Clarifying the complex:
New guidance for rare disease care

Krista Recsei, Elizabeth Lissiman, Andrew Knight, Hiba Gundru, Natalie Roberts, Lauren McKnight, Adam Jaffe, Elizabeth Emma Palmer

Background
Rare diseases, defined as conditions with a prevalence of less than one in 2000, are a public health priority, as they are collectively common and associated with poor outcomes. General practitioners (GPs) are central to improving outcomes for people living with rare disease by providing holistic, lifelong and family-centred care. However, the complexity, number of rare diseases and system-wide limitations create challenges for GPs and patients alike.

Objectives
This article outlines the challenges faced by people living with rare disease and highlights supportive resources for GPs to provide, facilitate and coordinate care.

Discussion
The new National Recommendations for Rare Disease Health Care (the Recommendations), co-designed with people living with rare disease, provide practical guidance on supporting patients on their journeys. Using a case study, we show how GPs can use the Recommendations.

Even when a patient is still on a diagnostic pathway, or there is no specific treatment or cure, there is always management and validation. These are two things that can make a profound difference to a person's quality of life. And every doctor is capable of giving it.

One of the most helpful things was being consistently treated as part of our child's care team. They asked questions and listened, using this information to discuss decisions around treatment and management with our family. They supported efforts to become better informed by suggesting research papers and other resources. It was really empowering, especially because you often feel so powerless in the face of a rare disease diagnosis.

Quotes from people living with rare disease, Rare Disease Awareness, Education, Support and Training (RArEST) Project.[1] Reproduced from the National Recommendations for Rare Disease Health Care, published under a CC-BY 4.0 license.

A RARE CONDITION is one that affects fewer than one in 2000 people.[2] Over 70% of rare conditions have a genetic basis,[3] such as cystic fibrosis or Angelman syndrome. Others include autoimmune conditions such as sarcoidosis, cancers such as mesothelioma and infections such as Zika virus. In high-income countries such as Australia, rare diseases cause approximately 60% of childhood deaths.[4] People living with rare disease have more unplanned and prolonged hospital and emergency department attendances than people with common chronic conditions.[5–7]

There are over 8000 rare diseases affecting one in 12 people across Australia,[8] a similar prevalence to type 2 diabetes, making rare disease paradoxically common in general practice.[9] The specialist general practitioner (GP) is ideally placed to support people living with rare disease – encompassing people diagnosed with or suspected to have a rare condition, their families and support people.[10] Although knowing about every rare disease is impossible, common approaches to diagnosis and management can greatly assist clinicians in caring for their patients. However, GPs, like all clinicians, report challenges in recognising and enabling a diagnosis and knowing what supports they can access to deliver evidence-based, holistic care for these complex, chronic conditions.[9] The Australian Government and global authorities, including the United Nations and World Health Organization, have recognised rare diseases as a public health priority that requires innovative and coordinated actions.[8,11,12] In response to this need, the Australian Government funded the

Rare Disease Awareness, Education, Support and Training (RArEST) Project to co-design a suite of practical resources for people living with rare disease, health professionals, advocates and decision makers.[13] A key output is Australia's first National Recommendations for Rare Disease Health Care (the Recommendations; Figure 1).[1]

Following the framework of the Recommendations, this article outlines challenges identified by people living with rare disease, highlighting resources that support GPs in providing, facilitating and coordinating care, with an illustrative case example.

The role of specialist GPs in rare disease care

GP expertise in delivering person-centred primary care places them in a central position to help improve outcomes for people living with rare disease. GPs can shorten time to diagnosis by recognising rare disease red flags early (Figure 2) and organising appropriate testing and referrals.[14–16] GPs are perfectly placed to stay on the journey with patients and their families, helping them navigate complex health systems and manage unpredictable symptom emergence and progression.[14,17] This support can reduce unplanned hospital and emergency room visits,[18,19] and it can improve physical and mental health outcomes.[14,18,20–22]

However, GPs have not been well supported. Australia's fragmented and overburdened health system makes it challenging to provide high-quality rare disease care. Rare disease is not explicitly included in The Royal Australian College of General Practitioners (RACGP) or Australian College of Rural and Remote Medicine training curricula, with little continuing professional development available.

