Global health for rare diseases through primary care

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Rare diseases affect over 300 million people worldwide and are gaining recognition as a global health priority. Their inclusion in the UN Sustainable Development Goals, the UN Resolution on Addressing the Challenges of Persons Living with a Rare Disease, and the anticipated WHO Global Network for Rare Diseases and WHO Resolution on Rare Diseases, which is yet to be announced, emphasise their significance. People with rare diseases often face unmet health needs, including access to screening, diagnosis, therapy, and comprehensive health care. These challenges highlight the need for awareness and targeted interventions, including comprehensive education, especially in primary care. The majority of rare disease research, clinical services, and health systems are addressed with specialist care. WHO Member States have committed to focusing on primary health care in both universal health coverage and health-related Sustainable Development Goals. Recognising this opportunity, the International Rare Diseases Research Consortium (IRDiRC) assembled a global, multistakeholder task force to identify key barriers and opportunities for empowering primary health-care providers in addressing rare disease challenges.

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Introduction

WHO describes primary health care as a comprehensive approach to address broader health determinants; empower individuals, families, and communities; and meet essential, lifelong health needs of these individuals. Despite international variations in the definition of primary care, strengthening primary care systems has been shown to enhance the effectiveness and efficiency of health-care delivery. The significance of primary health care has been reaffirmed by the WHO Declaration of Astana where participants emphasised the importance of primary health care.[1] Family medicine physicians, general practitioners, nurses, midwives, and others who provide primary care services often serve as the initial point of contact for patients, responding to their concerns and enquiries. With the growing potential for genetic screening and the increasing availability of DNA-based tests for diagnosis and screening, primary care clinicians should be prepared to address patient requests for information or guidance on genetic testing. Primary health care, with its focus on community-based diagnosis, prevention, health promotion, treatment, rehabilitation, and palliation, plays a pivotal role in achieving health for all.

Primary care is a subset of primary health care, encompassing essential first-contact care provided in community settings. It can be delivered by a diverse range of health-care professionals, including doctors, nurses, allied health practitioners, community health practitioners, and pharmacists.[2] Primary care is foundational to health systems and is the only accessible care in some locations; it is, therefore, critical for the wellbeing of people living with rare diseases.

A particular concern is the potentially high proportion of individuals with rare diseases who are currently undiagnosed, who often present complex conditions to primary care providers with a myriad of symptoms that might resemble more common ailments. Without an accurate diagnosis, these individuals are unable to access the necessary services and support required, and are consequently stuck within the health-care system for extended periods.[3] Recognising complexity can lead primary care providers to suspicions of undiagnosed rare diseases, which can enable timely referrals to specialists for accurate diagnosis.

Despite the rarity of each specific disease, the collective impact of known rare diseases affects approximately 300 million people globally, with estimates suggesting the existence of between 6000 and 10 000 known rare diseases.[4] This recognition prompted the UN Resolution on Addressing the Challenge of Persons Living with a Rare Disease and Their Families, and alignment with the Sustainable Development Goals, signifying the emerging public health priority of rare diseases.[5,6]

Linking the services and care provided by primary care providers and acknowledging the role of primary care in service planning are crucial. The diversity, complexity, and multiplicity of rare diseases contribute to substantial disparities in scientific knowledge, clinical expertise, availability of diagnoses and treatments, patient outcomes, and quality of life. However, common elements exist across the diagnosis, therapy, and psychosocial care of rare diseases, which provide a foundation for primary care interventions to address their unmet needs.

The International Rare Diseases Research Consortium (IRDiRC) brings together national and international governmental and non-profit funding bodies, pharmaceutical and biopharmaceutical enterprises, medical device companies, umbrella patient advocacy organisations, and scientific researchers to foster global collaboration and advance rare disease research. IRDiRC covers Africa, Asia, Australia, North America, Latin America, and Europe, and aims to ensure an accurate diagnosis, care, and available therapy for all people with rare diseases within 1 year of seeking medical attention. This vision is accompanied by three goals for 2027: to improve and expedite the diagnoses of rare diseases; to contribute to the development of 1000 new therapies, focusing on rare diseases without

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For more on the **Genetic Testing Registry** see https://www.ncbi.nlm.nih.gov/gtr/

