

Rare diseases are a 'common' problem for clinicians



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Background

Approximately 8% of the Australian population live with any one of about 10,000 known rare diseases. This is similar to the proportion of people living with diabetes or asthma.

Objectives

The aim of this article is to review the impact of rare diseases on families and health services, and the role of the general practitioner (GP) and policy response in Australia.

Discussion

Research from the Australian Paediatric Surveillance Unit indicates that people living with rare diseases face significant challenges, including diagnostic delays, lack of available treatment and difficulty in finding the right health service. Families feel isolated, under-supported, and often face economic hardship. All GPs see people with rare diseases and have a crucial role in making appropriate referrals, coordinating care, supporting families, and linking them with psychosocial and other supports. GPs require access to current, relevant resources to assist them to help patients with rare diseases. A coordinated national approach to rare diseases is also needed in Australia.

Approximately 8% of the Australian population live with one of about 10,000 known rare diseases. This figure is similar to the proportion of people living with diabetes or asthma. People living with a rare disease, regardless of which specific disease they have, face significant challenges including diagnostic delays, lack of available treatments and difficulty in finding the appropriate health services. Families feel isolated, under-supported and often face economic hardship. General practitioners (GPs) caring for children and adults with rare diseases have a crucial role in making appropriate referrals, providing care coordination and linking families to psychosocial and other forms of support. It is important, therefore, that GPs are aware of information portals and educational resources that will assist them to help patients with a rare disease.

Rare diseases are common

Paradoxically, rare diseases are common. With advances in our knowledge regarding the human genome, we now know of more than 7000 genetic diseases.¹ Numbers of rare diseases are increased by rare injuries, infections, mental health disorders, cancers and adverse events associated with therapies.¹⁻³ Thus, although individually rare, these disorders are collectively common. It is highly likely that all GPs will regularly encounter patients with a rare disorder.⁴ Rare diseases are often complex and chronic. Usually, they have their origin in childhood and are associated with significant disability, impaired quality of life and premature death.² In a French study, 26% of children who attended a disability clinic had disabilities related to a rare disease.⁵ Such diseases place an enormous burden on families, society and health services.⁶ Yet, clinicians lack easy access to educational opportunities and information resources regarding rare diseases.²

A rare disease is defined as one with a population prevalence of less than 1 in 2000.² An estimated 8% of the population is born with, or develops, a rare disorder over their lifespan.^{1,2} However, there are few data sources or registries on rare diseases in Australia, which means these figures are rough estimates at best.

Since 1993, the Australian Paediatric Surveillance Unit (APSU) has collected national data each month on a range of rare diseases from paediatricians, to address knowledge gaps.³

Response to rare diseases in Australia and internationally

Although rare diseases are collectively more common than diabetes,⁷ and almost as common as asthma,⁸ they have been neglected by health providers, policy makers and research funders. The development of a coordinated national plan for rare diseases across the European Union⁹ and the establishment of an Office for Rare Diseases Research within the National Institutes of Health (NIH) in the US¹⁰ attest to the recognition of the importance of rare diseases. Despite calls for a coordinated national plan for rare diseases, Australia has adopted a 'piecemeal' approach (Box 1).^{11–13} The Undiagnosed Diseases Program within the NIH enables clinicians to seek information and advice from rare disease experts across the US to speed up diagnosis and initiation of appropriate treatment.¹⁴ The government of Western Australian has proposed a similar undiagnosed disease program and rare disease framework.^{15,16}

Drugs specifically for rare diseases, if available, are often expensive.¹⁷ Pharmaceutical companies are reluctant to invest in the development and clinical trials of drugs that will benefit a small market. Several countries, including Australia, have adopted 'orphan drug' programs to provide incentives for pharmaceutical companies to bring these drugs to market more quickly. However, few such drugs have been registered in Australia.^{2,17}

Box 1. Key components of a national plan for rare diseases*

- Raise awareness of the burden of rare diseases on families, health professionals, and the community
- Increase knowledge of the epidemiology and impacts of rare diseases in Australia
- Improve healthcare for people with rare diseases through better access to diagnostic tests, new treatments and specialised services
- Promote scientific and social research on rare diseases through the development of national and international multidisciplinary research partnerships
- Develop and disseminate information regarding rare diseases that is relevant to the Australian context for patients, parents, carers and the general public
- Provide educational resources and networking opportunities for health professionals to allow them to better identify and manage rare diseases
- Support families affected by rare diseases by facilitating the development of integrated peer support networks
- Advocate, in partnership with families, for people affected by rare diseases
- Promote development and funding of a national umbrella organisation addressing all aspects of rare diseases

