the various committees (NKSE, the National Office for the Implementation of NAP, the Advisory Board, and the Strategic Platform). Clarity on who is responsible for project and process management of the further implementation of the NAP was identified as a specific need.
Denmark	
▪ National Strategy for Rare Diseases 2014[24]	▪ The Danish Health Authority handles the secretariat function for the working group and can supplement the working group with relevant skills on an ad hoc basis, including possibly through the establishment of sub-working groups.
▪ National Strategy for Rare Diseases: Status Evaluation and Recommendations for Future Efforts 2018[25]	▪ The status evaluation was initiated in autumn 2016 with a collection of contributions from the parties who formed the original working group for the preparation of the national strategy. The contributions were used at an initial status meeting at the Danish Health Authority in October 2016, where the same parties were invited. At the status meeting, the participants agreed to form a follow-up group for further work towards the preparation of the status evaluation. The Danish Health Authority handled the secretariat function, and the status evaluation was prepared in collaboration with the National Board of Social Services. During the work, advice was received from the follow-up group. Members of this group included the Danish Society for general medicine, the Centre for Rare Diseases, the Ministry of Health and the Elderly and the Danish Paediatric Society.
▪ Evaluation of the National Strategy for Rare Diseases 2022[26]	▪ The Danish Health Authority holds an annual status meeting with group members and other invited parties. They discuss the status of the implementation of the recommendations and other relevant issues. The meetings create space for professional discussions of current development trends, issues and challenges in the field, and contribute perspectives on how the work with the recommendations develops in practice. Finally, it is ensured that the area is

Country Information Source	Governance
	continually adapted to national as well as international changes. Status group members include the Centre for Rare Diseases Aarhus University Hospital and Central Region, the Danish Society for Medical Genetics and the National Board of Social Affairs and Health (for full list please see Appendix B, Table B8). It is recommended that the commitment and participation of patient associations is supported.
England ▪ England Rare Diseases Action Plan 2022[27] ▪ England Rare Diseases Action Plan 2023: Main report and Annexes[28]	See 'United Kingdom' in this table for details of overarching UK governance structures. ▪ The England Rare Diseases Framework Delivery Group develops, oversees, and coordinates delivery of England's action plans. It has brought together publicly-funded delivery partners across the health system including NHS England and NHS Improvement; the National Institute for Health and Care Excellence; the Medicines and Healthcare Products Regulatory Agency; Health Education England; the National Congenital Anomaly and Rare Disease Registration Service; Genomics England; the National Institute for Health and Care Research, and the Medical Research Council, as major funders of rare diseases research; and representatives of rare disease patient and public voice and the clinician community. Over the course of 2021, the delivery group met every 6 weeks to develop and agree on actions, which formed the basis of the plan. The action plan sits within a wider system, which includes organisations such as charities, patient advocacy groups, philanthropically funded organisations, independent policy institutes and industry and will help to facilitate continued engagement, increased coordination and more joined up working with others. The Framework Delivery group will work with the rare disease community to develop an approach for monitoring and evaluation.
Finland National Programme for Rare Diseases 2019-2023[50]	A number of parties have or are proposed to have responsibility for the development and coordination of roles related to rare diseases: ▪ Ministry of Social Affairs and Health: steering of legislation, resources and information, general supervision, assessment, EU cooperation, cooperation in Nordic networks ▪ Funding Centre for Social Welfare and Health Organisations (STEA): funding of patient organisation activities in the field of rare diseases, assessment of effectiveness of such measures ▪ Healthcare and social welfare: production of services, improving the availability of expertise, agreeing on service pathways and referral practices ▪ University Hospital Districts: regional cooperation and coordination tasks in accordance with the Centralisation Decree (582/2017), information production to Health Village, international research activities, coordination of centres of expertise and ERN healthcare providers, care instructions ▪ National Institute for Health and Welfare (THL): information guidance, maintenance of networks, project steering, comprehensive research, assessment and maintenance of services, functioning measures, ORPHAcodes, knowledge-bases and registries ▪ Council for Choices in Healthcare in Finland (COHERE Finland): knowledge steering, assessment of inclusion of services and treatments in rare diseases in the service palette of national healthcare ▪ Social Insurance Institution of Finland: reimbursement of medicines, costs of cross-border care, other benefits and services, rehabilitation ▪ Finnish Medicines Agency (FIMEA), Pharmaceuticals Pricing Board (HILA): marketing authorisation of medicinal products, assessment of benefits to treatment from orphan drugs, conditions for reimbursement of medicines ▪ Finnish Network for Rare Diseases: to influence matters promotion of joint lobbying of organisations, communication, compiling and disseminating information

Country Information Source	Governance
	▪ Finnish Alliance of Rare Diseases and Disabilities Organisations (HARSO): promotion of organisations' joint activities to influence matters ▪ Norio Centre of Rare Diseases: maintenance of the Finnish Orphanet website, international cooperation.
France French National Plan for Rare Diseases 2018-2022[51]	The Strategic Committee ensures application of the plan by mobilising partners and resources. It guides its implementation and proposes adjustments to the plan on the basis of the evolving context. It validates the annual report proposed by the operational committee that it submits to the Prime Minister. The Committee is chaired by the cabinets of the Ministry of Solidarity and Health and the Ministry of Higher Education, Research and Innovation. The Strategic Committee meets at least once a year. Membership of the committee included representatives from government departments, rare disease clinical networks and the project leader of the France Genomic Medicine 2025 plan. The Operational Committee is responsible for implementing the actions of the Plan and reporting back to the Strategic Committee. It ensures actions are implemented in accordance with the scheduled calendar, assesses the results of the Plan using indicators and monitors spending compared to the scheduled budget. It prepares the annual report for the Plan. The Operational Committee is chaired by two people who have been appointed by the Ministry of Solidarity and Health and the Ministry for Higher Education, Research and Innovation (chair and vice-chair), who are assisted by the rare diseases mission, composed of members of both ministries, and the secretariat of which is handled by the Directorate General for Care Provision. The Operational Committee meets at least once a year. Membership of the committee included representatives from patient associations and rare disease clinical networks (see Appendix B Table B12 for list of committee members).
Germany ▪ National Plan of Action for People with Rare Diseases 2013[32] ▪ Interim report on the implementation of the National Action Plan for People with Rare Diseases 2017[31]	▪ The German Federal Ministry for Education and Research, the Alliance of Chronic Rare Diseases, and the National Action League for People with Rare Diseases (NAMSE) are responsible for coordinating and publishing work in relation to their work regarding rare diseases. The main aim of the NAMSE is to provide advice on a National Action Plan for People with Rare Diseases by 2013 and support the establishment of national centres of expertise. Further roles of the Action League include implementing the Recommendations of the Council of the European Union, including: drafting a National Action Plan for Rare Diseases and implementing and monitoring the Plan (supporting the establishment of centres of excellence is also recommended by the European Union Council). As outlined in section 3.2.3, organisations responsible for implementing individual actions include; the German Hospital Federation; the Ministry of Health; the German Federal Ministry for Education and Research and the German Research Foundation. See Appendix B, Table B13 for the full list of such organisations.
The Netherlands ▪ National Plan for Rare Diseases 2013[52]	▪ The government is responsible for areas such as prevention and early detection (newborn screening) of diseases and the financing of orphan drugs. The strategy also outlines the requirement to appoint a director and or coordinator for the recommendations to promote coherence and help prevent fragmentation and unnecessary duplication. Additionally, each individual recommendation names one party that should take primary responsibility (see section 3.2.3). The action plan tries to encourage these parties to feel responsible for the recommendation and to encourage action to be taken. Most recommendations also include suggestions for organisations with which to collaborate on the action point and or recommendation.

Country Information Source	Governance
Coordination Consultation for Rare Diseases: Final Advice 2017[53]	▪ The national policy regarding the powers and responsibilities of expertise centres lies primarily with the Ministry of Health, Welfare and Sport. Health insurers have a role when it comes to purchasing care in expertise centres and the surrounding network. The Health and Youth Care Inspectorate will monitor quality and safety. The Netherlands Healthcare Institute has several roles. It advises the Ministry of Health, Welfare and Sport on the inclusion of orphan drugs in the package and can also stimulate the development of care standards for rare diseases, which often originate from scientific associations.
Northern Ireland ▪ Northern Ireland Rare Diseases Action Plan 2022/23[34] ▪ Northern Ireland's Rare Diseases Action Plan: Progress Report Year 1 (March 2022 – March 2023)[33]	See 'United Kingdom' in this table for details of overarching UK governance structures. ▪ The Northern Ireland (NI) Rare Diseases Implementation Group develops, oversees and co-ordinates delivery of NI's Action Plan. The group is chaired by the Department of Health's Chief Scientific Advisor and Director of the Health and Social Care Research & Development. It brings together key stakeholders across the healthcare system, including representatives from relevant areas such as commissioning, public health, the rare disease patient voice via the voluntary sector, academia, adult social care, mental health, and genomic medicine. Over the course of 2021 and 2022, the Implementation Group met regularly to develop and agree the actions, which form the basis of the plan. The Implementation Group has worked in partnership to develop this action plan, bringing together representatives from the rare disease patient and public voice, and the clinical community. The NI Rare Diseases Partnership actively lobbied on behalf of, and with support from, the rare disease community to successfully establish an All-Party Group for Rare Disease at the NI Executive. The All-Party Group will act as a mechanism to ensure that all future conversations around rare disease support and services have a direct conduit into the parliamentary structure at the highest level, while supporting awareness raising at an Executive and regional level. ▪ In considering how best to take forward the work, NI Rare Diseases Implementation Group grouped the 14 actions thematically, for example actions on information sharing or around education and training, and established five Working Groups to take forward each themed group of actions.
Portugal ▪ Integrated Strategy for Rare Diseases 2015-2020[35] ▪ Annual Plans 2016,[36] 2017,[37] 2018,[38] and 2019[40] ▪ Interim Report on the Implementation of the Integrated Strategy for Rare Diseases 2015-2020 – Year 2017[39] ▪ Annual Report Integrated Strategy for Rare Diseases 2015-2020 – Year 2018[41]	The Inter-ministerial Commission created to implement the Integrated Strategy for Rare Diseases 2015-2020, was chaired by the Director-General of Health and consisted up of representatives from various bodies, namely: the National Institute of Health; Central Administration of the Health System; National Authority for Medicines and Health Products; Social Security Institute; National Institute for Rehabilitation; Foundation for Science and Technology; and Directorate-General for Education in the area of special educational needs. A number of parties were invited to participate in operationalising the priorities set out in the Integrated Strategy for Rare Diseases 2015-2020 such as: health professionals, rare disease patient representative associations, National Association of Portuguese Municipalities, National Association of Parishes and Social Sector partners.

Country Information Source	Governance
Scotland Rare Disease Action Plan 2022[42]	See 'United Kingdom' in this table for details of overarching UK governance structures. ▪ The Rare Disease Implementation Board (RDIB) was formed to develop the Rare Disease Action Plan. The RDIB brings together those with clinical expertise, representatives of patient advocacy groups and other NHS Scotland third sector representatives (such as, Genetic Alliance UK, Medics 4 Rare Diseases, and the Office for Rare Conditions) to work on the Plan. The RDIB will work with NHS Scotland Boards and with NHS Scotland's National Services Division to ensure that all actions required to improve the lives of people with rare diseases can be embedded into standard practice across Scotland. The National Services Division are particularly important as they deal with national and specialist services for small patient groups, which is often the case for the care and treatment of rare diseases. The "Once for Scotland" strategy that the National Services Division apply will also help with better coordination of care.
United Kingdom The UK Rare Diseases Framework 2021[29]	The UK Rare Diseases Framework is a UK-wide document. However, each of the four UK nations has its own delivery or implementation group responsible for drafting and monitoring nation-specific action plans. To further help with implementation of the Framework, two UK-wide boards have been created: ▪ The UK-wide UK Rare Diseases Framework Board provides strategic oversight and facilitates alignment of policy across the 4 UK nations. ▪ The UK Rare Diseases Forum provides a means of engagement with the community. The forum has two parts: a core membership which meets twice a year, and an online knowledge and collaboration platform for continual engagement with a broad range of stakeholders, which both feed into the strategic UK Rare Diseases Framework Board. A UK-wide newsletter is also produced which provides policy updates on implementation and progress as well as relevant news on rare disease developments in each country.
Wales Wales Rare Diseases Action Plan 2022 - 2026[43]	See 'United Kingdom' in this table for details of overarching UK governance structures. The Wales Rare Disease Implementation Group works with health boards and partner organisations acting as the mechanism for the development and oversight of the action plan for Wales. The Wales Rare Disease Implementation Group will continue to meet regularly to report on progress. This will include a process of constant review and any changes to the plan will be considered on an annual basis. This will include those actions completed during the year and timescales for those not completed and barriers to completion. A number of developments will be subject to agreement of available resources and ongoing and or successful business cases. By developing the plans in a clear way with: ▪ actions ▪ delivery partners and or stakeholders ▪ timelines ▪ measures and or outcomes it will provide a platform for objective measurement of the success of the plan.

Key: BMG: Federal Ministry of Health (Austria); COHERE: Council for Choices in Healthcare in Finland; DGOS: Directorate General for Care Provision (France); EU: European Commission; ERN: European Reference Network; HSE: Health Service Executive; NAMSE: National Action League for People with Rare Diseases; NAP: National Action Plan (Austria); NI; Northern Ireland; NKSE: National Coordination Centre for Rare Diseases; NHS: National Health Service; RDIB: Rare Disease Implementation Board (Scotland); Rare Voices Australia; UK: United Kingdom; USA: United States of America.

3.2.5 Funding model

Seven of the selected countries outlined funding allocated toward either overall strategy implementation, individual strategy priorities and or individual strategy actions (Australia,[22] England,[27, 28] Finland,[50] France,[51] Germany,[32] Scotland[42] and Wales[43]) (see Table 3.7). In addition, while the Netherlands did not outline a funding model for overall strategy implementation, one of their strategic actions related to enabling funding of care in designated centres of expertise through health insurers. Government funding committed to strategy implementation was outlined by England,[27, 28] Scotland[42] and Wales.[43] England[27, 28] outlined that funding would be provided either through delivery partners' existing organisational budgets, or accounted for in the previous year's autumn budget and spending review. Funding included £340 million for the Innovative Medicines Fund, and a £5 billion increase in health-related research and development. This funding for health-related research included allocations to support Genomics England's research initiative, a national research pilot testing 100,000 newborns using whole genome sequencing to detect rare diseases with a genetic cause. Scotland[42] outlined that the Scottish Government supported strategy implementation through significant investment, with £5 million committed for 2022 and 2023. Wales[43] stated that the Rare Diseases Implementation Group secured Welsh Government funding for strategy coordinator support, a new all-Wales Clinical Lead for Rare Diseases, and the setup of a two-year pilot for a Syndrome Without A Name (SWAN) Clinic.

Finland[50], France[51] and Germany[32] also stated sources of research funding such as the European Joint Programme on Rare Diseases (Finland[50]), the Ministry for Solidarity and Health (France[51]) and the German Research Foundation.[32] Finland[50] also described funding for patient representative organisations, while Germany[32] outlined that centres of expertise would be funded within the existing legal framework. The French Action Plan[51] listed estimated costs and the funding bodies for all strategy actions; examples included: *Action 1.1: Encourage the management of any person with or suspected of having a rare disease within a rare disease reference centre* at a cost of €119 million per year (€597 million over five years dedicated to rare disease reference centres), funded by the Ministry of Health and Prevention.

While Australia did not outline a funding model within their strategy,[22] a key representative confirmed that over $4 million was provided for strategy implementation actions from 2020 to 2021.[56] One million dollars of this was provided for rare disease awareness and education activities, with the remaining $3 million provided to undertake development and delivery of education resources for health professionals, and activities to support people living with a rare disease.

Finland[50] was the only country included to perform economic analysis in relation to strategy funding. Finland estimated the following costs for strategy implementation:

- approximately 1.6 additional person-years would be needed for physicians and 0.8 person-years for nurses at the national level, with a cost of approximately €200,000 per year
- at least two person-years are required for the national coordination tasks, including the communication of information, coordination of networks, update and maintenance of the ORPHAcodes, and Orphanet activities. Resources are also required for development of the database and the maintenance of a registry for rare diseases. In total, these amount to €200,000 to €300,000 per year
- if the centres of expertise joined all 24 ERNs during the programme period, the total amount of work would be between 20 and 25 person-years, at a cost of approximately €2 million per year.[50]

Five of the countries included did not outline a funding model or budget mechanism, or else outlined that there was no budget ring-fenced for strategy implementation and or activities, in their respective national rare disease strategy (Austria,[47] Denmark,[24] the Netherlands,[52] Northern Ireland[34] and Portugal[35]). All of these countries outlined that a lack of funding presented a challenge to, or constraint on, strategy implementation, and this was particularly apparent in strategy evaluation documents.[26, 33, 39, 41, 48, 53]

Table 3.7 Funding models identified in the national rare disease strategies of Ireland and the selected countries.

Country Information Source	Funding model(s)
Ireland	
▪ National Rare Disease Plan for Ireland 2014 – 2018[19]	▪ The implementation of this National Rare Disease Plan shall be set in the context of re-orienting current resources for the purposes of advancing these recommendations in the health service, given the prevailing financial constraints. The present budgetary environment shall be explored to identify and exploit all opportunities for progressing this national plan as the future platform to address the care and treatment of people with rare diseases.
▪ Interim Report on National Rare Disease Plan for Ireland 2014-2018 (Interim Report on Implementation[45] and Summary of Recommendations[46])	▪ References to funding are included in progress reports on recommendations 4, 6, 8, 10, 16a, 20, 22, 29 and 45 (see Appendix B, Table B16).
Australia	
▪ National Strategic Action Plan for Rare Diseases 2020[22]	▪ Not mentioned. Funding gaps and recommendations for funding priorities noted in Actions 1.1.1, 2.2.2, 2.2.4, 2.3.2, 2.4.2, 2.4.3, 3.2.2, 3.2.3, 3.3.2 and 3.4.1 (see Appendix B, Table B1).
▪ Information provided by email from key representative in Australian Government Department of Health and Aged Care to HIQA[56]	▪ "Funding of $4.03 million over four years from 2020-21 is being provided for implementation activities that align with the Action Plan. Of this funding, $1 million is being provided for rare disease awareness and education activities. The remaining $3.03 million is being provided to undertake development and delivery of education resources for health professionals, and activities to support people living with a rare disease."
▪ Implementing the National Strategic Action Plan for Rare Diseases: May 2023 Status Report[23]	▪ All governments must urgently invest in the rare disease sector. To drive systemic change, investments should leverage and build on existing expertise, knowledge, resources and infrastructure. Learnings from the activity scan also highlight the need to invest in regular reviews of Action Plan progress to support iterative implementation plans for a responsive, dynamic, transformative and targeted approach.
Austria	
▪ National Action Plan (NAP) for Rare Diseases 2014-2018[47]	▪ The costs associated with the implementation of the measures must be taken into account when planning. There is currently no defined budget available; budget frameworks set for several years may need to be taken into account. The actual costs for each individual measure proposed in NAP are determined during the planning and definition of the respective implementation process. The institutions involved in the implementation are included in the cost estimate so that the potential financiers can plan the required budget. At the end of the term of the current NAP (2018), the health ministry, with the support of the National Centre for Coordination of Rare Diseases, will provide a summary of the total funds used for the development and implementation of the NAP. Additionally, funding institutions are outlined for Priority 5: Promoting research in the area of rare diseases: ▪ Fund for the Promotion of Scientific Research ▪ Austrian Research Promotion Agency

Country Information Source	Funding model(s)
▪ Evaluation of the NAP for Rare Diseases 2020[48]	▪ Austrian Business Services Society ▪ Anniversary Fund of the Austrian National Bank ▪ Federal state-specific funds ▪ The most common reason why measures are not (yet) implemented or not fully implemented was the lack of clarity regarding the financing of implementation, partly also a lack of monitoring of implementation, but also the prioritisation of actions relating to the designation of centres of expertise. All experts and stakeholders stated that the question of financing had been deliberately left out. In the discussions in the Strategic Platform and the Advisory Board for Rare Diseases it was repeatedly stated that the NAP should not incur any additional costs. The majority of the experts and stakeholders surveyed stated that the NAP was an action plan that did not take financial considerations into account and was not predetermined to have a schedule. There is a lack of clear commitment from the financiers involved when it comes to implementation. Some interviewees suggested creating a slimmed-down new version of NAP, but one that would be feasible and more concrete. Appropriate financing of the measures should also be taken into account. This could take the form of an implementation plan coordinated with all stakeholders involved. Further findings around the financing of the NAP, from interviews with experts, are outlined in Appendix B, Table B5.
Denmark ▪ National Strategy for Rare Diseases 2014[24]	▪ No specific funding of the overall strategy mentioned. The financing of the RAREDIS database has been based on grants from private funds, despite the Danish Health Authority's recommendation and approval as a clinical quality database. Stable, lasting funding is therefore an important prerequisite for further expansion and development of the database.
▪ Evaluation of the National Strategy for Rare Diseases 2018[25]	▪ There is no associated funding for the national strategy. Current expenditure for rare diseases, as for all other diseases, is within the general health system budget of the regions and municipalities.
▪ Evaluation of the National Strategy for Rare Diseases 2022[26]	▪ No specific funding of the overall strategy mentioned. However, there are a number of initiatives which are outlined to require stable funding including: ▪ Medical Handbook rare articles (in relation to Theme 5). The Medical Handbook is an online medical encyclopaedia aimed primarily at Danish General Practitioners. It contains approximately 2,500 medical articles about conditions, symptoms, treatments, and health and aims to provide reliable online health information.[57] ▪ A project for virtual rare patient education inspired by the "Learn to tackle" model. The background for the initiative was funds allocated with the Ministry of Health's empowerment grant 2018/2019-2021 for Rare Diagnoses, which were earmarked for patient education. However, the project description was never assessed, which resulted in unused funds from the empowerment grant in the Health Pool from 2018-2021. These were instead partially channelled into funding Helpline 2021/2022. ▪ Helpline – has been financed by a temporary grant, but is not financially secure for the future. If the consultancy is to continue, funds must therefore be added. Sjældne Diagnoser (the Danish umbrella association of rare disease patient representative organisations) estimates that additional funding is needed from and including the 4th quarter of 2023 and up to and including 2025 in order to keep the offer alive.

Country Information Source	Funding model(s)
	A need for clarity around finances has also been outlined in the strategy evaluation: several of the efforts initiated in connection with the status evaluation in 2018 are based on temporary funding. The particular challenge with temporary funding in this area is that it has been difficult to maintain competencies. This is crucial, as the complexity of the field means that building skills takes extra time. Loss of knowledge at the end of a project is thus more difficult to handle here than in other areas.
England ▪ Rare Diseases Action Plan 2022[27]	▪ Funding for all the actions listed is already committed, either through delivery partners' existing organisational budgets, or accounted for in the 2021 autumn budget and spending review. In the 2021 budget, the Chancellor announced a £5 billion investment over the next three years to increase health-related research and development. This includes funding to support Genomics England's research initiative, a national research pilot testing 100,000 newborns using whole genome sequencing to detect rare diseases with a genetic cause. **Progress to date:** An additional £340 million of funding has been announced, for the Innovative Medicines Fund, which will provide early access to promising new medicines, including cutting-edge gene therapies.
▪ Rare Diseases Action Plan 2023[28]	▪ The commitments outlined in this action plan 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. Specific examples of research-related funding are outlined below. For further details, see Appendix B, Table B10. ▪ **The Syndrome Without A Name (SWAN) pilot:** During 2022, NHS England (NHSE) developed a proposal for a 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 (related *to Priority 1: helping patients get a final diagnosis faster*). ▪ **The Innovative Medicines Fund (IMF):** In June 2022, NHSE and NICE launched the 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 (related to *Priority 4: improved access to specialist care, treatment and drugs*). ▪ **The National Institute of Health and Care Research (NIHR) BioResource**: In the 2022 action plan £40 million of funding was announced for the NIHR BioResource, 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. ▪ **Mapping the Rare Disease Landscape:** In 2022, a commitment was made to mapping the rare disease research landscape, in collaboration with the Medical Research Council (MRC) and the NIHR. Analysis has 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. ▪ **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. 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 with call outcomes expected in April 2023.