For more on the **International Rare Diseases Research Consortium** see https://irdirc.org

approved treatments; and to develop methods for measuring the impact of diagnoses and therapies on patients with a rare disease. The IRDiRC has assembled task forces and working groups to address actionable topics identified by the consortium in achieving its vision and goals. IRDiRC established the Primary Care Task Force by convening international representatives from stakeholders who were essential to identifying priority rare disease research areas within primary care. Acknowledging the broad scope of primary care, the Task Force identified four key areas while recognising the potential for future IRDiRC activities to address additional areas of importance with future task forces and working groups. The four key areas discussed in this Health Policy are: access to diagnosis and therapies and awareness of rare diseases; training and education on rare diseases; referral pathways and care coordination; and data sharing and digital health.

Methods

In 2020, IRDiRC launched a call for activity proposals to address gaps in rare disease research from within its consortium. The IRDiRC Consortium Assembly comprised executives and leaders from 30 major funding bodies, 12 industry representatives, 17 patient advocacy group representatives, and six scientific experts serving as chairs of the IRDiRC scientific committees. The consortium identified primary care as a crucial area in rare disease research that lacked attention. Consequently, it was established as an IRDiRC Task Force in 2021. The current objectives of the Task Force are to bring together stakeholders to identify priority research areas in primary care that align with IRDiRC goals, and to identify the challenges and opportunities for rare disease research in primary care.

To ensure a global perspective, the IRDiRC Scientific Secretariat recruited global opinion leaders in rare disease specialist and primary care through social media and the IRDiRC website. Umbrella rare disease patient advocates, who work with diverse groups of rare disease patient advocates, were also recruited through the same channels. The Task Force included family medicine doctors, nurses, pharmacists, patient advocates, people with rare diseases and their family members, geneticists, genetic counsellors, funders, researchers, and industry representatives, and spanned a broad geographical coverage.

Key findings of the Task Force

Access and awareness of rare diseases

The accurate and timely diagnosis of rare diseases is crucial in facilitating early intervention and avoiding extended diagnostic odysseys, which are characterised by misdiagnosis and diagnostic delays.[7] Despite a lack of readily available treatments for most rare diseases, people with rare diseases can still benefit from various therapies, such as physiotherapy and speech and language therapy, which can support childhood development and mitigate the burden of rare diseases. However, primary care providers have expressed concerns about the ethical dilemmas and profound psychosocial effects of genetic testing in their daily practice, which indicates the need for improved education and support in managing these challenges.[8] The involvement of primary care providers in the care of people with rare disease remains unclear, highlighting the importance of identifying and integrating these people with rare disease in primary care systems for improved health-care planning and epidemiological research.[9]

Genetic testing shows promise in diagnosing people with rare diseases, as over 72% of rare diseases have a genetic basis.[10] Next-generation sequencing and other technologies have facilitated the time-effective and cost-effective diagnosis of most genetic diseases, but substantial challenges hinder widespread adoption. The lack of genetic workforce capacity is a global concern, even in high-income countries,[11] with many regions and countries lacking sufficient genetic expertise. The low reimbursement by governments and private insurers for genetic services also poses an additional barrier. The combination of these factors prevent primary care providers from referring people with suspected rare disease to specialists, which delays diagnosis and treatment. The diagnostic odyssey might also be extended due to inappropriate testing, which could also incur financial loss for both people with a rare disease and health-care systems, due to single gene tests being ordered instead of genomic testing. The misinterpretation of genetic test results, such as false-positive diagnoses or the incorrect labelling of variants of unknown significance as diagnostic, could have devastating consequences. A failure to identify and address these risks (eg, presymptomatic testing, incidental findings, or false positives) when testing people for rare diseases can lead to further action, such as the need for cascade testing in families.

To address these challenges, health-care systems need to widen the availability of genetic services and ensure appropriate reimbursement. Primary care providers might require additional education to enhance their knowledge of and confidence in genetic testing. They might also need guidance on when and where to refer patients, along with how to effectively collaborate with medical geneticists and genetic counsellors for diagnosis and care that extends from preconception, preimplantation, and prenatal testing to palliative care.