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Impacts on families and support needs

Dr Sandra Dunkelberg, a parent of a child with a rare, undiagnosed disease, said of her experience:

*'I had to find the right doctors, to be insistent but not obstinate. On the one hand, I had to save Mathilda from unnecessary diagnostic tests, often saying "no" and "why?." On the other hand, I had to ensure that she received everything she needed.'*¹⁸

Table 1. Examples of organisations providing information and support to families living with rare diseases

Organisation name	Services provided*
Genetic Alliance Australia www.geneticalliance.org.au	<ul style="list-style-type: none"> • Peer support and linkage with other families • Educational resources and opportunities • Group and individual counselling services
Centre for Genetics Education www.genetics.edu.au	<ul style="list-style-type: none"> • Educational resources for families, including disease fact sheets, pamphlets and other publications • Information regarding newborn screening and genetic testing • List of genetic services • List of genetic counselling services
Steve Waugh Foundation www.stevewaughfoundation.com.au www.stevewaughfoundation.com.au/the-foundation/programs	<ul style="list-style-type: none"> • Grant support for children and families living with rare diseases • Fundraising and networking events • The SNUG (Special Needs Unlimited Group) program provides retreats for families caring for a child with a rare health condition
Variety – The Children's Charity www.variety.org.au	<ul style="list-style-type: none"> • Equipment, medical assistance, and supporting children in educational, sporting, or artistic endeavours and experiences
Rare Voices Australia www.rarevoices.org.au	<ul style="list-style-type: none"> • Advocacy on behalf of the Rare Disease Community • Awareness raising campaigns
Orphanet – the portal for rare diseases and orphan drugs (European-based organisation) www.orpha.net/consor/cgi-bin/index.php	<ul style="list-style-type: none"> • Information regarding rare diseases (searchable by disease or by symptom) • Directory of patient organisations • Directory of clinical trials and research studies
National Organisation for Rare Diseases (US-based organisation) https://rarediseases.org	<ul style="list-style-type: none"> • Information regarding rare diseases • Orphan drugs • Clinical trials • Events and awareness raising

**Examples of services/information only. Please visit the organisation's website to find out more.*

This example illustrates some of the difficulties faced by parents caring for a child with a rare disease. In 2012, the APSU initiated a large study, supported by the Australian Research Council (grant number LP110200277), on the 'Impacts of rare diseases on families'. Australian families reported significant stress as a result of inadequate services and treatment options, the frequent need to seek medical care, feelings of isolation, high costs of caring for a family member with a rare disease, delays in diagnosis, and misdiagnoses.⁶ APSU research suggests that delays in diagnosis and the way in which the diagnosis is given contribute to family distress. One parent said the doctor was 'very clinical and abrupt ... didn't listen to our concerns or offer support'.⁶ Few families received the psychological support they wanted and needed at the time of diagnosis.⁶ Out-of-pocket expenses are significant as families fund equipment and home modifications, which are not funded by health services or other government agencies. *Table 1* lists organisations that provide information, financial support and peer support for families living with rare disease that may be of use to GPs.

Health services needs

It has been said that 'families affected by rare diseases represent a medically disenfranchised population that falls through the cracks of every healthcare system in the world'.¹⁹ The complexity of rare disorders and the need for multidisciplinary care has a significant impact on health providers and health budgets. Hospital admissions and the use of emergency services are common. For example, each year, girls with Rett syndrome have, on average, nine medical appointments and one-third are admitted to hospital.²⁰ Health costs in managing rare diseases are substantial.^{21,22} Overseas, specialist 'rare disease' clinics such as the Agrenska Centre, which cares for multiple rare disease groups, provides multidisciplinary care and has links to peer support groups, costs one-third of the cost of conventional services.²² In Australia, there is a limited number of multidisciplinary clinics for specific rare disorders or groups of disorders (eg genetic metabolic disorders, connective tissues disorders, neuromuscular disorders, Angelman syndrome and Rett syndrome). Many of these clinics are under-resourced, lack sustainable funding and most are located in tertiary children's hospitals, making access for families who live in rural or regional areas of Australia challenging. As Australian doctors increasingly adopt telemedicine into their routine clinical practice, the development of an 'Undiagnosed Diseases Program'¹⁴ could support earlier diagnosis and treatment. This would be achieved by improving access to experts in rare diseases via a virtual clinic for families, GPs and other clinicians working outside of specialised centres.