Country Information Source	Funding model(s)
	▪ **Digital, data and technology:** A joint funding package of up to £200 million between NHSE, DHSC and the Department for Business, Energy & Industrial Strategy 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. A number of actions related to commissioning or funding were also outlined: Actions 11, 12, 15, 17, 20, 21, 23, 24, 28 and 29 (see Appendix B, Table B10).
▪ The UK Rare Diseases Framework 2021[29]	▪ Not mentioned.
Finland National Programme for Rare Diseases 2019-2023[50]	**Some cost estimates for initiatives within the strategy are provided below:** ▪ The strategy estimates that approximately 1.6 additional person-years would be needed for physicians and 0.8 person-years for nurses at the national level. The cost effect would be approximately €200,000 per year. ▪ National coordination requires personnel resources in the national coordination unit. According to Subcommittee calculations, at least 2 person-years are required for the national coordination tasks, including the communication of information, coordination of networks, update and maintenance of the ORPHAcodes, and Orphanet activities. Resources are also required for development of the database and the maintenance of registry for rare diseases. In total, these amount to €200,000 to €300,000 per year. ▪ The European Commission grants the European Reference Network (ERN) centres operating in Finland a small amount of financial support for ERN activities. For healthcare providers to fulfil the quality requirements for ERN centres, an additional amount between €20,000 and €40,000 per year is needed, for maintenance of required procedures and quality systems. Participation in an ERN uses an input equal to 0.1 person-years for each sub-group in the network. In total, there may be up to ten of them. If centres of expertise joined all the 24 ERNs during the programme period, the number of Finnish centres would total approximately 30. The total amount of work would be between 20 and 25 person-years. The imputed costs are about €2 million per year. It has been estimated that an input of less than €1 million is used to maintain the necessary systems in the year a centre is established and about half of that in the following years. **Examples of research funding:** ▪ The Academy's Research Council for Biosciences, Health and the Environment had granted just over €20 million to 57 research projects focusing or touching upon rare diseases between 2011 and 2017. Excluding research in rare cancers and infectious diseases, the overall funding for research in rare diseases was €19 million. This is less than 10% of funding from the Research Council. ▪ Of the 24 rare disease groups included in the ERNs, 10 research fields remained completely unsupported during the time of the estimate, despite internationally effective research in many of them. ▪ There are other funding sources for research conducted on rare diseases in ERN centres and universities. In the total funding, the importance of short-term funding from research foundations has increased while – due to cuts in government research funding – the number of research personnel has reduced and fewer research equipment updated. ▪ A significant part of scientific research in rare diseases focuses on patients identified during clinical practice in university hospitals and on the ensuing translational studies collaboratively carried out by the clinician and basic researchers. In such studies, continuous governmental research funding granted to hospital districts plays a vital role. ▪ In 2019, a five-year funding project by the European Commission, the European Joint Programme on Rare Diseases was launched. The objective of this project is to improve the quality of life for individuals with rare diseases by increasing knowledge about the

Country Information Source	Funding model(s)
	diagnostics, treatment and care of rare diseases. The project brings together research sponsors, research institutes, universities, university hospitals, ERN Centres of Expertise and patient organisations. The Academy of Finland has participated in this from its beginning. ▪ The Virtual Hospital 2.0 project (2016-2018) of the five university hospitals is funded by the Ministry of Social Affairs and Health. **Funding for the empowerment and involvement of people with rare disease in society and their communities:** Several organisations, associations and interest groups receive support from the Funding Centre for Social Welfare and Health Organisations. It channels net revenue from the Finnish gaming company Veikkaus. Enabling support to small associations and to rare disease patients without any remains challenging.
France French National Plan for Rare Diseases 2018-2022[51]	Costs of each Focus Area and Funders are outlined in Implementation (see Appendix A, Table A1, and Appendix B, Table B12).
Germany National Plan of Action for People with Rare Diseases 2013[32]	**Funding for Centres of Expertise:** Type A, Type B and Type C centres are to be funded by the existing legal framework. The following were discussed in detail with respect to their suitability for funding the three types of centres of expertise: ▪ highly specialised outpatient care (§116b Social Code Book V) ▪ care by panel doctors and dentists (§§95ff Social Code Book V) including care provided by hospital physicians or clinics authorised to provide outpatient care (§§116, 116a Social Code Book V) ▪ enabling provisions for university outpatient clinics (§117 and 120 Social Code Book V) as well as social-paediatric centres (§119 Social Code Book V). In addition, besides the collective agreements, there are the selectively contracted conditions for: ▪ remunerating special services within the framework of integrated care (§§140a ff Social Code Book V) or specialised medical care (§73c). ▪ However, selectively contracted solutions have proven to be unsuitable for ensuring universal access to care for the small numbers of persons affected because of the specific challenges faced in the area of rare diseases. Instead, the existing funding possibilities offered by collective contracts are to be used to finance the systematic implementation of the three-tiered structure of centres for rare diseases. The NAMSE partners will urge that the necessary funds that are not already included in the existing standard remunerations be made available by the payers. ▪ This funding will be assessed in proposed action 1, whereby representatives of patient interests will work together with representatives of both healthcare providers and the third party payers to clarify the common criteria and requirements for funding centres. Funding will be reviewed (two years after implementation) to determine whether the funding elements contained in the existing standard remunerations are sufficient to fund the centres of expertise (two years after implementation) in proposed action 3. **Research funding:** ▪ Diagnostic test systems developed and employed at the research level will have to be funded through public subsidies. ▪ Investigator-initiated trials are presently being funded by the German Federal Ministry for Education and Research (BMBF) and the German Research Foundation. ▪ The BMBF has funded ELSA research since 1997 and proposed action 13 is to continuing this funding.

Country Information Source	Funding model(s)
	▪ The ERA-Net Initiative "E-Rare" collects information about research going on into rare diseases in countries, to strategically coordinate activities and to fund transnational research projects. Germany is a partner and proposed action 15 aims to continue this research funding. ▪ Funding and support for research is also identified as proposed action 16 (see Appendix A, Table A1).
The Netherlands ▪ National Plan for Rare Diseases 2013[52]	▪ The Ministry of Health, Welfare and Sport has not allocated a budget for proposed measures and activities to this plan. Of course, recommendations are also made that do not have to cost extra money. These recommendations relate to a different approach within existing structures and organisations.
▪ Coordination Consultation for Rare Diseases: Final Advice 2017[53]	▪ The document mentions throughout that funding is required but does not specify where from. Funding issues are outlined related to: ▪ measures for reimbursement of orphan drugs ▪ measures that remove barriers to cooperation between specialists and the different echelons, especially with regard to financing chain care and shared care ▪ reimbursing or subsidising the setting up of a network structure ▪ facilitating measures (training, financing) for the participation of patients (organisations) ▪ health insurers to finance care and ensure continuity, such as financing network care and expertise centres within expertise networks ▪ innovative ways (of financing) are needed to organise care for patients with a rare disease.
Northern Ireland ▪ Northern Ireland Rare Diseases Action Plan 2022/23[34]	▪ **A funding model is not described, however there are a number of specific Actions which refer to funding:** **Action 1:** It will also be important to secure funding for a dedicated person(s) (to include rare diseases navigators) to take the Information Hub work forward, therefore a relevant business case or funding application will be developed. **Action 2:** We will also work to agree an investment and implementation plan by the end of the first year. **Action 4:** Part of the work in developing a NI registry will be to scope the logistics for accommodating the registry; a scoping review is expected to be completed and a business case developed as part of this Year 1 Action Plan, to include necessary resources to take the registry work forward. **Action 5:** We will develop a cost and or benefit analysis to support a bid for additional resources, including a dedicated education coordinator to take the education and training work forward. **Action 7:** One of the outcomes will be to explore the requirement for a physical space and developing a business case and implementation plan for an expert centre by the end of year one. **Action 13:** Whilst it is recognised that our healthcare system continues to meet significant resource challenges, opportunities for research training to increase the capability and capacity of our Health and Social Care rare disease workforce will be actively identified and disseminated, and support provided in identifying and securing appropriate funding for rare disease research studies.
▪ Northern Ireland's Rare Diseases Action Plan: Progress Report Year 1 (March 2022 – March 2023)[33]	▪ A funding model is not described, however a number of funding challenges outlined below: ▪ The absence of a fully functioning Executive, along with associated budgetary and planning issues, continues to hinder progress in many areas across health and the NI Rare Diseases Action Plan is no exception.

Country Information Source	Funding model(s)
	▪ The Department is projecting a funding gap of some £764 million for the 2023/24 financial year and the current priority is to mitigate where possible both the immediate impact on frontline services and long-term irreversible consequences for the health and care system. ▪ The lack of confirmed recurrent funding is constraining not only the action outputs and out-workings of the Working Groups, but also the ability to make effective progress at pace. ▪ Currently in NI, there are a number of large Strategic Programmes and Projects taking forward the Health and Social Care Transformation agenda. While some of these will inevitably define the feasibility of some rare diseases actions (for example those that involve encompass) and effective input is required at design stage, the available expertise is currently over-stretched and under competing time and work priorities. ▪ Opportunities to partake in wider UK and European research studies with potential associated funding have been made more difficult by the demanding time commitments commanded by the projects.
▪ The UK Rare Diseases Framework 2021[29]	▪ Not mentioned.
Portugal ▪ Integrated Strategy for Rare Diseases 2015-2020[35] and Annual Plans for 2016,[36] 2017,[37] 2018[38] and 2019[40]	▪ Not mentioned.
▪ Annual Report Integrated Strategy for Rare Diseases 2015-2020 – Year 2018[41]	▪ The absence of a specific budget allocated to the activities of the Integrated Strategy for Rare Diseases 2015-2020 and the inability of the entities involved to accept external financing from private, for-profit entities, is one of the biggest constraints on the implementation of the annual plans. In view of the above, the activities planned for 2019 should continue to be programmed within the strict domain of skills and resources available to the different partners of the Strategy, with possible limitations in the definition of some objectives.
▪ Interim Report on the Implementation of the Integrated Strategy for Rare Diseases 2015-2020 – Year 2017[39]	▪ Some initiatives were not fully implemented due to local constraints related to: ▪ Budget cuts made at the beginning of 2017 in the order of 30%, in some partner institutions. ▪ Lack of specific budget allocated to the activities of the Integrated Strategy for Rare Diseases 2015-2020. ▪ Impossibility for the entities involved to accept external financing from private, for-profit entities.
Scotland ▪ Rare Disease Action Plan 2022[42]	▪ *Mentioned under Action 1:* The Scottish Government will support this strategy through significant investment, with £5 million committed for 2022/23 alone, previous investment of £8 million since 2017. This is in addition to almost £20 million of funding allocated to the four genetic laboratories annually in Scotland by NHS Boards through NHS National Services Division commissioning arrangements. *Mentioned under Action 3:* Initial funding to establish Congenital Conditions and Rare Diseases Registration (CARDRISS) was provided by the Scottish Government to NHS NSS Information Services Division and latterly to Public Health Scotland (PHS), the current home of

Country Information Source	Funding model(s)
▪ The UK Rare Diseases Framework 2021[29]	CARDRISS, over the three-year period October 2018 to March 2022. Work will be done with PHS to understand the options to expand CARDRISS. Extensions are likely to require financial investment by the Scottish Government, which will be considered as part of future budgetary considerations. ▪ Not mentioned.
Wales ▪ Wales Rare Diseases Action Plan 2022-2026[43] ▪ The UK Rare Diseases Framework 2021[29]	▪ The Rare Disease Implementation Group have successfully secured Welsh Government funding for co-ordinator support, a new all-Wales Clinical Lead for Rare Diseases, and setting up a two-year pilot for SWAN Clinic. ▪ Not mentioned.

Key: BMBF: German Federal Ministry for Education and Research; CARDRISS: Congenital Conditions and Rare Diseases Registration; ERN: European Reference Network; IMF: Innovative Medicines Fund (England); MRC: Medical Research Council (England); National Action Plan (NAP); NI: Northern Ireland; NIHR: National Institute for Health and Care Research (England); PHS: Public Health Scotland; SWAN: Syndrome Without A Name; UK: United Kingdom.

3.3 Comparison with the National Rare Disease Plan for Ireland 2014 – 2018

The following sections compare the strategy contents for the selected countries, as described in section 3.2, with the contents of the *National Rare Disease Plan for Ireland 2014 – 2018*.[19] Information from the interim report on the implementation of the plan[45] and the accompanying summary of recommendations[46] is also included, where relevant. Similarities and differences are highlighted.

3.3.1 Timeline and aims

The Department of Health published the National Rare Disease Plan for Ireland in 2014,[19] with a projected timeline running until 2018. An interim report on its implementation and a summary of recommendations were also published by the Department of Health in 2017.[45, 46] As seen in Figure 3.1, Austria's national strategy followed the same timeline,[47] with Portugal's national strategy covering a similar timeline (that is, 2015 to 2020).[35] However, unlike Ireland, Austria conducted an evaluation following the conclusion of their national strategy's timeline, with recommendations for further strategy implementation.[48] Other countries that adopted a different approach to Ireland were Australia,[22] Denmark,[24] Germany,[30] and the Netherlands,[31] as these countries published open-ended strategies, without a defined end date for implementation.

The aims of the *National Rare Disease Plan for Ireland 2014 – 2018*[19] aligned with many of the aims outlined in the strategies of the selected countries. Improving screening, diagnosis, treatment and care were specifically mentioned as strategic aims for Ireland and 10 of the 12 selected countries. Although Denmark[24] and Germany[32] did not mention them explicitly in their aims, both countries addressed these topics in the themes and priorities of their national strategies.

The *National Rare Disease Plan for Ireland 2014 – 2018* also aimed to ensure that the Irish health system recognised, understood and addressed the needs of people with rare diseases in terms of policy, services, and research and or information systems.[19] This was addressed by the majority of selected countries, with strategic aims relating to patient involvement, education, health literacy, improving communication and coordination of services. The French national strategy's aims related to promoting innovation[51] were not specifically mentioned in Ireland's strategic aims.

3.3.2 Themes and priorities

Each of the themes and priorities identified across the national rare disease strategies of the selected countries was addressed in the *National Rare Disease Plan for Ireland 2014 – 2018*,[19] with the exceptions of 'health workforce education and

training' and 'access to mental health and psychology services'. Although it was not a distinct theme or priority, recommendations relating to education and training on rare diseases for healthcare professionals were included in the *National Rare Disease Plan for Ireland 2014 – 2018*.[19] Of the nine selected countries that included 'health workforce education and training' as a theme or priority, Australia outlined the most extensive planned approach, as they listed the development of a specific national rare disease workforce strategy as a priority.[22]

'Access to mental health and psychology services' was a theme and or priority in the national strategies of Australia,[22] England,[28] and Scotland,[42] and was added as a theme in the strategy evaluations conducted by Denmark.[25, 26] All of these documents were published after the conclusion of the *National Rare Disease Plan for Ireland 2014 – 2018*.[19]

Themes and priorities addressed by Ireland and all 12 of the selected countries were:

- screening and diagnosis
- access to healthcare and coordination of services
- rare disease research
- patient representation and empowerment.

Ireland also included certain strategic themes and priorities that were not addressed by the majority of selected countries. Equity was one of the five guiding principles of the *National Rare Disease Plan for Ireland 2014 – 2018*,[19] yet was only specifically addressed in the themes and priorities of national strategies for England[27] and Australia.[22] Australia also addressed pre-conception genetic testing and counselling under their strategic priority of 'facilitating increased reproductive confidence'.[22] This was addressed in the *National Rare Disease Plan for Ireland 2014 – 2018* under the theme of 'prevention, diagnosis and care'.[19]

3.3.3 Implementation

Ireland outlined a number of recommendations which were envisaged to be implemented throughout the duration of the strategy, similar to Austria,[47] Finland,[50] France,[51] Scotland[42] and Wales.[43] A different approach was adopted by England,[27, 28] Northern Ireland[34] and Portugal,[36-38, 40] who published annual plans outlining the short-term actions to be completed.

Across all of the selected countries, and in Ireland, the actions outlined in national rare diseases strategies focused on achieving the strategic aims, themes and priorities, within the specific national context of the country in question. Examples of actions that demonstrated both similarities and differences between the national strategies of Ireland and the selected countries were as follows:

- In terms of health information systems, both Denmark[24] and Ireland[19] included recommendations relating to the consolidation of fragmented national rare disease patient registries, the use of rare disease codes in patient records, and planning for Orphanet participation. Denmark's subsequent strategy evaluations showed the progression of these recommendations over time, with the expansion and consolidation of their RAREDIS national database, the use of OMIM (Online Mendelian Inheritance in Man) codes and ORPHAcodes, and the identified need for resources to enable Orphanet participation.[25, 26] At the time of publication of Ireland's interim report in 2017,[45, 46] a number of preliminary actions were described as being in progress or having been completed. For example, the National Rare Diseases Office (NRDO) had performed a preliminary analysis of existing rare disease registries and was in the process of assigning those registries on the Irish national Orphanet site.[46]
- Ireland[19] and 10 out of the 12 selected countries included actions in their national strategies related to screening for rare diseases. These countries were Australia,[22] Austria,[47] Denmark,[24-26] England,[27, 28] France,[51] the Netherlands,[29, 33, 34] Northern Ireland,[33, 34] Portugal,[35-37] Scotland,[42] and Wales.[43] Ireland's recommendations focused on using epidemiological surveillance to inform screening, the role and composition of the National Newborn Bloodspot Screening Programme Governance Group, and the development of a policy framework for population-based screening programmes by the Department of Health. Similarly, Austria included an action focused on implementing evidence-based governance structures, in the form of setting up a scientific advisory board at ministerial level for their newborn screening programme.[47] Examples of other actions with a different focus included: raising awareness of screening opportunities (Australia);[22] designing an ethically approved research study on whole genome sequencing for screening in healthy newborns (England);[30] and expanding the number of diseases screened for and increasing investment in newborn screening programmes (France).[51]
- A number of actions related to enhancing access to appropriate drugs and technologies were also outlined by Ireland.[19] These included developing appropriate decision-making criteria for the reimbursement of orphan drugs and technologies.[19] Similarly, the Netherlands[52] also outlined that a consistent policy regarding entitlement and reimbursement of orphan drugs was required.
- A small number of recommendations relating to genetic testing and data use were included in the *National Rare Disease Plan for Ireland 2014 – 2018*,[19] while no recommendations specifically referred to genomics. However, genomics featured prominently in strategic actions for Australia,[22]

England,[30] Northern Ireland,[34] Scotland,[42] and Wales.[43] Each of these national strategies was published during or after 2020.

- Mapping and development of care pathways, with an emphasis on the transition from paediatric to adult care, were specific actions in the Irish national strategy, and were also included as actions for Denmark,[27-30] Northern Ireland[34] and Wales.[43] Broader actions related to mapping care pathways for people with rare diseases were included by England and Scotland, while Scotland also included a specific action to develop a pathway for people with ultra-orphan diseases (that is, diseases affecting fewer than 1 in 50,000 people).
- As in Ireland, most EU countries listed actions relating to participation in ERNs, including supporting national centres to seek recognition as designated Centres of Expertise. Austria included multiple actions in their national strategy relating to designating Centres of Expertise, integrating these centres into the national healthcare landscape, and facilitating their integration into ERNs.[47] Their strategy evaluation noted this as a particularly successful area of strategy implementation.[48]
- Innovation was specifically addressed in one recommendation in the Irish national strategy: *"Sponsors could be offered an incentive to run trials in Ireland increasing access to innovation for Irish patients"*. In comparison, innovation was the focus of a number of actions within the French national strategy,[51] including establishing an innovation coordinating body, promoting the development of innovative diagnostic products and treatments, and facilitating access to innovative treatments by patients.
- The importance of personalised medicine in the treatment of rare diseases was acknowledged in the Finnish national strategy,[50] and hopes for its future significance were noted in Denmark's 2022 evaluation.[26] Finland outlined how a number of projects linked to their national strategy would improve the use of personalised medicine, for example, the planned establishments of four National Centres of Excellence and a national Genome Centre.[50] Personalised medicine was not distinctly addressed in the recommendations included in the Irish national strategy.

Ireland's national strategy outlined a number of 'recommendations',[19] with strategies from Denmark[27-30] and the Netherlands[29, 33, 34] using the same terminology. Other countries that outlined more definitive 'actions' in their strategies included Australia,[22] England,[27, 28] France,[51] Northern Ireland,[34] Scotland[42] and Wales.[43]

Similar to Northern Ireland[34] and Scotland,[42] the Irish strategy listed implementation agencies for some, but not all, recommendations. In contrast, Austria,[47] England,[27, 28] France,[51] Germany,[32] the Netherlands[52] and Wales[43]

specified the stakeholders responsible for leading and or collaborating on the implementation of each action. Portugal did not initially specify implementation agencies in their main strategy,[35] or their annual plans for 2016[36] and 2017,[37] but changed their approach to list stakeholders responsible for implementation in their 2018[38] and 2019[40] annual plans.

Ireland listed a number of key outputs within their recommendations, against which strategy implementation could be measured.[19] Examples included: the Health Identifier Bill and Health Information Bill, a periodic national report on the epidemiology of rare diseases in Ireland, and an All-Ireland Network of Rare Disease Registries. However, unlike the approaches adopted by England,[27, 28] Northern Ireland,[34] and Wales,[43] not every recommendation in the Irish strategy had a clear, measureable output or outcome.

Aside from Ireland,[19] Denmark[24] was the only country that stated within their national strategy that they intended to use the EUCERD core indicators[58] to monitor progress. These indicators were noted in the Dutch national strategy,[52] but it was not explicitly stated that they would be used to monitor implementation of the strategy. Although Ireland's interim report on implementation[45] and summary of recommendations[46] did not explicitly report progress relative to the EUCERD indicators, some indicators were addressed, for example, participation of designated centres of expertise in ERNs, and the type of classification and or coding used by the healthcare system.

3.3.4 Governance and or organisational models

A number of aspects of the governance and or organisational models outlined in the *National Rare Disease Plan for Ireland 2014 – 2018*[19] were similar to those of the selected countries. For example, the Steering Group established by the Department of Health to oversee the development of the National Rare Disease Plan was comparable to the working group established by the Danish Health Authority.[24]

In the National Rare Disease Plan for Ireland,[19] the HSE Service Plan mechanism was noted as the system through which implementation of recommendations applicable to the health and social care system would be monitored. An Oversight Group was also established in 2015 to oversee the implementation of the plan.[46] This group reported to the Department of Health, and was largely comprised of members from the original Steering Group that led on drafting the national plan. This Oversight Group was similar to the follow-up group outlined in the Danish evaluations of their national rare disease strategy,[25, 26] which included representatives from the Ministry of Health, the Danish Health Authority, medical specialists, and patient representative organisations. The Danish follow-up group included representatives from regional and local governments and the National Board of Social Affairs, unlike the Irish Oversight Group. It also included a greater

number of members from relevant professional societies, as well as national Centres of Expertise.

A number of the selected countries established dedicated governance structures as part of their national rare disease strategies, which acted as coordinating bodies that assigned responsibility for implementation to named stakeholders and or collaborators. For example:

- the strategic and operational committees established in France[51]
- the inter-ministerial commission in Portugal[35]
- the UK Rare Diseases Framework Board and Forum, and national implementation or delivery groups for England, Northern Ireland, Scotland and Wales.[29]

In Ireland, organisational structures within the health system that led on rare disease strategy implementation included the National Clinical Programme for Rare Diseases (NCPRD), established in 2013 as a joint initiative between the HSE and the Royal College of Physicians of Ireland with this programme having responsibility for strategy, and the NRDO, established in 2015 by the HSE with responsibility for operationalising or assisting with a number of strategic recommendations.[19, 45, 46] As outlined in the interim report[45] and summary of recommendations,[46] responsibility for implementing a number of recommendations lay outside the NCPRD or NRDO. For example, implementation of rare disease coding was noted to be progressing under work associated with the e-Health Strategy and Knowledge and Information Strategy, and the establishment of a National Genetic and Genomic Medicine Network was proposed to deliver integrated genetic medicine services.[46]

These organisational structures are somewhat similar to those seen in Austria,[47] where the National Coordination Centre for Rare Diseases (NKSE) was responsible for similar actions in their national strategy, such as guiding the coordination of healthcare services for rare diseases, acting as an information hub, and multiple actions relating to national Centres of Expertise and promoting participation in ERNs. However, the NKSE differed in that it was set up by the Austrian federal government as part of their healthcare research and planning institute, Gesundheit Österreich GmbH, rather than being part of an organisation responsible for the provision of national public healthcare services. The NKSE was also established prior to the development of their national strategy and led its development. In Austria's strategy evaluation,[48] the role of the NKSE was noted to have changed over time, with coordination tasks moving to the newly-established National Office for the Implementation of NAP from 2019.