Figure 1. The eight recommendations for rare disease healthcare (https://rarediseasesnsw.au/home/national-recommendations).[1]

Challenges faced by people living with rare disease

The rarity of each condition creates shared challenges for affected individuals, their families and health professionals. Most patients have a long diagnostic odyssey, seeing an array of different clinicians over an average of 4–5 years and experiencing at least one misdiagnosis.[23,24] An estimated 50% of people with a suspected rare disease remain undiagnosed.[25] Even with a diagnosis, people living with rare disease and their clinicians face uncertainty on the best next steps because of limited natural history data, consensus management guidelines and treatment options.[26] This uncertainty, along with social, educational and financial impacts, contributes to high rates of mental health conditions among people living with rare disease, as well as frustration and disempowerment for their clinicians.[14,27]

National Recommendations for Rare Disease Health Care

The Recommendations are a new resource providing practical guidance for clinicians on supporting patients on their diagnostic odysseys and beyond.[28] Collaboratively written by a multidisciplinary team of clinicians, researchers, educators and people living with rare disease, they have been recognised as an Accepted Clinical Resource by the RACGP.[1]

The Recommendations are 'disease-agnostic' and outline eight actions health professionals can take to provide high-quality rare disease care (Figure 1). Each recommendation explains why the action is important and how it can be implemented, suggests evaluation indicators, then links to tools, resources and continuing professional development.

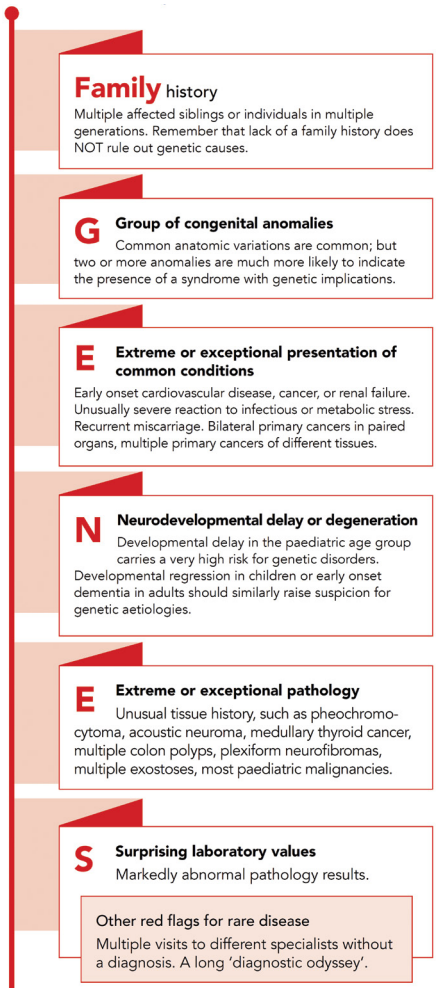

Figure 2. Family GENES tool.[1]

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Conclusion

Efforts to improve outcomes for people living with rare disease are gaining momentum. The Recommendations provide practical, disease-agnostic guidance where little existed previously, emphasising the core importance of empowered clinicians and providing resources to help them walk alongside families.

The Recommendations have acknowledged limitations. Research into rare diseases is limited, both individually and collectively.[1,13] This resource is therefore framed as 'recommendations' based on the existing evidence. It is acknowledged that there are also system-level challenges that health professionals cannot address individually. Future directions include creating rare disease guidelines or standards and developing models of care to address systemic issues. Another role for GPs is to facilitate conversations and connections about research and clinical trials, given that 95% of rare diseases lack a targeted treatment. One ideal opportunity is to link families with patient registries, where they exist, as well as a growing number of disease-agnostic registries such as the Genomics of Rare Disease Registry, launched by the Garvan Institute of Medical Research.[29]

We foresee that GPs will be at the forefront of improving outcomes for patients living with rare disease because of their broad clinical knowledge and expertise in lifelong, person-centred care. It is envisaged that their critical work will be enabled by digital innovation, bringing up-to-date diagnostic tools, clinical guidelines and research opportunity alerts into their practice databases, as well as clear pathways and partnerships with centres of rare disease expertise, co-designed with the rare disease community.[28]

Case study: Mai is searching for answers

We recognise some resources, services and supports in this case study are not currently available to all GPs.

Mai is a single mother aged 22 years whom you supported in her first pregnancy. Her son, Kiêt, was hypotonic at birth and was referred to a neurologist. You saw him often in his first year of life as he had challenges establishing feeding and weight gain, and he experienced recurrent ear infections.

