The landscape for rare diseases in 2024

By definition, rare diseases affect a small number of individuals (fewer than 1 in 2000 people in any WHO region); yet, with more than 7000 types of rare disease in existence, the burden worldwide is not insignificant. To date, approximately 300 million people live with rare diseases. Such individuals are often a neglected and marginalised group, especially those in low-income and middle-income countries. Around 80% of rare diseases have a genetic cause, almost 70% of which present in childhood; about 95% lack approved treatments; the average time for an accurate diagnosis is 4·8 years; and about 30% of children with a rare disease die before age 5 years. In 2021, the UN embraced the first resolution on addressing the challenges of persons living with a rare disease and their families, calling on Member States to provide access to safe and affordable health services, particularly at the primary-care level. As we approach Rare Disease Day on Feb 29, what does the current landscape look like for people living with rare diseases?

Achieving precise and early diagnosis poses challenges because of the low likelihood of such a disease occurring, and poor knowledge among patients and health-care workers of their typical signs and symptoms. However, substantial diagnostic advances have been made using whole-genome sequencing. For example, in their paper in *The Lancet Neurology*, Kristina Ibañez and colleagues showed that whole-genome sequencing had high sensitivity and specificity in identifying rare neurological disorders caused by increased numbers of repetitive short tandem DNA sequences, partly addressing the challenge that up to 70% of patients with rare neurological conditions remain genetically undiagnosed. Advances in early and precise diagnosis are of key importance, since rapid diagnosis can enhance health outcomes and improve quality of life. Having an early genetic diagnosis has also been associated with a reduction in both treatment costs and the incidence of financial hardship related to rare diseases.

Since the market potential for drugs addressing rare conditions can be economically less attractive than for common conditions, policies and legislation have been proposed to facilitate the development of treatments for rare diseases, also called orphan drugs. The Orphan Drugs Act, signed in the USA in 1983, provides incentives such as tax credits and access to research grants, fostering the approval of hundreds of orphan drugs in the USA, and leading to similar legislation in other regions such as Europe. Groundbreaking novel therapeutic strategies such as gene therapy have also brought hope for patients and their families with rare genetic disorders.

However, even when we do have treatments, there is no promise of accessibility for all. For instance, Hemgenix, a gene therapy to treat haemophilia B based on an adeno-associated virus vector, costs up to US$3·5 million per case in the USA. The affordability challenges go beyond diagnosis and treatment. Since most people living with rare diseases need specialised treatments, which are often only available in specific high-income countries, medical tourism can be the only option available, but it is not feasible for most. A Health Policy paper in *The Lancet Regional Health—Americas* highlighted that, in Latin America, less than 3% of the population would be able to afford to travel for treatment abroad.

Parents and carers of a child living with rare diseases can also be substantially affected: insufficient information, few treatments or management options, and financial concerns can contribute to psychological distress. Due to frequent medical admissions and appointments, many parents and carers are forced to reduce their employment hours or to leave the workforce, posing additional financial difficulties. People living with a rare disease can also experience stigmatisation. Insufficient awareness of their rare disease among health-care staff and communities can result in patients' symptoms being invalidated, visible symptoms of the disease can result in social discrimination, and schools and employers can fail to address accessibility needs.

Overall, the 2024 Rare Disease Day is marked by both advances and persistent challenges. Urgent attention is needed to prioritise early and precise diagnosis as well as effective treatment of rare diseases via specific policies and funding for research and development. A collective approach involving integration of rare diseases into the health-care system, inclusion of mental health considerations in rare disease services, and increased awareness efforts will be essential for fostering progress and addressing the unmet needs of those affected by rare diseases. ■ *The Lancet Global Health*

For more on **rare diseases** see https://globalgenes.org/rare-disease-facts/

For the **UN resolution** see https://www.rarediseasesinternational.org/wp-content/uploads/2022/01/Final-UN-Text-UN-Resolution-on-Persons-Living-with-a-Rare-Disease-and-their-Families.pdf

For more on **whole-genome sequencing for diagnosis of neurological rare diseases** see **Articles** *Lancet Neurol* 2022; **21:** 234–45

For more on the **costs of rare diseases** see **Articles** *Lancet Reg Health West Pac* 2023; **34:** 100711

For more on **costs of haemophilia gene therapies** see https://www.reuters.com/business/healthcare-pharmaceuticals/uptake-new-hemophilia-gene-therapies-slow-field-assesses-options-2023-12-15/

For more on **rare disease policy in Latin America** see **Health Policy** *Lancet Reg Health Am* 2023; **18:** 100434

For more on **parents' perspectives on navigating the health-care system for children with rare diseases** see *J Genet Couns* 2018; **28:** 80–90