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Paradox of possibilities: the *rare* landscape in the Asia Pacific Region

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Abstract

The Asia-Pacific (APAC) region, home to 60% of the global population, has the highest number of Persons Living with a rare disease (PLWRD). To promote more equitable societies, the Asia Pacific rare disease Organization (APARDO), established in 2015, has been developing its regional position to promote collaboration, increase awareness among stakeholders, explore equitable and affordable diagnosis and treatment, and improve health outcomes and quality of life for all PLWRD. The APAC region's heterogeneous population and complex healthcare environment pose distinctive challenges in addressing rare diseases. Through conferences, webinars, and contributions to global initiatives, APARDO is fostering connectivity and providing a platform as a part of the global rare disease (RD) community to address shared challenges. The development of APARDO to strengthen its global presence as the representative of the APAC RD region is vital for a more equitable world.

Keywords: RDs, patient organizations, Asia-Pacific, policy, diversity

INTRODUCTION

The Asia-Pacific (APAC) region perhaps best illustrates the well-known paradox of rarity: With over 4.7 billion people, or more than half of the world's population, residing in this region[1], it is characterized by extreme heterogeneity of cultures, languages, and socioeconomic backgrounds. Within this large population, it is estimated that more than 258 million individuals are living with rare diseases (RDs)[2-4]. The region's heterogeneous population and complex healthcare environment pose distinctive challenges in addressing RDs. At the same time, the magnitude of the region, the size of the RD population, and the readiness of various stakeholders hold the promise of possibilities for novel solutions and approaches towards health equity. Many countries in the region increasingly recognize the importance of developing comprehensive policies and strategies to support persons living with RD (PLWRD) and their families through concerted efforts in research, diagnosis, treatment, patient support, and public awareness initiatives[5-7]. Nonetheless, the establishment of collaborative initiatives among healthcare professionals, researchers, patient organizations, and governmental entities remains vital to ensure equitable access to comprehensive care and support for PLWRD throughout the APAC region. Towards this goal, Asia Pacific Alliance of Rare Disease Organisation (APARDO) was created to effectively and collectively address the challenges and enhance outcomes for PLWRD in the APAC region[8]. This article presents the perspective of APARDO on the learning of collaboration among RD patient groups, as well as the opportunities for strengthening efforts across the heterogeneous region.

APAC regional RD policy context

Despite the consolidated acronym APAC, which may imply a unified approach, the reality presents a diverse landscape with varying strategies and levels of recognition of the pressing challenges faced by PLWRD and their families. Make towards this aim, over the past thirty years, many countries have set up dedicated policies or legislation to provide provisions to address the needs of PLWRDs. Japan remains one of the first countries to implement a dedicated policy in 1993[5-7]. The 1993 Japanese Pharmaceutical Affairs Law (now the Pharmaceuticals and Medical Devices Act) was revised to define rare and intractable diseases, collectively referred to as NANBYO. Furthermore, under the same law, measures were taken to promote research and development of orphan drugs, and review procedures were improved. Similarly, Australia has demonstrated leadership in forward-thinking RD policies. The Australia Therapeutic Goods Regulations 1997 provided guidance for orphan drug programs and incentives to market these medicines. In 2020, the "National Strategic Action Plan for RDs" was launched in Australia, focusing on collaboration between healthcare providers, researchers, patient organizations, and the government to improve coordination, research, and treatment access for RDs. Between 2000 and 2010, dedicated legislations on RD or orphan medicines were set up in Singapore, South Korea, Taiwan, and subsequently, between 2010-2021, in Hong Kong and the mainland of China, India, Indonesia, Malaysia, Philippines, and Thailand[9-12]. Further, while New Zealand has made a commitment to a strategy for RDs, no policy has been established yet[13]. Despite the existence of RD policy, many countries do not have a specific policy context for RDs. The extent and focus of the policies differ across countries, ranging from public awareness, patient support, research, diagnosis, and treatment access. Hence, the level of implementation varies vastly within the APAC region.

Unique characteristics of APARDO

APARDO, established in 2015 and as stipulated in the strategic plan, seeks to provide a patient advocacy-led alliance of RD stakeholders from the APAC region representing rare-disease organizations and operates under a constitution[8]. The Alliance's mission is to work effectively with national and regional policy makers, industry, and healthcare professionals to increase awareness, facilitate collaborations to explore equitable and affordable diagnosis and treatment, and improve health outcomes and quality of life for all patients and their caregivers. By 2023, APARDO has grown to an alliance of 29 member organizations from 15 countries.