In 2019, Yang and colleagues[12] reviewed 223 early neonatal deaths by whole exome sequencing and identified that a quarter could have had improved treatment with timely genetic diagnosis and counselling. For presymptomatic neonates, neonatal screening can identify genetic and other disorders to prevent or ameliorate illness. Traditional mass spectrometry can screen some metabolic genetic diseases with blood

biomarkers, whereas genomic sequencing can delineate the range of detectable diseases.

Primary care settings can provide an opportune environment for supporting the early diagnosis of rare diseases. Primary care providers can be educated about the warning signs of rare diseases, such as family history, groups of congenital anomalies, extreme or unusual presentations of common conditions, neurodevelopmental delay or degeneration, and extreme or exceptional pathology. These warning signs, also sometimes referred to as red flags, can be incorporated into primary care pathways to enhance the detection and referral of rare diseases.[13] The use of artificial intelligence (AI) and machine learning algorithms can support the identification process by analysing electronic health records, and developing prediction models to expedite diagnosis and improve care, while reducing costs. Morley and colleagues,[14] established a machine learning prediction model to identify people with suspected genetic diseases from electronic health records; this model could be used to speed up diagnosis, improve care, and reduce costs. Bastarache and colleagues[15] also designed phenotype risk scores to detect Mendelian disease patterns that can be used to identify people with undiagnosed Mendelian disease.

Increased access to and understanding of genetic and genomic testing does not guarantee treatment with a pharmaceutical agent for an individual with a rare disease. First a pharmaceutical agent must be designated an orphan drug, and after this designation the journey to patient access varies internationally. The term orphan drug is frequently used for rare disease therapies as, colloquially, rare diseases are often considered orphans due to a relative absence of attention to rare diseases and the development of treatments. The Orphan Drug Act defines orphan drugs as "a medicine, vaccine, or in vivo diagnostic agent that meets the requirements of regulation 16J of the Therapeutic Goods Regulations 1990".[16] Health technology assessment bodies have been created to scrutinise an innovation's quality of evidence to inform decision making on its health-care coverage and reimbursement.[17] Orphan drugs which are not aligned with health technology assessment standards are likely to face delays in patient access, which can be overcome by designing more flexible and fit-for-purpose health technology assessment processes. Early multistakeholder collaboration and scientific dialogue, particularly those that have included people with rare diseases, have been identified as effective paths in improving evidence-based decisions in rare disease.[18]

Once a country, government, or payer decides to reimburse a rare disease product, access to these orphan drugs is given to pharmacists in hospitals and in the community. The coordination of primary care providers, such as doctors, nurses, and pharmacists through targeted education, enhanced referrals, and best practice guidelines will provide the knowledge and pathways to improve the patient's adherence to medication, early detection of side-effects, reimbursement issues, and clinical follow-up. Compounding of pharmaceutical products can be done by community and hospital pharmacists for commercially unavailable products or during medicine shortages.[19] Awareness of rare disease trials in primary care can assist with the recruitment of people with a rare disease. Additionally, decentralised clinical trials within primary care for therapies could be further explored to increase access and equity.

Multidisciplinary clinical approaches, including pharmacists and general practitioners, combined with state-of-the-art genomic technologies, need to be implemented with agility to identify people with a rare disease earlier by referring these individuals, in a timely manner, to an expert centre. People with a rare disease can find information about their disease on websites such as Orphanet, the National Organization for Rare Disorders, and the US National Institutes of Health Genetic and Rare Diseases Information Center.

For more on **Orphanet** see https://www.orpha.net

For more on the **National Organization for Rare Diseases** see https://rarediseases.org/

For more on the **Genetic and Rare Diseases Information Center** see https://rarediseases.info.nih.gov/

For more on the **primary care collaborative** see https://www.pcpcc.org/about/medical-home

Training and education in rare diseases

Primary care plays a crucial role as the initial, and sometimes the sole, point of contact for people with a rare disease, and has the potential to serve as their medical home.[9,20] It is, therefore, important to prioritise education and capacity building in rare diseases in primary care, including the integration of education with specialist services, to enhance diagnosis and care.

Primary care providers should comprehensively understand the characteristic features and needs that intersect rare diseases, and be equipped to address the physical, mental health, and social needs that are common among people with rare diseases. This responsibility includes accessing reliable and up-to-date disease-specific information, guiding people with a rare disease towards appropriate advocacy and patient support resources, and possessing the necessary skills to appropriately identify, manage, and refer people with a rare disease.

