A RESEARCH REVIEW™
SPEAKER SERIES

Awareness of Rare Disorders

Making Education Easy 2022

About the speaker

Lisa Foster
Prior Chief Executive of Rare Disorders New Zealand

Lisa holds a BSc (Hons) degree in biomedical science, with experience as a research scientist in the field of genetics. Lisa also holds a Diploma in Anatomy, Physiology and Massage along with a Certificate in Psychology and a Diploma in Herbal Studies. She has worked extensively in the New Zealand health industry for over 15 years. The range of her experience covers assessing and facilitating care packages for older people, employment and education support in the mental health area and leading a team providing peer led crisis respite care and transitional housing for youth. Lisa was also part of the Be Leadership graduates in 2014. Lisa has a passion for holistic healing and teaching resilience techniques using positive neuroplasticity models.

As well as being the prior Chief Executive Officer for Rare Disorders New Zealand, Lisa is a Board member for the Asia Pacific Alliance of Patient Organisations plus World Health Organisation Collaborative Global Network for Expert Centres.

She is wholeheartedly committed to amplifying the voice of people living with rare disorders to ensure a truly inclusive health system which leaves no-one behind.

Lisa Foster, the prior Chief Executive of Rare Disorders New Zealand, presented this workshop as part of the GP CME meeting held in Rotorua in June 2022 in order to provide improved awareness of rare conditions and offer opportunities, knowledge and resources that allow community practitioners to be better prepared for identifying and managing undiagnosed and rare patients.

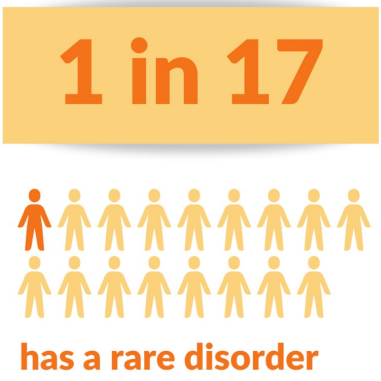
What is a Rare Disorder?

Currently, there is no definition for a Rare Disorder in New Zealand. A disease or disorder is defined as 'rare' in Europe when it affects less than 1 in 2000. Additionally, rare diseases are defined by the European Union as life-threatening or chronically debilitating diseases with low prevalence. They may have aspects of mental health burden and will need multidisciplinary care. Examples include Dravet Syndrome, Tuberous Sclerosis, Muscular Dystrophy, Achondroplasia, Fragile X, and Infective Endocarditis, among many others. Although 80% have a genetic origin, 20% have other areas of causation such as Guillain-Barre syndrome, a rare autoimmune disorder that leads to peripheral neuropathy which is thought to be triggered by an infection.

Why should we care about rare?

Rare Disorders affect a significant proportion of patients and can be very tricky to diagnose and manage.

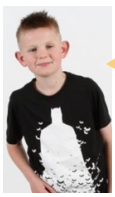
Data from a UK analysis showed that up to 1 in 17 people can be affected, therefore there are an expected 300,000 New Zealanders living with a Rare Disorder.[1] According to the research, conducted using a review of the Orphanet database, rare diseases currently affect at any point in time 3.5% – 5.9% of the worldwide population, equivalent to a conservative estimate of 300 million people worldwide (4% of an estimated world population of 7.5 billion).[1] Improvements in genomics and diagnostic techniques will lead to an increase in this estimation. Orphanet is a 37-country network, co-funded by the European Commission that aims to increase knowledge on Rare Disorders so as to improve the diagnosis, care, and treatment of people with Rare Disorders. Their database is a comprehensive, manually curated and expert reviewed knowledgebase specific for Rare Disorders.



Another reason to care for rare is the massive impact it has on people's lives and a desire to be prepared to support those affected.