Transitional care for young people living with rare disease

Because more children with rare diseases are surviving into adulthood, there is increasing demand for transitional care and appropriate services in adult hospitals.²³ Teenagers often feel

abandoned by health services and struggle to negotiate changes in service providers during the turbulence of adolescence.

*'I'm still transitioning, but it's been a trial. I'm too old for paediatrics, but too difficult a case for adult services to treat. I am worried about my health ... I don't know who will treat me properly if I end up in hospital ...'*²³

Table 2. Useful resources for clinicians on the epidemiology, clinical features, diagnosis and management of rare diseases

Organisation name	Services provided*
Orphanet – the portal for rare diseases and orphan drugs (European-based organisation) www.orpha.net/consor/cgi-bin/index.php	<ul style="list-style-type: none"> • Information regarding rare diseases (searchable by disease or by symptom) • Directory of clinical trials and research studies • Directory of centres of expertise
Centre for Genetics Education www.genetics.edu.au/ www.genetics.edu.au/Professionals/genetics-in-general-practice	<ul style="list-style-type: none"> • Educational resources for clinicians, including disease fact sheets, guidelines on genetic testing • A specific resource for general practitioners • List of genetic services • List of genetic counselling services
OMIM – Online Mendelian Inheritance in Man: An online catalogue of human genes and genetic disorders www.omim.org	<p>Comprehensive database of genetic disorders providing information regarding:</p> <ul style="list-style-type: none"> • disease characteristics • diagnosis • prevalence • genotype-phenotype correlations • associated genetic anomalies
National Institutes of Health, Office for Rare Diseases https://rarediseases.nih.gov	<ul style="list-style-type: none"> • Information regarding rare diseases • Genetic educational tools and fact sheets • Information regarding genetic testing and treatments
Australian Paediatric Surveillance Unit www.apsu.org.au www.inopsu.com	<ul style="list-style-type: none"> • Information regarding selected rare childhood diseases including: <ul style="list-style-type: none"> – Australian incidence estimates – diagnosis – disease features and study summaries – national platform for the study of rare childhood diseases; international collaboration via the International Network of Paediatric Surveillance Units • Research on health services utility and health service costs and psychosocial and economic impacts on families living with rare disease

*Examples of services/information only. Please go to the organisation's website to find out more.

Services such as Trapeze (www.trapeze.org.au) and the Agency for Clinical Innovation Transition Care Network in New South Wales (www.aci.health.nsw.gov.au/networks/transition-care/about) provide support during transition. GPs have an important role in coordinating care and brokering linkages with specialist health and social support services for adolescents living with a rare disease.

GPs and rare diseases

GPs have a key role in supporting patients living with a rare disease across the lifespan. Our research showed that 80% of children with a rare disease had visited their GP at least once in the previous 12 months, with an average of eight visits and a range of 1–240 visits each.⁶ Taking a detailed family history, carefully documenting presenting symptoms and signs, and making early referral to specialist services will help decrease diagnostic delays and allow earlier intervention.⁴ GPs have an important role in developing and implementing appropriate care plans and case coordination. In the APSU survey of approximately 462 families, most said they were ‘highly stressed’ (unpublished data). GPs can provide invaluable psychosocial support, referral for support for parents and siblings, and information on parent support groups. Families also reported significant out-of-pocket expenses and the GP can assist families in accessing government (disability and carers allowance) and philanthropic support (*Table 1*). Many families believe their GP is the best source of information regarding their child’s condition (*Table 1*). Routine preventive care, such as vaccination and screening for potential complications of a rare disease, is also important.

Access to information and training

GPs cannot expect to have detailed knowledge of even a fraction of the huge number of known rare diseases, and these cannot be adequately covered in undergraduate or postgraduate medical training. In France, all health professionals, medical doctors, midwives, nurses and paramedics attend a 2-hour training session on rare diseases, which raises awareness and identifies sources of information on rare diseases for health professionals.⁹ All third-year medical students at the Necker-Cochin Faculty of Medicine in Paris are offered an optional 30-hour training course on rare diseases, in addition to the routine genetics training.⁹ Similar courses could be offered in Australia. Our challenge is to enable GPs and other clinicians to have easy access to accurate, locally relevant information that will assist them in making an early diagnosis, providing optimal management and support, and advocating for families living with a rare disease. Some educational resources and information portals relevant to GPs are shown in *Table 2*.

Conclusion

GPs play an important role in healthcare delivery for people living with a rare disease and their families, especially in care coordination, preventive care and enhancing quality of life. GPs should be an integral part of any initiatives undertaken nationally to improve the diagnosis and management of rare diseases.