For more on the **International Network of Agencies for Health Technology Assessment** see https://www.inahta.org/

People with rare diseases often present with many symptoms affecting multiple organ systems. Consequently, they often require multiple appointments with various specialists, across numerous care sites. Given the complexities of the diagnostic journey and the challenges associated with managing rare diseases, two critical intervention points emerge; namely, the identification and referral process and care coordination.

Primary care providers, such as general practitioners and paediatricians, are often the first point of contact and the referring physician for people with a suspected rare disease. However, some people with a rare disease are seen by specialists directly to manage individual phenotypes. These individuals are often adults or in countries where the health-care system is decentralised. For example, a person with Fabry disease (also known as α-galactosidase-A deficiency, which occurs when the

enzyme α-galactosidase-A cannot efficiently break down lipids into energy-providing components) might be followed up by a cardiologist for cardiomyopathy, a nephrologist for renal impairment, and a neurologist for a neurovascular event. Under-recognition of the unifying diagnosis prolongs the diagnostic odyssey and leads to suboptimal care. In the given example, Fabry disease is treatable with enzyme replacement therapy, which, if received early, reduces morbidity and mortality.[21,22] A common strategy is to educate the individual specialist, especially with the warning signs that would generate suspicion of a rare disease, although there are few data on the efficacy of this approach. [7]

Given the complexity and lifelong impact of rare diseases, multidisciplinary and coordinated cross-sector care (eg, physical and mental health, education, employment, and disability) are crucial to health and wellbeing. Multidisciplinary care clinics or networks allow for streamlined care with reduced burden for the individual and their family.[23] Many such networks, including those that provide care to people with cystic fibrosis or neurofibromatosis types 1 and 2, are often affiliated with patient organisations to enhance and facilitate access. However, a survey of these networks showed access limitations, especially for adult patients and those with rarer conditions.[24] When these networks are unavailable, effective communication between geneticists, medical specialists, and primary care providers is imperative for optimising patient care. Equally, in the presence of such clinics, active primary care provider participation can improve outcomes. Collaboration between primary care providers, health pharmacists, and allied health providers is important as orphan drugs are deployed in the community, as collaboration allows the dissemination of information on use and contraindications and can collectively ascertain real-world data to advance development and improve outcomes. Research on how best to support the increased participation of primary care providers in multidisciplinary clinics and in care for rare disease is needed.

For more on **Rare Voices** see https://rarevoices.org.au/

A mixture of approaches is required to educate the diversity of primary care providers in responses to the unmet needs of people living with rare diseases (eg, early identification and referral, care and co-ordination, mental health and social support) and to accommodate rare disease interventions in often time-constrained primary care workflows. To complement much needed embedding of rare diseases in undergraduate training across the full spectrum of health-care providers, accessible approaches that use adult learning approaches that can evolve are required. Project ECHO is an adaptable, robust, and internationally deployed online method that creates communities of practice through a combination of case-based and interactive learning to educate between primary care provider and specialist care. ECHO has been used for both rare diseases and other diseases. Additionally, Rare Disease 101 by Medics4RareDiseases is a series of online modules that originated in the UK and are being updated and adapted for other jurisdictions, such as Australia and Africa, and could be tailored to various health-care roles. On-the-go education could also be built into primary care provider electronic health records. Research is required to further advance, implement, and assess these methods to develop other approaches, including those that can be deployed through mobile health platforms and in areas with little or no internet connectivity. Developing strategies that cater to multiple languages and cultural contexts is crucial to ensure inclusivity and relevance.

For more on **ECHO** see https://hsc.unm.edu/echo/

For more on **Medics4RareDiseases** see https://learn.m4rd.org/

Lessons from low-income and middle-income countries, such as the door-to-door efforts of the Accredited Social Health Activist workers in Telangana state in India,[25] offer adaptable solutions for high-income countries. In remote Western Australia, the role of Aboriginal Community Health Worker was created to engage communities, with rare disease education integrated into their training. The training modules cover warning signs, common challenges, family history taking, and sociocultural aspects. The modules are in Aboriginal languages, aligned with Aboriginal narratives, and cover real-world capacity building, telehealth, and online communities. General practitioners in rare diseases Centres of Expertise link practical expertise to primary care, as occurs in the Rare Care Centre,[26] whereas the Rare Disease Awareness, Education, Support, and Training project by Rare Voices Australia develops resources for self-advocacy among Aboriginal people with a rare disease, guiding interactions with health-care providers.

