

National Strategic Action Plan for Rare Diseases

The evidence base for the National Strategic Action Plan for Rare Diseases

A companion document to the National Strategic Action Plan for Rare Diseases

February 2020

We acknowledge Traditional Owners of Country throughout Australia and recognise the continuing connection to lands, waters, and communities. We pay our respect to Aboriginal and Torres Strait Islander people; and to Elders both past and present.

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Introduction

The collaborative development of the National Strategic Action Plan for Rare Diseases (the Action Plan) and its companion documents was led by Rare Voices Australia (RVA), with funding from the Australian Government Department of Health.

This document provides an overview of evidence to support the development of the Action Plan, as well as its key Priorities, Actions and three Pillars. The document also highlights the challenges of rare diseases and areas where there are gaps or limitations in the available evidence.

What is a rare disease?

While individual rare diseases may be rare, collectively, approximately eight per cent of Australians live with a rare disease¹. Extrapolated to an Australian population of over 25 million people², this equates to around two million Australians. The most widely accepted definition is that a rare disease is one that affects less than five in 10,000 people^{3,4}. Approximately 80 per cent of rare diseases are of genetic origin⁵. While estimates of the number of rare diseases may vary between countries and studies, due to differing definitions and challenges with data collection, it is prominently cited that there are more than 7,000 different rare diseases⁶.

Rare diseases, like many other chronic diseases, are often serious and progressive. They are often difficult to diagnose, not only due to their rarity but also because of their high level of symptom complexity. Health professionals are not typically taught sufficiently about rare diseases as part of their standard training⁷. Significant diagnostic delay and misdiagnosis is common.

While there is large variation among rare diseases, people impacted by rare diseases face common challenges. They include the struggle for a timely and accurate diagnosis, limited care and support options and a lack of research into rare diseases, despite recognised knowledge gaps⁸.

Rare diseases pose many challenges for all: from the person living with a rare disease, to their family and carers, rare disease organisations, the wider community, health professionals, researchers, the pharmaceutical industry, and governments.

Stakeholder consultations undertaken during the development of the Action Plan indicate that progress in the rare disease sector has been fragmented and undertaken in isolation. State, national, and international partnerships have been lacking, made even more difficult by Australia's disjointed health and social systems. There has been a lack of funding towards national leadership, and the coordination and facilitation of partnerships. Currently, data for most rare diseases is not captured in either health information systems or registries⁹ and there is no coordinated strategy to collect, measure, build and translate data that does exist. As acknowledged in the Asia-Pacific Economic Cooperation (APEC) *Action Plan on Rare Diseases*, as rare disease is often absent from policy, "it is difficult for health policymakers to allocate resources and design health interventions for rare diseases"¹⁰.

Priority Populations

Relevant implementation recommendations in the Action Plan identify the need to undertake targeted activities to improve health and wellbeing outcomes for priority populations which include: Australians living with a rare disease; Australians living with an undiagnosed rare disease; 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 (CALD) backgrounds; and people experiencing socio-economic disadvantage.

Rare diseases and Aboriginal and Torres Strait Islander people

While Aboriginal and Torres Strait Islander people are not necessarily at greater risk of rare diseases, several factors increase the potential impact of rare diseases on Aboriginal and Torres Strait Islander people. The lack of research into rare diseases means our knowledge on which rare diseases are most prevalent within the Aboriginal and Torres Strait

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Islander population is incomplete. Given the genetic basis of most rare diseases, research exploring this is vital. The following factors further contribute to the challenges faced by Aboriginal and Torres Strait Islander people:

- while the areas of genetics and genomics are expanding rapidly, inequity exists in the inclusion of Aboriginal and Torres Strait Islander people genetics, genomics, and clinical phenotype diagnostic support tools¹¹. International Rare Diseases Research Consortium (IRDiRC) members, which in Australia includes the Western Australia (WA) Department of Health and RVA¹², are committed to reducing existing and potential disparities between Indigenous and non-Indigenous Australians. The IRDiRC states that this “requires Indigenous-specific reference genetic data sets to improve clinical diagnosis and optimize therapies,” anticipating that “this research will not only benefit rare disease patients worldwide, but also have impacts in the wider context of personalized medicine”¹³. Numerous studies support this call for Indigenous-specific reference genetic data sets^{14,15,16}. The exomes of 72 Aboriginal Australians were recently sequenced¹⁷, and the National Health Genomics Policy Framework prioritises the promotion of “culturally safe and appropriate genomic and phenotypic data collection and sharing that reflects the ethnic diversity within the Australian population, including for Aboriginal and Torres Strait Islander people”¹⁸. These initiatives provide a starting reference point for genomic studies on Aboriginal and Torres Strait Islander people;
- many Aboriginal and Torres Strait Islander people have Indigenous language/s as their first language/s. As a result, diagnostic and clinical concepts, including around emerging health technologies, can be challenging for non-Indigenous Australian practitioners to adequately convey¹⁹. More work is also required to understand the health information needs of Aboriginal and Torres Strait Islander people with rare disease (and their families and kinship groups) to ensure available information and services are culturally safe and appropriate²⁰;
- proportionately, more Aboriginal and Torres Strait Islander people live in regional, rural, and remote areas, which can pose significant challenges to their ability to access services²¹;
- the Aboriginal and Torres Strait Islander population has a relatively young age profile compared with the non-Indigenous Australian population. As articulated in the National Aboriginal and Torres Strait Islander Health Plan 2013-2023, “[t]he younger age profile... requires a focus on well-designed and implemented antenatal care... along with effective interventions to support young adults to adopt healthy lives”²². This may have implications in relation to culturally safe and appropriate transitions between rare disease care services; and
- while only five per cent of Aboriginal and Torres Strait Islander people (compared with 16% of non-Indigenous Australians) are aged over 65 years, chronic health conditions affect 88% of Aboriginal and Torres Strait Islander people over 55 years of age²³. As stated by the Australian Human Rights Commission, “[i]n recognition of the unique status of Australia’s first peoples and in recognition of lower life expectancy levels, certain services are specifically designed for Aboriginal and Torres Strait Islander people”²⁴. As an example, Indigenous Australians have lower age eligibility for aged care programs²⁵. This may have implications in relation to culturally safe and appropriate transitions between rare disease care services.

Development of the Plan on a Page

The Action Plan has three Pillars:

Pillar 1: Awareness and Education

Pillar 2: Care and Support

Pillar 3: Research and Data

Each Pillar outlines Priorities, Actions and Implementation areas. The Pillars were established from discussions that took place at stakeholder consultations conducted during the development of the Action Plan. Throughout these consultations, stakeholders called for effective rare disease policy reform to be underpinned by three foundation principles:

1. Person-centred
2. Equity of access
3. Sustainable systems and workforce

Additionally, the following critical enablers were developed from Action Plan stakeholder consultations:

- multi-stakeholder involvement and engagement;
- collaborative governance and leadership;
- state, national and international partnerships; and
- high quality, comprehensive collection, and effective use of rare disease data.

These outcomes align with and build on previous stakeholder consultations from the 2011 inaugural Awakening Australia to Rare Diseases international symposium of over 200 delegates and RVA's national roadshow to progress a national rare disease plan in 2014.

Evidence for each Pillar

Awareness and Education

Lack of awareness and education about rare diseases for the general public

The lack of awareness about rare diseases often contributes to people feeling isolated and misunderstood. Personal stories sent to RVA by Australians living with a rare disease indicate that it is common for people to have never heard of the rare disease with which they, or their child, are diagnosed²⁶. These personal stories also suggest that increased awareness and education about rare diseases at the individual and community level is vital in empowering people living with a rare disease to become active participants in their rare disease journey²⁷. Education needs to respond to the fact that people living with a rare disease are constantly learning and at the same time, teaching others about their disease²⁸.

During stakeholder workshops at the 2011 inaugural Awakening Australia to Rare Diseases international symposium, the “need for increased public awareness, education and engagement programs was consistently suggested by symposium participants”²⁹. Information for people “living with a particular rare condition can be very limited especially if there is no patient support organisation for that particular condition or others diagnosed with the same condition”³⁰. In a 2016 survey of Australian adults living with a rare disease, around one in five respondents (19%) had not received any information about their condition at the time of diagnosis. Of those that did receive information, only half (50%) indicated they understood the information provided. “Information to patients and families must be provided in a range of formats and at various levels of medical and scientific detail to ensure full understanding and informed decision making.” Almost a third (31%) of survey respondents reported receiving verbal information only³¹.

Lack of awareness and education about rare diseases for health professionals

Personal stories sent to RVA by Australians living with a rare disease highlight that people often find it difficult to find a practitioner who is educated about their disease³². Stakeholder workshops at a symposium to inform the development of an Australian national plan for rare diseases revealed that “health professionals are perceived to need greater support to provide effective services for those affected by rare diseases”³³. Overseas, a United Kingdom (UK) study found that “patients and families worry about the level of awareness of rare diseases among healthcare professionals”³⁴.

A 2017 review of 11 national policies for rare diseases identified that rare disease education for health professionals is an important strategy that is being promoted in many countries³⁵. Similarly, the International Joint Recommendations to Address Specific Needs of Undiagnosed Rare Disease Patients outline the importance of systemic education and awareness of the care and support workforce, in the context of undiagnosed rare disease³⁶. Research out of Germany and Belgium suggests that up-to-date information that is easy to find (online), highly accessible, and co-located in a central repository can help overcome information deficiencies for people living with a rare disease; their families and carers³⁷; and health professionals³⁸.

Australian paediatricians caring for children with rare diseases have reported feeling that rare diseases were inadequately covered during university and in subsequent training, consequently, they feel unprepared to care for these patients³⁹. Paediatricians find the lack of clinical guidelines frustrating. Results from a national survey of paediatricians “support the need to raise awareness of rare disease resources” and indicate that “multiple strategies” are needed⁴⁰. “Embedding specific teaching about rare diseases in undergraduate and postgraduate medical curricula would better equip future paediatricians to care for children with rare diseases”⁴¹. Paediatricians have proposed the listing of specialist referral services, and online education modules about rare diseases that could be accessed from a “single online repository of a wide range of resources”⁴². This could support “dissemination of rare disease guidelines, referral pathways and coordination services relevant to health professionals”⁴³.

