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National Policy on Rare Diseases Living with Dignity: In Search of Solutions for Rare Diseases

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** The views and opinions expressed in this paper are those of the author and do not necessarily represent IDEAS*

What are Rare Diseases?

The World Health Organization (WHO) defines rare disease, also known as orphan disease, as any disease which affects a small percentage of the general population. Although individually rare, collectively there are over 6000 types and this constitutes a large number of patients, who share many issues in common (EURORDIS, 2009). About 80% of rare diseases are genetic in nature while those that are caused by other factors such as exposure to environmental factors, chemicals during pregnancy, infections and rare cancers are not inherited. About 30% of rare disease patients die before the age of five. About 9% or 45 million people in South East Asia are afflicted by orphan diseases (Right Diagnosis, 2015). Examples of rare diseases include inherited metabolic diseases such as lysosomal storage diseases; neuromuscular diseases such as Duchenne muscular dystrophy and spinal muscular atrophy; blood diseases such as haemophilia; bone disorders such as brittle bone disease and achondroplasia; and adult-onset diseases such as Huntington's disease and motor neurone disease.

Patients with rare diseases and their affected families face many challenges. As these conditions are often debilitating and chronic, they pose considerable long term psychological, medical and financial burden on the patient as well as their parents, siblings and extended family. Listed below are a number of key areas that have been identified that contribute to the challenges faced, and recommendations for the government to adopt in order to improve healthcare for the affected individuals.

Lack of recognition and inclusiveness

Rare disease patients in Europe are represented by the European Organisation for Rare Diseases (EURORDIS), a non-governmental patient-driven alliance of over 761 rare disease patient organisations in 68 countries. EURORDIS defines rare diseases as those affecting less than five people in 10,000 of the general population (EURORDIS, 2009). Meanwhile, the United States of America (USA) defines a disease as rare if it affects less than 200,000 persons out of the total population. In Taiwan, rare diseases are acknowledged not in terms of their prevalence but by their inclusion in the Rare Disease registry by name.

In Malaysia, thus far there is no official definition as to what is regarded as a rare disease. As the first step to providing a definition for local families, the Malaysian Rare Disorders Society (MRDS) has decided upon a classification on the basis of prevalence, that is, one in every 4,000 people of the general population. Having an official and accurate definition is paramount to addressing a multitude of issues faced by families living with rare diseases in Malaysia. For example, not having a clear definition leads to many issues with indifference from the policy makers, inadequate healthcare provisions and restricted access to crucial life-changing medication.

Rare diseases tend to draw the short straw in the current climate of competing healthcare resources. As they are presumed to only affect a very small number of Malaysians and are considered as non-communicable diseases, little attention is paid to these diseases and there is limited data, if any, on their prevalence and burden in Malaysia. In 2016, the Malaysian Ministry of Health (MOH) published the National Strategic Planning for Non-Communicable Diseases (NCDs) 2016-2025 where the report focused on lifestyle risk factors such as hypertension, obesity, cancer and hypercholesterolemia, as well as control of tobacco use, salt and alcohol consumption (Ministry of Health Malaysia, 2016). Indeed, there was no data on NCDs for segments of the population below 15 years old nor strategic planning for control and treatment needed for rare diseases in Malaysia. In addition, Malaysia currently spends only 2% of GDP on healthcare. Therefore, there is an urgent need to address the shortcomings of the national strategy especially the lack of funding in healthcare services. Proper acknowledgement of rare diseases, beginning with an official definition and recognition as a national healthcare issue, will help to garner more attention towards these conditions in addition to providing support for the patients and families. Although rare diseases are characterised by their low prevalence individually, in reality these conditions collectively impact the lives of a large number of Malaysians as patients and caregivers are faced with the financial, psychological and social burden. Many who suffer from rare diseases often feel isolated, uncared for and vulnerable. Being properly recognised as a serious healthcare matter and making rare diseases an inclusive issue will help to garner more awareness and respect for these individuals.

Lack of awareness and comprehensive healthcare provisions

As the conditions are rare, many healthcare professionals may be unfamiliar about the signs and symptoms of the various types of rare diseases, and consequently lack knowledge of what immediate treatment is necessary, and what to advise the patients and parents. Diagnosis is often delayed, even in developed countries such as the USA and Britain, by five to seven years. Early diagnosis reduces long term complications in the patients, lessens anxiety amongst family members, enables proper planning, and in many cases, genetic counselling could be provided to assist the parents for family planning and future prenatal diagnosis. Thus, it is imperative that the current and future healthcare professionals – and more generally the public – are better and more comprehensively educated about rare diseases.