At his 18-month vaccinations, Mai tells you she is worried there may be something 'not quite right' with Kiêt. You notice his facial features are quite distinctive, with widely spaced teeth and a smaller head. Kiêt has no clear words, is not walking and is quite unsteady. You check Kiêt's history against the red flags for rare disease (Figure 2) in *Recommendation 2: Timely diagnosis* (https://rarediseasesnsw.au/home/national-recommendations) and note Kiêt has several features suggestive of a genetic rare disease. You and Mai discuss referral to the local genetics service and a paediatrician. In view of Kiêt's developmental delay, you support Mai's application for funding for appropriate early intervention.

The genetics service requests that you organise some testing. You ask their genetic counsellor for advice about ensuring informed consent. You learn more about chromosomal microarray (CMA) and fragile X syndrome testing through the RACGP (www.racgp.org.au/clinical-resources/clinical-guidelines/key-racgp-guidelines/view-all-racgp-guidelines/genomics-in-general-practice/genetic-tests-and-technologies/chromosome-microarray) and the Centre for Genetics Education (www.genetics.edu.au/SitePages/Home.aspx), and you organise this first-tier testing for Kiêt through your local pathology provider.

Your longstanding relationship with Mai means you are comfortable discussing her anxiety. You provide her with relevant online resources, such as those listed in *Recommendation 5: Mental health, social and emotional wellbeing*, while you plan a long consultation to develop a Mental Health Treatment Plan.

Case wrap-up

The CMA indicates Kiêt has Angelman syndrome. The on-call genetic counsellor provides you with links to patient support organisations and plain language summaries on this rare condition. These resources are also signposted in *Recommendation 3: Share knowledge*.

The clinical genetics service re-triages Kiêt with this result. The family is seen more quickly and offered professional genetic counselling and a referral to an Angelman syndrome Centre of Expertise (CoE), found on the Australian RARE Portal (https://rareportal.org.au). The CoE clinic coordinator offers phone support to Mai and sends you the latest clinical guidelines.

You join a multidisciplinary case conference including Kiêt, the clinical geneticist, the neurologist, the nurse specialist and the clinic's physiotherapist and speech therapist (Medicare Benefits Schedule [MBS] item 758 via telehealth). You support Mai in recounting Kiêt's medical history and conveying her concerns, and you ask your

own questions so you are clear on a plan for ongoing support. The CoE provides you, Kiêt's other specialists and therapists and Mai with a 'rare disease passport' summarising clinical guidelines, research/clinical trial opportunities, and patient support groups (as suggested in *Recommendation 4: Advocacy, research, and new therapies*).

You continue to see Kiêt regularly, providing routine preventive care, updating his management plan and applying appropriate MBS items from the GP chronic care management plan suite (www.servicesaustralia.gov.au/mbs-billing-rules-for-gp-chronic-condition-management-plans?context=20). You provide Mai with information about the International Angelman Syndrome Registry, as she raised interest in being part of global knowledge gain about this rare condition.

You keep yourself, Mai and Kiêt up to date with advances in management for Angelman syndrome as Kiêt transitions into adult services (refer to *Recommendation 1: Person-centred care* and *Recommendation 6: Integrated and coordinated care*).

Key points

- Rare diseases affect one in 12 Australians.
- Currently less than 5% of rare diseases have a curative treatment, and health outcomes are poor, so access to clinical trials, research and psychosocial support for the whole family is paramount.
- GP involvement can reduce diagnostic delay and improve physical and mental health outcomes for people living with rare diseases.
- The National Recommendations for Rare Disease Heath Care are a practical disease-agnostic resource that can support GPs as they care for their patients living with rare disease.
- Further investment is required to develop national standards and novel models of care.

Authors

Krista Recsei BIntStud, MHC, Program Manager, RArEST Project, Discipline of Paediatrics and Child Health, School of Clinical Medicine, Faculty of Medicine & Health, UNSW Sydney, Sydney, NSW

Elizabeth Lissiman MBBS (Hons), FRACGP, Dip Child Health, Year 2 PBL Lead, Lecturer, Curtin Medical School, Curtin University, Perth, WA

Andrew Knight MBBS, MMedSci (ClinEpid), PhD, FAICD, FRACGP, Senior Staff Specialist, Primary and Integrated Care Unit, South Western Sydney Local Health District, Sydney, NSW; Conjoint Senior Lecturer, Discipline of General Practice, School of Clinical Medicine, UNSW Sydney, Sydney, NSW

Hiba Gundru MBBS, FRACGP, General Practitioner, Nurtured Medical, Sydney, NSW

Natalie Roberts BMedSc (Hons), MSc, Project Officer, RArEST Project, Discipline of Paediatrics and Child Health, School of Clinical Medicine, Faculty of Medicine & Health, UNSW Sydney, Sydney, NSW

