Recommendations for a National Approach to Rare Disease Data

Findings from an Audit of Australian Rare Disease Registries

Rare Voices Australia and Monash University

July 2023

Acknowledgement of Country

We acknowledge Aboriginal and Torres Strait Islander peoples as the Traditional Owners of Country throughout Australia and their continuing connection to both their land and seas. We also pay our respects to Elders – past and present – and generations of Aboriginal and Torres Strait Islander peoples now and into the future.

About Rare Voices Australia

Rare Voices Australia (RVA) is the national peak body for Australians living with a rare disease. RVA provides a strong, unified voice to advocate for policy as well as health, disability and other systems that work for people living with a rare disease. Our person-centred focus sees us working with all key stakeholders including governments, key peak bodies, researchers, clinicians and industry. RVA's work is non-disease specific and is based on the commonalities of rare disease. Our advocacy focuses on rare disease policy, processes and systems. RVA advocates for the best outcomes for Australians living with a rare disease.

In 2018, the Australian Government commissioned RVA to lead the collaborative development of the National Strategic Action Plan for Rare Diseases (the Action Plan).[1] The Action Plan is the first nationally coordinated effort to address rare diseases in Australia and was informed by an extensive multistakeholder consultation process led by RVA. The Minister for Health launched the Action Plan in February 2020, with bipartisan support. RVA continues to work with State and Federal Governments, as well as other stakeholders, in leading the collaborative implementation of the Action Plan.

Rare Voices Australia website

About Monash University's Registry Science and Research Program

The School of Public Health and Preventive Medicine (SPHPM) has extensive experience in the establishment and maintenance of clinical registries. These registries collect an identical minimum data set from patients treated in multiple hospitals or clinics throughout the country. Consistency is ensured through the use of identical definitions and data collection procedures.

Monash University currently operates over 40 major state or national clinical registries. Monash University clinical registries comply with the Australian Commission's Operating Principles and Technical Standards for Clinical Quality Registries (2008) and Framework for Clinical Quality Registries (2014), ensuring a high quality of data integrity, privacy and legislative compliance.

SPHPM's Clinical Outcomes Data Reporting and Research Program comprises and accesses expertise in management and governance, stakeholder engagement, data collection and management, data linkage, legal and ethical requirements, data quality assurance, biostatistics and reporting, communications, design and publications.

Monash University works closely with a wide range of stakeholders throughout the registry development and implementation process, including clinician leads and registry participants, hospital executive staff and ethics committees, data centres and repositories, governments, private health insurers, industry and consumers to ensure that their registries meet all stakeholder needs and governance and reporting requirements.

School of Public Health and Preventive Medicine (SPHPM) website

Authors

Dr Falak Helwani (PhD, BSc (Hons))

Falak is the Research and Evaluation Manager at Rare Voices Australia (RVA). Falak completed her PhD in molecular cell biology at the Institute for Molecular Bioscience, University of Queensland, in 2007. She has 5 years of postdoctoral experience in stem cell research at the Mater Medical Research Institute and has co-authored several peer-reviewed papers. In her role at RVA, Falak is involved in the development of the Rare Awareness Rare Education (RARE) Portal (a national website with information and resources for all rare disease stakeholders) and management of RVA research partnerships progressing different areas of the Australian Government's National Strategic Action Plan for Rare Diseases. Additionally, she has co-authored a White Paper and Strategy for Australia's rare metabolic diseases health workforce. Falak is also a mother to 2 children living with rare disease.

Dr Rasa Ruseckaite (PhD, MCompSc, BCompSc)

Dr Ruseckaite has a Senior degree in Science, Master of Science and 2 PhDs; one in Applied Computer Science Research Fellow and a Deputy Head (Qualitative Research) with the Clinical Outcomes Data Reporting and Research Program at the School of Public Health and Preventive Medicine, Monash University. With an undergraduate in Neuroscience.

Dr Ruseckaite is a co-founder of the Australian Special Interest Group for the International Society of Quality of Life, and she designed a short course entitled 'Patient Reported Outcome Measures (PROMs) for Clinical Registries' for clinicians, healthcare researchers, clinical registry coordinators and anyone interested in PROMs in a clinical registry setting.

She has published over 80 peer-reviewed journals, 4 book chapters and is also a reviewer for numerous journals, including the BMC Health Services Research, Journal of Cystic Fibrosis, PLOS One, and the Quality of Life Research Journal. Dr Ruseckaite is the Editor-in-Chief for the Journal of Patient-Reported Outcomes and serves as an editorial board member for the Journal of Quality Management in Healthcare.

Professor Susannah Ahern (MBBS (Hons), MBA, FRACMA, PhD)

Professor Ahern is a medical administrator and academic in health services research and management at Monash University. As the Head, Clinical Outcomes Data Reporting and Research Program, she is the Monash University Academic Lead for 6 national clinical quality registries, including in dementia, cystic fibrosis, breast devices, spine surgery and pelvic floor procedures.

Professor Ahern is a member of several national and state-based committees regarding clinical quality registries, including the Clinical Principal Committee; Clinical Quality Registries Expert Advisory Group; the Breast Implant Expert Working Group of the Australian Government Department of Health and Aged Care; the Clinical Quality Registries Framework Review Advisory Group of the Australian Commission of Safety and Quality in Health Care; and the Clinical Quality Registries Working Group, Victorian Agency for Health Innovation of the Department of Health and Human Services Victoria. She is also co-chair of the Australian Clinical Trials Alliance Registry Special Interest Group and a member of both the International Collaboration of Breast Registry Activities and the Cystic Fibrosis Registries International Data Harmonization Working Group. Professor Ahern has contributed to state and national registry policy and practice, and since the release of the National Clinical Quality Registry Strategy and Virtual Registry Strategy 2020—2023, this work is increasing in national significance.

Acknowledgements

RVA acknowledges our Scientific and Medical Advisory Committee (SMAC) for their ongoing commitment to registries for rare disease. The collective expertise, guidance and professional networks of RVA's SMAC were key to the audit of rare disease registries. RVA's SMAC and Round Table of Companies (industry representatives) also contributed to the co-development of the strategic recommendations and associated implementation priorities. Additionally, RVA thanks the registry managers and rare disease groups/organisations, including RVA Partners, who contributed to the research.

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EXECUTIVE SUMMARY

A nationally coordinated and systemic approach to the collection and use of rare disease (RD) data, including registries, is a key priority of the Australian Government's National Strategic Action Plan for Rare Diseases (the Action Plan).[1] The strategic recommendations and implementation priorities detailed in this report are a critical step towards achieving this goal. This report explores the landscape of Australian rare disease registries (RDR) and databases. The report's strategic recommendations and implementation priorities were co-developed with Rare Voices Australia's (RVA) Scientific and Medical Advisory Committee (clinicians and researchers) and industry representatives through RVA's Round Table of Companies (RTC).