3.3.5 Funding model

Ireland[19] outlined that no specific funding model or budget mechanism was allocated to strategy implementation; this was similar to Austria,[47] Denmark,[24] the Netherlands,[52] Northern Ireland[34] and Portugal.[35] It was outlined that current resources in Ireland would be re-orientated, where possible, to address the care and treatment of people with rare diseases. For example, there was no commissioning model proposed for initiatives such as designated Centres of Expertise, European Reference Network (ERN) healthcare provider support, care pathways, and rare disease coding. However, the interim report on implementation noted staff resources that had been allocated to the NRDO since its establishment, specifically the NCPRD Clinical Lead, supported by an Information Scientist, part-time Administrative Officer, part-time Genetic Counsellor and a 0.2 full-time equivalent Consultant Geneticist.[45]

In contrast, countries such as Australia,[22] England,[27, 28] Scotland[42] and Wales[43] outlined government funding that was committed to strategy implementation in the short- to medium-term. Detailed information on funding was included in the national strategies of Finland[50] and France.[51] Finland[50] was the only country included to perform economic analysis in order to estimate the costs of implementation for their strategy. The French national strategy listed estimated costs and the funding bodies for all actions, for example, significant funding was dedicated to supporting the registration of rare diseases at Centres of Expertise through deployment of the national rare diseases data bank (BNDMR).[51]

4 Discussion

Rare diseases present a number of challenges and barriers to effective and efficient healthcare delivery, including difficult and delayed diagnosis, a small number of patients often widely geographically dispersed, and a lack of clinical expertise.[59] To try and unify approaches to tackling rare diseases in Europe, the European Commission's Communication[2] in 2008 and the Council of the European Union's *Recommendation on an action in the field of rare diseases*[6] in 2009 promoted the development of national rare disease strategies by all EU member states. However, the domain of rare diseases is evolving, and therefore an updated understanding of national rare disease strategies may help further knowledge of the key aims, priorities, and actions relevant to rare disease. This will support the development of an updated national rare disease strategy in Ireland. An international review of national rare disease strategies for 12 countries was therefore undertaken; these countries were selected based on a combination of factors including having a national strategy published more recently than or at a similar time to Ireland's strategy, geographical proximity to Ireland, and population size. A descriptive analysis of the selected countries' strategies was undertaken, and compared to the *National Rare Disease Plan for Ireland 2014 – 2018*.[19] Information from the interim

report on the implementation of Ireland's plan[45] and the accompanying summary of recommendations[46] was also included, where relevant.

4.1 Developments in national rare disease strategies over time

The Council of the European Union recommended in 2009 that member states should adopt a national rare disease plan or strategy, preferably by the end of 2013 at the latest. This contributed to a subsequent increase in national rare disease strategy development, with Hedley et al.[5] noting that while only five European member states had developed national rare disease strategies or plans in 2009, this had risen to 25 member states by 2020. However, the authors also noted that a number of countries' strategies had 'expired' by late 2020, as they were time-bound strategies that were largely adopted in the period from 2009 to 2013, in line with the Council Recommendation, and had yet to be formally updated or replaced.[5] This was reflected in the findings of the current review, as a number of the selected countries, namely Austria,[47] Denmark,[24] Germany,[32] and the Netherlands,[52] published their first national rare disease strategies in 2013 or 2014. Like Ireland,[19] Austria's strategy[47] could be considered to have 'expired' at the time of conducting the current review, with both strategies having run from 2014 to 2018. Neither Germany[32] nor the Netherlands[52] had specified end dates for their strategies, whereas Denmark had extended their strategy, reviewing and refining their priorities with each of their strategy evaluations.[25, 26]

Other selected countries with strategies that reached, or were about to reach, the end of their timelines and were in the process of being replaced at the time of writing this report were Finland,[60] France,[61] and Portugal.[62] A key representative from Finland confirmed that the publication of an updated national rare disease strategy was due in January 2024.[60] This strategy, the *National programme for rare diseases 2024-2028*,[63] was published on 30 January 2024 and was therefore not eligible for inclusion in the current review. The strategy consisted of a single, concise main strategy document, and focused on tangible objectives that could be implemented within current resources. Its overarching aim was similar to the aims of the reviewed national rare disease strategies, that is, strengthening the treatment and participation of people with rare diseases. It shared many similar themes and priorities with the reviewed strategies and with Finland's *National programme for rare diseases 2019-2023*,[50] for example, strengthening national and international healthcare structures relating to rare diseases, preparing care pathways, facilitating rare disease research, and promoting inclusion of people with rare diseases.[63] Notably, it also included two themes not distinctly addressed in Finland's previous national strategy,[50] namely, building patient registries, and ensuring access to medicines, particularly orphan medicines.[63] A key representative from Portugal

confirmed that an intersectoral working group had been established in May 2023 to develop an updated national rare disease strategy.[62] The representative did not note an expected date of publication, however, the inter-ministerial order that established the working group stated that a proposal for the strategy was expected to be prepared by late 2023.[62] As such, for these countries, and for all of the selected countries, the information in this review is a summary of the available information at the time of publication of their most recent national rare disease strategy, and any strategy evaluations or supporting documents. Further developments that may have taken place after the publication of the included documents are therefore not captured in this review. For example, in Ireland, the National Screening Advisory Committee was established in 2019, after the publication of the national strategy and interim report documents included for comparison in this review.[19, 45, 46] Additionally the *National Strategy for Accelerating Genetic and Genomic Medicine in Ireland* was published in December 2022.[64] Equally, work towards implementing electronic health records and enabling sharing of health data is still in progress as of 2023, and will support the implementation of national rare disease coding in Ireland.[65]

Like Ireland, the reviewed strategies for Australia,[22] Austria,[47] Denmark,[24] Germany,[32] and the Netherlands[52] were those countries' first national rare disease strategies. Overall, the reviewed strategies from countries that had previous national rare disease strategies tended to be more specific in terms of their implementation plans than those for which the reviewed national strategy was their first strategy. For example, countries such as England,[27-30] Northern Ireland[33, 34] and Portugal[35-41] published annual action plans to accompany their high-level main strategies, while France[51] indicated that more detailed action plans would be prepared by the relevant theme or priority leader and other stakeholders.

4.2 Current and future strategic themes and priorities

The overarching aim of improving treatment and coordination of care for rare diseases was outlined in the majority of included national rare disease strategies, including the Irish strategy.[19] Several further aims were also identified, including improvements in diagnosis of rare diseases; increasing awareness and or communication in the area of rare diseases; and educating and involving patients with respect to their rare disease. These aims either broadly align with, or address, a number of the overarching trends in rare diseases outlined by the Rare 2030 Panel of Experts.[66] These trends, developed through a series of consultations and meetings held in 2019 (such as the EURORDIS Membership Meeting, the Panel of Experts Workshop, the EURORDIS Council of National Alliances and Council of European Federation meeting), have been identified as instrumental to shaping the future of rare disease policy.[66] Examples include, *"Increasingly empowered rare disease patient and the patient advocacy evolution"*; "*Rise of pan-European multi-*

stakeholder networks to advance diagnostics, treatment and care for rare diseases"; and "*New technologies and advanced therapeutics"*.[66]

While distinct themes and priorities were identified across the selected national rare disease strategies, a number of these themes and priorities, or aspects of them, were interrelated. For example, 'rare disease research' was a broad theme identified across all strategies reviewed. However, in the national strategies of Germany[32] and France,[51] research was also relevant to their priorities of promoting evidence and innovation in orphan medicines and innovative health technologies. Similarly, the theme of 'awareness and information for patients and the public' was linked to 'patient representation and empowerment' in the national strategies of Australia[22] and Denmark,[24] where providing access to information and education for people with rare diseases aimed to empower patients to be active participants in their care.

The themes and priorities addressed in the national rare diseases strategies of Ireland and all 12 of the selected countries (that is, 'screening and diagnosis', 'access to healthcare and coordination of services', 'rare disease research', and 'patient representation and empowerment') also broadly aligned with the Rare 2030 recommendations. These recommendations arose from the two-year iterative participatory Rare 2030 Foresight Study with over 200 thought leaders in the field of rare diseases and with thousands of people living with rare diseases, and aimed to set out a roadmap for rare disease policy in Europe from 2020 to 2030.[13] The main recommendation from that study that was not reflected in the national rare diseases strategies reviewed was the establishment of a long-term, integrated rare policy framework at European level. This recommendation, if adopted, has the potential to support future rare disease strategy development and implementation at a national level across Europe.

Patient representation and participation was a key theme spanning many facets of the reviewed national strategies. Patient representative organisations were listed as lead or collaborative stakeholders in strategy implementation, and were also involved in advocating for and driving strategy development. A notable example of this was Australia, where Rare Voices Australia was commissioned by the Australian Government Department of Health and Aged Care to lead the development of the national strategy[22] and to conduct a status report on strategy implementation.[23] In Ireland, patient representative organisations have advocated for rare disease policy and strategic priorities through the Rare Disease Taskforce, a collective comprising Health Research Charities Ireland, the Irish Platform for Patient Organisations, Science and Industry, and Rare Diseases Ireland.[67] The Rare Disease Taskforce report, published in 2020,[67] identified the key priorities for the Programme for Government 2020 and beyond, including a number of the themes and priorities identified in the reviewed national rare disease strategies; these included, for example, providing additional resources for prevention, diagnosis and care;

improving access to and time to reimbursement of new and innovative medications; and addressing healthcare costs and social service supports. Aside from this role in influencing strategic priorities from the perspectives of people living with rare diseases, there is also evidence that active patient representative organisations may positively impact on research and development activity in the field of rare diseases, particularly in relation to more prevalent rare diseases.[68]

A further priority identified in the Rare Disease Taskforce report was the mainstreaming of rare diseases into national health reform strategies, particularly Sláintecare.[67] One of the key visions of Sláintecare is the delivery of integrated care throughout all stages of a person's life,[69] characterised by features such as appropriate care pathways and seamless transitions. Progress in this regard was made in line with the *National Rare Disease Plan for Ireland 2014 – 2018*,[19] with the publication of a *Model of Care for Transition from Paediatric to Adult Healthcare Providers in Rare Diseases*,[70] together with a guide to support its implementation in practice,[71] and the *Model of Care for Rare Diseases*.[72] In the selected countries, a similar focus on transition from paediatric to adult healthcare services was seen in Denmark,[24] Northern Ireland[34] and Wales,[43] with a broader focus on mapping and development of care pathways in England[27, 28] and Scotland.[42] The rarity and diversity of rare diseases naturally present challenges to developing and implementing disease-specific care pathways. However, a generic care pathway for people with rare diseases may be feasible to design and implement, as demonstrated in Germany.[73] In Ireland, a model for designing rare disease care pathways has been developed and piloted by the National Rare Diseases Office,[74] and has been cited as an example of best practice by EURORDIS.[75, 76] A number of condition-specific care pathways have been developed according to this model.[77] However, no specific funding for such pathways was outlined in the HSE's 2023 National Service Plan,[78] in comparison to the HSE-funded 'Modernised Care Pathways'.[79]

4.3 Approaches to implementation

Approaches to strategy implementation varied greatly across the selected countries, with variation apparent across the actions planned, the stakeholders responsible for implementation, and outcomes or measures for monitoring and evaluating strategy implementation. While the majority of countries outlined specific strategy actions, it was also noted that strategy review, and or review of the current state of rare diseases, impacted these strategic actions and overall implementation. For example, Denmark reduced over 100 recommendations across 13 themes, outlined in their 2014 main strategy,[24] to 23 recommendations across six themes in their 2018 strategy evaluation.[25] This was to ensure all included recommendations were action oriented, and was further reviewed and adapted in their 2022 strategy evaluation.[26] This is supported by research in the field of rare disease guidelines, with Gittus et

al.[80] identifying that the feasibility of guideline recommendations impacts the overall implementation of the associated guidelines.

The nature of the implementation actions was also seen to change over time in the reviewed strategies, in line with advances in technology. An area of particularly rapid advancement in the decade since the publication of the *National Rare Disease Plan for Ireland 2014 – 2018*[19] is that of genetics and genomics. For example, genomic sequencing did not feature in the *National Rare Disease Plan for Ireland 2014 – 2018*[19], whereas England's action plan for 2023 included an action to design a research study on whole genome sequencing for screening in healthy newborns.[30] Furthermore, the results of a survey conducted in 2023 by the International Rare Diseases Research Consortium indicated that there are currently 14 studies planned across a number of European countries to trial initiatives in next-generation sequencing for newborns.[81] Access to mental health and psychology services has also been outlined as an area of importance in more recent national rare disease strategies, with Denmark including this as a theme in their 2018 and 2022 strategy evaluations.[25, 26]

In Ireland, a coordinated approach to genetics and genomics was outlined in the *National Strategy for Accelerating Genetic and Genomic Medicine in Ireland*, published in December 2022.[64] A number of the principles seen in the key strategic areas of focus for that strategy bear similarities to those identified in the reviewed national rare disease strategies, such as ensuring patient and public involvement and partnerships, building a workforce for the future, and strengthening data infrastructure. A notable difference between the structure of that strategy and that of the *National Rare Disease Plan for Ireland 2014 – 2018* was the publication of an accompanying Strategy Implementation Plan for 2023,[82] which detailed the activities and outputs to be delivered in the first year of the strategy, including assigned leads responsible for each. This structure was also adopted for the national rare disease strategies of a number of the selected countries, such as England,[27, 28] Northern Ireland[34] and Portugal.[36-38, 40]

Specific outcomes or measures linked to strategy actions were only outlined for four of the 12 selected countries. This is despite EURORDIS highlighting the monitoring of rare disease strategies as a strategic area which should be taken into account when building a national strategy.[15] Furthermore, EUCERD published recommendations on core indicators to capture relevant data and information on the process of planning, implementing and monitoring of these plans and strategies.[58] However, Ireland[19] and Denmark[24] were the only countries included within the current review to outline within their strategies that these core indicators would be used. Furthermore, neither country explicitly reported on these indicators in documents that provided updates on strategy progress[45, 46] or in strategy evaluations.[25, 26]

An element of the Rare 2030 recommendations applicable at national level is the recommendation that national plans and strategies should be sustained on a long-term basis, with adequate funding.[13] One aspect of this sustainability is the need for enduring governance and organisational structures, to ensure that coordination and progression of strategic actions are maintained over time. For example, in Germany, a report published in February 2023 recommended that the National Action League for People with Rare Diseases (NAMSE) should be maintained and sustainably financed into the future[44] in order to continue the successful work it carried out as part of their national strategy.[32]

In Ireland, a significant change in rare disease governance that occurred since the publication of the documents included in this review was the transfer in 2020 of the functions of the NCPRD to the NRDO, which operates within the Acute Operations governance structures of the HSE.[71] Maintaining adequate financing over time is another aspect of this sustainability. While the majority of countries in the current review outlined some type of funding for the implementation of their national rare disease strategy, five of the selected countries and Ireland either did not indicate allocated funding, or outlined that no funding was in place. When reviewing European rare disease policies in 2015, Rodwell et al.[83] also outlined that a number of rare disease strategies had insufficient or no funding, and suggested this was as a result of the wider economic context at the time. This was noted to impact the extent to which those national rare disease strategies were implemented, a finding echoed in the current review.

Finally, a number of the selected countries, such as England,[27, 28] Finland[50] and France,[51] outlined specific amounts of funding allocated to support rare disease initiatives. It should be noted that these absolute amounts are not comparable across countries, due to differing population sizes, as well as differences in overall budgets available, and in costs and purchasing power between countries and over time. Furthermore, even for these countries, limited information was provided within the reviewed national strategies on how funding allocation decisions were made. Finland provided estimates of the costs required for strategy implementation, particularly healthcare staff for specialist services,[50] but did not specify planned sources of funding. Additionally, the reviewed strategies that included details on costs and or funding generally focused on healthcare costs and research funding. For example, in France, where costs and sources of funding were listed for most strategic actions, no cost information was provided for actions that related to promoting social integration among people with rare diseases and their carers.[51] This is consistent with findings from scoping reviews on cost-of-illness studies and economic evaluations in rare diseases, which found that non-medical costs, lost productivity, and informal care costs were relatively less frequently included in such studies than medical costs.[84, 85]

4.4 Limitations

While this review presents a comprehensive descriptive analysis of the national rare disease strategies of 12 selected countries and Ireland, there are notable limitations.

Firstly, this review is a purely descriptive analysis of the included national rare disease strategies. Although strategy evaluations and or progress reports published by the selected countries were included, where available, this review does not include an evaluation of the strategies overall. National rare disease strategies consider issues related to rare diseases within the national context of the country in question, and these issues may vary from country to country. The rare disease landscape is complex, spanning multiple sectors such as health, social care, disability, social protection, education and research, each of which may also vary between countries. This limits the ability to evaluate the highest priority issues across countries, or which implementation strategies may be feasible or successful in different countries. Equally, due to their intersectoral nature, national rare disease strategies often address broad themes and priorities at a high level. While relevant data on broad topics such as rare disease research and orphan medicines was extracted and summarised in this review, the depth of such summaries was limited by the depth of the information published the included documents.

Furthermore, the countries selected for inclusion may not represent the scope of all national rare disease strategies published internationally. While efforts were made to include the most relevant countries, by considering factors such as when their most recent national rare disease strategies were published, geographical proximity to Ireland, population size, and a similar organisation of health services, countries of relevance may have been omitted. Additionally, while key representatives for all selected countries were contacted to confirm resources and or provide additional relevant resources, contact could not be made with two countries. While national rare disease strategies were identified within the document search for these countries, these were not confirmed by key representatives.

5 Conclusion

A national rare disease strategy aims to reduce the burden of rare disease, and ensure access to good quality healthcare for people with rare diseases. The current review identified an overall aim of improving treatment and coordination of care, and reoccurring strategy aims around improving rare disease diagnosis, increasing awareness and or communication in the area of rare diseases, and educating and involving patients with respect to their rare disease. All of the included national rare disease strategies outlined themes and priorities related to: screening and diagnosis; access to healthcare and coordination of services; rare disease research; patient representation and empowerment. The *National Rare Disease Plan for Ireland 2014*

– 2018 largely shared similar aims, themes and priorities to the reviewed national rare disease strategies. However, unlike Ireland, themes of health workforce education and training, and access to mental health and psychology services were prioritised by a number of countries.

The governance and or organisational structures through which strategies were developed, implemented, monitored and evaluated varied between countries, involving existing health authorities, newly-established dedicated bodies, or a combination of both. Implementation actions varied across strategies to reflect the national context of each country and the time of strategy development and publication; for example, strategies published in recent years included actions related to advances in genetics and genomics. Governing bodies ultimately accountable for national rare disease strategies included national ministries for health, or equivalent, as in Ireland. Collaboration from ministries with responsibilities for sectors such as education, research, and social security was seen in some countries.

The current review of national rare disease strategies in selected countries provides insights into what countries identified as issues of importance, the actions undertaken, and the governance and funding structures used to support strategy implementation. This review will support the development of an updated national rare disease strategy in Ireland.

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Appendix A

Table A1. Implementation actions, agencies and measures or outcomes identified in the national rare disease strategies of Ireland and the selected countries.

Country Information Source	Implementation action(s), agency(ies) and measure(s) or outcome(s)
Ireland National Rare Disease Plan for Ireland 2014 – 2018[19]	…it is envisaged that the National Rare Disease Plan will be implemented on the basis of the recommendations set out in the report, supported by high-level outcomes underpinned by a series of key outputs/action areas with designated lead agencies. The Steering Group recommends: **Recognition of rare diseases – Information and research** 1. Guidelines be developed on coding and recording of rare diseases within relevant Irish health data systems that are consistent at European and global level. The Health Information and Quality Authority (HIQA) will have a role in this, given its functions regarding information standards, including coding standards. 2. The publication of the Health Identifier Bill and the forthcoming Health Information Bill. 3. The Department of Health and the Health Service Executive (HSE) put in place over 5 years a coherent system to conduct broad epidemiological surveillance of rare disease in Ireland. This epidemiological surveillance should include profiling of rare diseases among high-risk cultural and ethnic minority groups for the purposes of appropriate neonatal screening and improving diagnosis and outcomes. 4. A periodic national report on the epidemiology of rare diseases in Ireland be published by the Department of Health, similar to that prepared for the European EUROPLAN report, and that reporting on rare diseases be integrated into the existing HSE reporting on health and disability services. 5. All existing databases to be mobilised. Systems be put in place to enhance the utility of data held in relevant health service-based information systems, including hospital record, laboratory cytogenetic and molecular genetics data. 6. Irish data on Orphanet be reviewed and a plan for its development agreed, including an assessment of its relocation to an Irish centre if appropriate. This function should be supported by a National Office for Rare Diseases *(further information on the role of this proposed new office is provided in Chapter 4).* 7. Appropriate support be given for the ongoing involvement of Irish registries in relevant European collaborations, including the RARECARE and EUROCAT registries. 8. An All-Ireland Network of Rare Disease Registries, covering the island of Ireland, be developed and that this network work towards enhancing and standardising rare disease registries in line with HIQA draft guidelines, data protection legislation and international best practice. This function should be supported by the new National Office for Rare Diseases. 9. The development of any future information systems provide for a rare disease code in a patient's record in order that all people with rare diseases may be easily identified. The development of a Rare Disease ID Card that could be linked to a person's Personal Public Service Number should also be explored once the provisions of the proposed Information Bill have been enacted and promulgated. 10. A rare disease research network be developed to: a. enhance the quality and relevance of rare disease research on the island of Ireland in a strategic manner in line with the priorities of this National Rare Disease Plan; b. support the integration of rare disease research within relevant forthcoming Government research policy and legislation;

Country Information Source	Implementation action(s), agency(ies) and measure(s) or outcome(s)
	c. develop a clearly identifiable online presence, which would act to attract international interest and research partnerships; d. actively pursue potential international research partners; e. signpost new and established researchers to relevant resources and contacts; f. facilitate greater international collaboration with relevant registries, organisations and consortia, including the International Rare Disease Research Consortium; g. make proposals to the Department of Health with regard to Irish involvement in international networks such as E-Rare and engage in the rare diseases aspects of BBMRI-ERIC, ECRIN-ERIC and other EU infrastructures. 11. Research on rare disease in Ireland adhere to the EURORDIS guiding principles for conducting rare disease research. 12. The role of the designated Centres of Expertise in Ireland should include research relevant to rare disease, in particular with regard to registries, health service and translational research. 13. Ireland becomes a member of ECRIN-ERIC in due course and that the capacity of Ireland's five clinical research facilities to engage in rare disease research nationally or in collaboration with international collaborative research be enhanced. 14. The potential for industry collaboration in research relevant to rare diseases is explored, particularly with regard to research relevant to the diagnosis, treatment and management of rare disease. 15. The forthcoming national biobanking plan provides national coordination and quality standards for biobanking and embraces all opportunities for rare disease research and Ireland becomes a full member of BBMRI-ERIC when the national coordination of biobanking has been established. **Prevention, Diagnosis and Care** 16. With respect to pregnancy: a. Where family members are known to be at risk of being carriers of genes for rare diseases, they have appropriate access to pre-conception genetic testing and counselling, which can inform them about the risks involved in becoming pregnant; b. Making evidence-based, high-quality pre-conceptual care available to women at higher risk of having babies with rare congenital anomalies (e.g. women with diabetes or epilepsy); c. Women are supported regarding preparation for a healthy pregnancy, including healthy diets and lifestyles, folic acid supplementation and good maternal ante-natal care, which can have a role in the prevention of a small number of rare conditions. 17. The HSE Governance Committee/Group on Newborn Screening within the Integrated Services Directorate be expanded to include a patients' advocate. The Committee should consider the population benefits of newborn screening, including whether programmes need to be expanded or modified, and the need for carrier screening. The Department of Health should also provide a policy framework for population-based screening programmes. 18. The Department of Health consider addressing the need for a review of legislation that indirectly impinges on the Newborn Bloodspot Screening Programme. 19. Governance arrangements for 'send out' genetic tests be strengthened. This should include clinical guidelines for 'send out' tests and yearly audits of the quality and diagnostic yield of tests sent out from non-hospital sources in order to minimise wastage. A national funding perspective is required to maximise quality and cost-efficiency. Centres involved in testing should develop and use guidelines regarding the most commonly tested conditions. 20. The National Clinical Programme for Rare Disease through a National Office for Rare Diseases develop the clinical and organisational governance framework that will underpin care pathways and access to treatment for rare disease patients, particularly in the context of the transition from paediatric care to adult care.