As Malaysia's healthcare continues to improve with a reduction in mortality rates from malnutrition and infectious diseases, chronic NCDs such as rare diseases, congenital malformations and birth defects are becoming the main causes of under-5 childhood mortality. While rare diseases should be handled by multi-disciplinary teams in tertiary centres, there is a need for increased awareness and funding for screening, diagnosis, treatment as well as research and educational programs on these conditions (The Star, 2017). Information on rare diseases is often difficult to understand and mainly focuses on the more severe end of the spectrum. Patient support groups like the Malaysian Rare Disorders Society, Rare Disease Alliance Foundation Malaysia and Malaysia Lysosomal Diseases Association increasingly play an emerging role in the dissemination of information to increase awareness as well as the provision of advisory services, fund-raising and patient advocacy. Very often, empowering patients and families with knowledge provides multiple beneficial effects: the caregivers are more likely to take charge of treatment regimes, show better medication compliance, are active in advocacy roles and provide essential support for each other (Malaysia Rare Disorders Society, 2013).

However, due to limited financial support and resources as well as persistently low levels of awareness, many patients with rare diseases remain undiagnosed or are not given the appropriate treatment. In addition, parents of these young patients do not receive adequate support or respite care and many continue on a 'diagnostic odyssey' for years. A concerted effort on behalf of the government ministries must be made to address this issue and to expand the effort towards awareness and greater welfare support.

Lack of access to medications

There are only a few rare diseases which have pharmaceutical treatment options (Cremers and Aronson, 2017). These pharmaceutical treatments, termed 'orphan drugs,' are often life-changing treatments but are only available for a very select number of rare diseases. This is partly due to the fact that the biopharmaceutical industry regards these orphan drugs as uneconomical to produce due to the vast amount of investment needed for the initial research and development, difficulties with small cohorts for clinical trials, and the relatively small 'customer' pool to recoup the investment. Hence, research and development in rare disease therapeutics is likely to be costly and financially risky for the pharmaceutical industry. A recent report has indicated that orphan drugs are listed as the world's top ten most expensive drugs (PhRMA, 2015), putting them out of reach for most patients to afford privately.

The United States Congress passed the Orphan Drug Act (ODA) in early 1983. The ODA provides a special status to pharmaceutical agents or biological products that treat a rare disease or condition upon the request of a sponsor. For a drug to qualify for orphan designation, the drug and the disease must fulfil certain criteria as specified in the ODA and FDA regulations (Hunter, Rao, and Sherman 2017). Orphan designation enables various development incentives such as tax credits for clinical testing. A marketing application for a drug product that has received orphan designation is not subjected to a prescription drug user fee unless the application included an indication for anything other than the rare disease or condition for which the drug was designated to treat. In addition, the manufacturer is also provided with various forms of research support and a seven-year exclusivity period for emerging therapies. More than 600 drugs and biologic products have been approved for treatment of rare diseases since the ODA was passed, and over 230 new drugs have been approved in just the last ten years, indicating a growing interest by the biopharmaceutical companies to develop these drugs (PhRMA, 2015).

Although this is an encouraging trend, these developments only represent medication for less than one in ten patients with a rare disease. Furthermore, while these efforts have brought new treatment options to patients with rare diseases, the medication is still unaffordable to many patients in low and middle income countries. Equitable access to treatment for rare disease patients is in line with United Nations Sustainable Development Goals, one of which is ensuring healthy lives and promoting well-being for all at all ages, leaving no one behind. The European Commission, in its White Paper "Together for Health: A Strategic Approach for the EU 2008-2013" identified rare diseases as a priority for action.

Lack of protection of the rights and dignity of individuals with rare diseases

In Malaysia, dedicated financial support for genetic diseases began in the first decade of the 21st century with reimbursements for the purchase of iron chelators for treatment of iron overload in patients with beta thalassaemia major. In the early 2000s, through the work of early clinical geneticists and paediatricians, funding of approximately RM8.5 million was obtained for enzyme replacement therapy (ERT) for the treatment of patients with lysosomal storage diseases (LSD) from the Ministry of Health. However, with the increasing number of patients and the chronic nature of these rare diseases, the funding allocated to the MOH has become insufficient. Many patients are not receiving the correct dose for their treatment and the number of new patients who continue to await treatment is increasing annually. An additional RM10 million was allocated in 2017 to address some of these issues (The New Straits Times, 2017). However, ERT funding is only available to MOH patients while some patients are diagnosed in university hospitals and private healthcare facilities. Limiting nationwide access to ERT only to Hospital Kuala Lumpur (HKL) for MOH patients from Peninsular Malaysia further increases patient congestion and exacerbates the challenges of delivering treatment to patients who may have difficulties accessing HKL. Efforts to raise funding for ERT via charitable organizations, mass and social media events and private companies as well as compassionate use of ERT were occasionally met with limited success, but ultimately unsustainable for medium and long-term needs. A Technical Committee for ERT was established and a guideline on the indications and use of enzyme replacement therapy for lysosomal diseases in Malaysia was issued by the MOH in 2009 and updated in 2017 (Ministry of Health 2017). Whilst this example shows the challenges faced by LSD patients, it is likely that this too would be the same experience for other rare disease groups and their drug treatments in the near future.