Referral pathway and care coordination

Equipping primary care providers with adequate education in genetics and genomics, as well as access to rare disease case-finding resources can enhance referrals to specialist services for people with a rare disease.[27] Additionally, clear guidelines from clinical geneticists and other specialists can support the appropriate use of genetic services by primary care providers. Equitable access might be an issue when genetic services are siloed within tertiary centres, especially for marginalised and underserved populations. In their scoping review, Chou and colleagues[27] describe barriers to the integration of medical genetics into primary care, particularly in medically underserved communities, and potential strategies to overcome them. To effectively bridge the gap in primary care provider clinical genetics and rare disease knowledge, while increasing capacity and augmenting access to genetic services, three evidence-based strategies were proposed: telegenetics (a method that uses different technologies to provide genetic services); learning communities; and a partnership trio between primary care providers, people with a rare disease and their families, and clinical genetics providers—effectively creating a version of the patient-centred medical home.[28] Further research is needed to explore how these

service-delivery models in primary care are experienced by referring primary care providers, and the potential impact of these models on people with a rare disease.

Genetic conditions are complex, multisystem diseases; thus, their case management is cross-disciplinary. Primary case managers act as a patient's primary coordinator, facilitator, advocate, and record keeper. Prediagnosis, the person with a rare disease or their family member interacts primarily with the soon to be case manager, in conjunction with a primary care provider. Referrals to specialists might occur, resulting in growing challenges for patients and their families as their levels of involvement in health care deepens.

However, care coordination could be fragmented, with specialists focusing solely on their fields as an isolated entity (eg, cardiac or respiratory) without considering the broader context. This can result in patients and their families facing time constraints, scheduling conflicts due to multiple appointments or competing appointment spots, and challenges in managing their care effectively.

Once a diagnosis is obtained, a specific case manager might be assigned. Even with case management, undiagnosed patients and their families consistently struggle to justify their eligibility for financial support and funding for access to services and treatment. Post diagnosis, effective case management empowers and assists patients and their families, through early education and timely genetic counselling, to advocate for their tailored health needs and fosters a sense of self-efficacy and understanding. Addressing this essential aspect of holistic, cost-effective health care should be prioritised.

Patient-centred care is a standard model adopted in health-care services but due to the rarity, complexity, and high psychosocial burden of rare diseases, people with rare diseases and their families play a more integral role in the care team, compared with those with non-rare diseases.[29] Two-way learning between health-care providers and affected individuals is crucial to reshape the patient–clinical partnership. The health literacy of people with a rare disease and their families directly impacts their ability to navigate and access health-care services effectively. In this context, patient advocacy groups play an important role in enhancing health literacy and guiding families through complex health-care systems. In both low-income and high-income countries, primary care providers and community health workers might lack information on rare diseases, relying on patient groups and organisations for guidance to optimise care pathways. Patient groups and organisations serve as valuable referral sources, particularly when primary care providers suspect a rare disease, as these organisations possess in-depth knowledge of the system, including available resources and expertise. Connecting with a national alliance for rare diseases can be particularly beneficial for primary care providers in accessing expertise and resources.

Drawing insights from economies where rare disease care is still developing, people with rare diseases and patient groups have emerged as leaders in the development of referral pathways. Rare disease referral pathways intersect the research and health-care systems, highlighting the importance of their integration to ensure that patients receive optimal care while benefiting from research infrastructure, such as the potential for diagnosis through a research pathway. By merging care and research within referral pathways, health-care systems can create a more comprehensive and cohesive approach to rare disease management. This integration ensures that people with a rare disease receive appropriate care, and benefit from the advancements and resources available within the research setting.

Data sharing and digital health

Data accumulated via longitudinal records are a key enabler of understanding the natural and treated history of rare diseases across the lifespan, underpinning progress on diagnosis, treatment, and ongoing care.[30] Unfortunately, the flow of data in the overall diagnosis process is often non-existent, or reliant on unstructured artifacts (eg, emails, faxes, and printed or electronic documents). This fragmented data exchange between primary care providers and specialists during the diagnostic journey leads to individual data artifacts focused on localised health issues. To expedite the diagnostic process, capturing, coding, and sharing data effectively is crucial.