This work also responds to the United Nations Resolution on *'Addressing the Challenges of Persons Living with a Rare Disease and their Families'*. Specifically, point 5 encourages Member States, including Australia, to:

> 'Collect, analyse and disseminate disaggregated data on persons living with a rare disease, including by income, sex, age, race, ethnicity, migration status, disability, geographical location and other characteristics relevant in national contexts, where applicable, to identify discrimination and to assess progress towards the improvement of the status of persons living with a rare disease.'

Rare diseases are not routinely counted or recorded in Australia. Extrapolated from international data sets, an estimated 2 million Australians live with a RD.[2] To ensure evidenced-based planning and an accurate contextual understanding of the economic burden of RD, it is necessary to systematically count RD. This can be achieved by adopting national routine coding of RD patients at the point of care and extracting data from existing registries and health records to capture existing patients.

Registries are fundamental instruments for pooling health-related data and are essential for RD where prevalence is low and knowledge is limited. According to EURORDIS-Rare Diseases Europe, a world leader in RDR, registries are 'indispensable infrastructure tools for translating basic research and clinical expertise into therapeutic tools'.[3] The value of registries is also recognised by Australians living with a RD. A 2016 Australian study found almost 90 per cent of respondents living with a RD were interested in joining a patient registry in recognition of the key role registries play in linking people living with a RD to clinical trials, which are often the only available treatment option.[4]

In response to Action 3.1.4 of the Action Plan, *'Develop a national approach to person-centred rare disease registries to support national standards, best practice and minimum data sets'*, RVA engaged registry experts at Monash University to undertake an audit of existing RDR and databases collecting Australian RD data. The audit showed RD data in Australia is housed across multiple registries and databases with each containing unique data sets, under varied governance, controlled by different custodians and built for different purposes. This heterogeneity highlights the need for a standardised approach to RD data in Australia.

In response to this gap, based on the RDR audit and international best practice, RVA, Monash University, RVA's SMAC, and RVA's RTC co-developed 8 strategic recommendations for a national approach to RD data, summarised below. RD data that can be easily shared, and uniformly measured and reported across jurisdictions and health services, are vital to informing an evidence-based

nationally consistent approach to high quality RD care and support. These data are also vital to responding to inevitable new challenges on the horizon, including for cell and gene therapies, which must be managed with evidence, including natural history and clinical data.

IMPLEMENTING THE NATIONAL STRATEGIC ACTION PLAN FOR RARE DISEASES

Pillar 3: Research and Data

Priority 3.1 and Action 3.1.4 of the Action Plan must be addressed to ensure all eligible and consenting Australians living with a RD are counted and supported.

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.

Action 3.1.4

Develop a national approach to person-centred rare disease registries to support national standards, best practice and minimum data sets.

Aspirational Vision for Australian Rare Disease Data

A single national person-centred approach to RD data that is:

- Flexible and responsive, to enable changes and additions to the data set;
- Modular, to enable interoperability and linkage with individual RDR and other relevant data collections; and
- Mandated, to ensure all Australians living with a RD are counted, so no one is left behind.

Objectives for Australian Rare Disease Data

Develop and implement a framework for RD data that:

1. Promotes sustainability of individual RDR, and enables aggregated national RD data sets
2. Develops/leverages fit-for-purpose infrastructure for a national RDR that enables consented national data sharing and linkage, and safeguards privacy.
3. Develops a national minimum data set for RD that can drive evidence-based policy for improving and resourcing RD care.
4. Mandates the collection of RD data and the use of specific RD codes across government systems, including health and disability.

Critical Enablers for Nationally Consistent Rare Disease Data

- ***Commonwealth, state and territory involvement and engagement***
- ***Interoperable infrastructure, coding and digital tools across health services and other sectors***
- ***Mandatory high quality RD data collection and reporting***
- ***Streamlined consent processes***
- ***Multistakeholder partnerships***
- ***Patient-led governance and co-design***
- ***Data management workforce***

Related Australian Government Activity

In addition to progressing implementation of the Action Plan, the strategic recommendations and associated implementation priorities presented in this report are an opportunity for the Australian Government to leverage from, align with and progress several existing investments, commitments, initiatives, frameworks and strategies, including:

- The Australian Commission on Quality and Safety in Health Care's Clinical Quality Registry Framework (revised in 2023);[5]
- The National Clinical Quality Registry Strategy and Virtual Registry Strategy 2020—2023;[6]
- The Australian Government's $40 million investment in national clinical quality registries over 4 years from 2023;
- The Medical Research Future Fund's National Critical Research Infrastructure Initiative;
- Australia's National Digital Health Strategy;[7]
- 2021 National Research Infrastructure Roadmap;[8]
- National Health Reform Agreement – Addendum 2020–2025;[9]
- The Australia Data Council's Data Sharing on Birth Defects Initiative on secure data sharing and linkage (See the Case Study in Part 2 of this report);
- The National One Stop Shop and the National Clinical Trials Front Door;[10] and
- The United Nations Resolution on *'Addressing the Challenges of Persons Living with a Rare Disease and their Families'*, adopted by Australia as a Member State.[11]

Strategic Recommendations

Strategic Recommendation 1. Through multistakeholder partnerships, promote person-centred patient-led RDR with formal clinical oversight. RDR should be focused on a group of, or all, RD rather than a therapeutic intervention, in alignment with Key Principle 3 in the EURORDIS-NORD-CORD Joint Declaration.[12]

Strategic Recommendation 2. Mandate recording and surveillance mechanisms for RD, through a high-quality high-value national registry, that is clinical trial ready and implements RD coding across health and other settings. This should also enable the use of deidentified aggregated RD data for service planning and policy development.

Strategic Recommendation 3. Leveraging existing tools, develop validated person-centred metrics for high value RD care and support that crosscut all RD. This should include development of RD or domain-specific patient reported outcome measures and patient reported experience measures tools.

Strategic Recommendation 4. In response to the global health data standard World Health Organization mandate[13] and Action 3.1 in the Action Plan:

- Implement ORPHAcodes in reporting RD across all relevant government data collections;
- Contribute to the mapping and interoperability of existing health data sets to unlock RD knowledge from existing and new data; and
- Ensure RD are better represented in future implementations of classifications, such as the International Classification of Diseases 11th Revision - Australian Modification (ICD-11-AM).

Strategic Recommendation 5. Engage with experts to define the path towards a National Minimum Data Set (NMDS) for RD. This will include consultation with relevant organisations and data specialists, such as the Australian Digital Health Agency, the Australian Institute of Health and Welfare, and the National Health Data and Information Standards Committee (NHDISC).

Strategic Recommendation 6. Through dedicated Commonwealth funding, develop a NMDS for RD to be adopted by all Australian-based RDR. This needs to be supported by policy and legislation, as required. The NMDS should align with international recommendations for RD data to enable interoperability with international data sets.