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References

- Office of Rare Disease Research – US Department of Health and Human Services. About ORDR. Bethesda: ORDR, 2015. Available at <https://rarediseases.info.nih.gov/about-ordr/pages/30/about-ordr> [Accessed 20 July 2015].
- Zurynski Y, Frith K, Leonard H, Elliott E. Rare childhood diseases: How should we respond? *Arch Dis Child* 2008;93:1071–74.
- Zurynski YA, Peardon E, Bower C, Elliott EJ. Impacts of national surveillance for uncommon conditions in childhood. *J Paed Child Health* 2007;43:724–31.
- Knight AW, Senior TP. The common problem of rare disease in general practice. *Med J Aust* 2006;185:82–83.
- Guillem P, Cans C, Robert-Gnanasia E, et al. Rare diseases in disabled children: An epidemiological survey. *Arch Dis Child* 2008;93:115–18.
- Anderson M, Elliott EJ, Zurynski YA. Australian families living with rare disease: Experiences of diagnosis, health services use and needs for psychosocial support. *Orphanet J Rare Dis* 2013;8:22.
- Australian Institute of Health and Welfare. Incidence of type 1 diabetes in Australia 2000–2013. Diabetes series no.23. Cat no. CVD 69. Canberra: AIHW, 2015.
- Asthma Australia. Statistics. Available at www.asthmaaustralia.org.au/Statistics.aspx [Accessed 20 July 2015].
- European Union Committee of Experts on rare Diseases (EUCRED). 2013 Report on the state of the art of rare disease activities in Europe. Available at www.eucerd.eu/upload/file/Reports/2013ReportStateofArtRDActivitiesFR.pdf [Accessed 20 July 2015].
- National Institutes of Health. Office for Rare Diseases Research. Bethesda: NIH, 2015. Available at <https://rarediseases.info.nih.gov> [Accessed 20 July 2015].
- Jaffe A, Zurynski Y, Beville L, Elliott E. Call for a national plan for rare diseases. *J Paed Child Health* 2010;46:2–4.
- Kirby T. Australia makes up for lost time on rare diseases. *The Lancet* 2012;379:1689–90.
- Forman J, Taruscio D, Llera VA, et al. The need for worldwide policy and action plans for rare diseases. *Acta Paediatrica* 2012;101:805–80.
- National Institutes of Health. National Institutes of Health Undiagnosed Diseases Program. Bethesda: NIH, 2015. Available at www.genome.gov/27544402 [Accessed 20 July 2015].
- Western Australia Department of Health – Office of Population Health Genomics. The first Australasian Undiagnosed Diseases Program (UDP) Workshop, 2015. Available at www.genomics.health.wa.gov.au/home/undiagnosed_diseases_program_workshop.cfm [Accessed 20 July 2015].
- Government of Western Australia, Department of Health, Office of Population Health Genomics. WA rare Diseases Strategic Framework 2015–2018. Perth: UDP 2015. Available at <http://www.genomics.health.wa.gov.au/docs/Rare-diseases-strategic-framework.pdf> [Accessed 20 July 2015].
- McKell Institute. Funding Rare Disease Therapies in Australia: Ensuring equitable access to health care for all Australians. Sydney: McKell Institute, 2014. Available at http://mckellinstitute.org.au/wp-content/uploads/pdf/McKell_RareDiseases_A4-New-web.pdf [Accessed 20 July 2015].
- Dunkelberg S. A patient’s journey: Our special girl. *BMJ* 2006;333:430–31.
- Myers A. Rare Diseases: Our most common health problem. In: National Organization for Rare Disorders. *NORD Guide to rare Disorders*. Philadelphia: Lippincott, Williams and Wilkins, 2003;ix-x.
- Moore H, Leonard H, de Klerk N, et al. Health service use in Rett syndrome. *J Clin Neurol* 2005;20:42–50.
- Hime NJ, Fitzgerald D, Robinson P, et al. Childhood interstitial lung disease due to surfactant protein C deficiency: Frequent use and costs of hospital services for a single case in Australia. *Orphanet J Rare Dis* 2014;9:36.
- Olaison A. The Agrenska centre. A socioeconomic case study of rare diseases. *Pharmacoeconomics* 2002;20(Suppl 3):73–75.
- Zurynski YA, Elliott EJ. Challenges of transition to adult health services for patients with rare diseases. *Med J Aust* 2013;198:575–76.