Several other professions were identified as having insufficient levels of knowledge and experience of rare diseases to adequately meet the needs of people living with a rare disease and their families and carers⁴⁴. The identified professions included GPs; nurses; allied health professionals; social workers, psychologists and other relevant mental health and wellbeing professionals; dietitians; and specialists.

Awareness and Education

Why awareness and education of rare diseases for health professionals is critical

Many people have found that health professionals may contribute to the 'diagnostic odyssey' through insufficient awareness or 'suboptimal' knowledge of rare diseases^{45,46,47,48}. A 2016 survey of Australian adults living with a rare disease showed that health professionals' lack of awareness of rare diseases often contributes critical impacts such as to delays in diagnosis and treatment, potentially missing opportunities for early intervention and improved outcomes⁴⁹. Such experiences go beyond diagnosis. A 2016 survey of parents in Australia and New Zealand found that a majority (54%) were dissatisfied with health professionals' level of knowledge and awareness of their disease⁵⁰.

Researchers found that "health professionals may need greater awareness of rare diseases in order to improve the diagnostic process, and support to meet the information requirements of people newly diagnosed with rare diseases⁵¹." Due to the sheer number of rare diseases in total, "it is unrealistic to expect that health professionals would know about every rare disease⁵²." Instead it is suggested that more appropriate education would be to "reinforce to health professionals that when they see a patient whose symptoms they can't explain, usual practice is to ask whether the cause could be a rare disease⁵³."

Rare disease knowledge and awareness are lowest amongst frontline health professionals (GPs) and highest amongst specialists⁵⁴. Whilst unsurprising, due to the nature of their respective roles, frontline health professional awareness is critical as they are the first step in many Australians' diagnostic journeys. Red flags for rare disease are therefore critical elements of all physicians' academic and continuing professional education⁵⁵. Due to the sheer number of different rare diseases and the urgent need for diagnosis, any rare disease education for health professionals would ideally be supported by embedding red flags for rare disease diagnosis in health information systems⁵⁶.

Important role of rare disease organisations in awareness and education activities

Stakeholder consultations conducted during the development of the Action Plan highlighted that rare disease organisations are important to the rare disease sector and often fill gaps in the system. Research shows this is not just in terms of awareness and education, but also care and support and, increasingly, in the research sphere⁵⁷. Throughout the consultations, it was consistently noted that these organisations are often under-resourced, are largely volunteer-based and often have a limited ability to raise funds, posing a risk to their long-term sustainability⁵⁸. At the 2011 inaugural Awakening Australia to Rare Diseases international symposium, "participants suggested funding is required in a range of areas such as... support groups and organisations, for example: seed funding to fund project officers; ongoing funding for an umbrella organisation; administration support; conference attendance and website development⁵⁹."

Rare disease organisations and people living with a rare disease can be a source of "[s]ubstantial information... concerning medical, practical or legal topics⁶⁰." People living with a rare disease have reported finding the information received from others as highly trustworthy, and thus saw it of paramount importance to seek out rare disease organisations following diagnosis⁶¹. Patient organisations are often the main or only source of information for rare disease patients⁶². These findings were reiterated throughout the Action Plan stakeholder consultation process.

A review of awareness and education activities undertaken by Australian rare disease organisations also informed the Action Plan. The review indicates that rare disease organisations play a key role in raising disease awareness and providing person-centred information. These activities vary from organisation-to-organisation but typically involve the following activities: ensuring up-to-date information about a rare disease is accessible via their website; publishing regular e-newsletters and distributing them to their community; making closed Facebook groups available for people living with a rare disease; and running webinars about areas of interest specific to their community.

Prevention measures for certain non-hereditary rare diseases

Types of non-genetic rare disease make up 20% of rare diseases and include cancers, infections, and autoimmune

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disorders⁶³. Primary prevention of some of these non-genetic rare diseases is possible.

Some Australians are at an increased risk of developing or contracting certain rare non-hereditary diseases that are unrelated to pregnancy. Examples include: people who may be exposed to certain factors in their environment (such as rural populations or farm animal handlers to Q fever, or those living in areas where *Mycobacterium ulcerans* is present); and those with low immunity and thus increased vulnerability (such as newborns prior to receiving scheduled vaccinations (such as for whooping cough) or the immunocompromised). Rare non-hereditary diseases can be related to pregnancy. In certain instances, pregnant women may have an increased chance of being vulnerable to diseases such as rubella (German measles) and chickenpox (varicella). The passing of these infections onto an unborn baby may result in rare congenital disorders in the child, such as congenital rubella syndrome, or congenital varicella syndrome⁶⁴.

The importance of education for individuals and families following genetic testing or screening

Advances in genetics and genomics provide opportunities to increase our understanding of disease, including its prevention and treatment⁶⁵. Despite these advancements and the associated opportunities, there are still significant gaps in knowledge and understanding that limit our ability to interpret results, predict the consequences of mutations, and even diagnose some diseases, even after thorough genomic analysis⁶⁶. It is therefore important to recognise that there are clinical, ethical, legal, social, and economic (ELSI) implications associated with genetic screening⁶⁷, and that these implications impact on families and individuals. As most (80%) rare diseases are genetic in origin⁶⁸, information around genetic causes and inheritance patterns are of critical concern, not only for the individual in question, but for close relatives or future children. Individuals and families require detailed information to make informed decisions⁶⁹. This information helps to facilitate increased reproductive confidence.

Similar sentiments are echoed in *The UK Strategy for Rare Diseases* (the Strategy), which acknowledges that, while expansion of genetic testing and screening programmes will increase peoples' choices, it will also increase the complexity of questions relating to the ethical, legal and social issues/implications. Regarding diagnosis through genetic testing or screening, the Strategy notes that individuals and families will require timely access to reliable, and correct information about their condition to make informed choices. The type of information required includes how to connect with support groups, what the treatment options are, and whether there is any relevant research activity taking place⁷⁰.

Australian research currently underway involves ten thousand couples and will focus on reproductive carrier screening to identify those with an increased chance of having children with certain rare diseases. Researchers will evaluate the outcomes of screening; psychosocial impacts reported by couples; ethical issues raised by screening, and health economic impacts of this test⁷¹ providing an important opportunity to develop education materials for individuals and families after accessing rare disease genetic testing or screening.

Education about chronic conditions and rare congenital anomalies

Evidence indicates women who have, or may be at risk of developing certain chronic conditions, such as diabetes, epilepsy or thyroid disorders (for example, through family history of these disorders), may have an increased chance of having babies with rare congenital anomalies^{72,73}. There is good evidence for preconception care interventions related to these chronic conditions in order to prevent development of rare diseases in the unborn child.

The role of awareness and education in contributing to the prevention of congenital anomalies

The European Surveillance of Congenital Anomalies (EUROCAT) reports that many congenital anomalies are potentially preventable, and "liable to be reduced by an integrated strategy of primary prevention⁷⁴." The World Health Organization (WHO) recommends awareness and education activities as providing proven and effective prevention of development of congenital anomalies⁷⁵.

The *EUROCAT/EUROPLAN Recommendations on policies to be considered for the primary prevention of congenital*

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anomalies in National Plans and Strategies on Rare Diseases identify a number of types of preventative action including, “advice to future parents by health professionals during individual pre-conceptional and early pregnancy consultations, tailored for high and low (average population) risk couples” and “health education campaigns targeted to potential future parents⁷⁶.”

Australian GPs have identified that a major barrier to their ability to provide evidence-based, high-quality preconception care is a lack of women presenting in the preconception stage. There is evidence suggesting that women may not be aware of the benefits of preconception care. Barriers to GPs proactively investigating the need for preconception care are predominantly related to insufficient time and resources. Despite this, preconception care checklists, patient brochures, handouts and waiting room posters can be effective enablers to preconception care. The involvement of practice nurses in the preconception care model can optimise the effective and efficient use of resources⁷⁷.

Information and education that enables people to be active participants in their rare disease journey

Numerous stakeholder consultations, including consultations conducted as part of the development of the Action Plan, highlight people’s need for a broad range of information, including “disease etiology; treatment and management options; a directory of specialists, local medical and social services; entitlements (e.g. financial); and support groups⁷⁸.” These findings align with a German study that assessed the information needs of people living with a rare disease. Participants highlighted the need for care and support information regarding specialists treating rare diseases, including their location and accessibility; treatments/medical devices, such as wheelchairs, prostheses, dressing material; lifestyle factors, such as diet and exercise; and how to find rare disease organisations. The German study also found that people need information that is up-to-date with respect to research, clinical practice and personal experience; high quality and from trusted sources; and consolidated at a central point that is easily accessible. The study showed that a well-designed information portal can help to enable informed decision-making and simplify access to specialised services and providers⁷⁹. Similarly, Australians have “identified the need for publicly available information on rare diseases to be easily accessible, and centralised⁸⁰.” In a 2016 survey of Australian adults living with a rare disease, 77% of respondents reported that referral to a website was the most preferred format of information about their condition⁸¹.