Country Information Source	Implementation action(s), agency(ies) and measure(s) or outcome(s)
	21. National Centres of Expertise (CoEs) in Ireland be identified for groupings of rare conditions, based on clinical need and built on foundations already established. There is an urgent requirement for the HSE to map out CoEs and healthcare pathways, and to acknowledge the different role and competencies of CoEs and centres providing care at local level, such mapping to be aligned with the re-organisation of Irish hospitals into hospital groupings. It is also important that broader clinical guidelines take account of the requirements of rare diseases. The potential for cooperation on an all-Ireland basis should be realised. The designation of CoEs should be in accordance with the EUCERD quality criteria for CoEs. 22. The HSE integrate CoEs into national funding planning, with provision for adequate staffing for multidisciplinary care, as well as sustainable research infrastructure for clinical investigation in addition to competitive research. 23. The Department of Health and the HSE encourage and support the national Centres of Expertise (when so designated) to seek recognition as EU designated Centres of Expertise or associated national centres in ERNs for Rare Diseases according to the timeframe, framework and standards currently being developed at European level through the complementary work of EUCERD and the EU Cross-Border Healthcare Directive 2011/24/EU. 24. Residential respite care be available for children with rare diseases. 25. With respect to palliative care: a. access is provided to appropriate palliative care for people with rare life-limiting conditions; b. guidelines are developed in palliative care provision to address the complex and multisystemic nature of many rare life-limiting conditions; c. the National Development Committee for Children's Palliative Care, chaired by the HSE, take account of the particular needs of children with rare disease in its ongoing programme of work; d. the next National Cancer Strategy could elaborate further on how best to manage rare cancers, especially in the context of this National Rare Disease Plan, where there is a shared objective to detect and treat early patients with rare cancers. 26. Appropriate modules relating to rare disease feature within all undergraduate and postgraduate programmes of both medical professional and carer disciplines. In addition to developing competency requirements and training programmes for medical professionals and carers engaged with rare conditions, practical experience and exposure to patients with rare conditions is advantageous. 27. A system of training in rare diseases for healthcare professionals be addressed through their professional bodies with the support of all stakeholder groups, including patients and their families. Action in this area should build on initiatives already underway or in progress (as outlined in Recommendation 26). 28. The establishment of a National Clinical Programme for Rare Diseases. A key role for this clinical programme will be the mapping, development and implementation of care pathways for rare diseases. 29. The establishment of a National Office for Rare Diseases to facilitate the coordination and timely access to Centres of Expertise nationally and internationally, and to provide up-to-date information regarding new treatments and management options, including clinical trials. **Enhancing access to appropriate drugs and technologies** 30. The HSE develop a Working Group to bring forward appropriate decision criteria for the reimbursement of orphan medicines and technologies. The approach should include an assessment system similar to that for cancer therapies established under the National Cancer Control Programme and link with the Clinical Added Value of Orphan Medicinal Products at European level. 31. The HSE undertake a preliminary economic evaluation of current activity and costs for orphan medicine and technologies for rare disease patients across all hospitals settings. 32. Applications for the use of orphan medicines and technologies in hospitals be dealt with in the context of a national budget, rather than through individual hospital budgets, and that the HSE take account of this.

Country Information Source	Implementation action(s), agency(ies) and measure(s) or outcome(s)
	33. The HSE develop a publicly available annual report documenting the use of both existing and new-to-market orphan medicines and technologies in Ireland and a summary of applications received and decisions relating to those applications. 34. The existing horizon scanning between pharmaceutical companies and the HSE, including clinical value assessment authorities, continue and be enhanced so as to improve information available regarding orphan medicines in the pipeline and the future needs for these medicines. 35. The capacity to prescribe all orphan medicines and technologies for ultra-rare conditions be limited to specialist teams designated through the Centres of Expertise. 36. The HSE apply a set of guidelines on the prescribing of orphan medicines and technologies in Ireland. The HSE should evaluate clinical outcomes regarding use of orphan medicines. 37. Clinicians should provide data necessary to the monitoring of prescription patterns and pharmacovigilance, so as to ensure patients' safety and high-quality healthcare. 38. Early dialogue between the HSE and companies who are running clinical trials in Ireland with Irish patients where license approval is imminent. 39. Sponsors could be offered an incentive to run trials in Ireland increasing access to innovation for Irish patients. **Empowering, protecting and supporting rare disease patients and carers** 40. The principles of patients' empowerment be integral to all aspects of this National Rare Disease Plan for Ireland, both now and in the future, in recognition of the fact that patients and their carers require significant clinical and non-clinical support. 41. Arrangements be put in place to support the integration of the experience and expertise of rare disease patients' organisations in the implementation and review of this first National Rare Disease Plan for Ireland. 42. Patients' rights to appropriate assessment and treatment be realised through a recognised national Centre of Expertise or by linkage through the patient's healthcare provider to recognised ERNs and in the context of the EU Cross-Border Healthcare Directive 2011/24/EU. 43. The proposed National Office for Rare Diseases provide support and information to patients. 44. The National Rare Disease Plan for Ireland encompass a holistic and person-centred view of the lives of rare disease patients and their families, one that goes beyond healthcare issues. 45. The HSE and non-governmental organisations provide ongoing support for people living with rare diseases and that they cooperate and promote awareness of rare diseases. 46. The HSE and non-governmental organisations avail of the opportunity to promote awareness of and information on rare diseases on Rare Disease Day. **Implementation, Monitoring and Review of the National Rare Disease Plan** 47. An Oversight Implementation Group of relevant stakeholders, including patients' groups, led by the HSE be established to oversee and monitor implementation of the National Rare Disease Plan's recommendations and associated key outputs. The HSE will report to the Department of Health using key performance indicators on a periodic basis in accordance with reporting requirements under the National Service Plan. It should be noted that the European Union has mandated EUCERD's key performance indicators and that Ireland will have to report on these (see Appendix B, Table B15). 48. There should be an overall review of the National Rare Disease Plan prior to development of the next plan in 2019. **Appendix 5: EU EUCERD Indicators to monitor National Rare Disease Plans** ***Background indicators (preparation of the plan/strategy)***

Country Information Source	Implementation action(s), agency(ies) and measure(s) or outcome(s)
	1. Existence of regulations/laws or equivalent official national decisions that support the establishment and development of a Rare Diseases plan. 2. Existence of a rare diseases advisory committee. 3. Permanent and official patients' representation in plan development, monitoring and assessment. 4. Adoption of the EU rare diseases definition. ***Content indicators*** 5. Existence of a national policy for establishing Centres of Expertise on rare diseases. 6. Number of national and regional Centres of Expertise adhering to the national policy. 7. Participation of national or regional Centres of Expertise in ERNs. ***Information*** 8. Development of and or participation in a comprehensive national and or regional rare diseases information system. 9. Existence of helplines for rare diseases. ***Knowledge, classification/coding, registries and research*** 10. Existence of a national policy on rare diseases clinical practice guideline development and implementation. 11. Type of classification/coding used by the healthcare system. 12. Existence of a national policy on registries or data collection on rare diseases. 13. Existence of rare disease research programmes and/or projects in the country. 14. Participation in European and international research initiatives. ***Therapies*** 15. Number of Orphan Medical Products with a European Union marketing authorisation and available in the country (i.e. priced and reimbursed or directly supplied by the national health system). 16. Existence of a governmental system for compassionate use of medicinal products. ***Social services*** 17. Existence of programmes to support the integration of rare disease patients in their daily life. ***Financial support indicators (implementation of the plan/strategy)*** 18. Existence of a policy/decision to ensure long-term sustainability of the rare diseases plan/strategy. 19. Amount of public funds allocated to the rare diseases plan/strategy. 20. Specific public funds allocated for rare disease research. 21. Public funds specifically allocated for rare disease research actions/projects per year since the plan started.
Australia ▪ National Strategic Action Plan for Rare Diseases 2020[22]	▪ A number of specific actions were outlined. No implementation agencies were outlined, with the strategy stating that the implementation of any action is the decision of each stakeholder based upon their area of responsibility, governance remit, existing activities and future planning and directions in relation to rare diseases. No specific measures or outcomes were listed, although they may be contained within each action. **Action 1.1.1: Develop and conduct national awareness and education activities for rare diseases.** ▪ **1.1.1.1:** Analyse existing resources and distribution and build on these to continue media and communications and material that promotes and distributed the latest information relating to rare disease. Responsibility for deliverables will be identified as art of this process (see Appendix B, Table B1 for 1.1.1.2 to 1.1.1.4).

Country Information Source	Implementation action(s), agency(ies) and measure(s) or outcome(s)
	Action 1.1.2: Raise awareness of, and deliver, relevant prevention measures for non-hereditary rare diseases, such as cancers, infections and autoimmune disorders. ▪ **1.1.2.1:** Governments, healthcare services and stakeholder organisations raise awareness of, and educate about, relevant prevention measures for non-hereditary rare diseases, including through national and localised media and communications material (see Appendix B, Table B1 for 1.1.2.2). **Action 1.1.3: Develop, deliver and promote targeted awareness and education activity to support people in their preparation for conception and pregnancy.** ▪ **1.1.3.1:** Governments and healthcare services raise awareness of rare diseases and educate people preparing for conception and pregnancy. This is incorporated into existing pre-conception and perinatal care. This could include education and awareness pertaining to both preventative measures and rare diseases testing and screening opportunities such as: ○ pre-conception (carrier) testing and screening ○ pre-implantation genetic diagnosis (testing) and screening ○ ante-natal testing and screening ○ newborn testing and screening (see Appendix B, Table B1 for 1.1.3.2 and 1.1.3.3). **Action 1.2.1: Raise awareness among people living with a rare disease, and their families and carers, about the care and support services available to them.** ▪ **1.2.1.1:** Develop and maintain an accessible multi-purpose digital repository to detail available care and support services and to provide general rare diseases information. The repository can be used to identify gaps and opportunities for improvement. Promote the repository to rare disease organisations, for distribution to people living with a rare disease, and their families and carers (see Appendix B, Table B1 for 1.2.1.2). **Action 1.2.2: Improve consultation and communication between policy-makers and the rare disease community.** ▪ **1.2.2.1:** Rare disease organisations strengthen their connections with policy-makers. This would build on current coordination by existing national and state-based collaborations (see Appendix B, Table B1 for 1.2.2.2). **Action 1.3.1: Develop a national rare disease workforce strategy.** ▪ **1.3.1.1:** Identify existing gaps in the workforce that support people living with a rare disease and outline a path towards a sustainable workforce, taking into account the impact of genomics (see Appendix B, Table B1 for 1.3.1.2 and 1.3.1.3). **Action 1.3.2: Equip and encourage frontline health professionals to consider, investigate and refer for a potential rare disease diagnosis.** ▪ **1.3.2.1:** Develop and promote guidelines for Australia in line with the International Joint Recommendations to Address Specific Needs of Undiagnosed Rare Disease Patients. These guidelines will provide support for clinicians in identifying possible rare disease in people who present with complex symptoms. They will also articulate the key role that health professionals play in meeting the support needs of individuals and families through the diagnostic journey (see Appendix B, Table B1 for 1.3.2.2 and 1.3.2.3).

Country Information Source	Implementation action(s), agency(ies) and measure(s) or outcome(s)
	Action 2.1.1: Provide rare disease care and support that is integrated, incorporating clear pathways throughout health, disability and other systems. ▪ **2.1.1.1:** Establish standards for care and support that are integrated and incorporate clear pathways throughout all systems. Ensure these are informed by clinical and consumer rare disease experts and that such consultation informs policy development (see Appendix B, Table B1 for 2.1.1.2 to 2.1.1.4). **Action 2.1.2: Build a broad range of care and support services that are responsive to the changing needs of people living with a rare disease and their families.** ▪ **2.1.2.1:** Develop an accessible multi-purpose digital repository, incorporating elements targeted at the workforce that supports people living with a rare disease. With access to adequate information, healthcare and social support professionals will be equipped to support people living with a rare disease and their families to navigate health, disability and other systems (see Appendix B, Table B1 for 2.1.2.2 and 2.1.2.3). **Action 2.1.3: Ensure services support people living with a rare disease through significant life-stage transitions.** ▪ **2.1.3.1:** Enhance existing transition services to ensure people living with a rare disease experience seamless transitions between services as they move through life stages. Common transitions include: ○ reaching the age cut-off point for paediatric services (for example transitioning for child to adult hospitals) ○ relocating ○ when needs change significantly (such as the end-of-life) (see Appendix B, Table B1 for 2.1.3.2 to 2.1.3.4). **Action 2.1.4: Develop the capacity of rare disease organisations to represent and advocate for people living with a rare disease and their families.** ▪ **2.1.4.1:** Rare disease organisations represent and advocate for people living with a rare disease and their families through a range of activities including: ○ written submissions ○ consumer hearings ○ communicating with their community ○ representing their community to stakeholders, such as government and industry ○ advocating for reimbursement of health technologies after independent health technology assessment (HTA) has demonstrated effectiveness. Further support the current activities of rare disease organisations trough additional resourcing as well as further national collaboration (see Appendix B, Table B1 for 2.1.4.2). **Action 2.1.5: Embed the voice of people living with a rare disease and their families and carers throughout structures and systems that impact rare diseases.** ▪ **2.1.5.1:** Capture and promote the voice of people living with a rare disease and their families and carers by: ○ involving people living with a rare disease at every level of decision-making; ○ ensuring ongoing engagement to capture broader input from people living with a rare disease through surveys, focus groups, newsletters and representation on boards; and ○ calling for key structures and systems to routinely and effectively capture broader input from consumers, as done currently in some research settings and HTA (consumer hearings) (see Appendix B, Table B1 for 2.1.5.2).

Country Information Source	Implementation action(s), agency(ies) and measure(s) or outcome(s)
	Action 2.2.1: Ensure all Australians have equitable access to a range of diagnostic tools and tests, providing the best chance of early and accurate diagnosis. ▪ **2.2.1.1:** Further the development of, and investment into, the range of existing specialist diagnostic responses, such as genomics technology, including for Aboriginal and Torres Strait Islander people; interdisciplinary undiagnosed disease programs, clinical phenotype diagnostic support tools; centres of expertise; genetic counsellors and peer support groups (see Appendix B, Table B1 for 2.2.1.2 and 2.2.1.3). **Action 2.2.2: Develop policy that supports the implementation of diagnostic tools and tests.** ▪ **2.2.2.1:** Support national leadership and coordination of a range of screening and diagnostic tools and tests jointly funded by Commonwealth and state/territory governments, to enable more consistent service and equitable access (see Appendix B, Table B1 for 2.2.2.4 and 2.2.2.5). **Action 2.2.3: People with an undiagnosed rare disease are identified and have priority access to the most appropriate specialised and expert diagnostic response.** ▪ **2.2.3.1:** Flag in health information systems when someone presents with an undiagnosed rare disease (see Appendix B, Table B1 for 2.2.3.2 and 2.3.3.3). **Action 2.2.4: Support people with a suspected but undiagnosed rare disease on their diagnostic journey.** ▪ **2.2.4.1:** Undertake a survey on existing support for people with an undiagnosed rare disease delivered by rare disease organisations, to identify gaps and opportunities for improvement (see Appendix B, Table B1 for 2.2.4.2 to 2.2.4.4). **Action 2.3.1: Ensure individuals and families known to have an increased chance of being carriers of genetic variants for rare diseases have equitable access to peri-conception genetic testing and counselling, which can provide them with information about becoming pregnant and pregnancy.** ▪ **2.3.1.1:** Further to the National Health Genomics Policy Framework and Pregnancy Care Guidelines, develop consistent and comprehensive clinical guidelines for all relevant health professionals to support individuals and families to access peri-conception genetic testing, counselling and peer support groups (see Appendix B, Table B1 for 2.3.1.2 to 2.3.1.4). **Action 2.3.2: Women who have, or are at risk of developing, certain chronic conditions, such as diabetes, epilepsy or thyroid disorders, have an increased chance of having babies with rare congenital anomalies. Provide these women with access to evidence-based, high-quality pre-conception and peri-natal care.** ▪ **2.3.2.1:** Governments and healthcare services provide women planning a pregnancy with increased and equitable access to a pre-conception consultation program to investigate whether they have, or are at risk of developing, certain chronic conditions, such as diabetes, epilepsy or thyroid disorders, that may affect their pregnancy (see Appendix B, Table B1 for 2.3.2.2 and 2.3.2.3). **Action 2.4.1: Develop policy that supports people living with a rare disease to have timely and equitable access to new and emerging health technologies.** ▪ **2.4.1.1:** Broaden the description and understanding of the principles underpinning Australian HTA processes to acknowledge the challenges associated with assessing health technologies for rare diseases (see Appendix B, Table B1 for 2.4.1.2 to 2.4.1.5).

Country Information Source	Implementation action(s), agency(ies) and measure(s) or outcome(s)
	Action 2.4.2: Ensure funding and reimbursement pathways are fit-for-purpose and sustainable for current and new health technologies for rare diseases. ▪ **2.1.2.1:** Build on the current processes within the HTA to ensure all rare diseases submissions are flagged as complex and may require additional scoping and engagement to address potential challenges and uncertainties (see Appendix B, Table B1 for 2.4.2.2 and 2.4.2.3). **Action 2.4.3: Ensure people living with a rare disease have equitable access to medicines with demonstrated clinical benefit for a rare disease, including those that are already funded for another condition.** ▪ **2.4.3.1:** Ensure the HTA Consumer Evidence and Engagement Unit provides education and support to people living with a rare disease and their families and carers, and/or rare disease organisations to support them to take a more active role in HTA processes (see Appendix B, Table B1 for 2.4.3.2 and 2.4.3.3). **Action 2.5.1 Ensure people living with a rare disease, including their families and carers, receive the community, clinical and digital mental health supports and services they need.** ▪ **2.5.1.1.** Enable people living with a rare disease, including their families and carers (with appropriate consent) to access information and resources (including digital) customised for rare diseases as part of Chronic Disease Management Plans and Mental Health Care Plans (see Appendix B, Table B1 for 2.5.1.2). **Action 2.5.2: Implement care and support systems to address the mental health and wellbeing of Australians impacted by a rare disease.** ▪ **2.5.2.1:** Empower rare disease care and support providers to deliver the best possible mental health and social and emotional wellbeing support outcomes through a range of initiatives, including: ○ access to evidence that aids providers in their understanding of and ability to respond to mental health and social and emotional wellbeing support needs, such as a rare disease mental health checklist ○ awareness around the existing range of free or low cost digital mental health services that provide support, such as Head to Health; ○ education about how to access and utilise these services ○ cultural competency education that empowers providers to effectively support Aboriginal and Torres Strait Islander people (see Appendix B, Table B1 for 2.5.2.2). **Action 2.5.3: Develop the capacity of rare disease organisations to provide wellbeing and mental health support.** ▪ **2.5.3.1:** Better resource existing social and emotional wellbeing support provided by rare disease organisations including: ○ peer support ○ family days ○ community engagement ○ information sessions and workshops (see Appendix B, Table B1 for 2.5.3.2 and 2.5.3.3). **Action 3.1.1: Health information systems identify and measure rare diseases and undiagnosed rare diseases.** ▪ **3.1.1.1:** The Australian Institute of Health and Welfare re-establishes the Australian National Congenital Anomalies Register, including rare disease coding (ORPHAcodes). This will accelerate, extend and nationalise rare disease coding already underway in the Western Australian

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	Register of Developmental Anomalies, and contribute to International Classification of Diseases 11th Revision (ICD-11) preparedness (see Appendix B, Table B1 for 3.1.1.2 to 3.1.1.4). **Action 3.1.2: Undertake broad epidemiological surveillance of rare diseases to support decision-makers to access the information they need to improve the health and wellbeing of Australians living with a rare disease.** ▪ **3.1.2.1:** Building on existing newborn screening and congenital anomalies data collections, further develop Australia's monitoring of rare diseases and undiagnosed rare diseases. Examples may include and extend beyond: ○ newborn and paediatric age ranges; and ○ the rare diseases currently captured in newborn screening and congenital anomalies data collections (see Appendix B, Table B1 for 3.1.2.2). **Action 3.1.3: Improve rare disease data collection and use, including best-practice safe storage, data sharing, custodianship, analysis, reporting and privacy requirements.** ▪ **3.1.3.1:** Establish a dedicated Rare Disease Office within the Australian Institute of Health and Welfare. Included in its remit will be systematic improvements in rare disease data integration and interoperability (see Appendix B, Table B1 for 3.1.3.2). **Action 3.1.4: Develop a national approach to person-centred rare disease registries to support national standards, best practice and minimum data sets.** ▪ **3.1.4.1:** Develop a summary report of all existing Australian and relevant international rare disease registries, collecting information on: ○ governance standards ○ management practices ○ data sets, including patient numbers, estimated incidence, prevalence and coverage ○ classification systems used (for interoperability with other registries and health information systems). This information will support national coordination of rare disease registries and the establishment of minimum data sets, provide a better understanding of who is currently being counted and aid identification of best practice (see Appendix B, Table B1 for 3.1.4.2). **Action 3.2.1: Develop a national research strategy for rare diseases, to keep pace with genomic advancements, precision medicine and innovation.** ▪ **3.2.1.1:** Undertake a national stakeholder consultation process to set agreed priorities for a national research strategy for rare diseases, including: ○ surveys ○ public forums ○ targeted themed roundtables ○ opportunities for public submissions (see Appendix B, Table B1 for 3.2.1.2). **Action 3.2.2: Proactively address evidence gaps in areas that are important to people living with a rare disease.** ▪ **3.2.2.1:** Ensure lived experience drives research by encouraging collaboration between researchers and people living with a rare disease through workshops, conferences and consumer reference groups (see Appendix B, Table B1 for 3.2.2.2 to 3.2.2.4).

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	Action 3.2.3: Support collaborative research into rare diseases in Australia and internationally. ▪ **3.2.3.1:** Encourage and facilitate greater research collaboration nationally, internationally and with industry. Examples of how this may be achieved include: ○ financial incentives for research teams that can demonstrate collaboration with national, international and industry partners ○ the development of customised research grants for rare diseases that require a degree of collaboration with national, international and industry partners. **Action 3.2.4: Building on existing initiatives, continue to foster an environment conducive to clinical trials for rare diseases taking place in Australia.** ▪ **3.2.4.1:** Develop recommendations to encourage and enable more clinical trials for rare diseases to take place in Australia (see Appendix B, Table B1 for 3.2.4.2 and 3.2.4.3). **Action 3.2.5: Investigate and promote options that enable Australians living with a rare disease to participate in clinical trials and other research activity, both in Australia and internationally (without needing to leave Australia).** ▪ **3.2.5.1:** Identifying and maximising utilisation of available resources and assets to the extent possible, link people living with a rare disease to research activity, such as data collection, registries, natural history studies, qualitative research and clinical trials based in Australia and internationally (see Appendix B, Table B1 for 3.2.5.2). **Action 3.3.1: Provide people living with a rare disease or an undiagnosed rare disease with the opportunity and support to participate in research.** ▪ **3.3.1.1:** Health professionals inform and connect people living with a rare disease to research as part of their ongoing care (see Appendix B, Table B1 for 3.3.1.2 and 3.3.1.3). **Action 3.3.2: Enable researchers, funders and policy-makers to access the voice of people living with a rare disease in driving and delivering research into rare diseases.** ▪ **3.3.2.1:** Develop and support consumer reference groups to promote additional pathways for researchers, research funders, policy-makers and other decision-makers to be informed about the rare disease community's needs and priorities. Wherever possible, leverage and build on the expertise and resources of existing groups and mechanisms (see Appendix B, Table B1 for 3.3.2.2). **Action 3.4.1: Support partnerships between researchers and clinicians in research into rare diseases.** ▪ **3.4.1.1:** Research funding bodies prioritise research proposals and applications for rare diseases that can demonstrate support from, and close working relationships with, clinicians (see Appendix B, Table B1 for 3.4.1.2). **Action 3.4.2: Identify, leverage and enhance existing capability and infrastructure to ensure appropriate and experienced resourcing is available within clinical teams that deliver rare disease care.** ▪ **3.4.2.1:** In partnership with industry, philanthropy and trial sites, identify and enhance existing capability and infrastructure within clinical centres to ensure appropriate capability is available to support the operation of clinical trials for rare diseases (see Appendix B, Table B1 for 3.4.2.2).