Strategic Recommendation 7. Leverage learnings from existing national data sharing and linkage models and customise these for RD. Any data sharing and linkage models for RD should streamline data custodianship guidelines and enable interoperability of different state and territory linkage platforms.

Strategic Recommendation 8. Promote sustainability of existing, and enable development of new, RDR.

INTRODUCTION

What are patient registries and why do they matter?

A patient registry is a collection of standardised information about a group of patients who share a condition or health experience.[14] Patient registries serve a variety of purposes, including epidemiological surveillance, and evaluation of disease outcomes and treatments. Registries can also facilitate patient access to clinical trials and novel therapies. This is vital in the context of RD, where clinical trials may be the only way to access treatment.[1]

Registries can also be broad in scope, from simple contact registries to more detailed clinical quality registries (CQRs) capturing information on symptoms, test results, diagnosis, treatments and patient-reported outcomes.

Registries provide an important evidence-base for systems change through policy reform. A well-run registry operating under national arrangements collecting data over time can be a mechanism for monitoring and evaluating health systems, treatment interventions, outcomes and economic burden of disease. This information can inform health service planning, changes in interventions, models of care, health care processes and access to appropriate and consistent care, improving outcomes such as quality of life, quality of care and survival.[14,15]

In 2020, the Australian Government and the Australian Commission on Safety and Quality in Health Care (ACSQHC) published the National Clinical Quality Registry and Virtual Registry Strategy 2020–2030 (National Strategy)[6], which aims to drive continuous improvements in the value and quality of patient-centred health care to achieve better outcomes for all Australians.

The value of health data collection and the current challenges were originally acknowledged in 2014 in the ACSQHC's Framework for Australian Clinical Quality Registries (the Framework for CQRs)[5], as follows:

> 'In Australia there is limited capacity to measure and monitor the degree to which health care benefits the patient and how closely that care aligns with evidence-based practice. Currently, only a small number of data collections capture and report process and outcomes data for specific clinical conditions or interventions. This results in significant gaps in current Australian health information regarding the appropriateness and effectiveness of specific healthcare interventions. The development of national clinical quality registries is a cost-effective way of addressing these gaps.'[5]

The inherent rarity of RD exacerbates the gaps highlighted in the Framework for CQRs. This makes the need to routinely collect RD data to inform systems and processes for equitable access to high-quality care and reimbursed health technologies even more vital. As the national peak body for Australians living with a RD, RVA contributed a written submission to the consultation for the Framework 2nd Edition in 2023, highlighting the need to ensure that the strategic principles enable the development of CQRs for RD.[16]

The Need for Rare Disease Registries and Data

Limited data in RD means the burden and public health impacts of RD in Australia and overseas are underestimated. Low prevalence, high burden of disease and high levels of unmet need, met with limited treatment options, make data collection a critical first step for informing better outcomes for people living with a RD. RDR are an international priority and have been the focus of research in

several countries, including Europe, Japan, Slovenia, the United States of America and Canada. In 2012, umbrella RD organisations, EURORDIS, the National Organization for Rare Disorders (NORD) and the Canadian Organization for Rare Disorders (CORD) published the 10 Key Principles for Rare Disease Patient Registries,[12] the first of which states, 'patient registries should be recognised as a global priority in the field of rare diseases'.

In 2022, in recognition of the challenges of fragmented RD patient data, 24 members of the European Reference Network (ERN) came together to establish the FAIRification Steward team to better define the challenges and devise solutions to harmonise the collection of RD data across Europe.[17] The Findable, Accessible, Interoperable, Reusable (FAIR) and Collective Benefit, Authority and Control, Responsibility and Ethics (CARE) Principles[17,18] should become the cornerstone for a national approach to collecting RD data in Australia.

EURORDIS-NORD-CORD Joint Declaration of 10 Key Principles for Rare Disease Patient Registries[19]

NORD EURORDIS Rare Diseases Europe CORD Canadian Organization for Rare Disorders

EURORDIS-NORD-CORD Joint Declaration of

10 Key Principles for

Rare Disease Patient Registries

1. Patient Registries should be recognised as a global priority in the field of Rare Diseases.
2. Rare Disease Patient Registries should encompass the widest geographic scope possible.
3. Rare Disease Patient Registries should be centred on a disease or group of diseases rather than a therapeutic intervention.
4. Interoperability and harmonization between Rare Disease Patient Registries should be consistently pursued.
5. A minimum set of Common Data Elements should be consistently used in all Rare Disease Patient Registries.
6. Rare Disease Patient Registries data should be linked with corresponding biobank data.
7. Rare Disease Patient Registries should include data directly reported by patients along with data reported by healthcare professionals
8. Public-Private Partnerships should be encouraged to ensure sustainability of Rare Disease Patient Registries.
9. Patients should be equally involved with other stakeholders in the governance of Rare Disease Patient Registries.
10. Rare Disease Patient Registries should serve as key instruments for building and empowering patient communities.

The Need for a National Approach to Rare Disease Data in Australia

By global estimates, approximately 3.5 to 6.9 per cent of the world's population is living with a RD at any given time.[20] Forgoing extrapolation from these global statistics, there is no true measure of the number of Australians living with a RD. Without a national data set and an accurate baseline, it is impossible to empirically measure and define areas of unmet need and address well-known inequities in access to care for Australians living with a RD.[1,21]

Multiple research papers and stakeholder consultation processes in Australia have identified the need for a national, coordinated, and systematic approach to the collection and use of RD data, including registries.[1] Such an approach will enable monitoring and the accumulation of knowledge about RD to inform clinical practice, research and health service planning.[1] For key decision-makers

at all levels, greater knowledge of RD can facilitate more responsive and appropriate services for people living with a RD and their families and carers.

In a 2020 white paper, variation in care was highlighted as a key concern for Australians living with a rare metabolic disease.[21] Alarmingly, the management, care and outcomes for this particular umbrella group of RD patients depend on where they live. Variations in care can lead to serious consequences for people living with a RD, and high costs to the healthcare system. RDR—particularly clinical quality RDR—are vital instruments to quality improvements for consistent and equitable care. Addressing variation in care is also one of the priorities for registry development in Australia according to the ACSQHC's, 'Prioritised list of clinical domains for clinical quality registry development'.[22]

The Action Plan calls for the 'development of a national approach to person-centred rare disease registries to support national standards and minimum data sets' (Action 3.1.4).[1] The first step to achieving this is outlined by implementation step 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; and
- Classification systems used (for interoperability with other registries and health information systems).'

This information will support national coordination of RDR and the establishment of minimum data sets, provide a better understanding of who is currently being counted and aid in the identification of best practice. A critical enabler of the Action Plan highlights the need for 'High-quality comprehensive collection and effective use of rare disease data.'[1]

The research presented in Part 1 of this report is the fulfilment of this implementation step and only one of many steps needed to define and deliver a national approach to RD data in Australia.