Lack of workforce capacity

Lack of awareness and education about rare diseases is often compounded by the lack of workforce capacity. In 2005, the Human Genetics Society of Australasia (HGSA), with input from the Australasian Association of Clinical Geneticists, Australasian Society of Cytogeneticists, Australasian Society of Genetic Counsellors and the Australasian Society for Inborn Errors of Metabolism, responded to the Productivity Commission’s (PC) Issues Paper. The response informed the PC of supply shortages and knowledge gaps in four key rare disease workforce components; clinical geneticists, genetic counsellors, cytogenetic scientists and metabolic teams, as well as complementary workforces such as dietitians, nurses and laboratory scientists⁸². The PC released a research report in 2006 that presented findings of a study investigating health workforce supply and demand issues and proposed solutions. While a number of general workforce issues were discussed that would have broad applicability to a rare disease context, matters of direct relevance to rare diseases were not included in the report⁸³. These long-standing issues may not have been sufficiently addressed given participants in Action Plan stakeholder consultations identifying some parts of the workforce as having insufficient capacity for current and/or future demand. This includes genetic counsellors; clinical geneticists; researchers with rare disease interests; and specialists, including metabolic specialists⁸⁴. However, these challenges are not unique to Australia. In 2005, a United Kingdom (UK) needs assessment and review recommended an approximate doubling of the metabolic workforce, including specialists, nurses, and dietitians, to meet demand for services⁸⁵.

The complexity in rare diseases highlights the need for multi-disciplinary clinics for specific or groups of rare diseases. Resourcing of these multi-disciplinary clinics has also been identified as an issue both in terms of funding and

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staffing⁸⁶. In a survey of Australian adults living with a rare disease, half of the respondents felt they did not receive “sufficient psychological support”. Researchers concluded that “mental health professionals should be considered a key part of a multi-disciplinary approach, given half of our respondents perceived they did not receive sufficient psychological support”⁸⁷.

It has been well documented that with the growth in genomic testing, there has been a significant increase in demand for clinical geneticists and genetic counsellors^{88,89}. A 2017 report commissioned by the New South Wales Ministry of Health articulated “the changing landscape” in which genetic counsellors are currently operating, noting that technological advancements have led to rapidly increasing potential to access genomic information, and this has led to a significant and widening gap between supply and demand of genetic counsellors and the services they offer⁹⁰.

A more thorough audit of rare disease workforce gaps would need to be undertaken to get a full picture of the situation as the above information only highlights some areas in which workforce capacity needs to be increased.

Evidence for each Pillar

Care and Support

Lack of integration in rare disease care and support

People living with a rare disease have more complex care needs than the general population. In a 2016 study of Australians living with a rare disease, in the 12 months prior:

- 81% of respondents had seen a medical specialist compared to 35% of the general population;
- 40% of respondents had accessed an outpatient clinic compared to 9% of the general population;
- 28% of respondents had been a hospital inpatient compared to 13% of the general population;
- 33% of respondents had presented at the Emergency Department compared to 12% of the general population; and
- nearly 40% of respondents consulted three or more specialists yet only 9% had a designated care coordinator⁹¹.

At RVA's national roadshow to progress a national rare disease plan in 2014, stakeholders reported that it is "not uncommon for 10 or more specialists to be involved in patient care⁹²."

At an international level, the WHO and the Organisation for Economic Cooperation and Development have both advocated for integrated care services^{93,94}. With respect to rare disease, there is international recognition that "integrated and coordinated strategies are necessary to ensure holistic access to care and treatment for patients⁹⁵."

Implementation of integrated rare disease care and support are key recommendations of three important 2019 reports: the McKell Institute's *Disability & Rare Disease: Towards Person Centred Care for Australians with Rare Diseases*⁹⁶; the European Organization for Rare Diseases (EURORDIS) position paper *Achieving Holistic Person-Centred Care to Leave No One Behind*⁹⁷; and the *APEC Action Plan on Rare Diseases*⁹⁸. In Australia, based on health systems information, the PC has echoed the call for integrated care services, as have a number of consumer representative bodies, including the Consumers Health Forum of Australia⁹⁹.

Australian research shows that, due to disease complexity and associated disability, "children living with rare disease often require specialist care from large teams of health professionals¹⁰⁰." Stakeholders have called for "coordinated and integrated approaches to care... to meet the complex needs of all people with a rare disease¹⁰¹." Stakeholders have also called for a wide range of health and social support services and complex case management support to facilitate "access to a range of specialists, services and programs; coordinated and integrated care so that there are no gaps in service delivery across the lifespan, including transitions from paediatric to adult care¹⁰²."

The importance of person and family-centred approaches

Rare disease care and support must be person and family-centred, while being integrated and appropriate for all Australians living with a rare disease. Person-centred care involves measuring all outcomes that matter to people living with a rare disease. Due to the fragmentation and siloed nature of Australian health systems, which are organised by medical specialties, documentation of "patients not being considered as a 'whole person'; both at the time of diagnosis and during ongoing care and disease management," is not uncommon¹⁰³.

Patient-Centred Outcome Measures have been a focus of the IRDiRC since 2016.

Because a rare disease affects every aspect of their daily life, patients and their caregivers become experts of the rare condition and of the important outcomes of diseases that need to be addressed. It is thus critically important to partner with and listen to them¹⁰⁴.

Numerous stakeholder consultations, including consultations undertaken as part of the development of the Action Plan, have confirmed that living with a rare disease does not only affect a person's health: it impacts every facet of their life, including education, employment and mental and physical health^{105,106,107}. For example, it is currently difficult for people living with a rare disease to navigate their way through the health and disability systems as there is a lack of clear referral pathways^{108,109}. Additionally, a number of notable Australian rare diseases studies and stakeholder consultation processes call for greater integration of care as a means for improving outcomes for Australians living with a rare disease^{110,111,112}.

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Organised calls for rare disease care and support for Australians living with a rare disease that is integrated can be traced back to 2011¹¹³. There is evidence that coordinated care prevents hospital encounters, decreases emergency presentations, significantly lowers family travel requirements, and boosts school attendance, in addition to producing notable economic savings¹¹⁴.

Understanding that people's needs are broader than the health system alone

An Australian survey found that only a minority of people living with a rare disease agreed that they had received sufficient social (34%), financial (15%) and psychological (20%) support¹¹⁵. The “complexity and chronicity means that children need ongoing multidisciplinary care from paediatric specialists, allied health professionals and disability services¹¹⁶.”

Key findings from RVA's national rare disease roadshow in 2014 indicate, “there is significant potential to extend coordinated care beyond the medical model to include, for example, how young people living with a rare disease interact with health, education, training, disability and other services¹¹⁷.”

Increasing the utilisation of telehealth and other digital health services

One Australian study showed that 39% of respondents travelled more than 50km to see medical specialists while less than 4% had used telehealth services¹¹⁸. These findings echo similar stakeholder consultations that indicate people living with a rare disease need “care closer to home by people who are informed about their rare disease¹¹⁹.”

The utilisation of digital health services, including virtual clinics and telehealth (telemedicine) services, is a key component of modern health care and social support. This is arguably of even greater importance in a rare disease context, where individuals experience great complexity, conditions are often chronic, prevalence is low and both people living with rare disease and rare disease expertise is geographically dispersed. Australia's *National Digital Health Strategy* (2017) noted that the benefits of coordinating care for people with chronic and complex conditions are “significant and compelling”¹²⁰. My Health Record has the explicit objective of improving the coordination of care and planning for people with chronic and complex conditions¹²¹.

An evaluation of the use of telehealth in the Northern Territory by individuals living in rural and remote areas who typically needed to travel to access medical care, found that implementing telehealth contributed to greater appointment attendance rates, resulted in high levels of satisfaction of both health professionals and patients and led to reduced travel expenditure¹²². Other case studies exploring the use of telehealth in Australian chronic and/or complex disease contexts have demonstrated far-reaching benefits for all stakeholders, including the potential for significant reductions in expenditure, as well as reduced hospital admissions, length of stay and reduced mortality. Both patients and health professionals were satisfied with the technology and would continue its use¹²³.

Responding to disability caused by rare diseases

Many rare diseases have the potential to see people requiring access to disability services. A 2019 McKell Institute paper, *Disability & Rare Disease: Towards Person Centred Care for Australians with Rare Disease*, found that “seven in 10 people with a rare disease report not having their health and disability care needs met¹²⁴.” Of particular concern is that “almost one in three people have experienced deterioration in the supports they receive under the National Disability Insurance Scheme (NDIS)¹²⁵.” The report also cites the lack of rare disease knowledge and expertise of customer-facing NDIS staff as the primary reason inadequate support is given, and finds that many people living with a rare disease incur significant out-of-pocket costs in meeting their needs. A key contributing factor is that the “NDIS is explicitly not designed to replace mainstream health services for people with a disability and consequently, only covers supports for activities of daily living and not medical expenses. For individuals who have a disability with an underlying and ongoing medical cause, such as people with rare diseases, there can often be grey areas in coverage creating delays and confusion. In addition, this delineation between health and disability services does not promote care integration that can best support the complex needs of people with rare diseases¹²⁶.”

Enhancing existing transition services

During Action Plan stakeholder consultations, the following significant life-stage transitions were identified: people reaching the age where paediatric services cease (e.g. transitioning from child to adult hospitals); relocating; and when needs change significantly (such as at end-of-life).

One of the most commonly cited and critical transitions is the transition from paediatric to adult services¹²⁷. A position paper looking into the transition from child centred to adult health care systems found that “patients require support to transition from paediatric to adult services.” Poor transition experiences have been linked to “increased long-term social and economic costs due to poor treatment compliance; disengagement from services; increased genetic risks; and higher rates of disease-related complications¹²⁸.”

In a study of Australian adults living with a rare disease, of those who had transitioned from paediatric to adult services, more than half had experienced problems with the transition¹²⁹. Many improvements have been suggested by people living with a rare disease and their families and carers, including:

- better preparation for transition, including adequate time;
- modifiable transition processes based on readiness of the individual;
- consultation with and involvement of all affected parties in the transition process;
- greater integration and coordination of care during the transition (by GPs) and once a part of adult health services; and
- greater resources for young people in transition, including access to education and employment, access to benefits, peer support and psychological support¹³⁰.