Some of the voices of those impacted explain the value of being an informed clinician:

"Sometimes it can be exhausting and incredibly stressful to look at what is happening an try to convey this to others."
Bernadette's Mum Elizabeth



"What would be great is if doctors had more understanding towards parents who know when something isn't right with their kids"
Jarod's Mum Alicia

"It is very scary and at times difficult to navigate the system"
Adam's Mum Michelle

"I have a crazy hope that one day New Zealand care would develop to where all patients are never invalidated or ignored"
Sarah

CASE STUDY: Adam, 15 yrs old

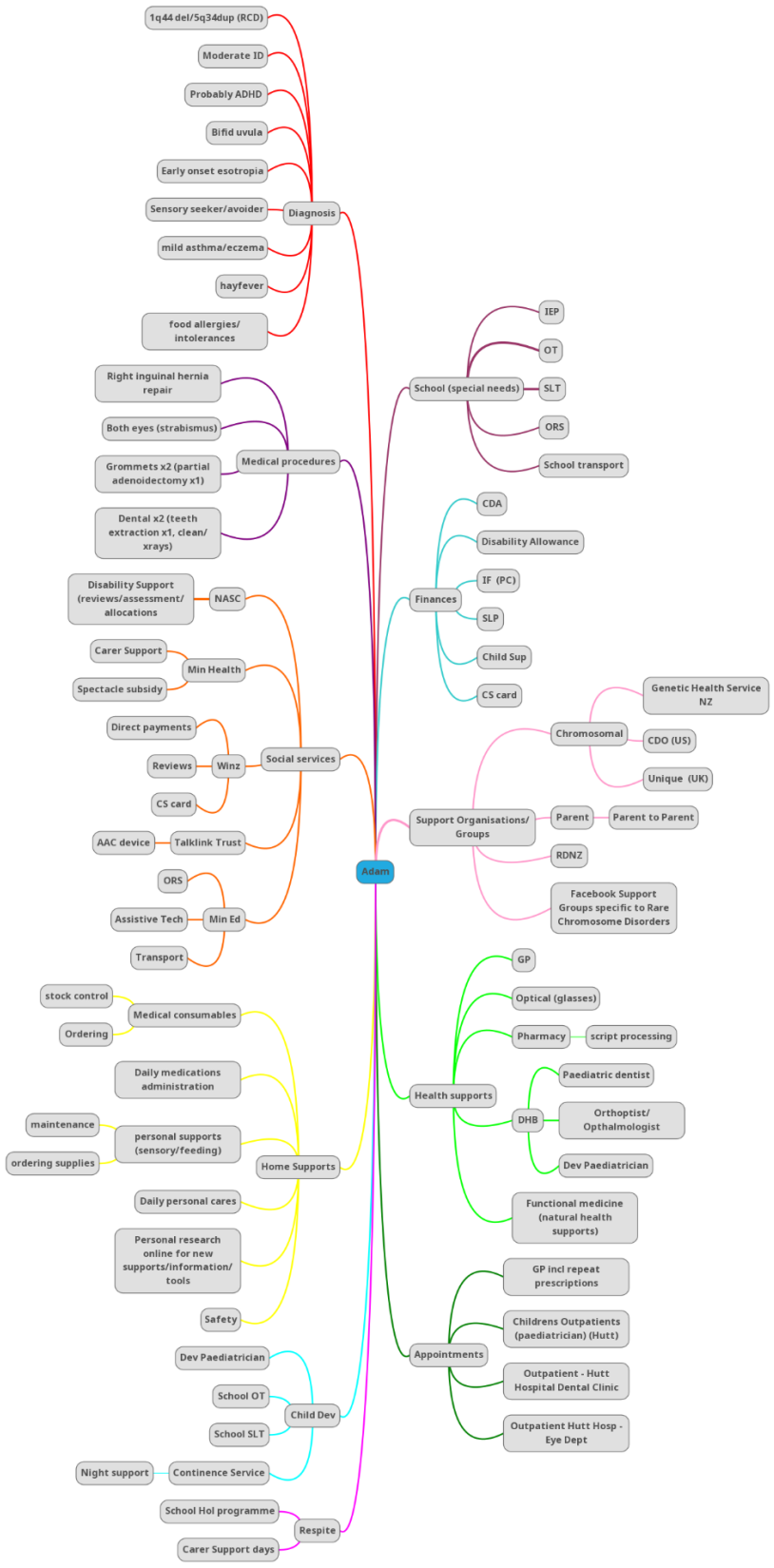


Figure 1: MindMap of complex care and supports in place for Adam

Figure 1 shows a current snapshot in time of the current care and supports in place for Adam who lives in Wellington and has a rare chromosome disorder known as *1q44 deletion* along with *5q34q35 duplication* which leads to a very complicated outcome of symptoms and management. Adam's specific rare chromosome disorder is ultra-rare (<1 in a million) and possibly unique.

Figures 2 and **3** outline the aspects of diagnosis and care that affect the Community Practitioners and other Practitioners including the Specialists caring for Adam. All other areas of Adam's care outlined on the MindMap in Figure 1 are organised by and/or provided by his parents.

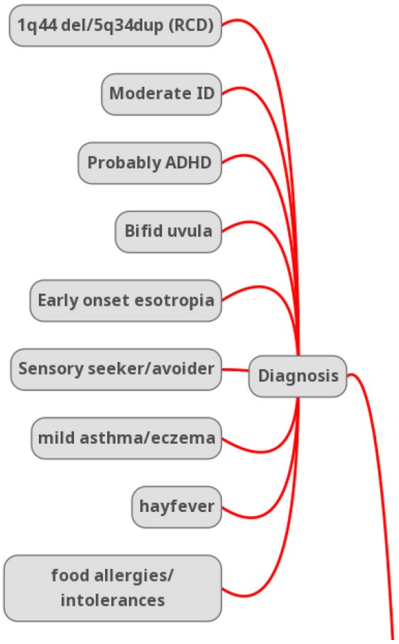


Figure 2: Adam's diagnosis journey

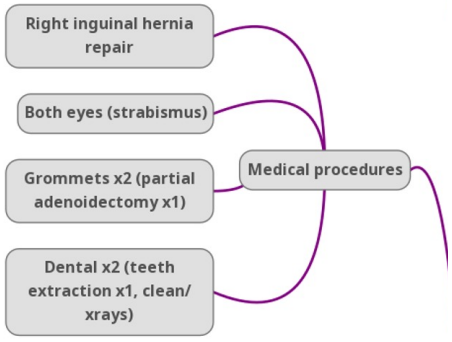


Figure 3: Medical procedures undertaken to assist Adam

The Facts

The *Voice of Rare Disorders* survey was conducted in November 2021 by Rare Disorders New Zealand to fill a significant data-gap in the New Zealand health system, due to the lack of official data collected on Rare Disorders.[2] It fills a vital data-gap in our health system to understand the impact that living with a Rare Disorder has on different areas of life, as well as where the needs are and what barriers exist that prevent people from accessing the treatment and care they need for a decent quality of life.

This survey, which was completed by 718 respondents, highlighted that the utilisation of health services by patients with rare disorders is high with 87% of respondents having seen a GP or specialist in the last 70 days, 1 in 3 presented to hospital per year and with an average of 13 days as an in-patient.[2] Additionally, it showed that the impact on a patient's life is high with 75% of respondents stating that the Rare Disorder made everyday tasks difficult.[2] It reportedly caused a decrease in income for 70% people.[2] In terms of treatment, the survey also addressed medicine access challenges with 85% of respondents taking medicine for their Rare Disorder however in the majority of cases this was to address symptoms of their disorder and not a specific medicine for their disorder.[2]

Other key findings of the survey:[2]

- Over half took longer than one year to get a diagnosis, and for one in five, it took over 10 years;
- There were few accessible, effective modern medicines available for the majority of people, with most being used to relieve pain and inflammation;
- The majority felt that communication and information exchange between different service providers was poor and that professionals are poorly prepared to support them;
- 70% had a decrease in income and limited employment options due to their disorder;
- 57% have experienced increased tension between family members, and 69% experienced isolation from family and friends, amplified by or caused by their rare disorder;
- One in three often felt unhappy and depressed and felt they could not overcome their problems.