ABOUT THE RESEARCH

RVA engaged researchers from Monash University's School of Public Health and Preventive Medicine (SPHPM) with expertise in clinical registries to conduct an audit of Australian RD data captured by existing registries and databases. RDR capturing Australian data were identified through literature search[23] and direct contact with RD organisations, including RVA Partners, and industry. Registry managers were asked to participate in a survey, and 40 were invited to semi-structured one-on-one interviews—8 took part. Through these 3 phases, data were collected around registry governance; management practices; data sets, including patient numbers, estimated incidence, prevalence and geographical coverage; the use of classification systems; as well as the impact of registries on outcomes and the enablers and barriers to meeting registry objectives.

These data, together with international best practice, relevant Australian policies (including the Action Plan), and multistakeholder input (including from registry experts, industry, consumers and representatives from all relevant government departments) have shaped the development of strategic recommendations for the future of RD data in Australia. The strategic recommendations will support ongoing advocacy efforts and next steps to achieving this goal.

Limitations of the research

It is important to keep in mind that this research did not identify every Australian RDR or data set. All RD data in electronic medical records or databases within hospitals and health clinics were not captured in this research. Nonetheless, the findings highlight significant heterogeneity in RD data sets and issues with the findability of RD data in Australia.

ABOUT THE REPORT

Part 1 of this report summarises the research findings—the current RD data landscape in Australia. It also lists common challenges and enablers to maintaining a RDR cited by registry managers who contributed to this research. Part 2 includes strategic recommendations and implementation priorities that will become a roadmap for a national approach to RD data in Australia.

PART 1. RESEARCH FINDINGS

This section summarises the landscape of Australian RD data (as at February 2022) based on an audit of 74 RDR and databases. It highlights missed opportunities in the current approach to RD data and the challenges and enablers of setting up and sustaining RDR in Australia.

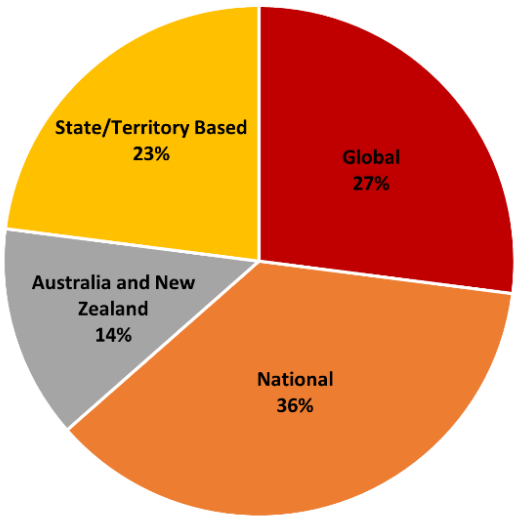
*Some of this work has been published in a peer reviewed journal.[23]

Australian Rare Disease Data: How and What Data Are Collected?

Key Finding 1. RDR Capturing Australian Data Vary in Jurisdictional Scope

Seventy-four registries (and databases) collecting Australian RD data were identified through this research. These registries vary in size, type and geographical scope**.** Nine are biobanks. Most registries capturing RD data have fewer than 1000 participants, and as few as 18, reflective of the low prevalence of RD. Figure 1 shows over one third of registries (36%) identified through this research capture national data across multiple centres.

Figure 1. Geographical Scope of Rare Disease Registries Collecting Australian Data



Missed Opportunities from Restricted Geographical Scope

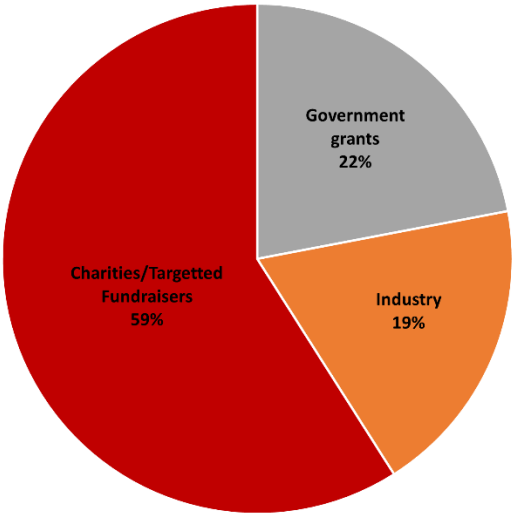
The variable and restricted geographical scope of many RDR collecting Australian data places limitations on data utility and interoperability. Australia's small geographically spread population further compounds data constraints from the inherently low prevalence of RD. So, while many of the registries identified in this research are purpose built, and capturing some data is better than no data at all, we must consider ways to expand the coverage of existing registries for national reporting. Registry managers need to be supported to recruit every possible consenting patient across Australia to ensure full coverage of the eligible clinical population. This aligns with the National Strategy and Framework for CQRs, and Principle 2 of the EURORDIS-NORD-CORD Joint Declaration of 10 Key Principles for Rare Disease Patient Registries[12]—*'Rare Disease Patient Registries should encompass the widest geographic scope possible'*.

Nationally consistent data sets, such as successfully implemented CQRs, can significantly improve safety and quality in health care. They can also lead to significant returns on investment through improvements in survival, quality of life and prevention of unnecessary treatments or hospital stays.[5] CQRs may not be the only answer to widening the reach of RDR, but relevant recommendations in the National Strategy and the Framework for CQRs should be leveraged in a national approach to RD data. Implementation priority 8.3 in Part 2 of this report mentions RDR should aspire to the standards of CQRs by meeting the Operating Principles for CQRs endorsed by the Health Minister in 2010 and listed in the Framework.[5]

Key Finding 2. RDR Capturing Australian Data Are Not Sustainably Funded

Funding for Australian RD data collection varies, and some registries are funded through a combination of sources. According to the audit findings, Australian RD data collection is primarily funded by charitable organisations and through direct fundraising. Only a fraction (22%) of the costs of these registries falls on governments and even less (19%) is covered by industry (Figure 2).