Key outcomes from stakeholder workshops to inform the development of an Australian national plan for rare diseases revealed the importance of coordinating whole-of-lifetime care: “Symposium participants expressed the view that there should be no gaps in service delivery across the lifespan of an individual; programs and services should seamlessly span transitions from paediatrics to adulthood to aged care. Participants suggested case coordinators are needed to be the first point of contact for patients, carers, and families. Case coordination should be individualised; be flexible and cost-effective for the health system; and be founded on national best practice standards. It was thought that a generic model(s) of care could focus on issues common to many types of rare diseases¹³¹.”

The need to enhance existing transition services is gaining importance as more children with rare diseases survive into adulthood. Transition is felt most acutely by teenagers who “often feel abandoned by health services and struggle to negotiate changes in service providers during the turbulence of adolescence”¹³². Greater awareness and education of rare diseases, by both GPs and specialists, would assist in the transition process for young people living with a rare disease¹³³.

The multi-faceted role of palliative care in rare diseases, including perinatal palliative care

Palliative Care Australia (PCA) describes palliative care as “person and family-centred care... to optimise the quality of life¹³⁴.” PCA considers the holistic nature of palliative care to include providing physical, emotional, spiritual, and/or social care, dependent on the individual's unique needs¹³⁵. While most people associate palliative care solely with end-of-life care, palliative care can provide a broader scope that “improves the quality of life of patients and their families facing the problem associated with life-threatening illness, through the prevention and relief of suffering by means of early identification and impeccable assessment and treatment of pain and other problems, physical, psychosocial and spiritual¹³⁶.”

Palliative measures can make significant improvements to individuals' quality of life where they experience complex symptoms as a result of a rare disease. Palliative care can also benefit the individual's family^{137,138}. There is a need for further research to investigate improvements to palliative care services for people living with a rare disease that could address the breadth and depth of their needs^{139,140}.

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Perinatal palliative care

The perinatal period is defined as starting at 20 completed weeks (140 days) of gestation and ending at 28 completed days after birth¹⁴¹. PCA has developed Guidelines that include a focus on perinatal palliative care¹⁴². The Australian Institute of Health and Welfare (AIHW) reported that in 2015 and 2016, the most common cause of perinatal death was congenital anomaly; which caused an estimated three in 10 (approximately 1710) perinatal deaths¹⁴³. Most congenital anomalies are considered rare diseases due to their low frequency¹⁴⁴.

For families that have, or will have, a child with a condition that means their death is imminent, perinatal palliative care is an invaluable resource¹⁴⁵. With a focus on both the foetus or infant and their family, this care is intended to prevent and relieve suffering and improve the conditions of the infant's living and dying. "It is a team approach to relieve the physical, psychological, social, emotional, and spiritual suffering of the dying infant and the family"¹⁴⁶.

The vital role of rare disease organisations in representing and advocating for their community

Stakeholder consultations undertaken as part of the development of the Action Plan confirmed that in Australia, valuable care and support is provided by rare disease organisations. This includes peer support, the provision of information, access to resources, and individual and systemic advocacy. Many rare disease organisations are run by people living with their own rare disease challenges, which can at times affect their ability to offer services and impacts the organisation's sustainability¹⁴⁷.

Importance of timely and accurate diagnosis

Personal stories of Australians living with a rare disease suggest that significant diagnostic delay and misdiagnosis, often referred to as the 'diagnostic odyssey', are common in rare disease¹⁴⁸. This is further supported by a survey of Australian adults living with a rare disease in which 30% of respondents were impacted by a diagnostic delay of more than five years, while almost half had received at least one misdiagnosis. Two thirds of respondents had needed to consult three or more doctors before they received a confirmed diagnosis¹⁴⁹. Similarly, another Australian study found almost 40% of families of children diagnosed with a rare disease believed they had experienced delayed diagnosis, with a similar number having consulted six or more different doctors in the lead up to receiving a definitive diagnosis. Twenty-seven per cent initially received a misdiagnosis¹⁵⁰.

Diagnostic delay and misdiagnosis causes "physical, psychological, emotional and financial costs for the person and family living with a rare disease¹⁵¹." Australian researchers note that the "value of a diagnosis cannot be underestimated, even in the absence of an effective treatment¹⁵²" and that "prompt, correct diagnosis is very important for families, as it enables them to explain their child's disease to others, to stop blaming themselves for their child's condition, it may restore reproductive confidence and alleviates some of the stress of not knowing what is wrong and what to expect in the future¹⁵³." RVA states that "early diagnosis enables the best clinical care, treatment options, access to services, peer support, increased reproductive confidence and access to participation in clinical trials (research)¹⁵⁴."

The important role of screening and diagnostic programs

Screening and diagnostic programs have an important role in the diagnosis of rare diseases. An international review of national policies for rare diseases found that an "accurate and timely diagnosis is predicated on availability of universal or highly accessible screening and diagnostic programs and services"¹⁵⁵. In relation to diagnostic responses, tools/ tests and screening, the Action Plan calls for further investment to address existing funding gaps and to continue working towards national coordination and equitable access. Screening and diagnostic programs have the potential to increase reproductive confidence. Further evidence is below.

Diagnostic response: Genomics technology

A growing number of studies demonstrate the cost-effectiveness, efficiency, and efficacy of genomics technologies in

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rare disease diagnosis¹⁵⁶. Australian studies worth noting include a 2019 article on population genomic screening and a 2018 article on Whole Exome Sequencing¹⁵⁷. Next-generation sequencing strategies have “accelerated the pace of discovery” of the genetic basis of disease, and thus changed the landscape of rare disease diagnosis¹⁵⁸.

Diagnostic response: Undiagnosed Diseases Programs (UDPs)

Internationally, the first UDP was established in the United States (US) in 2008 to provide answers to patients with mysterious conditions that have long eluded diagnosis and to advance medical knowledge about rare and common diseases¹⁵⁹. The UDP expanded over time to form the Undiagnosed Diseases Network in the US, after which emerged an international manifestation, the Undiagnosed Diseases Network International (UDNI). The core principle of UDPs is to “focus assessments and expertise in one place at one time and centred on one patient at a time¹⁶⁰.”

WA was involved in the formation of the UDNI and is Australia’s first UDP – the UDP-WA. The UDP-WA aims to provide a definitive diagnosis for people with complex and long-standing medical conditions. Australia’s UDP incorporates a team of doctors from a broad range of specialties working together in partnership with researchers¹⁶¹. A review of early outcomes include definitive diagnosis of some cases, refined management of the program, increased staff cohesion, dissemination of genomic and phenomic knowledge, supporting the training of junior medical staff, retaining/re-attracting workforce capacity and generating enthusiasm and engagement of medical students and researchers¹⁶². The UDP-WA has been recognised as an innovative model contributing to health system sustainability. It also seeks to address inequities for Indigenous and underrepresented populations on a local and global scale¹⁶³.

Diagnostic response: Clinical phenotype diagnostic support tools

Clinical phenotype diagnostic support tools can help to increase reproductive confidence. A person’s phenotypeⁱ is of great relevance in rare disease; many rare diseases can be considered to manifest along a spectrum of severity, and there is often great variation (heterogeneity) between individual cases of the same disease. In some cases, health professionals may assess that a person’s phenotype strongly suggests the presence of a genetic condition, yet a diagnosis that explains all symptoms is unable to be made¹⁶⁴.

FaceMatch is an example of a cutting-edge clinical phenotype diagnostic support tool. Using advanced facial recognition software, it is designed to help find a genetic diagnosis for children with significant developmental delay or intellectual disability by matching their facial features with already diagnosed children. Early studies have demonstrated the potential utility of FaceMatch to facilitate the interpretation of DNA sequencing data¹⁶⁵.

Diagnostic response: Newborn bloodspot screening in rare diseases

Newborn bloodspot screening (NBS) is offered to all newborns in Australia¹⁶⁶. While there are variations in the conditions screened for in each state and territory, approximately 25 rare and serious conditions are screened for. Approximately 99% of newborns are screened through the programs¹⁶⁷, making them potentially one of the most significant and early rare disease diagnostic tools available. The endorsement of the NBS Framework proposal provides an effective mechanism to add to screening panels, which will lead to earlier diagnosis of a greater number of rare diseases.

Previous advances in technology related to testing and management of conditions have had a significant impact on NBS programs. For example, the advent of tandem mass spectrometry led to rapid expansion of the Australian NBS programs¹⁶⁸. Current and emerging technologies, such as whole genome sequencing may also have significant impacts on NBS programs¹⁶⁹. As technology progresses and more rare disease treatments are developed, community attitudes towards testing will also evolve. A number of rare disease organisations are currently advocating for inclusion of screening for their specific rare disease.

The NBS National Policy Framework (the Framework) provides a mechanism for the review of diseases for their inclusion or exclusion in the NBS program. The Framework provides a mechanism to respond to evolving technology but has no ongoing funding. The NBS is a cost-effective approach to minimising disease burden, due to the ability to

i. A Phenotype is a term that refers to ‘the observable physical properties of an organism... [including its] appearance, development and behavior.’

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alter the disease course and thus improve health and wellbeing outcomes^{170,171}. However, to obtain maximum benefit from NBS programs, investment in the full screening pathway is required^{172,173}.

Priority access to the most appropriate expert diagnostic responses for Australians living with an undiagnosed rare disease

As defined in the International Joint Recommendations to Address the Specific Needs of Undiagnosed Rare Disease Patients¹⁷⁴, the undiagnosed rare disease population can be considered in two groups:

- “‘not yet diagnosed’ refers to a patient who lives with an undiagnosed condition that should be diagnosed but hasn’t been because the patient has not been referred to the appropriate clinician due to common, misleading symptoms, or an unusual clinical presentation of a known rare condition”; and
- “undiagnosed (Syndromes Without A Name or SWAN) refers to a patient for whom a diagnostic test is not yet available since the disease has not been characterised and the cause is not yet identified. This patient can also be misdiagnosed as his/her condition can be mistaken for others.”