Data sharing remains complex due to the involvement of numerous stakeholders and variables. Primary care providers' willingness to participate in data sharing initiatives depends on their perception of trust in the organisations receiving and analysing the data.[31] Regional or national programmes are crucial for people with rare diseases as they enable the collection of a critical mass of data that is necessary for developing appropriate care pathways from the bottom up. Concerns related to trust, governance, and secondary use of data continue to hinder data sharing, potentially impacting the business models of primary care providers.[31]

Patients, especially those with complex or unknown conditions, are usually willing to have their data shared within and beyond the practice for medical care purposes, such as seeking second opinions or referrals to secondary care. Primary care providers, in collaboration with advocates, need to develop policies on data sharing, raise awareness among people with rare diseases about the contents of their records, and improve patient understanding of data sharing processes.[31] Ensuring correct data sharing of orphan drug and device use between hospital, specialty, and community pharmacies is crucial for providing optimal care and treatment adherence.

Effective data capture and coding are products of the digital health strategy, which shapes practices and technological adoption. Embracing a digital-first approach in primary care can lead to a transition towards preventive

Panel 1: Key areas of focus and recommended interventions

Awareness and diagnostic access

Awareness and diagnostic access involves using the warning signs of rare diseases or using more sophisticated approaches, such as artificial intelligence, for early identification. It also requires a balanced approach that incorporates telehealth, builds local capacity, and ensures cultural safety and responsiveness. It is essential to increase access to genetic testing, coupled with training for primary care providers and specialists to support its safe and efficient use.

Training and education

There is a need for targeted training and education that focuses on the commonalities shared by all rare diseases. This targeted strategy should include the diagnostic odyssey, access to social services, mental health support, and the accessibility and coordination of care. The educational content should cover the needs of individuals before, during, and after a diagnosis. It is important to establish communities of practice that foster collaboration between primary and specialist care.

Referral pathway and care coordination

The referral pathway and coordination of care encompasses a wide range of interventions, including from prevention of symptoms of rare diseases to palliative care, involvement in both on-label and off-label use of drugs, intersectoral care integration, addressing mental illness and stigma, adopting family-based approaches, collecting real-world data, and facilitating participation in clinical trials and research. In a collaborative approach to primary care, a partnership between the patient's medical home and clinical, genetic, and other specialist service providers has been proposed as a model of service delivery to improve rare disease diagnoses and care. The impact of integrated and collaborative care models needs further research to optimise access and care for people with rare diseases. Primary care providers including pharmacists, doctors, nurses, and midwives can offer preconception counselling for those with known genetic risks.

Data sharing and digital health

Improved links between the expansion of neonatal screening programmes and primary care are needed. Collaboration across both data sharing and bidirectional care pathways with all stakeholders, including peak advocacy bodies, should also be encouraged. It is essential for safer and more effective care to share health data and information among all health professionals involved in a patient's care, including those outside the health-care sector, such as educational or social service entities. Primary care providers should play a role in placing patient care within a data-sharing environment and informing patients about the nature of data sharing according to local and national regulations. Efforts should also be made to address the additional needs of populations facing health inequities, such as those living in remote areas, residents of low-income and middle-income countries, and Indigenous communities.

Panel 2: Future directions for the management of rare diseases

- The implementation of aspects of existing conventions, policies, and strategies that identify the importance of primary care in improving the lives of patients with rare disease and their families, and creating revised or new ones that are tailored to primary care, should be supported.
- Advocacy for increased and more equitable funding of testing for rare diseases, and more globally connected services for people with rare diseases is needed.
- The mental health of people with rare diseases and their families requires increased focus.
- Strength-based approaches and two-way (eg, between Indigenous and non-Indigenous peoples and services) learning to develop better models of care are critical.
- Rare disease stigma must be addressed, so as to increase the equity of access and impact of services for people with a rare disease.
- Funding for rare diseases research within and for primary care must be increased.

and personalised medicine, which is critical for people with a rare disease. Telehealth, digital technology (ie, wearables and smart scales), and remote consultations offer opportunities to manage long-term conditions, improve health outcomes, and reduce hospitalisations.