Additionally, Rare Disorders continue to have a high impact on children and carers as 70% of rare conditions are exclusively childhood onset, while 20% childhood or adult onset which may be due to being undiagnosed or misdiagnosed earlier, with only 10% being adult onset only.

This data also highlights that while Community Medicine Practitioners may never see specific Rare Disorders, they should expect to see patients with Rare Disorders regularly.

Individually rare, yet collectively common - rare is everywhere!

Complexity and Uncertainty

Health systems are designed for common conditions and as such, Rare Disorders often fall through the gaps. There are mental obstacles created by expecting common things to be causations of symptoms yet the truth is that collectively rare disorders are common.

> *"When you have a rare disorder, you don't fit tick boxes. This automatically places you on the outer and everything you need becomes what feels like an impossible battle with our own health services."*

Rare Disorders often require an overlap of specialities with a broad stretch of need across specialties especially when one genotype of disorder can have drastically different phenotypes caused by processes such as variable penetrance and variable expressivity.

Additionally, obtaining a diagnosis is tough for both patient and health professional with 1 in 5 patients taking 10 years to gain a diagnosis, the majority had to visit 3 or more GPs and 62% of patients being misdiagnosed at least once.

Most Rare Disorder patients face similar challenges of dealing with attitude and dismissal, a lack of knowledge, understanding and expertise and the feeling of their issues being in the 'too hard basket' within an already stressed healthcare system. Once a diagnosis is received, patients often face issues with access to disability and social supports as often Rare Disorders do not fit the boxes to access the disability and health supports that are available. In addition, while medicines to treat a Rare Disorder may exist, the access may not be made available to the patient and their family in this country. The rarity of their condition impacts the patient, the care they receive and the equity of medicine access.

Patients would like their healthcare providers to be following planned pathways of care and using international best practice guidelines for diagnosis and treatment. Additionally, healthcare providers need to be collecting effective and comprehensive data with regard to these patients and their journeys in order to have an accurate picture of their requirements and their needs from the healthcare system in the future.