APARDO operates across a vast geographical area comprising 62 nations in Asia-Pacific [UNFPA][14] with an estimated 60% of the world population, including India and China, the two most populous countries globally. Notwithstanding the tremendous geographic and population spread, the alliance of Asian patient organizations is similar in its representation to other RD alliances operating at a regional level, such as the Rare Disease Europe (EURORDIS) and Ibero-American Alliance for Rare, Orphan or Infrequent Diseases (ALIBER). Such regional alliances typically leverage unifying aspects (e.g., common gaps, objectives) to facilitate operations and shared causes. In Europe, the European Union and the common market framework provided the first opportunity for EURORDIS to unify patient groups from European countries on a common objective. Similarly, ALIBER (a partnership between Ibero-American countries represented by the Portuguese National Alliance for Rare Diseases and the Spanish National Alliance for Rare Diseases) seeks to address the common challenges encountered in Spanish- and Portuguese-speaking regions. In contrast to the two alliances, APARDO operates in a broad geographical region with heterogeneous cultures, languages, and varying levels of development and readiness within health systems. While the organization draws on shared experiences with RDs and a commitment to tackle related issues and gaps, the lack of a unified economic or political framework (currently and in the near future) complicates the possibilities of working towards common goals. Nonetheless, such diversity has also yielded success stories through concerted and committed advocacy in the APAC nations (see Table 1 for a snapshot of the RD landscape in the countries represented in the APARDO membership). As Table 1 indicates, significant advances and developments are taking place across the region, among the higher-income and more technologically advanced countries/regions such as Japan, Korea, Taiwan, Hong Kong, China, and Australia, as well as those with developing or emerging RD research and health, social, and community services, notably India, Malaysia, Philippines, Indonesia, and Vietnam.

Looking ahead, the alliance has the potential to play a critical role in achieving health equity, improved diagnosis, and access to treatment and supportive care through strengthening its patient network, deepening engagement with stakeholders, and maintaining ongoing programs of education and capacity building. These objectives necessitate advocacy for contributing to specific policies to provide both visibility and improvement in the lives of those with RDs and their families.

Compared to EURORDIS and ALIBER, APARDO is the youngest regional alliance. The pioneer EURORDIS was established in 1997, ALIBER in 2013, and APARDO registered as recently as 2015. As a younger alliance, APARDO is on the path of strengthening as an organization and developing its membership. As of 2023, APARDO has no dedicated office space, has one part-time staff as an administrator, and relies heavily on the in-kind time contribution of its board of directors and members. Further investment is necessary to consolidate the organization and hire dedicated staff capable of handling secretarial duties, fundraising, and implementing strategic plans.

A review of APARDO activities and contributions

APARDO was set up as a patient alliance of RD stakeholders from the APAC region. Its objectives were to empower national RD organizations to advocate for better outcomes and quality of life for PLWRD and caregivers. It serves as a platform for promoting best practices and the exchange of information across the region. The focus of its initial activities has been to identify and assess solutions for gaps between patients and policies, as well as to amplify the voice of stakeholders, influence policies, and strengthen regional initiatives.

Along these lines, the organization has raised capital to enable the delivery of educational programs and organize annual conferences in Taiwan (2019), virtually in 2020 and 2021, and in Thailand in 2022 and in