Figure 2. Rare Disease Registry Funding Sources



Missed Opportunities from Lack of Sustainable Funding

Over reliance on charitable organisations is fuelling the lack of sustainable funding for RDR and this is likely to blame for incomplete or poorly curated RD data sets. Entering data into registries is laborious and time consuming for busy clinicians, patients, carers, and registry managers, and much of the work is unpaid. Without reliable and sufficient funding, efforts to collect RD data will remain limited in their scope, quality and ability to report accurately and meaningfully. The National Strategy for CQRs recognises the importance of sufficient and sustainable funding for national data sets, calling for prioritisation of sustainable funding models in partnership with multiple beneficiaries for national clinical quality data sets (see Priority 16 Actions).[6]

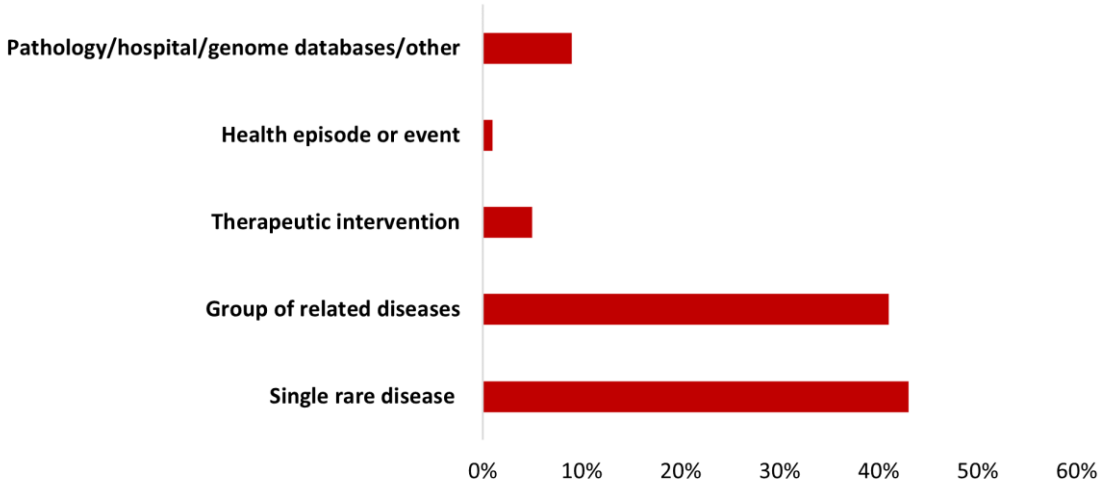
Governments should identify ways to better resource new and existing RDR to ensure sustainable and careful curation of accurate and reliable data that can be used for the quality improvement of care. This aligns with Strategic Priority 3 in Australia's National Digital Health Strategy[7], '*High-quality data with a commonly understood meaning that can be used with confidence*'. One way to ensure the sustainability of RDR and mitigate the current over reliance on charitable funds is highlighted in the 8th Key Principle of the EURORDIS-NORD-CORD Joint Declaration, *'Public-private partnerships*

should be encouraged to ensure sustainability of rare disease patient registries'.[12] This principle forms part of implementation priority 8.1 in Part 2 of this report.

Key Finding 3. There Is Wide Variation in RDR Scope

Most RDR captured in the audit were dedicated to a single RD or a group of RD. This aligns with the 3rd Key Principle of the EURORDIS-NORD-CORD Joint Declaration, *'Rare Disease Patient Registries should be centred on a disease or group of diseases rather than a therapeutic intervention'*.[12] Close to 20 per cent of registries captured data based on a health episode, a therapeutic intervention or were linked to pathology, hospital or genomic data sets (Figure 3).

Figure 3. Registry Scope



Key Finding 4. There Is Wide Variation in the Mechanisms for and Timing of RD Data Collection

Australian RD data are captured in different ways and at different intervals. Global registries (capturing Australian data) tend to collect data via online surveys completed by patients and carers. Data for Australian national registries are generally entered by clinicians or registry staff, including volunteers in patient-led support groups.

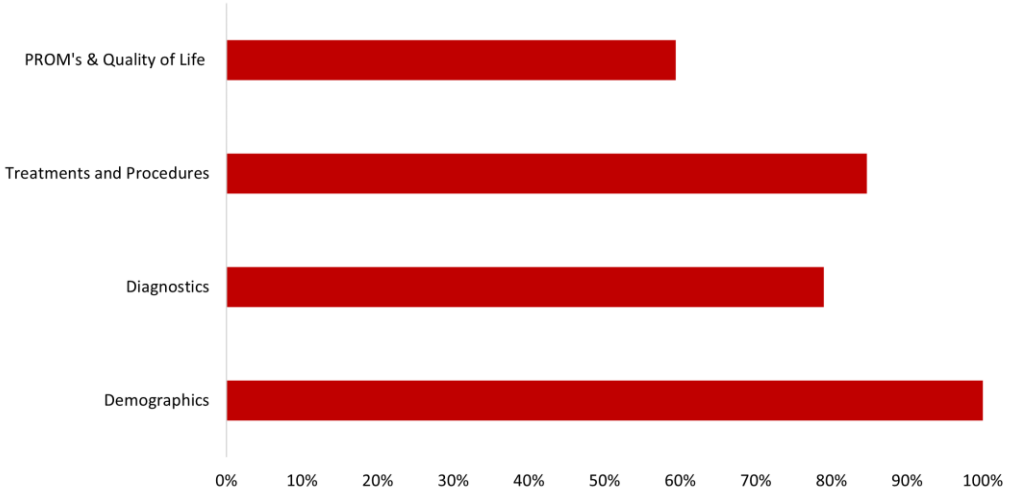
Of the 40 registries that responded to the survey arm of this research, 35 had consenting models for data collection, including both opt-in and opt-out models, and 34 had human research ethics approval. The details of consent for each RDR varied, with only some having considered consent for secondary use of data. This puts limits on the utility of data from these existing RDR, which likely diminishes potential benefits. Such limitations are not exclusive to RDR. The National Strategy for CQRs highlights that Australia is yet to harness the full potential of secondary uses for registry data.[6] It is important for RDR managers to leverage the recommendation from the National Strategy for CQRs to develop streamlined processes for consent, governance and ethics approval.[6]

Key Finding 5. There Are Gaps, Inconsistencies and Broad Variation in the Types of RD Data Collected

The 74 registries identified in this research captured different combinations of a broad range of data elements (Figure 4). Most data captured are related to the following key categories:

- **Demographics** (including given names, surnames, age, gender, country of birth, address, email, phone number, death date, race, insurance, education, employment status, family history, clinic and doctor details)
- **Diagnostics** (including date of diagnosis, age at diagnosis, clinical and diagnostic data and pathology, medical imaging and genetic test results, disease sequalae and outcomes)
- **Treatments and procedures** (including medications, supplements, surgeries, procedures and allied health interventions)
- **Patient Reported Outcome Measures (PROMs) and Quality of Life measures** (including mobility, self-care, pain, mental health and behaviour)

Figure 4. Proportion of registries capturing information from each data category



Missed Opportunities from Variable RD Data Sets

Highly varied data sets, and those with missing or poorly defined data elements, pose problems for interoperability, data sharing and reporting. To enable interoperability of data sets, it is important to have some level of standardisation and coordination around the types of data collected. The importance of interoperability of data collections is highlighted in Recommendation 5 of Australia's 2021 National Research Infrastructure Roadmap (the Roadmap), '*Drive a more integrated national research infrastructure ecosystem*'.[8] Under this recommendation, the Roadmap highlights '*data sets and collections are vital for all fields of research. Careful curation of (and improvements to) the reliability, interoperability, accessibility and management of data sets and collections is crucial to ensure use and reuse of data*.' Key Principle 4 of the EURORDIS-NORD-CORD Joint Declaration also encourages interoperability and harmonisation of RD resources.[12]