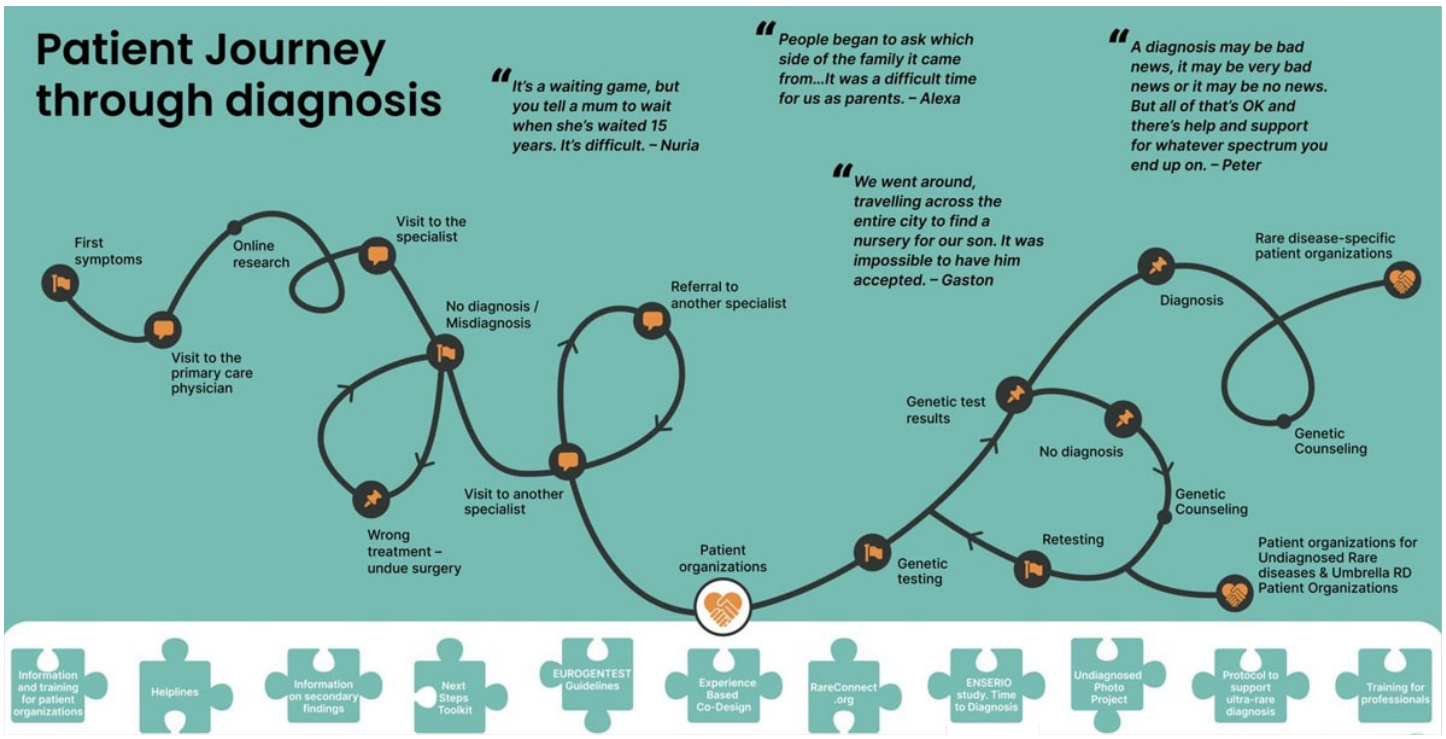
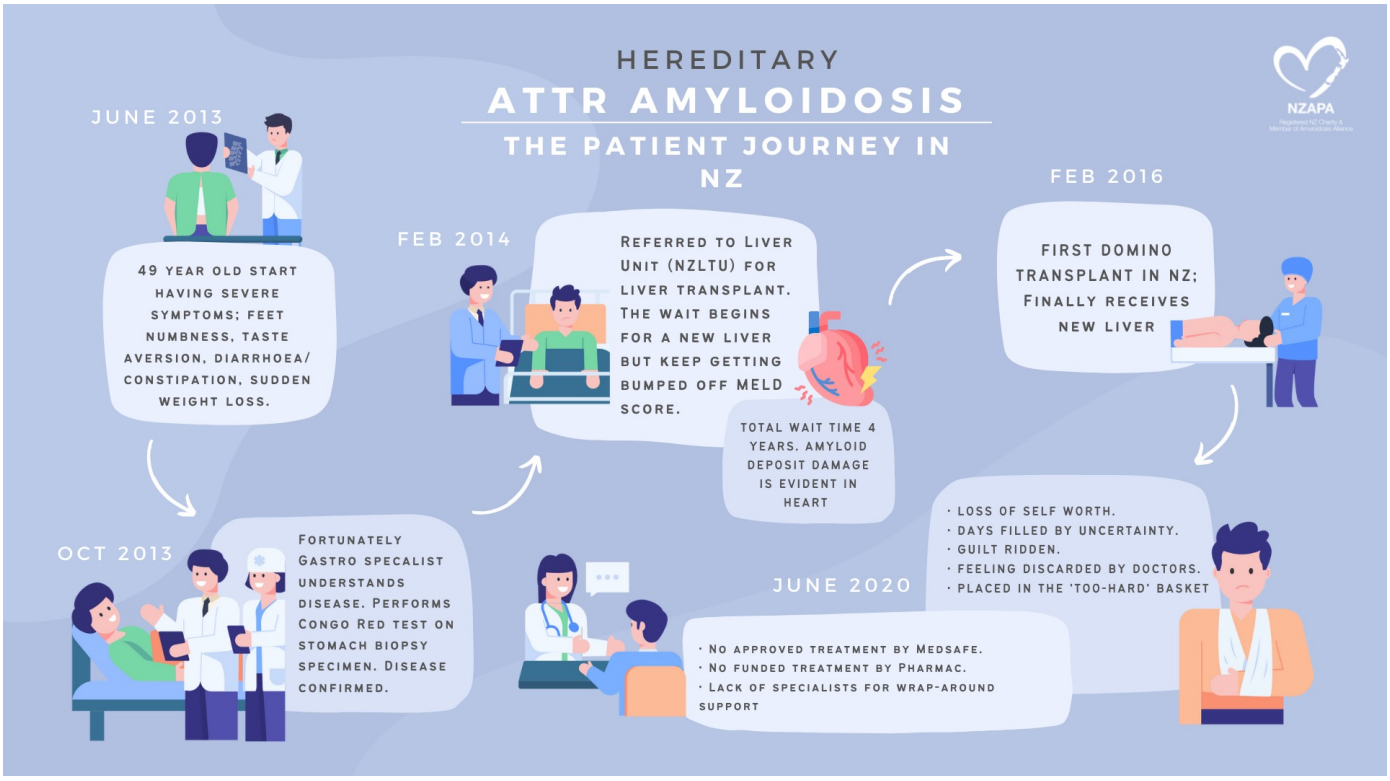