Prior to the 14th General Election, the Pakatan Harapan (PH) coalition issued a manifesto declaring in one of its promises that it *"will increase budget allocation and will provide incentives for the participation of private companies and charitable bodies to tackle rare diseases."* Specific measures and actions by PH government to follow through with this promise are highly anticipated. The government must look beyond the cost of these treatments and the rarity of the diseases and recognise that access to healthcare is a basic human right. Measures need to be taken to protect this fundamental human right and dignity. Thus, action is urgently required to establish legislation, regulations and national policies to address these issues. This is critical as the number of medications available for rare diseases is on the rise and increasing numbers of patient groups will advocate for access to these news drugs and treatments. The government must plan on how to address licensing regulations, pricing and distribution of these drugs. In addition, the government should also make provisions to encourage local research on rare diseases, and on the development of orphan drugs as a strategic biotechnological industry in Malaysia. Many countries across the world have established Rare Disease and/or Orphan Drug acts or policies, including at least five Asian countries such as Taiwan, Singapore, China, India and Japan (Gamme, Lu, and Babar 2015). Currently, Malaysia does not have similar legislation — it is thus time for Malaysia to advance this agenda.

Having highlighted the various issues faced by the patients and their families, the following are recommendations to address these issues.

Recommendations

1. Accurate data relating to rare diseases in Malaysia is needed:

- Resolve to have an accurate and representative definition for Rare Disease in Malaysia.
- Create and maintain an accurate and up-to-date national registry on rare diseases, including genetic and congenital conditions.

2. Legislation is needed to protect the rights of individuals with rare diseases:

- Rare Diseases and Orphan Drug Act legislation is urgently needed to protect the rights and lives of babies, children and persons with rare diseases. This is in keeping with international standards and practices and will help develop specific criteria for evaluating new orphan drug listing in the Ministry of Health Formulary.
- Adequate funding and resources must be allocated to provide access to diagnostic tests, treatment and rehabilitation to all patients with rare diseases and their families.
- Engaging the insurance industry to remove discrimination against patients with inherited rare diseases.
- Increase job opportunities and educational training and support for disabled persons with rare diseases.

3. Awareness and educational programs on rare diseases to patients, health professionals and general public:

- Commit to training more health professionals and genetic counsellors to help families with rare diseases and to avoid delay in diagnosis.
- Increase awareness amongst key stakeholders in Malaysia on rare diseases such as policymakers, academics, media organizations and non-governmental bodies.
- Networking, coalition building and media education to raise the profile and sensitization of the general public to the issue of rare diseases.
- Greater focus on the topic of rare diseases in medical training.

4. Pre-pregnancy and Pregnancy Care:

- Food fortification with folic acid to prevent neural tube defects.
- Educational programs for all women of childbearing age and healthcare providers regarding avoidance of teratogenic drugs.
- Educational programmes for sonographers, obstetricians, nurses and midwives to detect signs of possible rare disease during prenatal check-ups and upon birth.
- Educational programmes for nurses and midwives on how to provide immediate care for babies born with rare diseases, for example those with epidermolysis bullosa, osteogenesis imperfecta (brittle bone disease) and spinal muscular atrophy type 1.

5. Newborn screening program for diseases that cause severe disabilities and death:

- Newborn screening for inherited metabolic diseases to provide prompt diagnosis and treatment.
- Newborn screening for critical congenital heart diseases.
- Newborn screening for rare primary immunodeficiencies.
- Newborn screening for spinal muscular atrophy type 1.

6. Expertise and laboratory facilities to diagnose serious genetic diseases:

- Capacity-building in critical areas of expertise for rare diseases such as genomic scientists, clinical geneticists, genetic counsellors, genetic nurses and technologists and primary care providers.
- Create government posts for new areas of employment e.g. genetic counsellors and genomic scientists as well as data managers.
- Increased diagnostic laboratories for genetic and genomic diseases in various parts of the country.

7. Funding and expertise for treatment and rehabilitation services:

- Increase the budget for investigations, treatment and management of rare diseases in all types of healthcare facilities and university hospitals to achieve equity of care and services regardless where the patient is domiciled.
- Increase funding for rehabilitation services, including equipment and more qualified therapists.
- Increase accessibility for disabled persons in general, which would also incorporate those patients with rare diseases.
- Provision of respite care for parents and caregivers of patients with rare diseases that caused disabilities. Improve palliative care services for end-of-life situations in patients with rare diseases
- Improve palliative care services for end-of-life situations in patients with rare diseases.
- Improve inter-ministry collaboration in treatment of rare disease.

8. Research and development in rare diseases as one of the priority areas:

- More research funding is needed for rare diseases that may not be 'commercially' beneficial. Many new innovative pharmaceuticals and approaches to therapy are a result of new insights from research into rare diseases.
- Explore the possibilities for joint venture with pharma and biotechnology companies to produce biopharmaceuticals, biosimilar products, biosensors and medical devices locally, thus generating new industries in the field of rare diseases.

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