Table 1. RD legislation and orphan drug support in APARDO member countries

Country	Population size[15] (million)	RD policy/legislation	RD healthcare support or reimbursement	References
India	1,417.72	National Policy for Treatment of RDs (NPTRD) formulated by the Ministry of Health and Family Welfare, Government of India recognizing three groups of rare disorders: 1. Those requiring a one-time curative treatment 2. Diseases requiring long-term/lifelong treatment at a relatively lower cost 3. Diseases for which treatments exist but remain expensive	Under the NPRD, an allocation of approximately US$15 million to 12 RD Centres of Excellence announced in July 2023 The *National Policy on Research and Development and Innovation in Pharma-MedTech Sector in India* and the *Scheme for Promotion of Research and Innovation in Pharma MedTech Sector* announced in October 2023 aimed at improving accessibility and affordability of medicinal products including those for rare disorders	[16-18]
China Mainland	1,412.17	No national legislation on RD. The first list of 121 RD released in 2018, and the second listing of 86 more published in 2023	More than 90 RD drugs listed in the National Reimbursement Drug List (NRDL), with average patient copay ranging from 0% to 30% More than 100 RD drugs approved. Accelerated registration, priority review, and clinical trial waiver possible for RD drugs National Network for the Diagnosis & Treatment of RDs comprising 321 hospitals National RD Registry System (NRDRS) established by Peking Union Medical College Hospital (PUMCH) in 2018	[19-23]
Indonesia	275.5	No official definition or legislation for RD or orphan drugs	Nationwide newborn screening policy has not been established yet, except for congenital hypothyroidism In 2017, Indonesia opened its 1st CoE for RDs in Cipto Mangunkusumo Hospital in conjunction with Human Genetic Research Center and Indonesia Medical Education and Research Institute Universitas Indonesia (IMERI UI), and patient organization to support families affected by RDs	[24]
Japan	125.12	The 1993 Japanese Pharmaceutical Affairs Law (now the Pharmaceuticals and Medical Devices Act) revised in 2014 to define rare and intractable diseases, collectively referred to as NANBYO The current NANBYO Act applies to 338 disease groups	Medical expense subsidy system for severe pediatric specified diseases in 788 disease groups available Patients with milder conditions can access certain social welfare services	[25,26]
Philippines	115.55	Rare Disease Act of the Philippines since 2016	Defines RD, makes provision for diagnosis, and comprehensive medical care. Offers regulatory and fiscal incentives to encourage access to RD drugs Funding of approximately US$ 1.86 million allocated in 2022 for the implementation of the RD Act Newborn Screening available and covered by national- insurance since 2019	[27-29]
Vietnam	98.19	No legislation, and no official definition of RD and orphan drugs	The National Center for Newborn Screening and Management of RDs established at the National Hospital of Pediatrics (NHP) in 2013. Drug registration and RD drug accessibility accelerated by the 2016 National Assembly Law on Pharmacy	[30]
Thailand	71.7	No legislation, and no official definition of RD. The Thai FDA provides a definition for orphan drugs	24 RDs included in the National Health Security Office universal health coverage scheme Genomics Thailand program formed a national network for rare and undiagnosed diseases, 2019-2024	[31,32]
South Korea	51.63	Rare Disease Management Act of 2015 defines RD and commits to research and development, plans for diagnosis and treatment of RDs. National Health Insurance Scheme, the Medical Expense Support Project, and Support for Catastrophic Health Expenditure are programs supporting PLWRD Governmental Rare Disease Helpline website provides information and counseling services related to RDs	Ministry of Health and Welfare releases a 2017-2021 road map for the diagnosis, treatment, and management of RDs Korea Disease Control and Prevention Agency provides funding for research in RD	[33-36]

Malaysia	33.94	No formal legislation Health Ministry's National Strategic Plan for Medical Programmes currently under review	Allocation of approximately 5.3 million US$ has supported 60 patients thus far Private insurance coverage available for some RD Orphan medicine designation under the purview of NPRA	[37,38]
Nepal	30.55	No specific legislation on RD	Congenital disorders, because of their rarity, have not been addressed at the health policy level	[39,40]
Australia	25.98	2020 National Strategic Action Plan for RDs (the Action Plan) launched The Pharmaceutical Benefits Scheme (PBS) enables free medicines for 139 'life-saving and disease prevention' medicines	Most medicines subsidized through PBS RDs that are rejected by PBS on cost-effectiveness grounds are supported by the 1995 Life Saving Drugs Program	[41-45]
Taiwan	23.32	The RD and Orphan Drug Act was approved in 2000. The Act defines RD, and facilitates research, access of orphan drugs and special nutritional foods. The Act enables the prevention and early diagnosis of RDs	The Rare Disease and Orphan Drug Act provides grants, fast-track approval, protocol assistance, and market exclusivity	[46-48]
Hong Kong	7.35	No RD legislation	Clinical diagnosis and assessments, multi-disciplinary care and rehabilitation services, and subsidized drugs are available by the Hospital Authority, a statutory board that manages all public hospitals. Designated Orphan Drugs are covered by the government's annual financial budget allocated to the Hospital Authority and complimented by the Samaritan Fund (51 drugs) and the Community Care Fund Medical Assistance Programme (37 drugs) since 2021 for means-tested patients	[6,49,50]
Singapore	5.64	No formal RD legislation or definition of RD. Criteria for accessing the Rare Disease Fund stipulates rare as < 4/10,000 (i.e., < 1,600 people in Singapore). However, since the fund only covers ultra-rare diseases currently, the definition for ultra-rare is < 2 in 50,000 people (i.e., < 225 people with the condition in Singapore) Health Products Act governs orphan drugs as part of all therapeutic products	The Rare Disease Fund, a national multi-stakeholder charity fund set up in 2019, has provided financial support to 9 patients (as of March 2023) for 7 medicines approved for 5 RDs	[51-54]
New Zealand	5.12	No specific policy on rare disorders	The Pharmaceutical Management Agency (Pharmac) decides on behalf of Health New Zealand (Te Whatu Ora) which medicines and pharmaceutical products will be subsidized. The Pharmac Rare Disorders Advisory Committee evaluates funding applications and makes recommendations to the Pharmacology and Therapeutics Advisory Committee (PTAC) and Pharmac	[55-61]