Lauren McKnight BSc, PhD, Evaluation Lead, RArEST Project, Discipline of Paediatrics and Child Health, School of Clinical Medicine, Faculty of Medicine & Health, UNSW Sydney, Sydney, NSW; Education Advisor, Commonwealth Scientific and Industrial Research Organisation (CSIRO), Sydney, NSW

Adam Jaffe BSc (Hons), MD, FRCP, FRCPCH, FRACP, FThorSoc, John Beveridge Professor of Paediatrics, and Head, Discipline of Paediatrics and Child Health, School of Clinical Medicine, Faculty of Medicine & Health, UNSW Sydney, Sydney, NSW; Consultant in Respiratory Medicine, Sydney Children's Hospitals Network (Randwick), Sydney, NSW

Elizabeth Emma Palmer MBBS, HA (Hons), PhD, Clinical Associate Professor, Discipline of Paediatrics and Child Health, School of Clinical Medicine, Faculty of Medicine & Health, UNSW Sydney, Sydney, NSW; Clinical Geneticist, Sydney Children's Hospital Network (Randwick), Sydney, NSW

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Correspondence to:
Elizabeth.palmer@unsw.edu.au

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References

References are available online only.

correspondence **ajgp@racgp.org.au**

References

1. Rare Disease Awareness, Education, Support and Training (RArEST) Project. National Recommendations for Rare Disease Health Care. RArEST Project, 2024. Available at https://rarediseasesnsw.au/home/national-recommendations [Accessed 14 January 2025].
2. Wang CM, Whiting AH, Rath A, et al. Operational description of rare diseases: A reference to improve the recognition and visibility of rare diseases. Orphanet J Rare Dis 2024;19(1):334. doi: 10.1186/s13023-024-03322-7.
3. Nguengang Wakap S, Lambert DM, Olry A, et al. Estimating cumulative point prevalence of rare diseases: Analysis of the Orphanet database. Eur J Hum Genet 2020;28(2):165–73. doi: 10.1038/s41431-019-0508-0.
4. Gunne E, McGarvey C, Hamilton K, Treacy E, Lambert DM, Lynch SA. A retrospective review of the contribution of rare diseases to paediatric mortality in Ireland. Orphanet J Rare Dis 2020;15(1):311. doi: 10.1186/s13023-020-01574-7.
5. Walker CE, Mahede T, Davis G, et al. The collective impact of rare diseases in Western Australia: An estimate using a population-based cohort. Genet Med 2017;19(5):546–52. doi: 10.1038/gim.2016.143.
6. Navarrete-Opazo AA, Singh M, Tisdale A, Cutillo CM, Garrison SR. Can you hear us now? The impact of health-care utilization by rare disease patients in the United States. Genet Med 2021;23(11):2194–201. doi: 10.1038/s41436-021-01241-7.
7. Zurynski Y, Deverell M, Dalkeith T, et al; APSU Rare Diseases Impacts on Families Study group. Australian children living with rare diseases: Experiences of diagnosis and perceived consequences of diagnostic delays. Orphanet J Rare Dis 2017;12(1):68. doi: 10.1186/s13023-017-0622-4.
8. Australian Government Department of Health, Disability and Ageing. National strategic action plan for rare diseases. Australian Government Department of Health, Disability and Ageing, 2020. Available at www.health.gov.au/resources/publications/national-strategic-action-plan-for-rare-diseases [Accessed 17 January 2023].
9. Knight AW, Senior TP. The common problem of rare disease in general practice. Med J Aust 2006;185(2):82–83. doi: 10.5694/j.1326-5377.2006.tb00477.x.
10. Vidic N, McGlynn A, Abdi F, et al. Integrated care for people living with rare disease: A scoping review on primary care models in Organization for Economic Cooperation and Development countries. J Prim Care Community Health 2025;16:21501319241311567. doi: 10.1177/21501319241311567.
11. United Nations General Assembly. Addressing the challenges of persons living with a rare disease and their families: Resolution adopted by the General Assembly on 16 December 2021; A/RES/76/132. United Nations General Assembly, 2022. Available at www.rarediseasesinternational.org/wp-content/uploads/2022/01/Final-UN-Text-UN-Resolution-on-Persons-Living-with-a-Rare-Disease-and-their-Families.pdf [Accessed 12 February 2024].
12. World Health Organization (WHO). Rare diseases: A global health priority for equity and inclusion; EB156(15). WHO, 2025. Available at https://apps.who.int/gb/ebwha/pdf_files/EB156/B156_(15)-en.pdf [Accessed 16 June 2025].