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▪ Implementing the National Strategic Action Plan for Rare Diseases: May 2023 Status Report[23]	▪ The 2023 status report outlined that 380 activities could be identified that align with the Pillars and priorities in the Action Plan (see Appendix B, Table B2).
Austria National Action Plan (NAP) for Rare Diseases 2014-2018[47]	Implementation of the plan and its success to be monitored using specific indicators for each field of action, in line with European developments and procedures, which are still to be determined. The creation of the indicators was scheduled to be completed in 2015, however no indicators have been identified to date. No additional implementation actions, agencies, and measures or outcomes were identified in the Evaluation of the National Action Plan for Rare Diseases 2020[48]. Eighty-two actions and their associated responsible agencies are outlined according to the relevant field of action (in bold) and associated goal. For brevity, one action is outlined below for each goal. **Priority 1: Mapping/illustrating rare diseases in the health and social system.** **Goal 1:** Introduction of suitable documentation (coding) in all expertise centres and subsequently optional extension to other care levels. 1. Collaboration in the development of a coding system for rare diseases. a) Organising a workshop on coding with national and German participants. *Responsible*: BMG/NKSE. *Schedule*: 2014. b) Follow-up steps will be defined after the workshop. *Responsible*: BMG. *Schedule*: to be determined following a) (see Appendix B, Table B3 for actions 2 to 7). **Priority 2: Improving medical and clinical care for those affected by rare diseases.** *A. Designation of specialised centres* **Goal 1:** Summary of the individual rare diseases into medically meaningful disease groups. 8. Continue and complete work on grouping rare diseases (combining the individual diseases into medically sensible groups). *Responsible*: BMG/NKSE; medical professional societies. *Schedule*: 2014 (see Appendix B, Table B3 for actions 9 to 12). **Goal 2:** Designation of specialised centres for defined groups which are divided into three levels of care. 13. Anchoring the general performance and quality criteria for Type A, B and C centres in a suitable planning instrument. *Responsible*: NKSE/GÖG; Planning specialist group; hospital providers; Federal Health Commission. *Schedule*: 2014/2015 (see Appendix B, Table B3 for actions 14 to 20) **Goal 3:** Integration of these specialised centres through intensified networking. 21. Supporting horizontal and trans-sectoral networking of Types A, B and C centres with other care levels. *Responsible*: BMG/NKSE. *Schedule*: following Action 17. **Goal 4:** Providing framework conditions for the integration of Austrian expertise into European Reference Networks (ERNs). 22. Support for European networking with ERNs. *Responsible*: BMG/NKSE. *Schedule*: 2015.

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	B. Establishment of a national coordination office for rare diseases **Goal 1:** Identify deficits regarding rare diseases in the health and care system. 23. Assessing the care needs of patients with rare diseases in Austria. *Responsible*: BMG/NKSE. *Schedule*: completed in 2012. **Goal 2:** Develop a national strategy to address the identified deficits in the area of rare diseases (NAP). 24. Creating a National Action Plan for Rare Diseases (NAP). *Responsible*: BMG/NKSE. *Schedule*: 2013/2014 (publication 2015). **Goal 3:** Support the implementation of the NAP. **Goal 4:** Collection and structuring of the medical service offering in the area of rare diseases. **Goal 5:** Promote uniform access to medical care for rare diseases across Austria including therapies at the 'best point of service'. 25. Supporting the implementation process of the NAP. *Responsible*: BMG/NKSE. *Schedule*: 2014-2018. **Goal 6:** Information hub for rare diseases. 26. Providing relevant information on rare diseases for selected target groups. *Responsible*: BMG/NKSE. *Schedule*: constantly. **Goal 7:** Networking at European level to ensure continuous exchange in the area of rare diseases. 27. Participate in meetings of European commission bodies in the context of rare diseases. Optional: collaboration on European projects related to rare diseases. *Responsible*: BMG/NKSE. *Schedule*: constantly. *C. Continue and sustainably secure Orphanet as a comprehensive information system for rare diseases.* **Goal 1:** expansion of the contents of the database and ensuring long-term financing for Orphanet Austria. 28. Developing a concept for long-term financing for Orphanet Austria. *Responsible*: BMG/NKSE; Federal Ministry of Science, Research and Economy (BMWFW); federal states; HVB/Social Insurance; if necessary, other financiers. *Schedule*: 2014/2015 (see Appendix B, Table B3 for action 29). **Priority 3: Improving the diagnosis of rare diseases.** **Goal 1:** Development and implementation of quality and performance criteria for diagnostic laboratories for rare diseases. 30. Continue and complete the definition of performance and quality criteria for medical laboratories involved in the diagnosis of rare diseases. *Responsible*: BMG/NKSE; experts (selected members of the advisory board for rare diseases (see priority 8) as well as external experts). *Schedule*: 2015 (see Appendix B, Table B3 for action 31). **Goal 2:** Designations of specialised laboratories for rare diseases or groups of rare diseases. 32. Developing an application, assessment and designation process for medical laboratories involved in the diagnosis of rare diseases. *Responsible*: BMG/NKSE; coordination with HVB; federal states. *Schedule*: following Goal 1 (see Appendix B, Table B3 for action 33 to 35). **Goal 3:** Integration of these specialised laboratories into the Austrian healthcare landscape through close networking of all healthcare levels involved. 36. Supporting the nationwide networking of designated laboratories with each other and with other levels of care; Support in networking with Orphanet.

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	Responsible: NKSE; Orphanet Austria. *Schedule*: expected to be relevant from 2018. **Goal 4:** Development of financing models for laboratory diagnostic services for rare diseases. 37. Examination and possible revision of the relevant service catalogues. *Responsible*: Payer. *Schedule*: expected to be relevant from 2018. **Goal 5:** Development and implementation of uniform Austria-wide standards for instrumental diagnostics. **Goal 6:** Designation of specialised diagnostic facilities in accordance with the aforementioned Austria-wide standards. 38. Developing competency criteria for experts, who are involved in the diagnostics of rare diseases. *Responsible*: BMG/NKSE; experts; Quality specialist group. *Schedule*: expected to be relevant from 2018. **Goal 7:** Establishment of an official scientific advisory board at ministerial level for the Austrian newborn screening programme. 39. Setting up a permanent scientific advisory board for the Austrian newborn screening. *Responsible*: BMG and BMWFW. *Schedule*: 2015. **Goal 8:** Development of an Austrian "Undiagnosed Diseases Programme". 40. Development of a concept for an Undiagnosed Diseases Programme in Austria. *Responsible*: BMG/NKSE; experts. *Schedule*: 2016. **Priority 4: Improving therapy and access to therapies for those affected by rare diseases.** **Goal 1:** Networking at the European level to ensure sustainable financing of orphan drugs. 41. Participation in European cooperation projects to secure sustainable financing of orphan drugs, such as Mechanisms of Coordinated Access to Orphan Medicinal Products in Europe. *Responsible*: HVB; BMG; industry; support from NKSE. *Schedule*: 2014. **Goal 2:** Determine the costs of selected drugs without overlapping indications for the treatment of people with rare diseases in both general practice and institutional settings. 42. Price collection of selected orphan drugs in institutional and community-based sectors (including purchasing modalities such as joint purchasing and possible managed entry agreements) *Responsible*: NKSE/GÖG; HVB; hospital pharmacies; legal entity representatives of state hospitals; industry. *Schedule*: 2014/2015 (see Appendix B, Table B3 for action 43 and 44). **Goal 3:** Ensuring consistent access to therapies at the best point of service. 45. Establishing optimised supply processes at the respective "best point of service". *Responsible*: BMG; federal states; HVB; NKSE/GÖG. *Schedule*: 2016 (see Appendix B, Table B3 for action 46) **Goal 4:** Creation of a nationwide uniform catalogue of services for selected remedies (pilot project for rare diseases). 47. Establishing a discussion group to introduce a uniform service catalogue for medical devices (pilot project for rare diseases). *Responsible*: HVB; BMG; federal states; support from NKSE. *Schedule*: 2015. **Goal 5:** Ensure continuous access to adequate medication care. 48. Establishing a regular exchange between chief physicians, social health insurance and patient representatives. *Responsible*: Pro Rare Austria; HVB. *Schedule*: constantly (see Appendix B, Table B3 for action 49). **Priority 5: Promoting research in the field of rare diseases.** **Goal 1:** Make visible and create awareness of existing national and international funding opportunities for rare diseases in the "scientific community".

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	50. Providing specific information/links for rare disease relevant tenders on the NKSE website in cooperation with the relevant funding agencies and institutions. *Responsible*: NKSE as an information hub; BMWFW. *Schedule*: 2014 (see Appendix B, Table B3 for action 51). **Goal 2:** Creation of structural framework conditions to ensure high-quality applications (linked to Priority 2, designation of specialised centres). 52. Designation of expertise centres with a focus on research. *Responsible*: Expertise centres and expertise clusters (optionally also associated centres); hospital providers; if applicable, university management; NKSE as an information hub. *Schedule*: 2015. **Goal 3:** Networking domestic and other European centres of expertise in order to participate together in international funding programmes. 53. Austria's participation in ERN regarding research aspects. *Responsible*: Expertise centres and cluster model; NKSE as an information hub. *Schedule*: expected to be relevant from 2016. **Goal 4:** Coordination of support for rare disease-specific research initiatives in order to position Austria as a research location in the field of rare diseases. 54. Dialogue with the relevant stakeholders, especially with funding agencies and rare disease-relevant research institutions. *Responsible*: BMWFW; NKSE as an information hub. *Schedule*: 2014. **Priority 6: Improving knowledge and awareness of rare diseases.** **Goal 1:** Expansion of the level of knowledge of the most important sources of information. 55. Imparting basic knowledge about rare diseases and the possible options associated with it, treatment options. *Responsible*: health service providers; professional associations; BMG/NKSE; Pro Rare Austria. *Schedule*: 2014 (see Appendix B, Table B3 for action 56 to 59). **Goal 2:** Strengthening patient safety and health literacy through objective, quality-assured and target group-specific information. 60. Adding a focus on rare diseases in the health portal. *Responsible*: GÖG health portal; support from NKSE. *Schedule*: 2014. See Action 29: Providing quality-assured information on rare diseases. *Responsible*: Orphanet Austria. *Schedule*: 2014. **Goal 3:** Increase awareness of rare diseases in all target groups and raise awareness of the topic. 61. Definition of specific contact persons (person/department) for interest groups in the area of rare diseases. *Responsible*: all relevant system partners. *Schedule*: since 2011; Founding of NKSE, founding of Pro Rare Austria (see Appendix B, Table B3 for action 62 and 63). **Priority 7: Improving epidemiological knowledge in the context of rare diseases.** **Goal 1:** Establishment of a comprehensive, quality-assured epidemiological recording system for patients with rare diseases. 64. Inventory of existing patient registers for rare diseases and, if necessary, other relevant data collection systems in Austria. *Responsible*: Orphanet Austria; NKSE; Pro Rare Austria. *Schedule*: 2015 (see Appendix B, Table B3 for action 65). **Goal 2:** Consideration of interoperability with existing systems at national and European levels. 66. Ensuring interoperability with existing relevant national and international patient registries and data collection systems. *Responsible*: BMG/NKSE; federal states; Social Insurance; hospital providers. *Schedule*: as part of the definition and voting process. **Goal 3:** Coordination with current and future developments at European level. 67. Developing a minimum data set with international developments in mind.

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	Responsible: BMG/NKSE; hospital providers. *Schedule*: 2014 (see Appendix B, Table B3 for action 68). **Priority 8: Establishment of permanent advisory committees for rare diseases at the BMG.** **Goal 1:** Establish both committees. 69. Constituting the new "Rare Advisory Board" to replace the expert group for rare diseases as an advisory board in accordance with Section 8 of the Federal Ministries Act. *Responsible*: BMG. *Schedule*: 2014 (see Appendix B, Table B3 for action 70). **Goal 2:** National Advisory Council for Rare Diseases – continuous provision of expert knowledge from research and practice. 71. Participation in meetings of the Advisory Board for Rare Diseases and advisory role in the implementation of the NAP and other issues in the context of rare diseases. *Responsible*: BMG/NKSE; members of the Advisory Board for Rare Diseases. *Schedule*: 2014-2016 (see Appendix B, Table B3 for action 72). **Goal 3:** Strategic Platform for Rare Diseases – strategic support of NKSE work. 73. Participation in meetings of the Strategic Platform for Rare Diseases. *Responsible*: BMG/NKSE; Strategic Platform for Rare Diseases. *Schedule*: 2014-2016 (see Appendix B, Table B3 for action 74). **Priority 9: Recognition of self-help achievements.** **Goal 1:** Ensure Austria-wide representation for people with rare diseases. 75. Establishment of an Austria-wide umbrella organisation of self-help groups for people with rare diseases. *Responsible*: Pro Rare Austria. *Schedule*: founding of Pro Rare Austria in December 2011. **Goal 2:** Clarification of the role of self-help, promotion of independence and transparency with the aim of ensuring long-term financing. 76. Creating framework conditions to ensure long-term financing. *Responsible*: financiers; legislature (BMG); Working Group for Self-Help Austria (*ARGE Selbsthilfe Österreich*); Pro Rare Austria. *Schedule*: 2014 (see Appendix B, Table B3 for action 77 to 79). **Goal 3:** Recognition of the expertise and experiences of people with rare diseases and those of their relatives and creation of participatory decision-making structures. 80. Representation of self-help for rare diseases in decision-making bodies and inclusion in decision-making processes. *Responsible*: all system partners; Working Group for Self-Help Austria (*ARGE Selbsthilfe Österreich*); Pro Rare Austria. *Schedule*: Pro Rare Austria has been represented in the Expert Group for rare diseases of the BMG since 2011. **Goal 4:** Survey the health economic effects of self-help. 81. Initiating scientific studies to demonstrate the health economic effects of self-help. *Responsible*: relevant research institutions; Pro Rare Austria. *Schedule*: 2014. **Goal 5:** Strengthen the image of self-help among the public. 82. Public relations: e.g. contributions in media, events, public recognition. *Responsible*: all system partners; BMG/NKSE; Pro Rare Austria; media. *Schedule*: 2014.
Denmark ▪ National Strategy for Rare Diseases 2014[24]	During strategy evaluations in 2018 and 2022 strategy recommendations were narrowed to ensure they were action orientated. The recommendations of the 2022 evaluation are therefore the focus. ▪ The 2014 strategy outlined over 100 recommendations across 13 themes or chapters (see Appendix B, Table B6).

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▪ Evaluation of the National Strategy for Rare Diseases 2018[25]	▪ The 2018 strategy evaluation then narrowed down the 100 recommendations to 23 recommendations across 6 themes or chapters (see Appendix B, Table B7).
▪ Evaluation of the National Strategy for Rare Diseases 2022[26]	▪ The 2022 strategy evaluation then retained the 23 recommendations from the 2018 evaluation but also added two further themes, and Availability of Treatment and Implementation (outlined below). As this was a strategy evaluation, the recommendations were also assessed in terms of implementation, impact and relevance. This is outlined in Appendix B, Table B8. ***Theme 1: Rare patients in the hospital system and the municipality.*** **Recommendation 2:** The Danish Health Authority, with the involvement of the regions and centres for rare diseases, will initiate a process that clarifies the individual specialist guidelines in relation to the treatment of rare diseases, creates consistency between the specialist guidelines and ensures an appropriate organisation. **Recommendation 3:** The centres for rare diseases jointly and with the involvement of relevant parties draw up referral guidelines for how young and adult patients can enter the centres for rare diseases and for who can appropriately stay/not stay in the centres. The referral guidelines must take into account the speciality plan. **Recommendation 4:** Cooperation between clinical genetics departments, the centres for rare diseases and paediatric departments under regional auspices is strengthened and developed throughout the diagnostic process, including to ensure that new diagnostic methods are used for follow-up and diagnosis of patients who have not previously received a molecular genetic diagnosis. **Recommendation 5:** The genetic investigation and diagnostics are carried out under the auspices of the clinical genetic departments in order to ensure that the most suitable diagnostic methods are used and that the interpretation and dissemination of analysis results is carried out by professionals with clinical genetic specialist knowledge. **Recommendation 6:** The centres for rare diseases must: a) ensure an appropriate transition from child to adult. Below that guidelines are drawn up for how young and adult patients who need this can stay at the centres for rare diseases and for how the transition to other specialties is ensured for young people and adults who do not have to stay in the centres for rare diseases b) develop models and agreements on multidisciplinary teamwork, so that both children, young people and adults with a rare and complex disease are ensured a multidisciplinary, interdisciplinary and well-coordinated effort regardless of place of residence c) prepare patient course descriptions for the major rare diseases, based on national and international descriptions of "best practice" d) upgrade support functions, including psychological assistance, social worker assistance and physiotherapy depending on the local conditions. **Recommendation 7:** The Centres for Rare Diseases and the National Knowledge and Special Advisory Organisation must ensure easy access for professionals from all sectors to valid, user-friendly and up-to-date knowledge about rare diseases. **Recommendation 8:** The municipalities ensure holistically oriented and coherent process, e.g. through work with: a) establishment of one entrance and exit to/from the municipality. b) one coordinating case manager who can ensure coordination and handover of information between case managers, doctors and municipal specialist staff etc. as well as guide the citizen and contribute to minimizing the number of contacts in the citizen process. c) cross-cutting teams with a view to strengthening coordination across professional and administrative areas in cases with high complexity. This assumes that the citizen gives consent to the exchange of information.

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	d) creation of municipal networks across the country with a view to mutual learning and inspiration and uniform management of offers in the country. e) that municipalities with experience in coordinating courses for citizens with rare diseases in collaboration with the social services make their knowledge and experience available to the staff at centres for rare diseases, for example, through joint knowledge-sharing activities. ***Theme 2: Sector transitions, cooperation and coordination*** **Recommendation 9:** The centres for rare diseases strengthen course coordination, coherence and overview in the often very complex treatment courses, for example by strengthened use of functions such as the doctor responsible for the patient and the course coordinator function. This applies both to cooperation and the handing over of information between relevant hospital departments and across sectors. **Recommendation 10:** The Centres for Rare Diseases and the municipalities exchange patient data, and reciprocal access to contact about the individual patient is ensured between the course managers in the municipality and the Centre for Rare Diseases, respectively, and access for the municipalities to the medical expertise in rare diagnosis centres. **Recommendation 11:** Regions and municipalities in their collaboration consider rare diseases. This can be done, for example, by drawing up concrete agreements for the rare target group, or by including the rare target group in general health agreements, where patient processes cross regions, municipalities and general practice. **Recommendation 12:** The National Board of Social Affairs and Health, through the national coordination structure, follows the development of target groups, offers and efforts in the most specialised social and special education areas, and collects and disseminates knowledge about these, including publication of course description(s) for selected target groups. ***Theme 3: Patient education, coping and empowerment*** **Recommendation 13:** Regions, municipalities and patient organisations maintain and strengthen citizens' and relatives' ability to cope with to ensure optimal treatment results, increased quality of life and prevent social isolation, including: a) The patient organisations in collaboration with regions/Centres for Rare Diseases and municipalities develop offers for patient education at themed evenings, collaboration with voluntary organisations and virtual course material. The offers can be targeted at specific subgroups, including children, young people, adults, people with developmental disabilities or Danes with a different ethnic background. b) Initiate projects that aim to test/adjust/spread existing general models for other patient groups in need of help, so that they can also be applied to people with rare diseases. **Recommendation 14:** Patient organisations prepare/update information material with citizen-oriented knowledge and information about rare diseases, offers of support for coping, etc. with the involvement of professionals. **Recommendation 15:** Counselling services to promote patient empowerment must also be offered to people with rare diseases and their relatives in the future. ***Theme 4: International cooperation*** **Recommendation 16:** The regions are building up national cooperation with a view to Danish participation in international collaborations, including Danish participation in the ERNs and Orphanet. **Recommendation 17:** The regions build regional networks that support coordination of the regions' work between Danish ERN members, including the application process for the hospitals and contribute to the regional dissemination of relevant information from the Danish Health Authority.

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	Recommendation 18: The Danish Health Authority supports the regions in the above and strengthens Danish participation in ERNs during the construction phase by: ▪ clarifying that hospitals with highly specialised functions are recommended to be part of a ERN, if a relevant network exists ▪ supporting the incorporation of Danish hospitals into international collaborations by mediating contact and providing information, for example by holding an information meeting when the next application deadline is known participating in Nordic cooperation, including the Nordic Network on Rare Diseases and Nordic Cooperation on Highly Specialised Treatment and Clinical Trials, where, among other things, cooperation opportunities in relation to ERNs are discussed. ***Theme 5: Education and skills*** **Recommendation 19:** The teaching effort is strengthened, primarily in the specialist medical training programmes, in relation to diagnosis and treatment in rare diseases, so that all specialties in their target descriptions indicate learning competencies with a focus on the specialist being able to see symptoms as a possible part of a larger complex rare disease, so that relevant patients can be referred for investigation in the centres for rare diseases. **Recommendation 20:** Relevant medical scientific societies prepare a description of how an expert training/further training regarding rare diseases can be composed. **Recommendation 21:** It is being investigated how diagnosis descriptions for rare diseases can be anchored and expanded in the Medical Handbook in the future. **Recommendation 22:** The necessary competencies of other health personnel who deal with patients with rare diseases are strengthened. ***Theme 6: Registration, documentation and knowledge*** **Recommendation 23:** The regions and the Centres for Rare Diseases jointly: ▪ consolidate and expand the RAREDIS database nationally so that all relevant patients are included and strengthen the ongoing registration of rare diagnoses in clinical genetic departments ▪ ensure uniformly comprehensive registration practices, for example by using explicit codes that enable the identification of rare diseases ▪ map existing databases and registers and their potential use, for example, with a view to integration in RAREDIS in collaboration with the regions' clinical quality development programme strengthen research that includes patient processes both inside and outside the hospital. ***Theme 7: Availability of treatment*** Recommendation on access to and research in Orphan Medicinal Products (recommendations from 2014): ▪ That it is ensured that there is (continued) access to necessary Orphan Medicinal Products in Denmark, including that transparency is used in pricing and subsidy schemes. ▪ That there is general attention to the opportunities for research, development and initiatives in the field in Denmark, including recommending that the Danish Centre for Rare Diseases as well as other relevant hospital departments and research institutions participate and positively support research in Orphan Medicinal Products. ▪ Recommendation for support for participation in tentative experimental treatment (recommendations from 2014): ○ Preliminary experimental treatment should continue to be possible and carried out where appropriate. ○ That Denmark follows and participates in European initiatives in the field, such as clinical studies and collaboration on health technology assessments. ▪ Recommendation on the possibility of referral for research-related treatment abroad (recommendation from 2014):

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	○ Attention should be paid to the possibility of referral for specialised research-related treatment abroad, when there is a relevant opportunity for this. ***<u>Theme 8: Implementation</u>*** **Recommendation 1:** That the Danish Health Authority holds an annual status meeting with the parties involved for the next 3 years regarding to ensure implementation of the recommendations and continued dialogue in the area. ▪ Recommendation on the institutional involvement of patient associations (recommendations from 2014): ○ Voluntary associations should be involved in the work regarding the patient group's special problems, e.g. as a hearing party for new legislative proposals with relevance to the area, in relevant working groups etc. set up by public bodies and should be equipped to handle this task. ○ Patient associations can be involved with great advantage in gathering experience, satisfaction surveys, etc. ○ That you support the commitment and participation of the Patient Associations. ▪ Recommendation on the inclusion of EUROPLAN's proposals and recommendations (recommendation from 2014).
England ▪ The UK Rare Diseases Framework 2021[29] ▪ Rare Diseases Action Plan 2022[27] and Rare Diseases Action Plan 2023[28]	▪ See UK Rare Diseases Framework. ▪ 29 actions were identified across the 2022 and 2023 Rare Diseases Action Plan: Actions 1 to 16 were included in the 2022 action plan and include an owner, progress report, status, and metrics and or milestones for 2023. For brevity, the owner, status and one metric and or milestone is outlined below for each action. Actions 17 to 29 were included in the 2023 action plan and include lead organisations, outputs, outcomes and action-specific monitoring and evaluation. For brevity, the lead organisation, one output, one outcome and one monitoring and evaluation measure are outlined below for each action. ***<u>Priority 1: helping patients get a final diagnosis faster.</u>*** **Action 1: improving how decisions are made on newborn screening for rare diseases.** *Owner*: DHSC. *Action 1 status (ongoing, extended or concluded)*: ongoing. *Metrics and milestones for 2023*: the UK National Screening Committee will continue work to improve the evidence available to them in evidence reviews (see Appendix B, Table B10 for further metrics and milestones). **Action 2: whole genome sequencing (WGS) to screen for genetic conditions in healthy newborns – designing an ethically approved research study.** *Owner*: Genomics England, NHSE. *Action 2 status (ongoing, extended or concluded)*: extended. *Metrics and milestones for 2023*: optimal method for taking samples from newborns for the purposes of WGS (see Appendix B, Table B10 for further metrics and milestones).