The use of common data elements is one way to increase interoperability among registries, but implementation can be a challenge.[25] The need for a set of common data elements has been

explored in various countries, including Japan[24], Europe[25] and Slovenia[26], the United States of America[24] and Canada[24]. It is also highlighted in the Action Plan.[1] To keep pace with international impetus and progress implementation of the Action Plan, Australia should invest in the development and implementation of a nationally relevant and consistent set of common data elements for all RD data collections. Development of NMDS for RD, is covered in Strategic Recommendations 5 and 6 in Part 2 of this report. In Australia, NMDS are an important resource for estimating the public health impact of disease and accurately evaluating outcomes of interventions and their prospective savings to health and disability systems.[6]

Australia should also consider a move towards mandatory recording and surveillance of RD through a high-quality high-value national registry and the integration of RD coding across healthcare and other settings. This approach would make headway for the development of national statistics for RD in Australia and is covered in Strategic Recommendations 2 and 3 in Part 2 of this report. It would also improve the quality and utility of RD data, thereby facilitating improvements in diagnosis, clinical management and timely access to novel health technologies.

The utility of RDR is further contingent upon the quality and accessibility of data entered. If data quality is low, meaningful use of the data becomes impossible. In a paper investigating the determinants of maintaining high quality data in RDR, registry leads agreed that registries need procedures for checking data quality, and they should have clear definitions for each data element collected through formalised data definitions or dictionaries. Training registry users was also mentioned as integral to enabling quality data entry.[27]

Key Finding 6. RDR Capturing Australian Data Lack Transparency in Data Sharing and Reporting

Of the 74 registries and databases captured in this research, 40 did not share any information about their mechanisms for reporting. Of those that did share this information, 31 published data through newsletters, annual reports, or both. Some RDR reported at specific times (annually, monthly) and others provided reports on request.

Missed Opportunities from Lack of Transparency in Data Sharing and Reporting

Collaborative development of the Action Plan identified several key themes, which have become measures of Action Plan progress over time. Theme 4, 'The need to measure rare diseases' states,

> 'Limited data is a common feature in rare diseases. This is heightened by poor quality, disjointed collection methods and the ineffective use of data for rare diseases. Such limitations are evident across a range of areas, from health system classification to research. Research, monitoring and ongoing evaluation are critical in rare diseases because, ultimately, if we are not counting rare diseases, people living with rare diseases do not count.'[1]

One of the primary purposes of a disease registry or database is to collect longitudinal data for monitoring, evaluating and reporting on specific outcomes around disease prevalence, diagnosis, treatments and care. Limited data reporting among existing RDR collecting Australian data suggests a significant volume of these data are inaccessible to the public. This lack of transparency of data use may affect the trust of eligible participants causing them to question the purpose of their involvement. This poses a risk to recruitment and retention of patients to RDR more broadly. There is also a risk that the data collected are not being used for any clear purpose, which is a waste of limited resources and already scarce RD knowledge. The critical need for timely access to data to support shared patient-clinician decision making, improved service delivery, policy development and

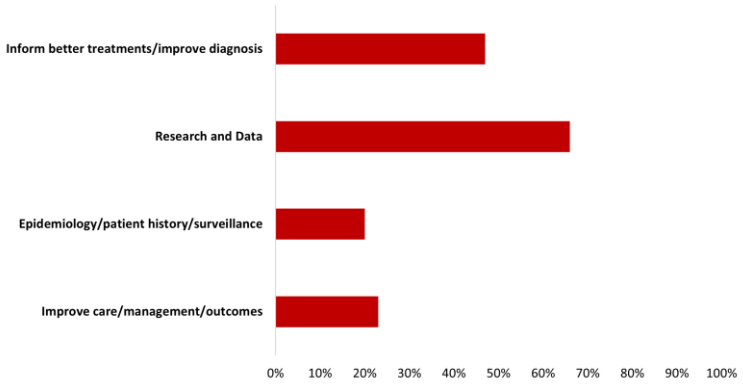
systems planning is cited in Schedule C, Long-Term Health Reform Principles, under 'Enhanced Health Data', of the National Health Reform Agreement – Addendum 2020–2025.[9] Such timely access to data for all of the purposes listed, is even more critical in RD, where progressive decline necessitates rapid decision making, and any data or knowledge could lead to better outcomes.

Key Finding 7. The Purpose of RDR Varies and Impact Is Not Routinely Measured

Registries and databases are usually established with a specific purpose or goal. Of the RDR captured through this project, 42 (66%) mention research and data in their purpose, 15 (23%) have a goal to improve care, management and/or outcomes, 13 (20%) are set up for epidemiology, patient history, surveillance, and 30 (47%) have goals to inform better treatments and improve diagnosis (Figure 5).

The majority of RDR and databases reported having made no identifiable impact on patient outcomes or the community. Survey respondents shared that either impact was not measured, or no direct impact had been made, mainly due to the small sample size of the registry or a slow rollout. It is worth noting here that RDR and databases found in the literature did not adequately report on the impact on patient outcomes, nor did they look into barriers or enablers to reaching their objectives or purpose.

Figure 5. Purposes of RDRs



Missed Opportunities from Varied RDR Purpose and Lack of Impact Measurement

As mentioned earlier, RDR—particularly CQRs—are vital instruments to quality improvements for consistent health care and, when built well, serve to inform cost reductions in the healthcare system. The impact of CQRs on quality of patient care and clinical outcomes is well-recognised. However, few RDR are enabled to reach this standard. This is a symptom of limited data, poor data quality, lack of standardised and validated data sets, and insufficient funding and resources.

Limited reporting on the impact of RDR signifies existing sources of RD data are not being used to their full benefit. Inherently small data sets together with few validated indicators, tools and standards of RD care impede the ability of RDR to reliably measure impact. More work is needed to build metrics or indicators for best practice in RD before true impact can be measured to determine the benefit of RDR on the health and wellbeing outcomes of people living with a RD. This work forms part of Strategic Recommendation 3 in Part 2 of this report.

Challenges and Enablers for Rare Disease Registries in Australia

To address the variation, inconsistencies and gaps in current RD data collected in Australia, it is important to highlight the common challenges faced by registry managers and leverage learnings and enablers. Registry managers surveyed and interviewed as part of this research shared the following common challenges and enablers of running a registry.

Challenges

- Insufficient funding and resources;
- Maintaining appropriate governance;
- Lack of sustainability;
- Transparency of data use;
- Lack of government support;
- Data completeness, including limitations on the types of data that can be collected by organisations that are not registered health providers;
- Difficulties with recruitment;
- Difficulties obtaining ethics approval; and some reported
- Barriers to collecting biological samples from rural and remote communities.

Enablers

- Dedicated registry staff;
- Contribution of clinicians' time to data collection;
- Enthusiasm and commitment from a steering committee;
- Well-defined registry scope and objectives;
- Site participation; and
- Sustainable funding.