RD: Rare diseases; CoE: centre of excellence; PLWRD: persons living with a rare disease.

Malaysia in 2023. APARDO has also organized a series of webinars on diverse topics, such as Essential Medicines and Cell and Gene Therapy. It has also partnered with organizations such as rare diseases international (RDI) for their initiative, the Global Network for RDs, and regionally, through support towards the RD Network, previously associated with the Asian Pacific Economic Cooperation (APEC) program. Over the years, the organization has collected data on patient needs and gaps and contributed to publications[8,48,62]. As a member of various global organizations such as RDI and the International Rare Diseases Research Consortium (IRDiRC), APARDO continues to contribute perspectives from the APAC region with the goal of improving the lives of PLWRD and their families.

Opportunities for strengthened collaborations

The hyper diversity of languages, cultures, paternalistic healthcare systems, and sparsity of developed patient organizations pose an enormous challenge for effective and efficient exchanges across APAC. Territorial differences ranging from vast areas (China, India, Australia) to thousands of islands (Indonesia,

Philippines) lead to barriers in outreach to RD patients, particularly in remote areas, making an assessment of needs, care integration and delivery, and dissemination of information and training a challenging undertaking. This is exacerbated by a lack of reliable epidemiological data on prevalence and socioeconomic burden, sparse diagnostic resources and patient registries, approved and/or funded medical treatment, and more. The lack of such understanding of the needs of the target population further impedes investment in RD research.

Nevertheless, there are great efforts across APAC to address challenges in different contexts. LMICs have useful skills and best practices to share, as demonstrated by responses to the COVID-19 pandemic. The experience of the SARS outbreak in 2003, as well as the ability to efficiently and creatively use limited resources for maximum impact, has come to the fore more than once. Examples include the ease of adapting telemedicine and digitalization of organizational operations for continuity and broadened impact[62,63]. Furthermore, despite its challenges, many countries have persevered to expand the protection of RD patients. For instance, expanded newborn screening programs are implemented in the Philippines, which is serving as a model for access across remote islands and limited resources[64].

Active patient engagement and advocacy, such as in Europe, has been successful in pushing changes in policies and supporting better diagnosis, treatment, and quality of life for PLWRD. However, most APAC countries lack the necessary support and motivation for patients and patient organizations to participate in various levels and topics related to their disease, and to speak out about gaps between their unmet needs and existing healthcare services. Global policy advancements, such as the UN Resolution "Addressing the challenges of persons living with a RD and their families" and Political Declaration on Universal Health Coverage including RDs, lend tools for national engagement and advocacy[65,66].

CONCLUSION

The APAC region, with approximately 60% of the global world population, is estimated to have the highest absolute number of people with RD. Therefore, further development of APARDO to strengthen its global position as the representative of the APAC RD region is vital for a more equitable world. This requires balanced sustainable resourcing, unified global commitments, agreements, and unified collaborations. To ensure that no one is left behind, it is imperative for the APAC region to adopt a holistic view of the global RD community, with an emphasis on active participation from developing and Low-Middle-Income Countries. A sustainable model for the APAC region would greatly benefit from enhanced connectivity and regional initiatives that encompass various RD stakeholders of the region and within the constraints and realities unique to APAC. This endeavor must start with the right mindset and commitment not only from developed nations but also (no matter how modest), developing ones. Such concerted efforts would empower the RD community, enabling more effective addressing of key issues such as access to therapeutics, care coordination, stigma and discrimination reduction, and the digitalization of patient organization operations.

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Authors' contributions

Made substantial contributions to the conception and design of the manuscript and performed data analysis and interpretation: Jain R, Wang CM

Contributed to the writing of the manuscript: Foster L, Nishimura Y, Li EY, Tsang KP
All authors contributed to the review and editing of the manuscript.

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