13. Rare Disease Awareness Education Support and Training (RArEST) Project. Final report. RArEST, 2024. doi: 10.5281/zenodo.13751238.
14. Ferreira RL, do Nascimento IJB, de Almeida VIA, et al. The utilisation of primary health care system concepts positively impacts the assistance of patients with rare diseases despite limited knowledge and experience by health care professionals: A qualitative synopsis of the evidence including approximately 78000 individuals. J Glob Health 2023;13:04030. doi: 10.7189/jogh.13.04030.
15. Boffin N, Swinnen E, Wens J, Urbina M, Van der Heyden J, Van Casteren V. General practice care for patients with rare diseases in Belgium. A cross-sectional survey. Int J Environ Res Public Health 2018;15(6):1180. doi: 10.3390/ijerph15061180.
16. Byrne N, Turner J, Marron R, et al. The role of primary care in management of rare diseases in Ireland. Ir J Med Sci 2020;189(3):771–76. doi: 10.1007/s11845-019-02168-4.
17. The Royal Australian College of General Practitioners (RACGP). Guidelines for preventive activities in general practice. 10th edn. RACGP, 2025. Available at www.racgp.org.au/clinical-resources/clinical-guidelines/key-racgp-guidelines/view-all-racgp-guidelines/preventive-activities-in-general-practice/about-the-red-book [Accessed 30 September 2025].
18. Auth R, Catanese S, Banerjee D. Integrating primary care into the management of cystic fibrosis. J Prim Care Community Health 2023;14:21501319231173811. doi: 10.1177/21501319231173811.
19. McClain MR, Cooley WC, Keirns T, Smith A. A survey of the preferences of primary care physicians regarding the comanagement with specialists of children with rare or complex conditions. Clin Pediatr (Phila) 2014;53(6):566–70. doi: 10.1177/0009922814528035.
20. Morris S, Hudson E, Bloom L, et al. Co-ordinated care for people affected by rare diseases: The CONCORD mixed-methods study. HSDR 2022;10(5). doi: 10.3310/LNZZ5321.
21. Noritz G, Naprawa J, Apkon SD, et al. Primary care and emergency department management of the patient with Duchenne muscular dystrophy. Pediatrics 2018;142(Suppl 2):S90–98. doi: 10.1542/peds.2018-0333K.
22. Willis A, Swann J, Thompson J. Childhood long-term conditions in primary care: A qualitative study of practitioners' views. Br J Gen Pract 2015;65(638):e593–600. doi: 10.3399/bjgp15X686509.
23. Crowe A, McAneney H, Morrison PJ, Cupples ME, McKnight AJ. A quick reference guide for rare disease: Supporting rare disease management in general practice. Br J Gen Pract 2020;70(694):260–61. doi: 10.3399/bjgp20X709853.
24. Faye F, Crocione C, Anido de Peña R, et al. Time to diagnosis and determinants of diagnostic delays of people living with a rare disease: Results of a Rare Barometer retrospective patient survey. Eur J Hum Genet 2024;32(9):1116–26. doi: 10.1038/s41431-024-01604-z.
25. Graessner H, Zurek B, Hoischen A, Beltran S. Solving the unsolved rare diseases in Europe. Eur J Hum Genet 2021;29(9):1319–20. doi: 10.1038/s41431-021-00924-8.
26. Fermaglich LJ, Miller KL. A comprehensive study of the rare diseases and conditions targeted by orphan drug designations and approvals over the forty years of the Orphan Drug Act. Orphanet J Rare Dis 2023;18(1):163. doi: 10.1186/s13023-023-02790-7.
27. Uhlenbusch N, Löwe B, Härter M, Schramm C, Weiler-Normann C, Depping MK. Depression and anxiety in patients with different rare chronic diseases: A cross-sectional study. PLoS One 2019;14(2):e0211343. doi: 10.1371/journal.pone.0211343.
28. Palmer EE, Recsei K, McKnight L, Roberts N, Jaffe A; RArEST Consortium. "You get left behind and lost in a complex world of rare care": Equity in access to rare disease care-learnings from the Australian Rare Disease Awareness, Education, Support, and Training (RArEST) project. EBioMedicine 2025;115:105710. doi: 10.1016/j.ebiom.2025.105710.
29. Kölker S, Gleich F, Mütze U, Opladen T. Rare disease registries are key to evidence-based personalized medicine: Highlighting the European experience. Front Endocrinol (Lausanne) 2022;13:832063. doi: 10.3389/fendo.2022.832063.