All 6 enablers in this list, overlap with enablers highlighted throughout the Framework for CQRs[5] and the National Strategy[6]. In addition to these, **supporting policy and legislation** have also been identified as vital for the success of registries. This is demonstrated through the success of legislated data collections such as the South Australian Birth Defects Register and Western Australian Register (SABDR) of Developmental Anomalies (WARDA), and numerous cancer screening registries.

To overcome the challenges highlighted above and avoid missed opportunities, it is important for RDR and databases to leverage all these enablers and establish a strong governance system. The Framework for CQRs5 provides useful guidance on the role and implementation of governance for CQRs, which all RDR should aspire to.

Part 1. Summary

The 7 key findings from this research have highlighted gaps and strengths in current RDR and databases. Additionally, the findings identified common challenges faced by RDR managers around collecting and reporting on data and sustaining the high volumes of work that come with running a registry. The findings have also identified several opportunities to progress and improve the collection and use of Australian RD data.

To transform opportunity into action, Part 2 of this report includes a set of strategic recommendations and implementation priorities for the first national approach to RD data collection in Australia. These recommendations and implementation priorities were informed not only by the research, but also by international best practice, Australian policies (including the Action Plan) and frameworks and extensive multistakeholder consultation. The recommendations will become a powerful advocacy tool and roadmap for building and maintaining RDR and databases in Australia. The end goal: to count RD so people living with a RD count.[1]

PART 2. STRATEGIC RECOMMENDATIONS FOR THE FUTURE OF RARE DISEASE DATA AND REGISTRIES IN AUSTRALIA

This section outlines strategic recommendations and implementation priorities for a nationally coordinated approach to RD data that supports national standards, best practice and minimum data sets, in alignment with Action 3.1.4 of the Action Plan.[1] These recommendations are based on the research findings presented in Part 1, the EURORDIS-NORD-CORD Joint Declaration of Key Principles for Rare Disease Patient Registries[12] and other international guidance, as well as relevant Australian policies, including the Action Plan[1], the Framework for CQRs[5] and the National Strategy.[6]

The collective goal for these recommendations is to enable the systematic collection, sharing and use of RD data, to reduce uncertainty, inform better outcomes and empower people living with a RD. The recommendations also highlight the need to leverage any existing RD data sets and establish RD coding in health and other systems for a more accurate national estimate of the number of Australians living with a RD. They lend themselves to improvements in the quality, utility, interoperability, accessibility and uniformity of Australia RD data that can inform all systems supporting Australians living with a RD. These recommendations should leverage and be considered in line with the National Digital Health Strategy[7]and all relevant government activities, including those listed on page 4 of this report.

RD data should also support fundamental and epidemiological research, patient access to clinical trials, health technology assessment processes for the reimbursement of new and repurposed drugs and health technologies, post-market surveillance of drugs and treatments, and inform service planning and improvements across health, social, disability, education, and other government systems.

Strategic Recommendations and Implementation Priorities

Strategic Recommendation 1. Through multistakeholder partnerships, promote person-centred patient-led RDR with formal clinical oversight. RDR should be focused on a group of, or all, RD rather than a therapeutic intervention, in alignment with Key Principle 3 in the EURORDIS-NORD-CORD Joint Declaration.[12]

> ***Implementation Priority 1.1*** *Develop formal mechanisms for community engagement in registries, including public-private partnerships to improve patient recruitment.*
>
> ***Implementation Priority 1.2*** *Embed registry enrolment into standard clinical care so clinicians are resourced to enrol patients and enter data.*
>
> *This aligns with Strategic Principle 5 in the Framework for Australian CQR, 'Dedicated investment in Australian clinical quality registries supports infrastructure, data cleansing, reporting and analysis of quality of care, based on succinct data sets captured routinely by clinicians at the point of care'.*[5]

Strategic Recommendation 2. Mandate recording and surveillance mechanisms for RD, through a high-quality high-value national registry that enables the use of deidentified aggregated RD data, is clinical trial ready and implements RD coding across health and other settings.

Strategic Recommendation 3. Leveraging existing tools, develop validated person-centred metrics for high value RD care and support that crosscut all RD. This should include development of RD or domain-specific patient reported outcome measures and patient reported experience measures tools.

Strategic Recommendation 4. In response to the global health data standard World Health Organization mandate[13] and Action 3.1 in the Action Plan:

- Implement ORPHAcodes in reporting RD across all relevant government data collections;
- Contribute to the mapping and interoperability of existing health data sets to unlock RD knowledge from existing and new data; and
- Ensure RD are better represented in future implementations of classifications, such as the International Classification of Diseases 11th Revision - Australian Modification (ICD-11-AM)

Strategic Recommendation 5. Engage with experts to define the path towards a National Minimum Data Set (NMDS) for RD. This will include consultation with relevant organisations and data specialists, such as the Australian Digital Health Agency, the Australian Institute of Health and Welfare, and the National Health Data and Information Standards Committee (NHDISC).

Strategic Recommendation 6. Through dedicated Commonwealth funding, develop a NMDS for RD to be adopted by all Australian-based RDR. This needs to be supported by policy and legislation, as required. The NMDS should align with international recommendations for RD data to enable interoperability with international data sets.

Implementation Priority 6.1 *Establish a working group to define a NMDS for RD, including a process for review. It must address the data needs of all government departments supporting Australians living with a RD.**

*This should include:

- Department of Health and Aged Care;
- Department of Social Services;
- National Disability Insurance Agency;
- Department of Education; and
- Health Technology Assessment committees (Medical Services Advisory Committee, Pharmaceutical Benefits Advisory Committee, the Life Saving Drugs Program).

The working group needs to include people living with a RD, RD advocates, governments, epidemiologists, health professionals, statisticians, informaticians, information technology systems designers and data managers, ontologists, registry managers, registry experts, industry and researchers.

The data elements in the NMDS for RD should:

- Be relevant, measurable, practical and reportable;
- Be centred around the Australian context and support international studies and interoperability;
- Capture a combination of clinical and patient-derived data, including real world data and patient reported outcomes and experience measures;[6]
- Be co-designed with patients, families, consumer organisations, clinicians and all other relevant experts;
- Be informed by international best practice;
- Show clear potential to improve the health and wellbeing outcomes of Australians living with a RD;
- Be clinical trial ready;
- Consider the needs of researchers;
- Address gaps in data needs and reporting standards of decision makers across all government support systems looking after Australians living with a RD, including health, health technology assessment processes, disability, housing, social, and mental health. This aligns with the Priority 9 Actions in the ACSQHC National Strategy;[6]
- Consider the needs of priority populations in the Action Plan, including Aboriginal and Torres Strait Islander people, people from culturally and linguistically diverse background and people living with a disability; and
- Include unique identifiers for priority populations in the Action Plan for Aboriginal and Torres Strait Islander people and people from culturally and linguistically diverse backgrounds.