Without a diagnosis, Australians living with an undiagnosed rare disease cannot be provided with an accurate prognosis and have no access to evidence-based treatment¹⁷⁵. SWAN Australia, an organisation that provides information and support to families caring for a child with an undiagnosed rare genetic condition, states that “when there is no formal diagnosis (parents) struggle to find the right direction to take and know which direction will best assist (their) child’s growth and development¹⁷⁶.” Also, their “medical conditions, physical condition, cognitive processes and behaviours might not make sense¹⁷⁷.” Parents may find it “difficult to connect and engage” with their children¹⁷⁸. Similarly, they can find it difficult to access other services and supports they need. A lack of diagnosis is reported as a roadblock to obtaining adequate funding from the NDIS¹⁷⁹.

There is international recognition that it is important that people with undiagnosed rare disease are identified and have priority access to the most appropriate specialised and expert diagnostic response. Alongside international counterparts, RVA co-authored joint recommendations calling for people with an undiagnosed rare disease to “be recognised as a distinct population with specific unmet needs by national authorities to enable the development of personalised health and social care¹⁸⁰.” This includes recommendations to implement systems to support health and social care professionals in the identification and care for undiagnosed individuals, and to make use of red flag indicators where a diagnosis is unlikely to occur, in order to fast-track a prioritised response¹⁸¹. One of the IRDiRC’s goals is that “all patients coming to medical attention with a suspected rare disease will be diagnosed within one year if their disorder is known in the medical literature; all currently undiagnosable individuals will enter a globally coordinated diagnostic and research pipeline¹⁸².”

Challenges with family planning

Diagnosis provides a critical starting point in providing knowledge for responding to the challenges of family planning in the rare disease context. As already stated, information is important to enable people to make the most informed choices. In an Australian and New Zealand study looking at the supportive care needs of parents with a child with a rare disease, almost half (46%) of the parents surveyed, were dissatisfied or extremely dissatisfied with the support received from health professionals regarding help with family planning. A high number of parents also reported that they were in need of professional support from a genetic counsellor for family planning advice¹⁸³.

The lack of specialist centres and equitable access

Consistency of care and equitable access is vital to people living with a rare disease. Key findings from RVA’s national roadshow on rare diseases in 2014 found that “patient and carer identified aims improve consistency of care and consistency in cost.” Additionally, all workshop groups expressed the view that patients must have fair and equitable access to services. Gaps in service delivery were perceived to exist across states and for those in rural and remote areas, while fragmentation within Australia’s health care system was another concern¹⁸⁴. “General paediatricians in rural

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Australia, where health services are limited, may experience problems when managing children with rare diseases, including obtaining specialist advice and accessing genetic testing and imaging technologies¹⁸⁵.”

Throughout the Action Plan stakeholder consultation process, participants consistently raised the need for centres of excellence or specialist centres for rare diseases. In a 2016 survey of Australian adults living with rare disease, only 22% knew of a specialist centre for their condition. Such centres can consolidate rare disease expertise, increasing continuity and coordination of care^{186,187} and facilitate the co-location of expert rare disease knowledge. Centres could also demonstrate strong collaborations with clinical teams, research teams and rare disease organisations. It has been perceived that “multi-disciplinary clinic(s) could facilitate case coordination. Such centres could undertake various roles including; establishing and managing clinical networks; acting as reference centres and... provide diagnosis, treatment, advice, follow-up care, information and entitlements in a coordinated cross-jurisdictional (e.g. state-state, state-national) manner¹⁸⁸.” These specialist centres could act as an opportunity to respond to implementation across all three Action Plan Pillars.

Internationally, the 2013 *UK Strategy for Rare Diseases* recommended the creation of specialist centres to deliver coordinated and expert care to meet the needs of people living with a rare disease. In France, rare disease centres of excellence are also responsible for improving the coordination of research¹⁸⁹. Elsewhere internationally, centres of excellence have brought together health professionals from a range of medical and allied health professions to provide team-based, integrated services for diagnosis, follow-up and management of people living with a rare disease. In some geographically dispersed regions, centres of excellence are linked by virtual networks. The European Reference Network is an example of this approach, which given the large land mass and relatively small population size of Australia, would be an appropriate approach for Australia. Centres of excellence executed in this manner have the potential to overcome the fragmented and siloed nature of Australia’s health system.

The lack of equitable access to the best available health technology

Why funding of health technologies for rare diseases is crucial

There are limited treatment options for rare diseases. Only a very small proportion of rare diseases have an available treatment; it is often cited that the figure is as low as five per cent¹⁹⁰. Even when a rare disease treatment does exist, financial support may not be available in Australia and thus access may be limited¹⁹¹. An Australian report released in 2014 found that “Australians are generally waiting from two to four years longer for access to rare disease therapies available in comparable countries like the UK, Canada, Germany and the Netherlands¹⁹².”

Stakeholder consultations undertaken in the development of the Action Plan highlighted the need to improve processes to enhance equity and timeliness of access to rare disease health technologies. Meanwhile, the IRDiRC identifies repurposing as a vital, innovative approach to achieving Goal 2 of its rare disease research goals for the next decade (2017-2027). Goal 2 states that “1000 new therapies for rare diseases will be approved, the majority of which will focus on diseases without approved options”¹⁹³.

Reimbursement of health technologies for rare diseases, using models designed for more common diseases, is challenging as smaller patient numbers impact cost effectiveness¹⁹⁴, and there is often less clinical evidence available due to the challenges of conducting large-scale clinical trials¹⁹⁵. This highlights the importance of alternative approaches to both identifying treatment options and funding health technologies for rare diseases¹⁹⁶.

There are many examples of an approved medicine (for a more common condition) demonstrating benefits for rare diseases¹⁹⁷. However, due to small patient numbers, it is not always commercially viable for companies to seek reimbursement for a rare diseases indication¹⁹⁸. Without government reimbursement, many rare diseases medicines are unaffordable for people living with a rare disease and their families. As many rare diseases are progressive, time is often critical, making timely and equitable reimbursement essential for people living with a rare disease to benefit from new and transformative health technologies¹⁹⁹.

Broadening existing HTA principles to acknowledge the challenges of HTA for rare diseases

The Australian Government health technology assessment (HTA) processes reflect the following principles: sustainable; transparent, accountable and independent; consultative and reflective of Australian community values; administratively efficient; flexible and fit for purpose: and informed by robust and relevant evidence²⁰⁰. Despite this, it seems there are still challenges for HTA for rare diseases. Recommendations from a 2014 report on the funding of rare disease therapies in Australia specifically include: “the process for assessing new therapies for rare diseases should be efficient, fit-for-purpose, transparent and informed by community and patient values”; and “the unique nature of therapies for rare diseases, including small patient populations and the implications this has for clinical trials, should be recognised in the evidence requirements for funding²⁰¹.”

Reimbursement pathways for rare disease health technologies

The main reimbursement pathways in HTA are:

- “The Pharmaceutical Benefits Advisory Committee (PBAC) for pharmaceuticals to be funded under the Pharmaceutical Benefits Scheme (PBS) and vaccines to be funded under the National Immunisation Program;
- The Medical Services Advisory Committee (MSAC) for medical services involving new procedures or health technologies to be funded under the Medicare Benefits Schedule (MBS) or other programs (for example, blood products or screening programs); and
- The Prostheses List Advisory Committee for prostheses to be funded through private health insurance arrangements under the Prostheses List²⁰².”

Each of these reimbursement pathways assess health technologies used for rare diseases yet none of these pathways is designed to specifically respond to the inherent features of rare diseases such as the complexity, small patient numbers, and limited data. For rare disease health technologies, these pathways are rarely streamlined or straightforward. “The process for listing a new therapy often involves making multiple submissions to Government, which adds to the costs of bringing new therapies to market and creates additional uncertainty for both patients and manufacturers²⁰³.”

The current HTA system is designed to gain efficiencies through achieving economies of scale and relies on evidence of, primarily, large randomised control trials. It can be challenging for many rare disease health technologies to meet the cost effectiveness and efficacy criteria required to receive reimbursement through reimbursement pathways.

Life Saving Drugs Program (LSDP)

The LSDP is the only reimbursement pathway that is designed to respond to some of the inherent features of a rare disease. It has been described as “an appropriate assessment for medicines that treat rare diseases, recognising the challenges in listing these drugs²⁰⁴.” The LSDP is only applicable to a very small subset of rare disease health technologies and has its own specific criteria relating to prevalence (1:50,000), life-extension, and application approval process. A number of reforms were made to this program in 2018, aiming to provide a “more structured system for consideration” and to “streamline administration²⁰⁵.” Reforms included the establishment of an Expert Panel to “provide advice and assistance to the Chief Medical Officer”; and the provision of a “mechanism to review the effectiveness of the medicines after 24 months²⁰⁶.”

The LSDP is an additional pathway rather than an alternative one, becoming an option after PBAC assessment for the reimbursement of health technologies for eligible individuals with rare and life-threatening diseases²⁰⁷. The LSDP pathway can only be considered if the Pharmaceutical Benefits Advisory Committee (PBAC) has decided that a medicine is clinically effective but not cost effective.

Ongoing review of policy in line with advancements in health technology

With advances in health care, science and technology, an increasing number of co-dependent and hybrid technologies are being developed. As defined by the Department of Health:

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Co-dependent and hybrid technologies can range from a single product with several components to several types of services linked along a clinical pathway. The use of diagnostic testing, including genetic testing, to refine patient selection and eligibility for high cost procedures, devices and particularly medicines, and the continued development of pharmacogenomics (also called 'personalised medicine'), will provide a new approach for tackling disease, and challenges for their assessment.²⁰⁸

These types of health technologies are at the forefront of rare disease care and were a focus of a 2009 *Review of Health Technology Assessment in Australia*. This review noted that, while these technologies “will provide a whole new set of tools and approaches for tackling disease,” they will also provide a range of challenges for their assessment. Central to these challenges is the question of the quality and quantity of available “robust and relevant” evidence, as well as which assessment pathway is most appropriate. The review discusses gaps in the evidence base for co-dependent and hybrid technologies, noting the challenge in establishing an appropriate comparator technology; evaluating the economic impacts of the technologies, such as diagnostic tests; proving cost-effectiveness in comparison with a do nothing comparison case; and conducting robust clinical trials and other studies²⁰⁹.