Figure 4: Rare Disorder Patient Journey

CASE STUDY: Aubrey, 58 yrs old



You may be the key to the lock

A person's experience of diagnosis is significantly influenced by the healthcare professionals involved in their care. An individual healthcare professional may offer the key for that person's lock and offer a pathway towards a diagnosis, connection and potential treatment. While marginalised communities experience the hardest pathway, GPs must be equipped to support people living with rare conditions.

Make the difference and turn a diagnostic odyssey into a diagnostic pathway

Prior to diagnosis, Rare Disorders can commonly become invisible illnesses where the struggle and burden is unseen and with patients obtaining the impression that it is all in their head. An important role of the healthcare professional is to let patients know they are heard and the practitioner is willing to ask questions to determine what is going on.

As a healthcare professional, it is important to ask yourself:

- Can you recognise rare flags?
- Do you expect to see patients with rare conditions, and do you know when to suspect one?
- Do you listen to the patient and follow up on symptoms, your own feelings or hunches, or things that don't fit the average diagnostic picture?
- Do you know where to find the resources or knowledge to assist them on their journey?

Community Practitioners cannot do all of the above alone. To be enabled to support people living with Rare Disorders is about having opportunities, resources and being empowered to know where to look. Communicate that while you don't have all the answers you are there with them on their journey, willing to ask questions and make the best effort you can with the time, energy and resources at your disposal.

An important opportunity available to Community Practitioners is sharing knowledge across specialties in to order to gain a diagnosis. A symphony of information can be gained by using a multi-disciplinary approach to help each other across specialities, especially when a Rare Disorder is involved.

With Rare Disorders, diagnostic bias is a challenging reality as 'anchoring' or sticking with a more common diagnosis that they feel the patient may have will affect a healthcare professional's judgement to order further testing, even if other evidence is brought to light. It is important to continue to revisit a previous diagnosis and check on new tests or resources that can be utilised.

Figure 5: Symphony not a Cacophony - Doctors disputing, the patient is ignored. Etching by D.N. Chodowiecki, 1781

To gain the best outcomes for a patient, especially one with a potentially Rare Disorder, it is important for a clinician to be able to listen to concerns, question potential diagnoses, be honest and open, ask for help, and be willing to learn alongside the patient.

Pathways and Resources: Be Rare Aware

Practitioners dealing with patients who may be suffering from Rare Disorders need access to resources and tools to help with solutions. A clinician also needs to feel comfortable in knowing what to do and where to go for up-to-date information.

Rare Disorders New Zealand

Rare Disorders New Zealand (RDNZ) is a central place for practitioners and specialists dealing with rare conditions to come for links, databases and information, and access to specific patient groups.