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	Action 3: continuously develop the National Genomic Test Directory, including rollout of WGS, which will play an important role in diagnosis of rare diseases. *Owner*: NHSE. *Action 3 status (ongoing, extended or concluded)*: concluded. *Metrics and milestones for 2023*: there will be future updates to the Test Directory (see Appendix B, Table B10 for further metrics and milestones). **Action 4: further develop the Genomics England clinical research interface – increase the number of diagnoses from genome data, and provide evidence to support the NHS Genomic Medicine Service in developing its diagnostic Test Directory.** *Owner*: Genomics England. *Action 4 status (ongoing, extended or concluded)*: concluded. *Metrics and milestones for 2023*: the clinical research interface is now embedded within Genomics England and within the NHS Genomic Medicine Service. Diagnoses continue to be made and returned to the NHS on a monthly basis for participants of the National Genomic Research Library (see Appendix B, Table B10 for further metrics and milestones). **Action 5: pilot new approaches for patients with undiagnosed rare conditions.** *Owner*: NHSE. *Action 5 status (ongoing, extended or concluded)*: ongoing. *Metrics and milestones for 2023*: the model is being discussed through NHSE governance and finance structures. If relevant funding is agreed, the SWAN pilot will be implemented in 2023 (see Appendix B, Table B10 for further metrics and milestones). ***Priority 2: increasing awareness of rare diseases among healthcare professionals.*** **Action 6: develop an innovative digital educational resource (GeNotes) – providing healthcare professionals with relevant and concise information to support patient management, linking to the NHS Genomic Test Directories, and signposting to extended learning opportunities.** *Owner*: Health Education England. *Action 6 status (ongoing, extended or concluded)*: extended. *Metrics and milestones for 2023*: evaluation of resources will continue through 2023 (see Appendix B, Table B10 for further metrics and milestones). **Action 7: determine how best to include rare diseases in UK health professional education and training frameworks.** *Owner*: Health Education England. *Action 7 status (ongoing, extended or concluded)*: ongoing. *Metrics and milestones for 2023:* the Genomics Education Programme (GEP) will undertake a desktop review of educational curricula, standards of proficiency and frameworks with a view to incorporating teaching opportunities using rare disease examples (for example, the inclusion of genomics in the Nursing and Midwifery Council standards with underpinning teaching materials developed by the GEP included in the nurse educator toolkit) (see Appendix B, Table B10 for further metrics and milestones).

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	Action 8: extend the remit of the Genomics Education Programme (GEP) to include non-genetic rare diseases. *Owner*: Health Education England. *Action 8 status (ongoing, extended or concluded)*: extended. *Metrics and milestones for 2023*: the GEP and Association of the British Pharmaceutical Industry will work together to incorporate greater understanding of future advances in medicines, including rare disease (see Appendix B, Table B10 for further metrics and milestones). **Action 9: publish high-quality epidemiological and research papers to increase the understanding of rare diseases, including papers looking at basic rare disease epidemiology, impact of COVID-19 on people with some rare diseases and cancer-related risk factors or outcomes for people with some rare diseases.** *Owner*: NHS Digital. *Action 9 status (ongoing, extended or concluded)*: concluded. *Metrics and milestones for 2023*: NCARDRS will report on the Altmetric scores on the 2022 papers in 2023 (where appropriate) as part of ongoing work under action 22 (see Appendix B, Table B10 for further metrics and milestones). ***Priority 3: better coordination of care.*** **Action 10: develop a toolkit for virtual consultations – improving use of videoconference and telephone clinic calls in services for patients with complex, multi-system rare diseases.** *Owner*: NHSE. *Action 10 status (ongoing, extended or concluded)*: ongoing. *Metrics and milestones for 2023*: NHS England will make its toolkit available to all highly specialised services clinical leads (see Appendix B, Table B10 for further metrics and milestones). ***Priority 4: improved access to specialist care, treatment and drugs.*** **Action 11: support rapid access to drugs for patients with rare diseases in the NHS, assessing the complexity of the service in which the drugs will be used, by mapping available access initiatives, identifying drugs and delivery challenges through horizon scanning, and listing drugs that have been identified for access.** *Owner*: NHSE. *Action 11 status (ongoing, extended or concluded)*: ongoing. *Metrics and milestones for 2023*: NHS England will produce an annual report by the end of the 2022 to 2023 financial year on access to drugs for patients with rare diseases at the point of delivery. This report will also include an analysis of overall uptake and geographical equity for those drugs recommended in the NICE Highly Specialised Technology Programme (see Appendix B, Table B10 for further metrics and milestones). **Action 12: develop a strategic approach for gene therapies and other advanced therapy medicinal products (ATMPs), based on horizon scanning by NHSE.** *Owner*: NHSE. *Action 12 status (ongoing, extended or concluded)*: ongoing. *Metrics and milestones for 2023*: development and implementation of the strategic approach will continue (see Appendix B, Table B10 for further metrics and milestones).

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	Action 13: capitalise on the changes made to NICE's methods and processes to ensure that NICE continues to support the rapid adoption of effective new treatments for NHS patients with rare diseases, implementing NICE's new methods and processes to support access to new treatments for rare disease patients. *Owner*: NICE. *Action 13 status (ongoing, extended or concluded)*: ongoing. *Metrics and milestones for 2023*: all actions have been implemented as business as usual for all new treatments starting evaluations with NICE (see Appendix B, Table B10 for further metrics and milestones). **Action 14: monitor overall uptake of drugs for patients with rare diseases and map geographical access to those drugs.** *Owner*: NHSE and NHS Digital. *Action 14 status (ongoing, extended or concluded)*: ongoing. *Metrics and milestones for 2023*: an annual report will be produced, and plans agreed as a way forward if access is deemed not equitable (see Appendix B, Table B10 for further metrics and milestones). **Action 15: map the rare disease research landscape to identify gaps and priorities for future funding.** *Owner*: DHSC and Medical Research Council. *Action 15 status (ongoing, extended or concluded)*: ongoing. *Metrics and milestones for 2023*: paper published by mid-2023 (see Appendix B, Table B10 for further metrics and milestones). **Action 16: reduce health inequalities in NHS highly specialised services, including considering health inequalities at highly specialised services annual clinical meetings, in service development and commissioning decisions, and in provider selection processes.** *Owner*: NHSE. *Action 16 status (ongoing, extended or concluded)*: concluded. **Actions for 2023 to 2024** ***Priority 1: helping patients get a final diagnosis faster.*** **Action 17: commission research on how best to measure the diagnostic odyssey.** *Lead organisation(s)*: DHSC. *Outputs*: funding call launched (see Appendix B, Table B10 for further outputs where applicable). *Outcomes*: establish a baseline time to diagnosis (see Appendix B, Table B10 for further outcomes where applicable). *Action-specific monitoring and evaluation*: funding call launched in early 2023 (see Appendix B, Table B10 for further monitoring and evaluation measures where applicable). **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.** *Lead organisations*: Genomics England, NCARDRS and NHSE.

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	Outputs: development of analytic plan for patients receiving tests against patients potentially eligible to receive a test, to investigate testing patterns and identify inequalities (see Appendix B, Table B10 for further outputs where applicable). *Outcomes*: the regulatory framework and technical pathway for sharing data within the healthcare ecosystem will be trialled as a proof of concept (see Appendix B, Table B10 for further outcomes where applicable). *Action-specific monitoring and evaluation*: By February 2024: one round of WGS data transfer from Genomics England to NCARDRS has taken place, analysis plan in place at NCARDRS, feasibility of transfer of non-WGS data from NHSE to NCARDRS assessed, workshop held with patient organisations (see Appendix B, Table B10 for further monitoring and evaluation measures where applicable). ***Priority 2: increasing awareness of rare diseases among healthcare professionals.*** **Action 19: publishing and implementing specific strategies for increasing awareness of rare diseases in the nursing and midwifery, pharmacy and primary care workforce.** *Lead organisation(s)*: Health Education England (HEE) (this enhances and is in addition to HEE's wider work to ensure all healthcare professionals are aware of rare disease). *Outputs*: GEP pharmacy lead in place to oversee education and training needs, including rare diseases (see Appendix B, Table B10 for further outputs where applicable). *Outcomes*: improved understanding of rare diseases amongst the nursing and midwifery, pharmacy and primary care workforce (see Appendix B, Table B10 for further outcomes where applicable). *Action-specific monitoring and evaluation*: updated curricula to feature content on genomics and rare diseases (see Appendix B, Table B10 for further monitoring and evaluation measures where applicable). ***Priority 3: better coordination of care.*** **Action 20: commission research to provide the evidence needed to operationalise better coordination of care in the NHS.** *Lead organisation(s)*: DHSC. *Outputs*: funding call launched (see Appendix B, Table B10 for further outputs where applicable). *Outcomes*: identification of the most cost-effective, tractable and impactful approaches to improving care coordination for people living with rare diseases (see Appendix B, Table B10 for further outcomes where applicable). *Action-specific monitoring and evaluation*: funding call launched in early 2023 (see Appendix B, Table B10 for further monitoring and evaluation measures where applicable). **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.** *Lead organisation(s)*: NHSE. *Outputs*: paper setting out requirements for any service specification involving patients with rare diseases to be formalised at the NHSE Specialised Commissioning Service Specification Tracking meeting (see Appendix B, Table B10 for further outputs where applicable). *Outcomes*: increased awareness of framework priorities among commissioners and service providers (see Appendix B, Table B10 for further outcomes where applicable). *Action-specific monitoring and evaluation*: from 2023, all new and revised service specifications include definition of care coordination (see Appendix B, Table B10 for further monitoring and evaluation measures where applicable).

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	Priority 4: improved access to specialist care, treatment and drugs. **Action 22: improved "findability" of people living with rare diseases using NCARDRS.** *Lead organisation(s)*: NCARDRS. *Outputs*: submission and/or publication of papers or reports describing methods to identify people with some rare diseases, including assessments on whether the methods might be applied to other diseases (see Appendix B, Table B10 for further outputs where applicable). *Outcomes*: improved national rare disease data for England, using peer-reviewed techniques that are potentially reproducible in the other countries and/or can be applied to other rare diseases (see Appendix B, Table B10 for further outcomes where applicable). *Action-specific monitoring and evaluation*: number specialised services sharing data with NCARDRS (see Appendix B, Table B10 for further monitoring and evaluation measures where applicable). **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.** *Lead organisation(s)*: NHSE. *Outputs*: PIAs considered in the development of all relevant commissioning policies (see Appendix B, Table B10 for further outputs where applicable). *Outcomes*: a continued and further developed process for ensuring that NHS England commissioning activities consider the impact of their activities on patients with rare diseases (see Appendix B, Table B10 for further outcomes where applicable). *Action-specific monitoring and evaluation*: number of PIAs considered (see Appendix B, Table B10 for further monitoring and evaluation measures where applicable). **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.** *Lead organisation(s)*: NHSE. *Outputs*: Highly Specialised Services Programme Board established to provide assurance that services for patients with rare diseases continue to have a high profile and are of high quality (see Appendix B, Table B10 for further outputs where applicable). *Outcomes*: role of NHSE in commissioning highly specialised services and wider services for patients with rare diseases strengthened (see Appendix B, Table B10 for further outcomes where applicable). *Action-specific monitoring and evaluation*: Highly Specialised Services Programme Board established by June 2023 (see Appendix B, Table B10 for further monitoring and evaluation measures where applicable). **Action 25: review the effectiveness of the Early Access to Medicines Scheme, the Innovative Licensing and Access Pathway and the Innovative Medicines Fund in supporting access to treatments for people living with rare diseases.** *Lead organisation(s)*: NHSE, NICE, Medicines and Healthcare Products Regulatory Agency. *Outputs*: report on number of applications and medicines made available through the schemes, which are treatments for rare diseases (see Appendix B, Table B10 for further outputs where applicable). *Outcomes*: improved understanding of the effectiveness of these schemes for improving and supporting access to rare disease medicines (see Appendix B, Table B10 for further outcomes where applicable). *Action-specific monitoring and evaluation*: proportion of applications which are rare disease medicines reported in 2024 action plan (see Appendix B, Table B10 for further monitoring and evaluation measures where applicable).

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	Action 26: registration of national data for exemplar rare genetic conditions which cause an inherited predisposition to cancer. *Lead organisation(s)*: NCARDRS. *Outputs*: outputs using the national data to possibly include publications, dashboards and data sharing of aggregate variant level data with relevant stakeholders including CanVAR-UK, DECIPHER and Genomics England (see Appendix B, Table B10 for further outputs where applicable). *Outcomes*: improved understanding of these diseases (including cancer risk), which will support better coordination of care, access to new treatments, and better outcomes for those that have them (see Appendix B, Table B10 for further outcomes where applicable). *Action-specific monitoring and evaluation*: number of conditions with a predisposition to cancer registered (see Appendix B, Table B10 for further monitoring and evaluation measures where applicable). **Action 27: improving the Be Part of Research platform for people living with rare diseases.** *Lead organisation(s)*: DHSC, National Institute for Health and Care Research. *Outputs*: further development of the Be Part of Research platform will be informed by feedback from the rare diseases community (see Appendix B, Table B10 for further outputs where applicable). *Outcomes*: the Be Part of Research platform will effectively meet the needs of the rare disease community (see Appendix B, Table B10 for further outcomes where applicable). *Action-specific monitoring and evaluation*: the rare disease community will be invited to take part in private beta phase testing of the Be Part of Research platform user interface by autumn 2023 (see Appendix B, Table B10 for further monitoring and evaluation measures where applicable). **Action 28: develop a plan to include rare diseases in NHSE'sCore20PLUS5 Framework.** *Lead organisation(s)*: DHSC, NHSE. *Outputs*: evidence collated to support the inclusion of people living with rare diseases in the 'PLUS' target population cohort (see Appendix B, Table B10 for further outputs where applicable). *Outcomes*: people living with rare diseases recognised by NHSE as a population group that are likely to experience poorer than average access, experience and/or outcomes in healthcare services (see Appendix B, Table B10 for further outcomes where applicable). *Action-specific monitoring and evaluation*: plan for how work will be carried out developed by autumn 2023 (see Appendix B, Table B10 for further monitoring and evaluation measures where applicable). **Action 29: commission portfolio level evaluation of England's Rare Diseases Action Plans with input from the rare disease community on design of metrics.** *Lead organisation(s)*: DHSC. *Outputs*: funding call launched (see Appendix B, Table B10 for further outputs where applicable). *Outcomes*: evaluation of the influence and outcomes of the framework using metrics co-developed with rare disease community (see Appendix B, Table B10 for further outcomes where applicable). *Action-specific monitoring and evaluation*: funding call launched in early 2023 (see Appendix B, Table B10 for further monitoring and evaluation measures where applicable).

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Finland National Programme for Rare Diseases 2019-2023[50]	*The Working Group did not want to make this National Programme into a detailed list of actions. Instead, the group wanted to describe the key principles and objectives guiding decision-making to improve the position of people living with rare diseases. As changes are needed in the healthcare and social welfare services, cooperation is required between regional and national operators to implement the objectives and actions proposed in this programme. In the time when the structure and organisation of healthcare and social welfare services is undergoing a major transformation at the national level, different operators must work together to identify regionally and nationally methods to implement the objectives. For brevity one objective and proposed action is outlined below.* **1. <u>Increasing knowledge on rare diseases and strengthening expertise.</u>** *<u>Increasing knowledge and awareness</u>* **Objectives and proposed actions:** ▪ Increasing cooperation between website administrators producing information (e.g. Duodecim, Health Village, National Institute for Health and Welfare (THL), Finnish Network for Rare Diseases, Orphanet) to improve the availability and coverage of information in Finnish and Swedish, and to avoid overlap (see Appendix B, Table B11 for further objectives and proposed actions). *<u>Strengthening the status of Rare Diseases Units and allocation of resources to them.</u>* **Objectives and proposed actions:** ▪ In all university hospitals, ensuring the allocation of resources to Rare Diseases Units and consolidating their tasks and positions (see Appendix B, Table B11 for further objectives and proposed actions). *<u>European Reference Networks (ERN)</u>* **Objectives and Proposed Actions:** ▪ Nationwide, to define the duties and responsibilities of ERN centres, to create cooperation practices between an ERN and other operators in its field of expertise, to integrate ERNs into the national service system (see Appendix B, Table B11 for further objectives and proposed actions). *<u>Promoting research</u>* **Objectives and proposed actions:** ▪ To keep rare diseases research as a focus area in national research funding (see Appendix B, Table B11 for further objectives and proposed actions). **<u>2. Strengthening of patient involvement in rare disease.</u>** *<u>Empowerment and involvement of people with rare diseases in society and their communities.</u>* **Objectives and proposed actions:** ▪ To encourage and direct individuals with rare diseases to contact relevant organisations and to seek peer support and other available services (see Appendix B, Table B11 for further objectives and proposed actions). *<u>Involvement of people with rare disease in developing healthcare and social welfare services in their own areas.</u>* **Objectives and proposed actions:**

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	▪ To strengthen the involvement of people with rare diseases by establishing customer panels in university hospitals. Customer panels will convene regularly to plan and to assess contemporary issues related to healthcare and social welfare services in rare diseases, together with Rare Diseases Units, centres of expertise and other actors to reach shared apprehension of matters to be discussed with experts by experience (see Appendix B, Table B11 for further objectives and proposed actions). *Safeguarding the involvement of people with rare diseases in their care and services* **Objectives and proposed actions:** ▪ To increase guidance, advice and information about the services available provided by professionals to persons with rare diseases and about the status of patients and clients in healthcare and social welfare (see Appendix B, Table B11 for further objectives and proposed actions). **3. Coordination of activities related to rare diseases.** *National coordination* **Objectives and proposed actions:** ▪ Clarification of national coordination and division of labour between the Ministry of Social Affairs and Health, THL and service providers (see Appendix B, Table B11 for further objectives and proposed actions). *Regional coordination* **Objectives and proposed actions:** ▪ Harmonising the regional operation of the units for rare diseases and strengthening the position of the units located in the specific catchment areas (see Appendix B, Table B11 for further objectives and proposed actions). *Coordination of care and services of a person with rare diseases.* **Objectives and proposed actions:** ▪ Planning and piloting a case manager model to ensure seamless care and services for those people with rare diseases requiring large numbers of services (see Appendix B, Table B11 for further objectives and proposed actions). **Practical implementation of the National Programme and monitoring it:** ▪ The Rare Diseases Units established to university hospitals play a key role in the coordination of the services required by people with rare diseases (see Appendix B, Table B11 for further objectives and proposed actions). The implementation of the programme requires all parties to commit themselves to achieving the jointly drawn up objectives.
France French National Plan for Rare Diseases 2018-2022[51]	*Each focus will be steered by a national project leader, who will work with the relevant players to develop detailed action sheets defining the schedule for roll-out of actions and follow-up and results indicators. The actions will be delegated to a national operator where appropriate. Patient associations and healthcare professionals will be closely involved in the roll-out of actions. All the actions will be conducted in accordance with the necessary ethical principles and with a view to reducing social inequalities.* *For brevity, one action in each focus area, the associated leader, cost and funder is outlined below.*

Country Information Source	Implementation action(s), agency(ies) and measure(s) or outcome(s)
	Focus 1: Reducing diagnostic delays and undiagnosed diseases. Action 1.1: Encourage the management of any person with or suspected of having a rare disease within a rare disease reference centre (CRMR) (see Appendix B, Table B12 for Actions 1.2 to 1.7, costs and timeline). **Leader:** ▪ Leader: Directorate General for Care Provision (DGOS). ▪ In collaboration with Directorate General for Research and Innovation (DGRI). **Cost:** Action 1.1: Encourage the management of any person with or suspected of having a rare disease within a rare disease reference centre: €119 million per year, i.e. €597 million over 5 years dedicated to rare disease reference centres (see Appendix B, Table B12 for costs of Action 1.5 and 1.7). **Funder:** Ministry of Solidarity and Health (MSS) funder for Focus 1 actions outlined above. **Focus 2: Improving neonatal screening and antenatal and preimplantation diagnostics to enable earlier diagnoses.** Action 2.1: Complete the regional and national reorganisation of neonatal screening in 2018, a necessary prerequisite to the implementation of new screening tests involving biomedical investigations (see Appendix B, Table B12 for Actions 2.2 to 2.7, costs and timeline). **Leader:** ▪ Leader: Directorate General for Health (DGS). ▪ In collaboration with DGOS, DGRI, Directorate for Social Security (DSS), French National Authority for Health, Biomedicine Agency, national ethics committee. **Cost:** Action 2.1: Project to extend neonatal screening from 2019 worth €1.8 million, i.e. €7.4 million over 5 years - pending, dependent on revision of the Bioethics law and the Social Security Financing Bill. **Funder:** MSS funder for action outlined above. **Focus 3: Sharing data to aid diagnosis and the development of new treatments.** Action 3.1: Deployment of the National rare disease data bank (BNDMR) in CRMRs in conjunction with hospital information systems (see Appendix B, Table B12 for Actions 3.2 and 3.3, costs and timeline). **Leader:** ▪ DGRI and DGOS. ▪ In collaboration with the DGS and the DSS. **Cost:** Action 3.1: BNDMR €600k/year, i.e. €3 million for the period of the plan to fund the operational unit, €3 million to support the deployment of the rare disease module in the computerised data records as a single instalment in 2018 (see Appendix B, Table B12 for costs of Action 3.2 and 3.3). **Funder:** MSS funding Action 3.1 and Ministry of Higher Education, Research and Innovation (MESRI) Investments for the Future Programme (PIA) funding Action 3.2 and 3.3. **Focus 4: Promoting access to treatments in rare diseases.** Action 4.1: Use existing upstream assessment mechanisms more systematically in order to accelerate the registration of medicinal products and medical devices (see Appendix B, Table B12 for Actions 4.2 to 4.4, costs and timeline). **Leader:** ▪ DGS and DSS

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	▪ In collaboration with the DGOS, French National Agency for the Safety of Medicines and Health Products, French National Authority for Health. **Cost and funder:** The pharmaceutical company covers the cost of follow-up of patients treated within the context of a temporary recommendation for use. However, since the follow-up of medicinal products prescribed off-label without a temporary recommendation for use is not funded, it will be necessary to find or unblock funding sources in order to guarantee – over the period of the plan – the establishment of registries by disease by the CRMRs, which forms one of the central ambitions of this working focus. The funding sources identified will be mobilised to enable the performance of the clinical trials required to improve our knowledge of a significant number of off-label prescribing practices identified in the context of the survey conducted by the rare disease clinical networks. **Focus 5: Giving new momentum to research in the field of rare diseases.** Action 5.1 Create a research group (see Appendix B, Table B12 for Actions 5.2 to 5.6, costs and timeline). **Leader:** ▪ Alliance for Life and Health Sciences (AVIESAN). ▪ In collaboration with the DGRI and the DGOS. **Cost:** Costs for actions 5.2 and 5.4 are outlined (see Appendix B, Table B12). **Funder:** MESRI – MSS – PIA funder for above actions. **Focus 6: Promoting the emergence of and access to innovation.** Action 6.1: Creation of a rare disease innovation coordination group (see Appendix B, Table B12 for Actions 6.2 and 6.3, costs and timeline). **Leader:** ▪ DGRI. ▪ In collaboration with the DGS, DSS, Directorate General for Enterprise and DGOS. **Cost:** No additional costs. **Focus 7: Improving care pathways.** Action 7.1: Develop information to make existing structures visible and accessible (see Appendix B, Table B12 for Actions 7.2 to 7.5, costs and timeline). **Leader:** ▪ DGOS. ▪ In collaboration with the DGS and the DSS. **Cost:** Action 7.1: €300K per year for the funding of Orphanet, €260K per year for the funding of MRIS, €70K per year for the funding of the Rare Diseases Alliance, i.e. a total for these 3 mechanisms of: €3.15M million over 5 years (see Appendix B, Table B12 for costs of actions 7.3 and 7.4). **Funder:** MSS is the funder for the above actions. **Focus 8: Facilitating the integration of people with rare diseases and their carers.** Action 8.1: Facilitate access to mechanisms, rights and services dedicated to disabled people and their carers (see Appendix B, Table B12 for Actions 8.2 to 8.6, costs and timeline). **Leader:** ▪ Directorate General for Social Cohesion

Country Information Source	Implementation action(s), agency(ies) and measure(s) or outcome(s)
	▪ In collaboration with the Directorate General for School Education, Directorate General of the Treasury, General delegation for employment and professional training, DGS and the National Solidarity Fund for Independent Living. **Cost:** No additional cost identified. **<u>Focus 9: Training health and welfare professionals to better identify and manage rare diseases.</u>** Action 9.1: Clarify the status of genetic counsellors and bioinformatics specialists and increase their training and recruitment (see Appendix B, Table B12 for Actions 9.2 to 9.4, costs and timeline). **Leader:** ▪ DGOS. ▪ In collaboration with the Directorate General for Higher Education and Professional Integration. **Cost:** Action 9.1, Action 9.2, Action 9.3 and Action 9.4: €2 million/year, i.e. €10 million over 5 years, will be dedicated to training. **Funder:** MSS will fund the above actions. **<u>Focus 10: Reinforcing the role of rare disease clinical networks in care and research issues.</u>** Action 10.1: Attribute additional missions to the FSMPs over and above their current missions (see Appendix B, Table B12 X for Actions 10.2 to 1.6, costs and timeline). **Leader:** ▪ DGOS. ▪ In collaboration with DGRI. **Cost:** Action 10.1: €119 million/year, i.e. €597 million over 5 years for the CRMRs, €12.7 million/year, i.e. €63.5 million over 5 years for the rare disease clinical networks (see Appendix B, Table B12 for costs of Action 10.6). **Funder:** MSS will fund the above actions. **<u>Focus 11: Specifying the positioning and missions of other national players in the field of rare diseases.</u>** Action 11.1: Maintain and amplify the contribution of patient associations and relatives' associations in the definition and implementation of rare disease policy (see Appendix B, Table B12 for Actions 11.2 to 11.4, costs and timeline). **Leader:** ▪ DGS, DGOS and DGRI. ▪ In collaboration with AVIESAN. **Cost:** See action 7.1.
Germany National Plan of Action for People with Rare Diseases 2013[32]	A number of recommendations and proposed actions are outlined for each action field and area. For brevity, one proposed action for each area along with their associated implementation and responsible bodies are outlined below (see Appendix B, Table B13 for further recommendations and proposed actions). **<u>Action Field 1: Care, centres, networks</u>** ***Area:*** The Centre Model for Rare Diseases.