The advance of co-dependent and hybrid technologies, and the resulting impact on HTA, highlights the importance of ongoing review of health technology policy. The IRDiRC has also identified this need, recommending that jurisdictions consider streamlining approval processes, increasing collaboration in review processes between regulators in different jurisdictions, and updating regulations to assist in the development of new health technologies²¹⁰.

Precision medicine presents a challenge to traditional public health decision-making²¹¹. “Advances in precision medicine, and the technologies that support it, are poised to reshape health care, invigorate biotechnology and ripple out to [other] fields.” Of great significance is the notable rate of advancement “demands that agile regulatory conditions... do not inhibit implementation”²¹².

Lack of access to repurposed medicines

There are many examples of an approved medicine for a more common condition demonstrating benefits for a rare disease²¹³. Due to small numbers, it is not always commercially viable for companies to seek reimbursement for a rare disease indication²¹⁴. Therefore, “in the absence of effective licensed medicines, unlicensed or off label medicines are an important route of access to treatment for rare disease patients”²¹⁵. Anecdotal reports to RVA from people living with a rare disease indicate people find it extremely frustrating and unjust that they have challenges accessing treatments that, in the medical opinion of their doctors, can help them. Particularly given these treatments are readily available for people with more common conditions.

The ability to identify therapeutic candidates for repurposing is likely to increase with the growing ability to undertake large-scale data analytics. Repurposing is one of the benefits of a proposed reconciliation between public health and precision medicine, making the link between the increasingly granular knowledge of disease and pathology, and the power of analyzing big data to reveal alternative uses for existing medicines²¹⁶.

Integrating mental health into rare disease care and support

Being diagnosed and living with a rare disease can be a significant psychological burden for both the individual and their family and carers^{217,218, 219}. Additionally, individuals seeking an explanation for their or their child's symptoms can be mistakenly diagnosed with a psychosomatic and/or psychiatric disorder. This was frequently reported in consultations undertaken during the development of the Action Plan and has been written about widely both internationally and in the literature^{220,221}. A survey into the supportive care needs of parents with a child living with a rare disease found that “parents expressed feelings of; anxiety, fear and worry, followed by anger, annoyance and frustration, and uncertainty, helplessness and vulnerability.” Twenty percent of parents surveyed reported taking medication in the previous week to help them cope emotionally. “A number of parents indicated they were being treated for mental health problems since the birth of their child with a rare disease; 37% of parents said they were being treated for depression, 41% for anxiety and 10% for other psychological problems²²².”

With respect to families, the causes of psychological burden are closely related to parents experiencing mental stress due to caring responsibilities, siblings receiving insufficient attention and partners experiencing relationship changes

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and/or feeling overly depended upon²²³. A survey of parents of children living with a rare disease in Australia and New Zealand found that almost half (46%) reported feeling socially isolated and desperately lonely. Similarly, the most frequent emotions expressed by parents in the week prior to completing the survey were anxiety and fear (53%), anger and frustration (46%) and uncertainty (39%)²²⁴.

Australia's Mental Health and Suicide Plan (the Plan) notes that "effective mental health care, in conjunction with quality physical health care provided early, improves life expectancy and quality of life for consumers and reduces the pressure on the health system." The Plan recognises the relationship between chronic or debilitating physical illness and impacts on mental health needs and highlights early interventions as part of a person-centred treatment and care plan as critical elements of care and support for this group²²⁵.

Peer support and mental health and wellbeing

A key role of rare disease organisations is to facilitate peer support between people living with a rare or undiagnosed disease. Peer support helps to reduce the isolation that comes with rare diseases. The Association for Children with a Disability states that "connecting with other families through peer support groups can help (people) feel more confident, capable and less isolated." This connection can help people to "overcome the challenges and celebrate the joys and gains, no matter how big or small²²⁶." Further investment into rare disease organisations is needed to continue facilitating this support. A survey of parents in Australia and New Zealand revealed that 42% of respondents had no access to a disease specific support group, and 75% had no contact with other parents with a child living with a similar disease²²⁷.

Evidence for each Pillar

Research and Data

The lack of research into rare diseases

For key decision-makers at all levels, greater knowledge of rare diseases can facilitate more responsive and appropriate services for people living with a rare disease and their families and carers. In a 2016 survey of Australian adults living with a rare disease, “respondents indicated an overwhelming desire to be involved in research into their condition²²⁸.” Research shows that “94% of rare diseases lack an approved treatment²²⁹.”

Limited rare disease data

Limited data is a common feature of rare diseases, often resulting in high uncertainty, which impacts every part of people’s lives²³⁰. Limited data is an inherent challenge for rare diseases, due to “low individual prevalence, and consequent propensity for variations in treatment and outcomes²³¹.” It has been stated that for most rare diseases in Australia, “even the most basic information, including incidence and prevalence, are merely estimates²³².” It is unclear “how many patients with a rare disease are receiving treatment; variation in the quality of care and health outcomes across the health systems; and the overall burden of rare diseases nationally²³³.”

The lack of a nationally consistent approach to rare disease data collection

Data collection and research are critical for knowledge building yet in the rare disease context, “there are no standardised data collections or registries for most disorders²³⁴.” 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 rare diseases data ^{235,236,237,238}.

During the Awakening Australia to Rare Disease international symposium, a number of key issues were identified in relation to information, data and evidence, including a nationally consistent approach to data collection by all Governments in Australia, which would allow for information exchange and aggregation²³⁹. These issues were also raised in the Communiqué to Progress a National Rare Disease Plan, which presented key findings from the 2014 RVA National Roadshow on Rare Diseases²⁴⁰, and in RVA’s 2017 advocacy document, *Call for a National Rare Disease Framework: 6 Strategic Priorities*²⁴¹.

The PC has identified that Australian Governments can do much more to allow researchers to access data and link data sets²⁴². Making health data more available could result in significant gains in efficiency, safety, productivity and improved decision-making²⁴³. A study exploring the collective impact of rare diseases in WA found a “marked disparity between the proportion of the population with a rare disease and their combined cost to the state health system²⁴⁴.” This study led to researchers extrapolating that just “inpatient hospital discharges for a cohort selected from the whole of Australia could be estimated as being in the range of AUD \$1.7 billion - AUD \$3.9 billion per year²⁴⁵.”

The PC also identified a need for nationally consistent and coordinated approaches related to genomics data²⁴⁶. It is important for Australia to develop the ability to collect, analyse, as well as safely and responsibly share data, particularly as it relates to precision medicine, which inherently involves personal data, which means privacy is of the utmost importance²⁴⁷. The potential for improvements in policy, research and clinical settings can be supported by access to interoperable datasets with, as framed in the National Health Genomics Policy Framework, “nationally agreed standards for data collection, safe storage, data sharing, custodianship, analysis, reporting and privacy requirements²⁴⁸.”

The importance of health information systems in identifying and measuring rare diseases

In Australia, data for most rare diseases is not captured in either health information systems or registries²⁴⁹ and there is no coordinated strategy to collect, measure, build and translate the data that does exist. “Instead, the impact of rare diseases remains largely hidden due to the inadequate information systems of a healthcare system designed to respond to individual diseases with much larger patient numbers²⁵⁰.”

At a symposium to inform the development of an Australian national plan for rare diseases, “stakeholders suggested that data collection by governments (State and Federal) be standardised so that information can be exchanged and

aggregated across jurisdictions. Participants identified a range of potential barriers in relation to data sharing, including ethical issues and policy requirements for health systems in different jurisdictions, privacy and confidentiality issues inherent in data linkage and ownership of the aggregated data²⁵¹.”

The importance of rare disease coding

The International Classification of Diseases (ICD) “is the global health information standard for mortality [death] and morbidity [disease] statistics.” The ICD enables diseases and health conditions to be recorded using a standardised coding system so that data can be tracked, analysed, and compared. More than 100 countries use ICD in clinical care and research settings for many purposes associated with health care. Approximately 70% of global health expenditure is allocated using ICD²⁵².

In Australia, hospitals have been using the tenth revision of ICD (ICD-10) for reporting mortality data, and an Australian modification of ICD-10 called ICD-10-AM for reporting morbidity data, since the late 1990s²⁵³. ICD-10 can only code 517ⁱⁱ of the almost 7,000 rare diseases listed by Orphanet, the global portal for rare disease²⁵⁴. This represents just over 7% of rare diseases. Additionally, ICD-10-AM is not cross-referenced to Orphacodes which is the universally recognised comprehensive classification and coding system for rare diseases²⁵⁵.

The WHO has initiated a process to update ICD to the eleventh revision (ICD-11)²⁵⁶. ICD-11 was released on 18 June 2018 for implementation from 1 January 2022²⁵⁷. ICD-11 brings mortality and morbidity coding into one classification. The AIHW has conducted a review of ICD-11 to inform and assist decision-makers about ICD-11 and its potential for adoption²⁵⁸. It is anticipated that the ICD update will have significant benefits for rare disease coding, with Orpha coding expected to be formally integrated within ICD-11. Accordingly, the number of rare diseases has increased by ten-fold compared with ICD-10, and 5,400 such diseases listed in the Orphanet database now have unique codes in ICD-11²⁵⁹. Early incorporation of Orphacodes into data collections has been proposed as a means of preparing for ICD-11, with the additional benefit of effectively bringing forward recording and reporting of local rare disease epidemiology²⁶⁰.