Who are we?

RDNZ is the only umbrella group for Rare Disorders in New Zealand and provides a strong common voice to advocate for an equitable healthcare system that works for the 300,000 Kiwis with a rare condition. Our rare collective is made up of more than 130 disorder-specific support groups.

What do we do that can help you?

RDNZ can link up practitioners with information and resources as well as offering referrals to patient groups and advocating for policy change for recognition, inclusion and action.

Additionally:

- RDNZ offers a platform and connector hub to link people to information and rare disorder groups specific to their disorder, and helps people navigate the health system.
- RDNZ provides a strong, unified voice to advocate for public health policy and a future healthcare system that works for those with rare disorders.
- They work with the Government, clinicians, researchers and industry to promote diagnosis, treatment, services and research.
- RDNZ continues to advocate for a national framework for rare disorders in New Zealand.
- They facilitate access to individual support groups and also provide a contact point for families who are affected by genetic conditions so rare that they do not have their own support group.
- RDNZ offers clear guidance and information on starting a new support group, plus connect groups to share their knowledge and expertise.
- They promote the issues faced by the rare disease community to increase understanding, motivation and empowerment.
- They work with rare disease groups to communicate their concerns to health officials/government to work for fairness within the health service. They also provide a central point for government to communicate with the rare disease community.
- RDNZ builds rare disease support group networks, and promote partnerships between these groups, clinicians, researchers, government agencies and industry.
- They educate physicians and other healthcare professionals about rare diseases to promote early diagnosis and optimal treatment.

RDNZ helps the many patient voices that they hear by creating clear communication to and through collaborations with: the Health sector including Primary Care; Te Aka Whai Ora/Māori Health Authority; Te Whatu Ora/Health New Zealand; Disability sector; Education sector; Consumer Advisory Groups such as Health Quality & Safety Commission Consumer Advisory Group; and Industry such as Pharma companies.

Collaborative Global Networks for Rare Disease

Healthcare networks for rare diseases are developing around the world, concentrating expertise and knowledge from China and Japan to the United States and across Europe. Networked care is scaling up as an effective model of care for rare diseases, with prevention, diagnosis, care and treatment administered locally, informed by the body of knowledge and expertise from the whole network. Rare disease expert centres will provide a global focus on solutions to reduce the diagnostic odyssey using technology pilots and ecosystem.[3]

Undiagnosed Diseases Network INTERNATIONAL

IRDiRC INTERNATIONAL RARE DISEASES RESEARCH CONSORTIUM

GLOBAL COMMISSION to End the Diagnostic Odyssey for Children with a Rare Disease

Figure 6: Rare Disorders New Zealand Vision

Other Resources

There are a number of online databases containing detailed information on rare disorders. This offers community health practitioners a place to learn more about potential or actual diagnosed rare disorders and can also provide clear, evidence-based material for their patients.

Orphanet (https://www.orpha.net/consor/cgi-bin/index.php?lng=EN) - A database dedicated to information on rare diseases and orphan drugs. Access is free of charge. It provides information on any disease that occurs less often than 1 in 2,000 in the population, whether genetic, auto-immune, infectious, cancers or diseases with no accurate diagnosis. It has most of the numerous rare diseases described in its database.

Find Zebra (https://www.findzebra.com/) - FindZebra is a tool for helping aid the diagnosis of rare diseases using freely available high quality curated information on rare diseases and open-source information retrieval software. FindZebra is intended primarily for physicians and other professionals concerned with diagnosis of rare diseases.

Genetic and Rare Diseases (GARD) Information Center (https://rarediseases.info.nih.gov/) - A public health program of the National Institutes of Health (NIH), National Center for Advancing Translational Sciences (NCATS) that provides health information about rare diseases for the public.

NORD Online Physician Guides (https://rarediseases.org/for-patients-and-families/information-resources/physician-guides/) - A resource for clinicians about specific rare disorders to facilitate the timely diagnosis and treatment of their patients.

