The RDI–*Lancet* Commission on Rare Diseases: improving visibility to address health-care disparities for 400 million people

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Rare diseases are complex and ubiquitous; they represent a global challenge that needs a global response. A rare disease is commonly defined as a medical condition that affects fewer than one in 2000 people.[1] There are thousands of different rare diseases[2] that collectively affect around one in 20 people (400 million individuals worldwide)[3] and include genetic diseases, cancer, infectious diseases, poisoning, immune-related diseases, idiopathic diseases, and undetermined conditions.[4] People living with a rare disease (PLWRD) and their families experience common and devastating challenges due to a unifying feature for all rare diseases: their individual low prevalence.[5] The provision of health care is a major challenge, and PLWRD often experience diagnostic delays, misdiagnoses, inadequate care, lack of treatment options, and, for a small subset of patients, very high-cost therapies. The social consequences of living with a rare disease are also devastating and include stigmatisation, difficulties with participation in education or the workforce, financial hardship, and social exclusion. However, approaches to rare diseases are shifting. Decades of work by grass-roots patient organisations and advocates, dedicated medical professionals, and motivated researchers has resulted in an unprecedented number of breakthroughs in rare disease gene discovery,[6] diagnostic technologies,[7] innovative therapies, and treatments.[8] Rare diseases are increasingly seen as a large group of diseases with common challenges for which shared solutions can have global impact.

Rare diseases are beginning to be recognised on the international policy stage. In 2021, the UN adopted a resolution on Addressing the Challenges of Persons Living with a Rare Disease and their Families[9] that recognised the unique difficulties in diagnosing and managing rare diseases.[9] This landmark resolution urges member states to improve health-care access, social inclusion, and equitable opportunities and calls for international collaboration to enhance support for this underserved population.[9] To achieve the 2019 UN Political Declaration on Universal Health Coverage (UHC),[10] which urges countries to accelerate progress towards achieving UHC by 2030, it is crucial that rare diseases are recognised as a global health priority to achieve UHC for all. Some member states have called for the World Health Assembly to adopt a resolution on rare diseases in 2025,[11] requesting WHO to develop a global action plan on rare diseases. This year is an important moment, with potential for change and tangible global impact to advance efforts to address rare diseases. To realise this potential, all stakeholders must leverage this momentum and translate it to benefits for PLWRD across the world.

The Rare Diseases International (RDI)–*Lancet* Commission on Rare Diseases is a new initiative dedicated to generating evidence-based and equity-informed recommendations that are implementable and impactful across all countries to improve the lives of PLWRD. This Commission unites 27 Commissioners who represent countries from around the world (all inhabited continents, Global North and Global South, low-income to high-income countries) and brings diverse perspectives (gender, lived experience) and expertise (ethics, clinical care, research, biostatistics, economics, regulatory, technology, and innovation) from a variety of health-care systems.

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Rare diseases are typically invisible, even though PLWRD encounter many medical specialties and health-care services and community workers. Data on rare diseases are often fragmented or do not exist. Therefore, there is no accurate representation of the burden of rare diseases. Poor visibility and recognition affect all aspects of the patient experience across multiple sectors, including health care, community, society, and home. Overwhelmingly, this lack of visibility and recognition for rare diseases and PLWRD is a fundamental gap underlying inequities in diagnosis, care, and support.

The Commission will therefore take a holistic and multidimensional approach to examine visibility and make specific actionable recommendations across five principal domains with associated working groups. The ethical and moral working group will examine the fundamental rights and entitlements of PLWRD through a human rights framework, aiming to ensure governments acknowledge their responsibilities and enact changes in law and policy. The data and metric working group will focus on collecting and analysing data to accurately represent rare diseases and count PLWRD, ensuring they are prioritised by governments, health-care systems, and researchers. The societal and health-care system working group will seek to reduce diagnostic odysseys and shorten the path to informed care by highlighting opportunities to identify PLWRD within society and health-care systems. The clinical pathway working group will explore integrating PLWRD into treatment pathways, shifting conventional models of care to include a broader understanding of treatment. Finally, the health-care professional competency working group will work to improve competency in rare diseases and foster participatory models of care to encourage health-care systems to listen to PLWRD and ensure they receive the care they need and want. Working groups will partner with PLWRD to understand their experiences and identify the services and supports they most need to generate concrete, actionable recommendations that can be applied globally.

The Commission is united in our commitment to seizing this moment and generating a robust dataset from which evidence-informed recommendations can be made and implemented around the world, contextualised for the local environment. We strive to ignite global action that amplifies the voices of PLWRD such that they are seen, heard, and cared for.

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**Kym M Boycott, Roberto Giugliani, on behalf of the Commissioners of the RDI–*Lancet *Commission on Rare Diseases†*
kboycott@cheo.on.ca

†The Commissioners of the RDI–*Lancet* Commission on Rare Diseases are Lama AlAbdi, Gareth Baynam, Kym M Boycott (Co-Chair), Juan Francisco Cabello, Yong Chen, Brian HY Chung, Roberto Giugliani (Co-Chair), Holm Graessner, Ada Hamosh, Susan Horton, Kirsten Johnson, Anneliene Jonker, Bartha Maria Knoppers, Helen Malherbe, Lucy McKay, José Elías García-Ortiz, Carmencita Padilla, Kimihiko Oishi, Juan Manuel Politei, Ratna Dua Puri, Ana Rath, Giuseppe Remuzzi, Anna Somuyiwa, Sharon F Terry, Durhane Wong-Rieger, Ignacio Zarante, and Shuyang Zhang. The members of the academic secretariat for this Commission are Sara Brambilla, Taila Hartley, Heather Howley, Alexandra Lianes, Alanna Miller, Alexandra Heumber Perry, and Mary Wang. Chloe Wilson is the Senior Editor at *The Lancet* working with this Commission.

Children's Hospital of Eastern Ontario Research Institute, University of Ottawa, Ottawa, ON K1H 8L1, Canada (KMB); Federal University of Rio Grande do Sul (UFRGS), Hospital de Clinicas de Porto Alegre (HCPA), Dasa, Casa dos Raros, Porto Alegre, Brazil (RG)

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