Strategic Recommendation 7. Leverage learnings from existing national data sharing and linkage models and customise these for RD. Any data sharing and linkage models for RD should streamline data custodianship guidelines and enable interoperability of different state and territory linkage platforms.

CASE STUDY: National Data Linkage Model

The Australian Digital Council (ADC, known as the National Digital Advisory Council, at the time of writing), was created to facilitate and drive better cross-government collaboration on data and digital transformation, and to improve services and policy outcomes for all Australians. The ADC commissioned the Western Australia (WA) Department of Health to partner with Commonwealth agencies to deliver data sharing across Australian jurisdictions. The Data Sharing on Birth Defects Initiative (the Initiative) aimed to understand the barriers to sharing sensitive personal data between the WA and Commonwealth governments and to identify a mutually agreeable method for the integration of cross-jurisdictional data sets. Birth defects (also called developmental anomalies or disorders of embryogenesis) are a large class of mainly RD. The Initiative was operationally led by the Western Australian Register of Developmental Anomalies (WARDA).

Following development and analysis of a suite of options to share the birth defects data, the Privacy Preserving Record Linkage (PPRL) approach was the preferred option for implementing the Initiative. The PPRL approach involves linkage by a third-party agency using only encoded personal identifiers. All data is encoded prior to leaving the data custodians, eliminating the need to share identifiable information between parties. The WA Department of Health assessed the feasibility of the PPRL approach for linking mothers in WA Health's WARDA and the Midwives' Notification System data sets to the Commonwealth's Medicare Enrolment File. Mothers were successfully linked proving the suitability and utility of the PPRL approach for sharing health data while preserving privacy.

The successful and high degree of data linkage attained through the Initiative is enabling Western Australian health researchers to investigate the effects of prescribed medications during pregnancy (ascertained through the national Pharmaceutical Benefits Scheme data set) on the likelihood of birth defects within WA (ascertained through the WARDA data set that includes ORPHAcodes). Researchers are also investigating the types of medications prescribed in pregnancy and the prevalence of birth defects following exposure to those medications in the first trimester of pregnancy. This is unlocking new RD knowledge from existing health and other government data sets. The success of the Initiative also provides opportunities to engage with private health sector bodies more broadly, who currently (at the time of writing), have limited participation in data linkage frameworks.

Strategic Recommendation 8. Promote sustainability of existing, and enable development of new, RDR.

Implementation Priority 8.1 *Develop a framework and infrastructure to sustain and support improvements in existing RDR and enable development of new registries This can be facilitated though incentivising public-private partnerships in alignment with Key Principle 8 in the EURORDIS-NORD-CORD Joint Declaration.*

Implementation Priority 8.2 *RDR should be supported to:*

- Develop and employ the appropriate workforce to support their operations. (As a guide, the Framework for CQRs mentions the following workforce for CQRs – clinical experts,

operational managers, data managers, statistical and epidemiological support, registry coordinators, and administrative and/or technical support.);[5]

- Expand their reach to recruit every possible consenting patient across Australia and ensure full coverage of the eligible clinical population;
- Develop sound ethics, governance and data custodianship principles that consider the FAIR[17] and CARE[18] Principles and align with the Data Governance Institute data governance principles in their operations;
- Engage with hospitals and relevant institutions and clinics across Australia; and
- Collaborate with relevant international registries or, where international registries do not exist, enable the participation of overseas patients – this is particularly important for ultra-RD.

Implementation Priority 8.3 *New and existing RDR should aspire to the standards of CQRs outlined in the Framework for CQRs.*[5]

NEXT STEPS

The ramifications of limited data in RD are far reaching, too often resulting in high levels of uncertainty that impact every part of people's lives. People living with a RD, health professionals and decision makers across all levels and sectors of government, face impossible choices based on incomplete knowledge and unclear pathways.

Data drives continuous improvements in the value and quality of care. The Action Plan acknowledges that greater knowledge of RD can facilitate more responsive and appropriate services for people living with a RD and their families and carers. In line with key priorities in the Action Plan, a strategy to count RD is the only way to accurately understand the impact RD has on people's lives, health and other systems and the economy.

This report details strategic recommendations to facilitate a coordinated and systemic approach to the collection and use of RD data. These recommendations are a critical step towards better informed choices for key decision makers, and more responsive and appropriate services for people living with a RD, their families and carers, health and other care professionals. Based on evidence and co-designed by experts, the recommendations leverage and include steps for better outcomes for all RD stakeholders, concurrently seeking to align with and progress implementation of several government frameworks, policies and investments. The recommendations are intended to guide and support the sustainable development of registries for individual RD, while also leveraging commonalities in RD, providing a roadmap for systemic collection of data across all RD.

'High quality, comprehensive collection and effective use of rare disease data' is a critical enabler of the Action Plan. Collaborative and timely implementation of the recommendations will address several priorities in the Action Plan.

All stakeholders and all governments have a role to play in the collection and use of RD data. Implementation of these recommendations requires systemic reform, which includes federal funding, legislation, mandates, infrastructure, resources and a dedicated workforce.

Following this report RVA will:

- Communicate the findings and recommendations with all stakeholders and encourage all relevant stakeholders to progress timely implementation of the recommendations;
- Seek meetings with Commonwealth, State and Territory Governments across all departments, including the Department of Health and Aged Care and the Department of Social Services, to discuss timely implementation of the recommendations; and
- As the national peak body for Australians living with a RD, work closely with experts, including researchers and registry managers, to progress timely implementation of the recommendations, where possible and n

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LIST OF ABBREVIATIONS

The Action Plan	The National Strategic Action Plan for Rare Diseases
ACSQHC	Australian Commission on Safety and Quality in Health Care
ADC	Australian Digital Council
CARE Principles	Collective benefits, Authority to control, Responsibility, Ethics Principles (for Indigenous data governance)
CORD	Canadian Organization for Rare Disorders
CQR	Clinical Quality Registry
ERN	European Reference Network
EURORDIS	Rare Diseases Europe
FAIR Principles	Findability, Accessibility, Interoperability and Reusability Principles
ICD-11-AM	International Classification of Diseases – 11th Revision – Australian Modification
National Strategy for CQRs	National Clinical Quality Registry Strategy and Virtual Registry Strategy 2020—2023
NHISSC	National Health Data and Information Standards Committee
NMDS	National Minimum Data Set
NORD	National Organization for Rare Disorders
ORPHAcodes	Orphanet nomenclature of rare diseases
PPRD	Privacy Preserving Data Linkage
PREM	Patient Reported Experience Measures
PROM	Patient Reported Outcome Measures
RD	Rare Disease(s)
RDR	Rare Disease Registry/Registries
SABDR	South Australian Birth Defects Register
The Framework	Framework for Australian clinical quality registries Second Edition
The Roadmap	2021 National Research Infrastructure Roadmap
WARDA	Western Australian Register of Developmental Anomalies