NORD's Rare Disease Database (https://rarediseases.org/for-patients-and-families/information-resources/rare-disease-information/) - Brief introductions for patients and caregivers to specific rare diseases.

Specific for clinicians, **Medics 4 Rare Diseases** (https://www.m4rd.org/) provides education and practical tools targeted at medical professionals, enabling them to reduce the diagnostic odyssey and improve the patient experience. Their online module, **Rare Disease 101** (https://learn.m4rd.org/), is freely available in Aotearoa and is aimed at medical professionals with little prior knowledge in rare diseases. It consists of the basic principles of what rare disease is, how you may suspect a rare disease, challenges faced by those living with a rare disease and how to support them.

Genetics in Primary Care UK (https://www.primarycaregenetics.org/?page_id=109&lang=en) developed a simple mnemonic, **Family GENES**, that alerts the clinician to consider genetic causes in the differential diagnosis. In addition to family history, the red flags include **Groups** of anomalies, **Early** or **Extreme** presentations of common diseases, **Neurodevelopmental** or **Neurodegenerative** conditions, **Exceptional** or unusual pathology, and **Surprising** laboratory values.

Lyfe Languages App – is a Universal Medical Translator which translates medical terminology into indigenous languages. It creates culturally appropriate indigenous translations which are available for Health Professionals to access and use from the app. This helps bridge the communication gaps that exist by creating accurate and safe language that is critical for healthcare. It is hoped that this technology may incorporate Te Reo Māori in the future.

In addition, new technologies are constantly being developed that will assist in the diagnosis of Rare Disorders including facial recognition and AI technologies. Where appropriate, genetic health services may also be useful to determine the genetic origin of a disorder and expert centers are being developed worldwide to assist with the diagnosis and management of patients with Rare Disorders.

New Zealand's Strategy for Rare Disorders

Recently, the Pharmac Review Panel has recommended that the Ministry of Health should 'develop a strategy that will lead to better, more timely services and more equitable support and outcomes for people and whānau with rare disorders'. Their report recognises that a cross-agency approach is needed to address the challenges faced by people living with rare disorders, and a Rare Disorder Strategy as part of the Pae Ora (Healthy Futures Bill), is the way forward to ensure improved health outcomes for this population group. This includes the call for rare disorder data to be collected in order to improve our understanding of the needs of this community.

The recently developed Rare Disease Framework from the United Kingdom provides an example of the priorities that a Rare Disorder Strategy may develop.

Rare Disease Framework 2021

Helping patients get a final diagnosis faster	• Rare disease patients across the UK to get a final diagnosis faster and for research into previously unrecognised conditions to identity new rare disease and provide new diagnoses.
Increasing awareness of rare diseases among healthcare professionals	• Healthcare professionals to have an increased awareness of rare diseases, use of genomic testing and digital tools to support quicker diagnosis and better patient care.
Better coordination of care	• Rare disease patients to experience better coordination of care throughout the patient journey.
Improving access to specialist care, treatments and drugs	• Rare disease patients to have improved access to specialist care, treatments and drugs

Figure 7: Rare Disease Framework (United Kingdom)

TAKE-HOME MESSAGES

- **Rare Disorders as a collective are common - prevalence as a whole is 300 million worldwide, 3.5 million in UK and 300,000 in NZ.**
- **Let your patients know they are heard and that you are willing to ask questions to determine what is going on.**
- **Create an access to resources and tools so you feel comfortable in knowing what to do and where to go for up-to-date information to help with solutions.**

REFERENCES:

1. Wakap SN, Lambert DM et al. European Journal of Human Genetics 2020; 28:165–173 https://doi.org/10.1038/s41431-019-0508-0
2. https://www.raredisorders.org.nz/assets/VOICE-OF-RARE-DISORDERS-White-Paper-February-2021-FINAL.pdf
3. Bolz-Johnson et al. Rare Dis Orphan Drugs 2022; 2: 9. DOI: 10.20517/rdodj.2022.01

RARE DISORDERS NZ