Country Information Source	Implementation action(s), agency(ies) and measure(s) or outcome(s)
	Proposed action 1: Existing funding options are to be used to ensure funding for the three-tiered structure of the centres for rare diseases. Special healthcare services for treating persons with rare diseases, in particular type A centres (reference centres), are to be taken into account within the framework of the negotiations for the remuneration of inpatient and outpatient care. In an advisory capacity, representatives of patient interests will work together with representatives of both the healthcare providers and the third-party payers to clarify the common criteria and requirements for funding the centres. They shall work together to ensure that the third-party payers can agree locally to provide the funds not already included in the existing standard remunerations. Once questions of funding and implementation have been resolved, it is recommended that the care providers implement the three-tiered model of "CenAction Field: Care, Centres, Network Centres for Rare Diseases (A, B, C)" in accordance with the suggested definition, taking into account the agreed preliminary list of the criteria to be met). **Implementation:** short-term (1 to 2 years). **Responsible bodies:** German Hospital Federation, Association of University Clinics in Germany, Federal Association of Statutory Health Insurance Funds, healthcare providers (see Appendix B, Table B13 for proposed actions 2 and 3). ***Area:*** Orphan Drugs, Off-Label Use and Evidence Generation. ***Proposed action 4:*** Given the problematic situation with orphan drugs (financing, interruptions in care), efforts are being made to determine whether further measures for procuring medicinal products for persons with rare diseases are still necessary once the centre model for rare diseases has been implemented. **Implementation:** medium-term (3 to 5 years) (once the centre has been established). **Responsible bodies:** German Federal Ministry of Health (BMG), the self-administration structure, ACHSE e.V. (Alliance for Chronic Rare Diseases), type A centres (reference centres), type B centres (centres of expertise) or type C centres (cooperating centres) (see Appendix B, Table B13 for proposed actions 5 to 7). **<u>Action Field 2: Research</u>** ***Area:*** Aetiology and Genome Analysis. ***Proposed action 8:*** Set up and expand sequencing centres for rare diseases. **Implementation:** short-term (1 to 2 years) (once the centre has been established). **Responsible bodies**: German Federal Ministry for Education and Research (BMBF), type A, type B or type C centres. ***Area:*** Pathophysiology and Disease Mechanisms. ***Proposed action 9:*** Support research projects on rare diseases that comprise the use of animal or cell models to elucidate the pathophysiology of rare diseases. **Implementation:** short-term (1 to 2 years). **Responsible bodies:** BMBF, German Research Foundation (DFG), other research sponsors. ***Area:*** Development of Diagnostic Test Systems. ***Proposed action 10:*** Intensify research to develop diagnostic procedures for rare diseases. **Implementation:** short-term (1 to 2 years). **Responsible bodies:** BMBF, DFG, other research sponsors, diagnostics industry. ***Area:*** Investigator-Initiated Trials: Prospective, Controlled Clinical Studies.

Country Information Source	Implementation action(s), agency(ies) and measure(s) or outcome(s)
	Proposed action 11: Specialisation of clinical research units dedicated to the study of rare diseases. **Implementation:** short-term (1 to 2 years) (once the centre has been established). **Responsible bodies:** Type A centres, BMBF. ***Area:*** Health Services Research. ***Proposed action 12a:*** Induce a multidisciplinary discussion on the state of health services research in order to take stock of and identify gaps in the research on the care of rare diseases as well as possible solutions. **Implementation:** short-term (1 to 2 years) (once the centre structure has been established). **Responsible bodies:** BMBF, BMG, ACHSE e.V (see Appendix B, Table B13 for proposed actions 12b). ***Area:*** Ethical, Legal and Social Aspects. ***Proposed action 13:*** Continuation of the ethical, legal and social aspects funding programme. **Implementation:** short-term (1 to 2 years) (once the centre structure has been established). **Responsible bodies:** BMBF. ***Area:*** Cooperation Between Academia and Industry. ***Proposed action 14:*** Implementation of a cooperative platform to broker the engagement between academia and industry. This should include patient organisations as well as small and medium-sized companies as part of a multistakeholder process. **Implementation:** short-term (1 to 2 years) (once the centre structure has been established). **Responsible bodies:** NAMSE coordinating office, BMBF, industrial partners (German Association of Research-based Pharmaceutical Companies and Federal Association of the German Pharmaceutical Industry), academic partners including type A, type B or type C centres, research associations of rare diseases. ***Area:*** Cooperation with International Partners. ***Proposed action 15:*** Continued strategic development of research funding of international cooperation in the field of rare diseases. **Implementation:** short-term (1 to 2 years). **Responsible bodies:** BMBF, DFG, other research sponsors. ***Area:*** Establishing Centres for Rare Diseases. ***Proposed action 16:*** Provide support for innovative concepts to connect the patient care and research at the individual locations in order to enable close cooperation between fundamental research on the one hand and clinical research on the other as well the effective translation of research results into actual care. This would be especially aimed at the type A centres (reference centres). **Implementation:** medium-term (2 to 5 years) (once the centre structure has been established). **Responsible bodies:** BMBF, BMG, NAMSE partners, university clinics, non-university research facilities. **Action Field 3: Diagnostics** ***Area:*** Initial Contact: Primary Care. ***Proposed action 17:*** Initiate as part of a pilot project an analysis of what is necessary to ensure cooperation between the centres and primary-care providers (e.g., the interface between the centres and primary care providers).

Country Information Source	Implementation action(s), agency(ies) and measure(s) or outcome(s)
	Implementation: short-term (1 to 2 years) (once the centre structure has been established). **Responsible bodies:** German Association of General Practitioners, German Society of Paediatrics and Adolescent Medicine (see Appendix B, Table B13 for proposed action 18). ***Area:*** Diagnostic Software Technologies. ***Proposed action 19:*** A uniform coding scheme for all patients with rare diseases employing the Orpha diagnostic coding system in conjunction with ICD-10 GM and in anticipation of the publication of ICD-11. **Implementation:** short-term (1 to 2 years). **Responsible bodies:** Orphanet Germany, German Institute of Medical Documentation and Information (part of the German Federal Ministry of Health) (see Appendix B, Table B13 for proposed actions 20 to 22). ***Area:*** Innovative Sequencing Technologies for Molecular Diagnostics. ***Proposed action 23:*** Take up consultations in the Evaluation Committee on the Uniform Fee Scale for Medical Procedures on the introduction of NGS technologies. **Implementation:** short-term (1 to 2 years). **Responsible bodies:** Health-care providers (preliminary stage), Evaluation Committee on the Uniform Fee Scale for Medical Procedures. ***Area:*** Guidelines. ***Proposed action 24:*** In order to support the development of guidelines for rare diseases, an electronic platform should be established with the expressed intent of setting up such guidelines. These guidelines should be adapted to the needs of the field of rare diseases in consultation with the Association of Scientific Medical Societies. The implementation of an electronic platform serves to save both time and costs, increase the transparency of the procedure and reflect the special needs of patients with rare diseases. **Implementation:** short-term (1 to 2 years). **Responsible bodies:** Technology, Methods, and Infrastructure for Networked Medical Research (TMF, sponsored by the BMBF), Association of Scientific Medical Societies (see Appendix B, Table B13 for proposed actions 25 and 26). **Cross-sections Action Field:** Registries ***Area:*** Web-Portal of Registries of Rare Diseases in Germany. ***Proposed action 27:*** Set up a web-portal of registries concerning rare diseases in Germany. **Implementation:** short-term (1 to 2 years). **Responsible bodies:** Orphanet Germany, TMF. ***Area:*** Steering Committee of Registry Operators for Exchanging Information on "Registries on Rare Diseases". ***Proposed action 28:*** Establish a steering committee "Registries of Rare Diseases" (e.g., operators of registries, experts) in collaboration with the TMF and the NAMSE coordinating office. **Implementation:** short-term (1 to 2 years). **Responsible bodies:** BMG, BMBF, NAMSE partners, TMF. ***Area:*** Development of Software for Establishing a Databank Prototype to Implement and Manage a Disease-Specific Registry for Rare Diseases.

Country Information Source	Implementation action(s), agency(ies) and measure(s) or outcome(s)
	Proposed action 29: Develop a prototypical registry for a "Disease-Specific Registries of Rare Diseases" (including a standardised registry for patients without a disease-specific registry, see Proposed Action 32 below) based on the provisions outlined in the draft by the NAMSE working group 'Registries'. This prototype – or individual software modules contained therein – should be adaptable for existing registries. A standardisation of all existing registries is desirable. **Implementation:** short-term (1 to 2 years). **Responsible bodies:** BMBF, BMG. ***Area:*** Registry of "Patients with an Unclear Diagnosis". ***Proposed action 30:*** Organise a workshop to gather and solve open questions concerning a registry for patients with an unclear diagnosis. **Implementation:** short-term term (1 to 2 years). **Responsible bodies:** Board of spokespersons of the networks for rare diseases sponsored by the BMBF, TMF (see Appendix B, Table B13 for proposed actions 31). ***Area:*** Project "Non-Disease-Specific Registry. ***Proposed action 32:*** Establish a project "non-disease-specific registry" based on (and thus subsequent to) the development of a prototype registry as suggested in proposed action 29. **Implementation:** long-term (over 5 years). **Responsible bodies:** Steering committee of the previously mentioned registry for rare diseases (proposed action 28). **Action Field 4: Information Management** ***Area:*** Adequate Patient Information on Rare Diseases. ***Proposed action 33:*** Develop a checklist "Criteria for Good Patient Information on Rare Diseases" based on the draft paper prepared by NAMSE. **Implementation:** short-term (1 to 2 years). **Responsible bodies:** ACHSE e.V., Agency for Quality in Medicine (see Appendix B, Table B13 for proposed actions 34 and 35). ***Area:*** Joint Communications on the Subject of Rare Diseases. ***Proposed action 36:*** Develop and implement a concept for joint communications and procedures for public relations in the realm of rare diseases. **Implementation:** short-term (1 to 2 years). **Responsible bodies:** NAMSE coordinating office, ACHSE e.V. ***Area:*** Central Information Portal. ***Proposed action 37:*** Draft a concept including suggestions for funding for the establishment of a central information for rare diseases with the aid of Orphanet resources. **Implementation:** short-term (1 to 2 years). **Responsible bodies:** Orphanet Germany, ACHSE e.V (see Appendix B, Table B13 for proposed actions 38 and 39). ***Area:*** Medical and Dental Training and Continued Education.

Country Information Source	Implementation action(s), agency(ies) and measure(s) or outcome(s)
	Proposed action 40: Establish a national, competence-based catalogue of learning objectives such that students of medicine and dentistry become so thoroughly acquainted with the special characteristics of rare diseases with respect to their symptoms, physiology, diagnostics, therapy and care that they acquire the necessary medical competence in all respects (cognitive, applied and emotional/reflective). In addition, students of medicine and dentistry should have all necessary information sources on rare diseases at their disposal. **Implementation:** short-term (1 to 2 years). **Responsible bodies:** German Association of Medical Faculties (see Appendix B, Table B13 for proposed actions 41 to 45). ***Area:*** Public Relations. ***Proposed action 46:*** Develop and implement a concept for public relations activities with respect to NAMSE and to the realisation of a National Action Plan. **Implementation:** short-term (1 to 2 years). **Responsible bodies:** NAMSE coordinating office. ***Area:*** Telemedicine. ***Proposed action 47:*** Identify and evaluate telemedicine offerings for rare diseases. **Implementation:** short-term (1 to 2 years). **Responsible bodies:** Joint representatives from the various centres, TMF, Association of Insurance Science and Practice e.V.: Committee on Telemedicine. **Cross-sectional Action Field: Patient Orientation** ***Area:*** Research. ***Proposed action 48:*** Include as appropriate the experiences gathered by patient organisations in the development and implementation of patient-oriented research and healthcare projects on rare diseases. **Implementation:** short-term (1 to 2 years). **Responsible bodies:** BMBF, DFG, BMG. ***Area:*** Expert Opinions by the Medical Advisory Service of the German Statutory Health Insurance. **Proposed action 49:** Improve the transparency surrounding the role and advisory capacity of the Health Insurance Medical Service. To this end, the Medical Advisory Service of the Federal Association of Health Insurance Funds can serve as contact point for patient organisations at the national level and can assume any necessary coordinating functions in the Health Insurance Medical Service community. **Implementation:** short-term (1 to 2 years). **Responsible bodies:** Central Association of Statutory Health Insurance Funds, Federal Association of Health Insurance Funds. ***Area:*** Support and Qualification of Patient Organisations. ***Proposed action 50:*** Within the limits of existing legal regulations, the NAMSE partners shall work to ensure the appropriate support for the activities of the patient organisations and their qualification. **Implementation:** short-term (1 to 2 years). **Responsible bodies:** BMG, ACHSE e.V., Federal Association of Self-help Organisations of People with Disabilities and Chronically People and Their Relatives in Germany (BAG SELBSTHILFE e.V.).

Country Information Source	Implementation action(s), agency(ies) and measure(s) or outcome(s)
	Area: European Networks. ***Proposed action 51:*** Provide support for integrating national patient organisations into Europe-wide cooperations concerning rare diseases. **Implementation:** short-term (1 to 2 years). **Responsible bodies:** BMG, the patient organisations. **Action Field 5: Implementation and Future Development** ***Proposed action 52:*** Even after passage of the National Action Plan NAMSE should continue its efforts with the collaboration of all previous partners, the goal being to evaluate and follow-up in due time the implementation of the Action Plan. To this end, the necessary structures and processes (e.g., Steering Committee, coordinating office, and means of communication) should be addressed in a separate organisational concept. **Implementation:** after passage of the National Action Plan. **Responsible bodies:** BMG, BMBF, ACHSE e.V.
The Netherlands ▪ National Plan for Rare Diseases 2013[52]	▪ **A number of recommendations and responsible agencies are outlined for each Theme. For brevity, one recommendation for each Theme is outlined below.** **Theme 1: Unfamiliarity with rare diseases** Recommendation: Encourage increasing general awareness of 'the phenomenon' of rare disease among healthcare and care providers, health insurers, (umbrellas of) patient organisations, policy maker in government and municipalities and the general public. ***1st point of contact*** *(other parties)*: **VSOP** (in collaboration with CG Council and NPCF Rare Disease Fund) (see Appendix B, Table B17 for further recommendations). **Theme 2: Information provision and communication** Recommendation: Improving differential diagnosis of rare diseases by: a) Use of ICT: e-learning and other ICT applications; b) Use of e-mail and video consultation from the expertise centre; c) Improving visibility of rare diseases (general) and information about centres of expertise. ***1st point of contact*** *(other parties)*: **NFU/STZ** (Patient organisations and health insurers) (see Appendix B, Table B17 for further recommendations). **Theme 3: Organisation of care and availability of therapy** **Diagnostics** Recommendation: Improve alertness to rare diseases. ***1st point of contact:*** **VSOP**/in collaboration with CG Council and NPCF Rare Disease Fund; **Framework plan for training doctors (NFU)** (in collaboration with scientific associations); **NFU/STZ** (Patient organisations and health insurers); **Dutch Society of General Practitioners and Doctors Youth Health Care Netherlands (and the Dutch Centre for Youth Health)** (in collaboration with other scientific associations) (see Appendix B, Table B17 for further recommendations). **Organisation of Care** Recommendation: Bring expertise centres for rare diseases under the Special Medical Procedures Act. ***1st point of contact*** *(other parties)*: **Ministry of Health, Welfare and Sport** (see Appendix B, Table B17 for further recommendations). **Availability of Treatment** Recommendation: When developing the policy regarding reimbursement for orphan drugs, specific features of the treatment of rare diseases (small groups of patients, great diversity) must be taken into account. ***1st point of contact*** *(other parties)*: **Ministry of Health, Welfare and Sport** (see Appendix B, Table B17 for further recommendations).

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	Theme 4: Research Recommendation: Improve instruments for signalling and recognition of rare diseases from general practice and youth healthcare. ***1st point of contact*** *(other parties)*: **Dutch Society of General Practitioners and the Dutch Centre for Youth Health** (see Appendix B, Table B17 for further recommendations). **Theme 5: Strengthening the voice of the patient with a rare disease** **Recommendation:** Increasing and expanding cooperation between patient organisations regarding generic aspects of rare diseases, especially for the purpose of advocacy, is necessary. ***1st point of contact*** *(other parties)*: **VSOP** (in collaboration with CG council and NPCF) (see Appendix B, Table B17 for further recommendations). **Theme 6: Direction and continuity** **Recommendation:** A director must be appointed who has primary responsibility for implementing the plan and initiating activities in the plan. ***1st point of contact*** *(other parties)*: **Minister of Health, Welfare and Sport** (see Appendix B, Table B17 for further recommendations). **Prioritised Recommendations** *Urgent/ short term (desired start next year 2014):* ▪ Appointing a director for the entire plan ▪ Clarity regarding policy for expertise centres and EU reference centres, mainly in the context of the Cross-border Care Legislation ▪ Promote timely and adequate diagnostics and promote alertness and knowledge about rare diseases or data regarding natural history. This also stimulates the development of a care chain *Medium term (starts in 2 to 3 years):* ▪ Designation of centres based on uniform criteria, the presence of multidisciplinary chain care and care pathways ▪ Coordination and coordination of care and sharing of information (shared care and chain care) ▪ Adequate financing of care (Diagnosis Treatment Combination chain) ▪ Follow-up funding for ongoing research programs in the field of rare diseases and orphan drugs. *Longer term (3 years or longer): Recommendations that will take a longer time to implement and/or for which it is currently unclear how (and when) these activities could start.* ▪ Financing new research/new programs regarding rare diseases (medical-scientific, social scientific) ▪ Adequate and uniform coding and national registration of rare diseases ▪ Long-term research into the natural course of the disease, early treatment options and measures to prevent and treat complications ▪ Development of new therapies by Dutch researchers and companies ▪ Evaluation of activities and returns of the plan. *Ongoing attention: There are a number of aspects that require continued attention, which do not benefit from a project based approach where the attention fades away after the end of the project. This concerns aspects such as:* ▪ Input from patient (organisations) in policy making and setting priorities strong advocacy for rare diseases

Country Information Source	Implementation action(s), agency(ies) and measure(s) or outcome(s)
	▪ Adequate education and training of healthcare providers and care providers with regard to rare diseases ▪ Knowledge and education, early detection and alertness for rare diseases ▪ Infrastructure for collecting knowledge about rare diseases and maintenance databases ▪ Entitlement to and financing of adequate treatment of rare diseases.
▪ Coordination Consultation for Rare Diseases: Final Advice 2017[53]	▪ The most important recommendation of the coordination consultation concerns the development of policy with which care (coordination), knowledge transfer and research are concentrated in the recognised expertise centres (recommended and implemented following the national rare disease strategy 2013) and can be expanded through their network for the benefit of people with rare diseases. In short, the recommendations from the coordination meeting relate to: ▪ care networks with expertise centres (also think of ERNs) as a 'spider in the web' with specific attention to the (psycho)social domain ▪ policy regarding monitoring and evaluation of expertise centres ▪ financing of (chain) care/shared care and healthcare purchasing ▪ financing coordination of care, preferably at patient or family level ▪ financing of treatment, including (orphan) drugs ▪ uniform coding, national registration of core patient data; serves for this purpose funding ▪ financing long-term research programs for rare diseases, both nationally and internationally, aimed at pathogenesis and (psychosocial) treatment ▪ quality standards for rare diseases ▪ infrastructure for collecting and sharing knowledge, sustainable use of eHealth and ICT options in healthcare ▪ structural input and financing of the contribution of patients (organisations) and stimulation of national and international exchange of knowledge and experience among organisations of people with rare diseases ▪ coordinating network for monitoring. The specific recommendations are broken into: **1. Direction and Continuity, role for the government** **2. Coordination, networking** **3. Improving the quality of care** For brevity, one specific recommendation in each area is outlined. **Direction and Continuity, role for the government** **Specific recommendations:** ▪ Develop sustainable policy with regard to expanding the tasks of expertise centres and setting up their networks between centres and care surrounding the patient group (in the patient's region). The centres function as a 'spider in the web' (see Appendix B, Table B18 for further recommendations). **Coordination, networking** **Specific recommendations:**

Country Information Source	Implementation action(s), agency(ies) and measure(s) or outcome(s)
	▪ Expertise centres (national) must share their experience about the organisation of care and therapy. Expertise centres can learn from other networks for chronic conditions, for example ParkinsonNet or oncology networks (see Appendix B, Table B18 for further recommendations). **<u>Improving the quality of care</u>** **Specific recommendations:** ▪ Recognition of (hereditary) rare diseases is not sufficiently guaranteed in basic medical training (framework plan) and in the training requirements of general practitioners and paediatricians. NFU and professional groups have a role to play in improving this (see Appendix B, Table B18 for further recommendations).
Northern Ireland ▪ The UK Rare Diseases Framework 2021[29] ▪ Northern Ireland Rare Diseases Action Plan 2022/23[34]	▪ See UK Rare Diseases Framework. ▪ A number of actions along with their key milestones and measures in Year 1 and related actions are outlined in each Priority. For brevity, one action in each Priority is outlined below. **<u>Priority 1: Helping patients get a final diagnosis faster</u>** **1. Information Hub** An online Rare Disease Information Hub established for Northern Ireland (NI), with a dedicated person employed to: ▪ collate relevant information; ▪ act as a contact point and source of advice for people living with a rare disease in NI and their families; ▪ connect those working in the rare diseases field. *Key milestones and measures (Year 1):* Scoping Group established (see Appendix B, Table B19 for further key milestones and measures). *Related Year 1 Action Plan actions:* 7. Expert centre; 9. Mental health needs; 10. Patient portal (see Appendix B, Table B19 for actions 2 and 3). **<u>Priority 2: Increasing awareness of rare diseases among healthcare professionals</u>** **4. Develop a Northern Ireland Rare Diseases Registry** A NI Rare Disease and Congenital Abnormality Registry to be established and linked to the new Encompass Integrated Care Record. *Key milestones and measures (Year 1):* Quarterly devolved nations meetings with registry colleagues to work towards a UK-wide national rare disease registration facility (see Appendix B, Table B19 for further key milestones and measures). *Related Year 1 Action Plan actions:* 1. Information Hub; 7. Expert Centre; 8. Care pathways/models; 9. Mental health needs; 10. Patient portal; 13. RD research awareness/participation (see Appendix B, Table B19 for actions 5 and 6). **<u>Priority 3: Better co-ordination of care</u>** **7. Develop an expert centre for Rare Diseases to include rare disease specialisms co-ordinator** Develop a national rare disease care centre acting as a central point of contact for rare disease across NI. Appoint a rare disease specialisms information coordinator.