Although concerns about losing the human touch initially dampened enthusiasm for telehealth tools from clinicians, trials have shown that telehealth is acceptable and beneficial to patients.[32] Patients found that telehealth increased the availability of services, although challenges related to access to and use of technologies were identified. Telehealth has also improved follow-up care and communication, as patients feel more at ease at home, and health-care providers can gather information from the patient's environment.[33] Remote consulting, cloud-based clinical applications, and patient self-help portals might provide solutions in the long term, particularly for Indigenous populations and those living in rural communities who face physical and technological access barriers and travel costs for health-care services. These populations are up to 70% more likely not to see a general practitioner, specialist, or other health professional when needed in high-income countries.[34] This rate is likely higher in low-income and middle-income countries due to lack of physical access to health-care services when compared with those in major cities. Children living in disadvantaged or remote areas also incur a higher burden of disease than those in more advantaged areas and cities.[35] As the front line of

medicine, primary care needs to focus on digital inclusion, and adopt a blended approach that combines in-person and virtual care to cater to both language and cultural differences.[33,36] Clinicians and managers must ensure that suppliers adhere to relevant privacy and security requirements.

The growth of digital health relies on investment in key areas, such as data standards, infrastructure, open electronic health records, interoperability, training, leadership, and governance. Successful examples of uninterrupted data flows exist within primary care networks and integrated care systems, facilitating enhanced communication between specialist centres and primary care in managing patients with rare diseases.[37] Although the integration of AI shows promise in improving diagnosis and care, further research is needed to define optimal use cases and ensure transferability across different digital platforms, health systems, cultures, and languages. Clinicians should recognise the potential biases and harms associated with AI technologies and ensure that they have undergone appropriate design, testing, regulation, and approval. Acknowledging that algorithms, even if technically robust, might be influenced by flawed, incomplete, unrepresentative, or outdated data or evidence is crucial. Therefore, although these methods hold promise, sound clinical judgement remains indispensable.[38]

Summary of recommendations

Until primary care is empowered by partnerships, knowledge, pathways, and tools to support diagnosis and care for people with rare diseases and their families, their needs will remain largely unmet. This need is particularly important in settings and populations with sparse access to specialist care, such as remote regions, low-income and middle-income countries, minoritised populations, and Indigenous people.

Unlocking the full potential of primary health care to address the unique challenges associated with rare diseases requires an approach that is both systemic and systematic. This approach should adopt a holistic perspective that considers the entire experience and course of the individual's life (panel 1).

Conclusion and future directions

Rare diseases are increasingly being recognised as a global health priority. Responding to the unmet needs of people with rare diseases and their families requires a coordinated and multifaceted primary care approach, especially in remote areas and low-income and middle-income countries where primary care might be the most or only accessible health care. Although individual themes of such a response will be internationally resonant, the exact nature of the responses will need to be tailored in culturally sensitive and responsive ways to each population and jurisdiction. Funding and delivery of the response will require coordinated multistakeholder advocacy for a range of activities delivered through both policy and practice. Future directions must, therefore, build on the aforementioned recommendations (panel 2).

Contributors

GB, ALH, and SG proposed, developed, and led the related IRDiRC Task Force; in addition, they wrote multiple sections, and performed overall review and editing of the Health Policy paper. MCVL participated in the related IRDiRC Primary Care Task Force and contributed to the coordination, editing, and review of the paper. MB-J, PC, ACG, XD, MD, LD, HG, AG, TG, EH, SSJ, BT, TV-L, SAW, and HB-P are members of the IRDiRC Primary Care Task Force and contributed to the analysis of gaps and opportunities in primary care for rare diseases, collection of literature and information, including structuring and writing of the paper. All authors read and approved the final manuscript.

Declaration of interests

PC is an employee of Medcan. HG receives grants or contracts from the European Commission and German Ministries for Health and Research; holds a leadership and fiduciary role as management team coordinating panel on rare neurological diseases, European Academy of Neurology; is a board member of association of German Centres for Rare Diseases; and is the chair of coordinators' group of European Reference Networks. AG is an employee of Sanofi. SG is a volunteer and a board member of Every Life Foundation. All other authors declare no competing interests.

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