Progress in WA

Just as Orphacodes provide a potential tool to track rare diseases, existing congenital anomalies data sets provide a potential source of rare disease data. Congenital anomalies are a large class of mainly rare diseases. The WA Register of Developmental Anomalies (WARDA) is Australia’s leading congenital anomalies data collection, with respect to rare disease coding. It is a statutory and state-wide combined congenital anomaly and cerebral palsy register and is a world affiliate member of EUROCAT and member of the International Clearing House of Birth Defects Surveillance Registers.

As part of a 2016 study, researchers in WA developed a data resource set based on Orphacodes that provided them with a better understanding of the epidemiology of rare disease in WA. This involved a significant matching and validation process, involving ICD-10 codes and ICD-10-AM codes²⁶¹. WARDA has implemented rare disease coding prospectively and is currently undergoing a matching exercise between the British Paediatric Association extension of the ICD ninth revision (ICD-9), ICD-10 and Orphanet, together with the WA Clinical Coding Authority, that also incorporates historical data and use case specific congenital anomaly coding. This is the basis for the introduction of Orphacodes into other health data sets²⁶².

The role of the AIHW and international best practice

The AIHW is committed to congenital anomalies as a core data collection in recognition that they remain a significant public health problem in Australia. However, the country does not have current quality national data on birth anomalies in Australia²⁶³. Despite congenital anomalies being the leading cause of perinatal deaths²⁶⁴, the most recent national publication was released in 2008 using 2002-2003 data²⁶⁵. Despite the 2004 report, *Recommendations for development of a new Australian Birth Anomalies System*, which set out initial parameters for a new Australian Birth Anomalies System, there has been little progress since²⁶⁶.

ii. Specifically, of the 6,954 clinical entities listed in Orphanet, 355 diseases have a unique and specific ICD-10 code, while a further 162 can be mapped to a specific set of ICD-10 codes.

Internationally, England's National Congenital Anomaly and Rare Disease Registration Service (NCARDRS) records people with congenital abnormalities and rare diseases across the whole of England²⁶⁷. The NCARDRS uses Orphanet definitions as the basis for case definition and congenital anomaly and cancer registration as a starting point to achieve a longer-term vision of collecting data on other rare diseases. The NCARDRS aims "to provide a comprehensive national registration service for all congenital anomalies and rare diseases diagnosed and treated in England to support a range of activities that registry data can be used for, including to support and empower patients, inform research and drive wider healthcare system aims, for example, as a data source for clinical audits, to monitor and evaluate the efficacy and outcomes of screening programmes and to evaluate treatment effectiveness." Importantly, despite increasing the coverage of congenital anomaly data collection by more than 100%, there has only been a 20% increase on previous registry budgets due to economies of scale²⁶⁸.

Epidemiological surveillance of undiagnosed rare diseases

SWAN UK estimates that 6,000 children in the UK are born each year with a syndrome without a name, "a genetic condition so rare that it is often impossible to diagnose"²⁶⁹. Extrapolated to an Australian population of over 25 million people²⁷⁰, this equates to around 2,200 children. There is no published data on the number of Australians living (prevalence), or born each year (incidence), with an undiagnosed rare disease.

Those without a diagnosis cannot be represented in ICD and, therefore, Australian health information systems cannot track those living with undiagnosed rare disease. Often, these individuals are formally recognised retrospectively once they receive a diagnosis. This approach has been undertaken to assess the impact of rare diseases on the UK's National Health Service. Once individuals received an accurate diagnosis, researchers then retrospectively studied 10 years' worth of data to understand the cost of their hospital visits and activity during their diagnostic odyssey²⁷¹.

Rare disease registries: importance of data collection

"For any given rare disease, without basic data available through a registry, it is often impossible to take the first critical steps towards improved management or new research²⁷²." Registries "enable the accumulation of relevant evidence" and "can be used to reduce variation in practice and strengthen the evidence base by generating hypotheses for new interventions and facilitating clinical consensus and practice guidelines²⁷³." "Registries, if populated with accurate and high-quality clinical data over extended periods of time, enable health service planning, epidemiological research, clinical trial recruitment and post-marketing drug surveillance²⁷⁴."

Rare disease organisations have expressed that "the environment for rare disease research in Australia would be greatly improved by a nationally coordinated approach to rare disease research infrastructure, in particular, through the establishment of patient registries and biobanks"²⁷⁵.

It is also well recognised that registries play a key role in linking people living with a rare disease with clinical trials for new health technologies (drug treatments and therapies). A 2016 Australian study found that almost 90% of respondents living with a rare disease were interested in joining a patient registry but only 20% were aware of one existing for their rare disease²⁷⁶. A number of rare disease registries have been created around Australia²⁷⁷. However, these registries are mostly being developed and organised independently of one another. Many problems have arisen due to this approach, including:

- duplication of effort;
- poor economies of scale due to the proliferation of disease-specific registries;
- an absence of consistent standards;
- a lack of sustainability due to various factors, including a lack of commitment from data providers, funding cessation, insufficiency or study termination;
- low interoperability of registries (i.e. information collected cannot be directly compared between registries, for example, due to different coding systems being used or different types of data collected);

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- low utility for research due to sub-standard quality control, lack of standardisation of data elements and absence of genetic data;
- low levels of data sharing;
- gaps in disease coverage;
- an absence of a strategic approach to registry creation and development, including some registries being created for short-term or single purpose use only; and
- inadequate involvement of people living with a rare disease and their families in registry creation and development^{278,279}.

The EURORDIS- National Organization for Rare Disorders (NORD)- Canadian Organization for Rare Disorders (CORD) 10 Key Principles for Rare Disease Patient Registries, state that rare disease registries should:

1. Be recognised as a priority in the field of rare diseases.
2. Encompass the widest possible geographic scope.
3. Be centred on a disease or group of diseases rather than therapeutic intervention.
4. Have interoperability and harmonisation between registries.
5. Consistently use a minimum set of common data elements.
6. Where possible, be linked with biobank data and biospecimen access.
7. Include the possibility of data directly reported by patients as well as healthcare professionals.
8. Encourage public-private partnerships to ensure sustainability.
9. Involve patients equally with other stakeholders in governance.
10. Serve as key instruments for building and empowering patient communities²⁸⁰.

In 2018, RVA established a National Alliance of Rare Disease Registries (the Alliance) with the aim to promote person-centred best practice, encourage uniformity around key principles and commit to developing a growing understanding of the national rare disease picture²⁸¹. The Alliance has articulated its alignment with internationally recognised key principles for rare disease registries²⁸² and calls for a nationally recognised, integrated process for ethics approval and consent²⁸³.

Investment into all types of research for rare diseases

At the 2011 rare disease symposium in Australia, stakeholders suggested a broad range of priority areas including “quality of life and social impact studies (e.g. needs of patients/carers); epidemiology and health economics (e.g. prevalence of rare diseases, burden of disease, cost-effectiveness of treatments and health services); and clinical trials (e.g. drug trials, novel therapies)²⁸⁴.” The IRDiRC states that people living with a rare disease need research into: diagnostics (including genomics); development and testing of new health technologies; precision or personalised medicine; and care and support²⁸⁵. Stakeholders at the Action Plan consultations also highlighted the need for research into rare diseases to inform evidence-based policy across all systems, extending beyond health to incorporate disability, social/welfare, mental health, education, employment, and housing.

Research priorities, depending on the specific rare disease, can be different. For example, while translational research may be important for many rare diseases, some rare diseases are not yet in the position to prioritise translational research. For certain rare diseases, the unmet research needs may be investment into data collection and natural history studies, or fundamental discovery (basic) research. Fundamental discovery research forms the foundation from which other types of research can develop²⁸⁶. A growing trend in fundamental discovery research is to focus on understanding the molecular mechanisms that lead to disease phenotypes, with a view to identifying potential therapeutics²⁸⁷ which holds great significance for rare diseases. Furthermore, this type of rare disease research often has implications for the understanding and treatment of more common conditions²⁸⁸. The US’ National Institutes of

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Health (NIH) National Institute of General Medical Sciences supports fundamental discovery research through direct investment into such research projects²⁸⁹ providing a potential model for Australia to customise.

Coordination and investment into rare disease research

Research into rare diseases must address existing gaps and the coordination of research projects must be prioritised²⁹⁰. Despite the unmet need, “there are no specific policies or programs supporting Australian rare disease research²⁹¹.” “In contrast, Europe and the US have significant government-funded programs and initiatives targeting rare disease research, including a strong development program for infrastructure such as registries and biobanks that can be used in the study of any rare disease^{292,293,294,295}.” Improved policy settings, and national and international collaborations, will help to drive strong research and innovation for all rare diseases²⁹⁶.

“In Australia, the National Health and Medical Research Council (NHMRC) is the peak agency for funding health and medical research. At the 2011 rare disease symposium in Australia, participants suggested that the NHMRC must recognise the value of research on rare diseases and allocate funding accordingly. Public/private collaborations and funding mechanisms should also be explored²⁹⁷.”

Stakeholders have also identified that in the rare disease research sector, “stronger research training, career pathways and the attraction and retention of research expertise are required²⁹⁸.” This is likely to occur as a result of increased investment into rare disease research.

Importance of sharing reports and outputs

It is important to continue building the body of rare disease evidence. “Publicly available information on rare diseases is needed for patients, families, health professionals, researchers, policy makers and other stakeholders²⁹⁹.” Two areas in which significant gains can be made are:

- greater reporting on rare disease research by research funding bodies; and
- the increased sharing of outputs from research and post-marketing surveillance, including publications and data.

The IRDiRC has stated that “[r]are disease research results should be rapidly shared and made highly visible to the scientific, health care, patient, pharmaceutical, and medical device communities³⁰⁰.”

This is consistent with the NHMRC’s Open Access Policy, which supports the sharing of outputs from NHMRC-funded research, including publications and data³⁰¹:

The aims of the NHMRC Open Access Policy are to mandate the open access sharing of publications and encourage innovative open access to research data... These approaches will help to increase reuse of data, improve research integrity and contribute to a stronger knowledge economy. Open access will also assist with reporting, demonstration of research achievement, improve track record assessment processes for the long term and contribute to better collaborations.