Country Information Source	Implementation action(s), agency(ies) and measure(s) or outcome(s)
	Key milestones and measures (Year 1): Scoping group captures the NI landscape plus further afield and develop an options appraisal (see Appendix B, Table B19 for further key milestones and measures). *Related Year 1 Action Plan actions:* 1.Information hub; 2. Genomics; 3. Registry; 8. Care pathways/models; 9. Mental health needs; 10. Patient portal (see Appendix B, Table B19 for actions 8 to 10). **<u>Priority 4: Improving access to specialist care, treatments, and drugs</u>** **11. Improve access to Rare Disease drugs** Ensure equity of access to rare disease medicines locally, regionally, and nationally by increasing health professional and patient awareness of the existing mechanisms to access available initiatives. *Key milestones and measures (Year 1):* Ensure appropriate rare disease representation and contribution (including patient voice) during the development of policy processes around access to, and managed entry of medicines, including the Individual Funding Request mechanism, into the NI healthcare system (see Appendix B, Table B19 for further key milestones and measures). *Related Year 1 Action Plan actions:* 7. Expert centre; 8. Care pathways/models; 10. Patient portal (see Appendix B, Table B19 for actions 12 to 14).
Portugal ▪ Integrated Strategy for Rare Diseases 2015-2020[35]	▪ A number of actions are outlined within each theme. For brevity, one action in each theme is outlined below**.** **Theme 1. Coordination of care** 1. Improve inter-ministerial, inter-sectoral and inter-institutional coordination of care, based on the complex needs of patients and their caregivers, and on the better use of national and regional resources, organising a coordinated approach of clinical and social services of both general and specialised support, by means of integrated plans of personal care (see Appendix B, Table B21 for actions 2 to 5). **Theme 2. Access to early diagnosis** 1. Promote access equity to early diagnosis and treatments based on scientific evidence, through specialised clinical centres (see Appendix B, Table B21 for actions 2 to 6). **Theme 3. Access to treatment** 1. Improve the access to early treatment by means of surgery, drugs or nutrition of serious rare diseases (see Appendix B, Table B21 for actions 2 to 6). **Theme 4. Clinical and epidemiological information** 1. Promote the systematic use of the European information system Orphanet, embracing it as the reference portal and credible information source about rare diseases, their characteristics, diagnosis and treatment possibilities (see Appendix B, Table B21 for actions 2 to 4). **Theme 5. Research** 1. Promote research through collaborative activity amongst health and social services with the scientific and academic community, and with the industry (see Appendix B, Table B21 for actions 2 to 6).

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	Theme 6. Social inclusion and citizenship 1. Develop training and education programmes for the health and social sector professionals, which will help their empowerment in the identification, treatment and rehabilitation of rare diseases (see Appendix B, Table B21 for action 2).
▪ Annual Plans 2016,[36] 2017[37] and 2018[38]	▪ A number of specific actions are outlined in the annual plans for 2016, 2017 and 2018 (see Appendix B, Tables B22, B23 and B24).
▪ Annual Plan 2019	▪ Planned activities and corresponding Responsible Entities listed for each strategic priority. **Theme 1. Coordination of care** **Activities planned for 2019:** Develop informative/educational material on the services/care available for people with rare diseases, with the involvement of associations of people with rare diseases and health professionals. ▪ *Responsible Entities*: All entities that are part of the Integrated Strategy for Rare Diseases (see Appendix B, Table B25 for further planned activities). **Theme 2. Access to early diagnosis** **Activities planned for 2019:** Recognition of pulmonary arterial hypertension treatment centres. ▪ *Responsible Entities*: Directorate-General of Health; Ministry of Health (see Appendix B, Table B25 for further planned activities). **Theme 3. Access to treatment** **Activities planned for 2019:** Development of informative material on nutrition care in the area of Rare Diseases. ▪ *Responsible Entities*: All entities that are part of the Integrated Strategy for Rare Diseases plus the Order of Nutritionists (see Appendix B, Table B25 for further planned activities). **Theme 4. Clinical and epidemiological information** **Activities planned for 2019:** Continued update of the Orphanet portal. ▪ *Responsible Entity*: Directorate-General of Health (see Appendix B, Table B25 for further planned activities). **Theme 5. Research** **Activities planned for 2019:** Monitoring the implementation of the Research, Development & Innovation in Rare Diseases Agenda prepared in 2018. ▪ *Responsible Entities:* Foundation for Science and Technology; National Institute of Health Doctor Ricardo Jorge (see Appendix B, Table B25 for further planned activities). **Theme 6. Social integration and citizenship** **Activities planned for 2019:** Publication of the Manual on the ISS website with all the Social Security Assistance services and social responses that provide support to people with rare diseases. ▪ *Responsible Entity:* Social Security Institute (see Appendix B, Table B25 for further planned activities).

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Scotland ▪ The UK Rare Diseases Framework 2021[29]	▪ See UK Rare Diseases Framework.
▪ Rare Disease Action Plan 2022[42]	▪ The Scottish Government strategy outlines a number of actions which they will implement across their strategy. Further information on each action is outlined in Appendix B, Table B28. **Action 1: Implementation of Genome UK** ▪ In Scotland specifically, we have recently established the Scottish Strategic Network for Genomic Medicine, as a 'front door' for engagement and strategy development. The Network will advise and make recommendations on genetic testing availability as well as supporting the planning for future capacity into areas such as Whole Genome Sequencing or expanding our Whole Exome Sequencing services, which we recognise are of huge importance to the rare disease community. The Network will have a crucial horizon-scanning function which will work with the Scottish Medicines Consortium, Scottish Health Technology Group, researchers, academia and our Innovation Pipeline to ensure people with a rare disease can access new genomic technologies and testing. **Action 2: Newborn Screening** ▪ For our year one action, we commit to continuing to participate in the UK NSC; to following guidance to ensure appropriate use of screening tools in line with UK National Screening Committee recommendation, and to work with the Committee to embed its new remit. **Action 3: Expanding the functionality of the Congenital Conditions and Rare Diseases Registration and Information Service for Scotland (CARDRISS).** ▪ In the first instance, CARDRISS will register babies affected by a major structural or chromosomal anomaly or recognised syndrome. This is in line with the standards recommended by the European Registry of Congenital Anomalies and Twins (EUROCAT), a European network of congenital anomalies registers. Live-born babies diagnosed within the first year of life; spontaneous stillbirths occurring at ≥24 weeks gestation; spontaneous late foetal losses occurring at 20–23 weeks gestation, and pregnancies terminated at any gestation due to an included anomaly will all be registered. **Action 4: Improving information about Rare Disease on NHS Scotland platforms** ▪ Over the next 12–18 months we will work with NHS Inform to improve information about rare diseases online. We recognise that due to the volume of rare diseases we will be unable to have bespoke information for each rare disease. However, as part of their patient journey, we want to ensure people have access to relevant information and are signposted to places for support while living with a rare disease or waiting to receive a diagnosis of their condition. **Action 5: Optimising Rare Disease Day** ▪ Rare disease day provides an important platform to raise awareness of rare diseases, and we will seek to optimise this platform to support the delivery of this priority. We will work with stakeholders to develop a suite of events which engage a broad range of people including clinicians, senior leadership in NHS Boards and those working within primary care. We recognise that raising awareness is about reaching those who aren't already engaged or have not yet gained some awareness of rare diseases. Those are who we will target through this action.

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	Action 6: Working with NHS Education for Scotland ▪ Over the next 12 months, we will work with NHS Education for Scotland to understand the existing rare disease training and education material already developed by a range of organisations like those developed by Genetic Alliance UK, Medics 4 Rare Disease and in other nations. We will consider where these training and education materials can be hosted to ensure optimal recognition and pick up across Health Care Professionals. **Action 7: Enabling opportunities for third sector organisations to raise awareness of rare diseases** ▪ Through partnership working, we will seek to work with rare disease organisations to enable opportunities for awareness raising. We will facilitate introductions and connections wherever possible between these organisations and their valuable expertise and NHS Scotland bodies like NHS Education for Scotland and NHS Inform to ensure that their work can reach the widest audience. **Action 8: Understanding and acting on the information needs of Health Care Professionals to raise awareness of rare diseases** ▪ Genetic Alliance UK's research team will develop a survey to understand healthcare professional's views of rare conditions, assess level of awareness and to identify gaps in information needs and how to address them. This will be distributed through Genetic Alliance UK's communications team, Office for Rare Conditions communications team and wider NHS Scotland networks. This will inform the development and distribution of information materials. **Action 9: Consider a future Care Coordination Service** We also began from the recommendation in the Framework that coordination of care should be improved, and also had recent reports to consider: ▪ The Scottish Parliament Cross Party Group on Rare, Genetic and Undiagnosed Conditions, via Genetic Alliance UK (the Cross Party Group secretariat) published the report Improving Care for Rare Conditions in Scotland in March 2021. The report recommended that a short-life group should be established to explore a coordination of care model for Scotland, and that the Scottish Government should commit to a pilot project for a care coordination service. **Action 10: Improving the use of Anticipatory Care Plans** ▪ We want to encourage take-up of Anticipatory Care Plans among healthcare professionals and signpost this information to clinicians and teams who care for people living with rare diseases. **Action 11: Digital Passports** ▪ To explore how this could benefit people living with a rare disease, we will work with third sector organisations who have used patient passports to understand how they could be better promoted for use by people living with rare diseases, their families and healthcare professionals. **Action 12: Supporting the Implementation of: It's OK to Ask** ▪ We would like to encourage the take-up of "It's OK to Ask" as widely as possible. Wider adoption of "It's OK to Ask" would also assist healthcare professionals in knowing a person's wishes and priorities, leading to more productive discussions at appointments. Transitions from paediatric to adult care can also benefit from this approach.

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	Action 13: Mental Health Strategy ▪ As part of our considerations for a future strategy, we will consider the mental health needs of all patient groups, including people living with rare diseases. Throughout the development we will work to ensure that we reflect the voice of those living with a rare disease in the refreshed strategy. **Action 14: Continuing to Promote and Embed Person Centred Care** ▪ We will continue throughout the lifespan of this person-centred framework to promote and embed person centred care ensuring those with lived experience are at the heart of the services we are delivering. **Action 15: Recognising the role of specialist services** ▪ We recognise that there are a wide variety of non-commissioned specialist services across Scotland, covering a range of rare conditions. These clinics or specialists are not always evident, and we will work to understand the landscape of care pathways across health and social care in Scotland, by initially focusing on an agreed set of rare conditions. **Action 16: Ultra Orphan Pathway** Since 2018, a number of medicines for rare diseases have become available through the Ultra-Orphan Pathway, such as nusinersen (Spinraza®) for the treatment of 5q spinal muscular atrophy, and burosumab (Crysvita®) for the treatment of X-linked hypophosphatemia in children and adolescents. The introduction of the Ultra-Orphan Pathway has and continues to support patients to receive faster access to new medicines for rare diseases. **Action 17: Digital Front Door** ▪ The Digital Front Door work will be a key enabler for people interacting with health and social care services in Scotland. This development will aim to allow anyone to book or rearrange appointments, order prescriptions, update their details and generally conduct routine 'transactions' online. This will support better coordination of care for people living with a rare disease and provide the ability for people to use digital products and services to manage their condition. This means being able to access health assessments, diagnosis, monitoring and treatments, making it an option for everyone with a long-term condition to use digital tools. This will be crucial to all of the priorities of this Framework in the short, medium and long term. **Action 18: Clinical Research for Rare Disease** We will focus on three areas: ▪ **Develop a Scottish Register for Rare Disease** ○ As covered in Action 3, in the short term, we are committed to consolidating the registration of congenital conditions covered by EUROCAT through the national congenital and rare condition registry service, CARDRISS. In time, we are also committed to extending the scope of the CARDRISS register to cover additional congenital and rare conditions covered by the pregnancy and newborn screening programmes. ▪ **Improve networking of research across Scotland** ○ We have established a collaborative group with representation that includes clinical investigators, NHS research Scotland and industrial partners. This group will identify the barriers to a "One Scotland" approach to conducting clinical research. Suggested improvements are

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	expected to include an improved governance structure that facilitates referral of patients to studies between regions and a hub and spoke model for the organisation of clinical trials. ▪ **Develop Genomics research infrastructure** ○ The most common clinical indication for whole exome or whole genome sequencing in Scotland is for the diagnosis of rare disease. The Rare Disease Implementation Board will, with the new Scottish Strategic Network for Genomics Medicine, seek to deliver safe storage of sequence data within a data system that includes research functionality, but also permits reanalysis of extant sequence data as knowledge improves, providing an increased diagnostic return on testing. **Monitoring and Evaluation** We recognise that measuring outcomes for patients, carers and families will be difficult. However, measuring the success of our actions in the short to medium term will be achieved in different ways, depending on what needs to be measured. Work such as better signposting of awareness-raising resources can be measured by assessing their take-up among healthcare professionals, and professional and patient reported improvements in the time taken to diagnose. We will look to develop metrics by which to measure the success of our various actions, such as patient-reported outcome measures.
United Kingdom The UK Rare Diseases Framework 2021[29]	**Principles of the UK Rare Diseases Framework** All 4 UK nations have signed up to the UK Rare Diseases Framework and have therefore agreed to collaborate to achieve the outcomes set out above. However, as health is a devolved matter, each nation will deliver these aims in a way which is most effective for their respective populations. Therefore, each nation will set out an action plan detailing the steps they will take to meet the aims of the framework within their own arrangements. In order to ensure cross-border collaboration and maximise the benefits of the framework for the rare disease community, each nation will follow the below core principles when delivering action plans and implementing the framework. Each nation will: ▪ Deliver the aims of the UK Rare Diseases Framework under each of the priorities and underpinning themes. ▪ Consider where action plans can contain specific and measurable commitments under each focus area and regularly review commitments (every 1 to 2 years). ▪ Develop policy commitments with expertise, in close collaboration with patients and others living and working with rare diseases. ▪ Ensure any impacts on health inequalities are considered when developing action plans. ▪ Ensure that the experiences of rare disease patients during the COVID-19 pandemic are reflected in the development of action plans and implementation of framework priorities and themes. ▪ Ensure that the voice of the rare diseases community is recognised across the system and that work as part of the UK Rare Diseases Framework is aligned with other relevant policy development, such as mental health and social care. ▪ Work collaboratively across nations to share knowledge and best practice. ▪ Review progress made towards the aims of the framework every 5 years and update priorities when necessary. Following the publication of the UK Rare Diseases Framework, all 4 nations will develop action plans which will set out how the priorities identified in the framework will be addressed, taking into account the underpinning themes. These action plans will be developed according to the principles of the UK Rare Diseases Framework and we will work closely with the rare diseases community to ensure the commitments developed are actionable and measurable. Where possible, each nation will aim to publish the action plans in 2021.

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Wales ▪ The UK Rare Diseases Framework 2021[29] ▪ Wales Rare Diseases Action Plan 2022-2026[43]	▪ See UK Rare Diseases Framework. ▪ The details of the plan are set out for each of the four main priorities. Each action is structured in a similar way: 1. Action 2. Delivery partners/Stakeholders 3. Timeline 4. Measure/Outcome For brevity, one action for each area, in each priority, is outlined below. ***Priority 1: helping patients get a final diagnosis faster*** ▪ **Whole Genome Sequencing (WGS) for rare diseases** 1.1 Increase Whole Genome Sequencing testing for rare diseases. AWMGS/WG/WHSSC. 2022/23. Increased number of tests performed. ▪ **Whole Exome Sequencing (WES) for rare diseases** 1.2 Return Foetal Whole Exome Sequencing trios testing (FAGP service) to Wales. AWMGS/WG/WHSSC. 2022/23. Number of tests performed/returned to Wales for testing. ▪ **Whole Transcriptome Sequencing for rare disease** 1.3 Ensure validation of a whole transcriptome service which will enable better understanding of RNA sequences to determine if a DNA sequence is turned on and whether proteins have changed. AWMGS. 2022/23. Validation of methodology. **Research Eco-system** 1.4 Ensure a consent strategy is developed that enables researchers to securely and safely access routine genomic data generated by AWMGS for translational research purposes. Wales Gene Park. 2022. Publication of consent strategy allowing improved access to genomic data for research purposes. Increased number of patients entering research studies (see Appendix B, Table B30 for Action 1.5). **Prevention and Early Detection** 1.6 Establish a public health and screening system in Wales that uses genomics to strengthen the current biochemical screening, diagnostic and care pathways in those at high risk. UK National Screening Committee, New-born Genomes Programme, Wales Screening Committee, Genomics Partnership Wales, Public Health Wales, National Screening Laboratory, WHSSC. 2022-2026. Increased number of rare diseases diagnosed by screening (see Appendix B, Table B30 for Action 1.7). **Service/Digital/Technical Infrastructure** 1.8 Ensure horizon scanning for commissioning requirements to inform the current National Genomic Test Directory for rare and inherited disease. AWMGS/WHSSC. 2022-2026. Improved test availability. ***Priority 2: increasing awareness of rare diseases among healthcare professionals*** **Lead Clinician for Rare Diseases**

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	2.1 Monitor ongoing role and work programme of Clinical Lead and Clinical Champion for rare diseases to raise profile of rare diseases. RDIG, health boards, trusts and all stakeholders. April 2022. Review of achievements of the role by RDIG, NHS Wales Health Collaborative and WG after two years in post. **Education and Shared Learning** 2.2 Survey qualified HCPs, undergraduates on their understanding and learning needs in rare disease. Use results to develop training and development plan from baseline information on HCP understanding of rare diseases. HEIW M4RD (undergraduate project in planning stage Universities Rare Diseases Nurses Network (RDNN). RDNN. 2023/24. Within two years: Improved awareness of rare diseases amongst healthcare professionals (see Appendix B, Table B30 for Actions 2.3 to 2.7). **Improving Awareness of Rare Diseases with Data** 2.8 Expand CARIS expansion to include adults affected by rare conditions. CARIS to collaborate with a small number of patient organisations to pilot research projects and generate patient data for a new adult register and allowing patients to self-report. CARIS, RDIG, WG, Genetic Alliance. 2022/23. Increased number of new conditions incorporated into the CARIS programme (see Appendix B, Table B30 for Actions 2.9 and 2.10). ***Priority 3: better coordination of care*** **Pathways of Care** 3.1 Ensure implementation of transition guidance with all paediatric patients transitioning to adult services should have a named worker and digital care plan linked to a patient passport. RDIG, WHSSC, WG. 2022-2026. Improved transitional care for rare disease patients (see Appendix B, Table B30 for Action 3.2). **SWAN Clinic** 3.3 Continue to build the establishment and assess/evaluate SWAN clinic. WG, WHSSC, Cardiff and Vale University Health Board. 2021-2023. Improved patient outcomes/diagnosis (see Appendix B, Table B30 for Action 3.4). **Digital Patient Record** 3.5 Establish an easily used "app" to enable a "patient passport" for rare disease patients. RDIG, Betsi Cadwaladr University Health Board, Life Sciences Hub Wales, Industry partners. 2022. All rare disease patients have access to a 'patient passport'. **Mental Health Services** 3.6 Ensure the mental health needs of rare disease patients and carers are considered as part of the overall mental health strategy for Wales and consider whether further guidance is needed such as a good practice guide for rare disease patients. RDIG, health boards, WG. 2022-2023. Improved mental well-being for rare disease patients. ***Priority 4: improving access to specialist care, treatments and drugs*** **Access to Medicines and Treatment** 4.1 Ensure continued access to orphan and ultra-orphan medicines in Wales. AWTTC, RDIG and WHSSC. 2022-2025. Improved access to orphan and ultra-orphan medicines (see Appendix B, Table B30 for Actions 4.2 to 4.4). **Access to Specialist Care** 4.5 RDIG to continue to work with WHSSC and HEIW to ensure appropriate consultant specialist services in Wales. (Note some services will need to be provided outside Wales for specific conditions to ensure appropriate expertise and critical mass of patients). RDIG, HEIW, WHSSC. 2022-2026. Rare disease patients have access to appropriate specialist opinions.

Key: ACHSE e.V.: Alliance for Chronic Rare Diseases (Germany); AVIESAN: Alliance for Life and Health Sciences (France); AWMGS: All Wales Medical Genomics Service; AWTTC: All Wales Therapeutics and Toxicology Centre; BBMRI-ERIC: European research infrastructure for biobanking; BMBF: Federal Ministry for Education and Research (Germany); BMG: Federal Ministry for Health (Austria or Germany); BMWFW: Federal Ministry of Science, Research and Economy (Austria); BNDMR: National rare disease data bank (France); CARDRISS: Congenital Conditions and Rare Diseases Registration; CARIS: Congenital Anomaly Register and Information Service; CG Council: Chronically Ill and Disabled Council (the Netherlands); CoEs: Centres of Expertise; CRMR: rare disease reference centre (France); DFG: German Research Foundation; DGOS: Directorate General for Care Provision (France); DGRI: Directorate General for Research and Innovation (France); DGS: Directorate General for Health (France); DHSC: Department of Health and Social Care (England); DNA: deoxyribonucleic acid; DSS: Directorate for Social Security (France); ECRIN-ERIC: European Clinical Research Infrastructure Network; ERN: European Reference Network; EU: European Union; EUROCAT: European Network of Population Based Registries; EURORDIS: Rare Diseases Europe; GEP: Genomics Education Programme; GÖG: Gesundheit Österreich GmbH; HCP: healthcare professional; HEE: Health Education England; HEIW: Health Education and Improvement Wales; HIQA: Health Information and Quality Authority; HSE: Health Service Executive; HTA: Health Technology Assessment; HVB: Central Association of Austrian Social Insurance Institutions; ICD: International Classification of Diseases; ICT: Information and Communications Technology; MESRI: Ministry of Higher Education, Research and Innovation (France); MSS: Ministry of Solidarity and Health (France); NCARDRS: National Congenital Anomaly and Rare Disease Registration Service; NFU: Dutch Federation of University Medical Centres; NHS: National Health Service; NHSE: National Health Service England; NI: Northern Ireland; NICE: National Institute for Health and Care Excellence; NKSE: National Coordination Centre for Rare Diseases (Austria); NPCF: Dutch Patients and Consumers Federation; PIA: Investments for the Future Programme (France); RAREDIS: database for rare diseases (Denmark); RDIG: Rare Diseases Implementation Group (Wales); RDNN: Rare Diseases Nurses Network; RNA: ribonucleic acid; STZ: Top Clinical Hospitals Foundation (the Netherlands); SWAN: Syndrome Without a Name; THL: National Institute for Health and Welfare (Finland); TMF: Technology, Methods, and Infrastructure for Networked Medical Research (Germany); UK: United Kingdom; VSOP: Association of Collaborating Parent and Patient Organisations for rare and genetic disorders (the Netherlands); WES: whole exome sequencing; WG: Welsh Government; WGS: whole genome sequencing; WHSSC: Welsh Health Specialist Services Committee.

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