In some countries, rare disease organisations have developed patient guides to rare disease research. This is in recognition of the knowledge that, in many cases, the people living with a rare disease and their family and carers are the experts in their disease and thus need to be able to understand the latest developments in any research that may relate to their disease³⁰².

Appropriate publishing of data collected under post-marketing requirements can be of great potential in rare disease, allowing researchers to make use of available data in an extremely data-poor environment³⁰³.

Collaborative research into rare diseases

Collaboration and stakeholder consultation are critical to effective rare disease research. Key players include people living with a rare disease; their families and carers; rare disease organisations; researchers; research institutions; clinicians; government; and industry³⁰⁴.

Collaboration is of central importance in precision medicine, which is arguably one of the most important up-and-coming research areas. Traditional siloes will need to be overcome in order to “take full advantage of this technological

shift; to build our scientific workforce; to encourage science, technology, engineering, mathematics and medicine (STEMM) education; to holistically address the ethical, regulatory and legal issues presented by new technologies; and to participate internationally in cooperative projects”³⁰⁵.

Clinical trials in rare disease

Clinical trials are critically important in rare disease. For many people living with a rare disease, participation in a clinical trial may be the only way to access treatment³⁰⁶. Yet there are many hurdles to overcome. For example, when targeted rare disease research funding for clinical trials was announced through the Medical Research Future Fund (MRFF) in 2017, RVA received many anecdotal reports that despite much unmet need, many rare disease communities could not apply as they did not have a registry.

At an Australian rare disease symposium, stakeholders highlighted that “bureaucracy needs to be minimised and the co-ordination of multi-institutional and/or multi-state research needs to be improved, including uniform ethics approval processes³⁰⁷.”

Rare disease research and unique trial designs

The small patient numbers in rare disease means that standard trial designs do not translate well to rare disease research. “The placebo/double blind trial design required by regulatory bodies is usually not possible and innovative trial designs should be recognised for rare diseases³⁰⁸.”

Traditionally, HTA relies on evaluations of efficacy and efficiency based on results of large randomised control trials (RCTs), or systematic reviews of RCTs^{309,310}. There are a number of barriers to RCTs taking place in rare disease, which in turn present challenges to building evidence in rare disease research. These include small and heterogeneous participant populations, and a high proportion of paediatric diseases (thus presenting challenges to participation). Alternative trial designs are therefore critical if people living with a rare disease are to have equitable access to care. The IRDiRC makes several recommendations relating to clinical trials including: considering multi-arm trials utilising international networks; strong engagement of people living with rare diseases in trial design and therapy development; and input from multiple regulatory agencies early and throughout the stages of clinical development (to ensure the trial design is likely to meet regulatory and HTA needs)³¹¹. Models that have been proposed specifically for rare diseases include cross-over trials, which involve administering one or more experimental therapies (often including placebos) sequentially in a specified or random order to the same group of subjects, and ‘N of 1’ trials, which are randomised cross-over trials in which an individual serves as their own control³¹².

The importance of rare disease research being collaborative and person-centred

The contribution of lived experience is of vital importance in rare disease research. It is common for rare disease research to focus on treatments (pharmacological interventions) and success is measured through what are known as surrogate outcomes, such as biochemical markers of the impact of the intervention³¹³. However, people with lived experience of chronic conditions, including children, their carers and the health professionals caring for them, often have markedly different research priorities and outcome measures^{314,315}. At the 2011 rare disease symposium in Australia, “symposium participants indicated... patients, carers and families should be directly involved in decisions about research on rare diseases³¹⁶.”

The policy position of the Australian Government encourages publicly funded researchers to include the voice of patients/consumers in their work. The NHMRC has formally published this position in the *Statement on Consumer and Community Involvement in Health and Medical Research* (2016)³¹⁷. This is in line with the position of other comparable nations and reflects a societal and political view that involving patients/consumers in research is the preferred ethical approach³¹⁸, and that they contribute a valuable perspective on lived experience. However, it has been observed that the presence of this policy position has not guaranteed that Australian rare disease organisations are involved in decision-making to do with research or policy³¹⁹.

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The James Lind Alliance in the UK, which is funded by the National Institute for Health Research, has developed a methodology that facilitates collaboration between the people receiving care, their carers and health professionals to prioritise research questions. The result was a 'top 10' list of clinical research questions that represent the priorities of the patient and professional communities equally. "Attractive to both researchers and funders" such an approach gives certainty to researchers and funders that research will be of significance to the people who will be most impacted³²⁰. When people with lived experience are involved in research priority setting, the identified priorities have a strong relationship to outcomes directly relevant and important to the stakeholders, and a lesser focus on treatments³²¹.

Researchers collaborating with people living with a rare disease

One of the major benefits for investigators collaborating with people living with a rare disease is that they gain a greater appreciation of lived experience.

Placing patients at the center of clinical research, drug development, and evaluation is increasingly recognized as paramount to fully understanding a disease and to identifying meaningful end points. Their knowledge, contribution, empowerment, and participation are crucial to increasing the efficiency of such efforts³²².

Because a rare disease affects every aspect of their daily life, patients and their caregivers become experts of the rare condition and of the important outcomes of diseases that need to be addressed. It is thus critically important to partner with and listen to them³²³.

There is an understanding in the Australian rare disease community that, while research may not lead to better outcomes for people currently living with a rare disease, participating in research may drive change for future generations. This is supported by outcomes of the Rare Barometer survey undertaken in February 2018 by EURORDIS³²⁴.

Researchers and rare disease organisations

There are "major initiatives in both Europe and the US to strengthen rare disease patient organisations' involvement in rare disease research³²⁵." Internationally, rare disease organisations are increasingly a primary source of funding for research investigating rare diseases³²⁶. An Australian study noted that despite not having this same level of investment in rare disease organisations (most are small volunteer-based groups), over 90% of the rare disease organisations surveyed "had a goal to promote or support research on the diseases affecting their members." Additionally, "nearly all (95%) had undertaken at least one research-related activity – such as providing funding or other support to researchers – in the previous five years³²⁷." "However, rare disease patient organisation leaders reported considerable challenges in meeting their research goals. Difficulties most frequently identified were insufficient rare disease patient organisation resources, and a perceived lack of researchers interested in studying their diseases. Other concerns included inadequate rare disease patient organisation expertise in governing research investments, and difficulty engaging researchers in the organisation's knowledge and ideas³²⁸." The study looks at these perceived challenges in light of two systemic issues: "the proliferation of and lack of collaboration between rare disease patient organisations, and the lack of specific governmental policies and resources supporting rare disease research and patient advocacy in Australia³²⁹."

Translation of research into clinical care

The translation of rare diseases research into clinical settings, while currently hampered³³⁰, is vital. Stakeholders at the 2011 Australian rare disease symposium identified "translating research into better prevention, early intervention, diagnosis and treatment to improve health and quality of life outcomes" as a priority³³¹. It was noted that "this requires the integration of research activity within the clinical context³³²." Such collaborations between clinicians and scientists undertaking fundamental discovery research provides benefits in the rare disease context³³³.

Appendix 1: Rare Voices Australia's Scientific & Medical Advisory Committee

Associate Professor Carol Wicking (Chair) – Independent Consultant

Associate Professor Gareth Baynam – Associate Professor, Western Australian Health Department

Professor Alan Bittles – Adjunct Professor and Research Leader, Murdoch University
and Adjunct Professor, Edith Cowan University

Lisa Ewans – Clinical Geneticist, Royal Prince Alfred Hospital and Clinical Associate Lecturer,
The University of Sydney

Professor Adam Jaffe – Head of the Discipline of Paediatrics, University of New South Wales,
Associate Director of Research, Sydney Children's Hospitals Network

Dr Paul Lacaze – Head of Public Health Genomics at Monash University

Dr Kristen Nowak – Director of the Office of Population Health Genomics

Dr Lemuel Pelentsov – Program Director, University of South Australia,
School of Nursing and Midwifery

Professor Jeff Szer AM – Director, Royal Melbourne Hospital

Associate Professor Yvonne Zurynski – Associate Professor, Macquarie University

Dr Kaustuv Bhattacharya – Metabolic Specialist, Queensland Lifespan Metabolic Medicine Service,
Queensland Children's Hospital

Appendix 2: Acronyms

AIHW – Australian Institute of Health and Welfare

CORD – Canadian Organization for Rare Disorders

ELSI – ethical, legal and social issues / implications

EUROCAT – European Surveillance of Congenital Anomalies

EUROPLAN – European Project for Rare Diseases National Plans Development

EURORDIS – European Organization for Rare Diseases

EU – European Union

HGSA – Human Genetics Society of Australasia

HTA – health technology assessment

ICD – International Classification of Diseases

IRDiRC – International Rare Diseases Research Consortium

LSDP – Life Saving Drugs Program

MBS – Medicare Benefits Schedule

MSAC – Medical Services Advisory Committee

MRFF – Medical Research Future Fund

NBS – Newborn bloodspot screening

NCARDRS – National Congenital Anomaly and Rare Disease Registration Service

NDIS – National Disability Insurance Scheme

NHMRC – National Health and Medical Research Council

NIH – National Institutes of Health

NORD – National Organization for Rare Disorders

PBAC – Pharmaceutical Benefits Advisory Committee

PBS – Pharmaceutical Benefits Scheme

PC – Productivity Commission

PCA – Palliative Care Australia

RCT – Randomised control trial/s

RVA – Rare Voices Australia

SMAC – Scientific & Medical Advisory Committee

SWAN – Syndromes Without A Name

UDP – Undiagnosed Disease Program/s

UDP-WA – Undiagnosed Disease Program Western Australia

UDNI – Undiagnosed Diseases Network International

UK – United Kingdom

US – United States

WA – Western Australia

WARDA – Western Australian Register of Developmental Anomalies

WHO – World Health Organization

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