Definition of Rare Diseases in South Africa

There is currently no global consensus on the universal definition of rare diseases (RD). Different countries and regions worldwide have implemented a variety of definitions and prevalence thresholds, often linked to local RD policy and legislation and other contextual issues. Within many countries or populations, including those with an agreed national definition of RD, there is often disparity on definition usage by different stakeholders operating in different contexts of the RD community.

In South Africa, there is no formally agreed definition of RD implemented at a national level and uncertainty continues to surround the use of this term. The lack of defined boundaries and clarity around this neglected health priority has implications for all stakeholders, and particularly for RD advocacy. This vacuum has largely been filled by the informal uptake of the European definition of RD in South Africa, which describes a RD as a condition affecting less than 1 in 2000 people in the population (equivalent to less than 5 in 10,000). This prevalence threshold was initially chosen by Rare Diseases South Africa NPO (RDSA), when the organisation was formally launched in 2013 and required a definition to implement. This choice was informed by the strength of agreement demonstrated by the European region and by similar rates of consanguinity observed with South Africa.

Research now offers an evidence-base to inform decision-making around the definition of RD, and prevalence thresholds. Work by Richter et al in 2015[1] provides an overview of the RD definitions used globally and findings of this study offer useful insights for consideration. Results of this study, which identified 296 RD definitions from 109 organisations in 32 international jurisdictions, included a range of prevalence thresholds from 5-79 cases per 100,000 people. The average prevalence threshold of most jurisdictions (66%) was between 40-50 cases per 100,000 people, with a global average of 40 cases per 100 000. Across the 32 jurisdictions, umbrella patient organisations tended to use more liberal and inclusive prevalence thresholds (47 per 100 000) whereas private payers used lower thresholds (18 per 100 000). The study recommended that qualitative descriptors be avoided and efforts to harmonize RD definitions should focus on standardizing objective criteria, such as prevalence thresholds[1].

These findings, together with prevalence thresholds from other studies, were used to compile and evaluate a number of options for a RD prevalence threshold in South Africa, summarised in Table 1.

Table 1: Summary of prevalence threshold for a rare disease and related descriptive statistics applied to the South African population 2020[1]

% of population	1 in *n* People Affected	Prevalence threshold (per 100 000)	Number affected in SA population	Citation Source
0.01	20,000	5.00	2,981	Richter et al 2015 (Korea)[1]
0.04	2,500	40.00	23,849	Richter et al 2015[1]
0.05	2,000	50.00	29,811	EU 1999[3], Richter et al 2015[1]
0.06	1,630	61.35	36,578	US Orphan Drug Act 1983[4] & Amendments
0.08	1,316	76.00	45,313	Richter et al 2015 (China)[1]

[1] Based on South African Population of 59,622,350[2]

Recommendation

Based on this study and taking into consideration the abundance of research on this issue in Europe, it is recommended that an individual RD in South Africa be defined as:

"*a condition affecting less than 1 in 2000 people (50 per 100,000 of population)"*

Based on the current population in South Africa[2], this equates an individual rare condition affecting 30,000 or less people. When considered as a collective of the 7000+ RD characterised to date[5], it is estimated that 6-8% of the population are affected, which equates to 3.5 million to 4.7 million South Africans (4.1 million) living with a RD.

Considerations

It is recommendations that the following considerations be taken into account:

- While further terms and inclusive nomenclature may be considered for use in the future (e.g. 'ultra rare' etc), the first step should be to adopt the recommended definition countrywide with buy-in and consensus by all stakeholders.
- Once adopted, implementation of the recommended definition should not be used as a tool to exclude patients or other stakeholders. A holistic, case by case should be applied, taking into account availability of clinical and therapeutic treatments, cost of treatment, severity of case, natural history of the condition and other factors relevant to the context, as well as the prevalence of the condition itself.
- As agreement and consensus is developed globally on a universal definition and prevalence threshold for a RD, this recommendation may be subject to revision.

References

1. Richter T, Nestler-Parr S, Babela R, et al. Rare disease terminology and definitions—a systematic global review: report of the ISPOR rare disease special interest group. Value Health. 2015;18(6):906-914.
2. Statistics South Africa. Statistical Release P0302. Mid-year Population Estimates 2020. Pretoria: Statistics South Africa; 2020.
3. European Union. Regulation (EC) No 141/2000 of the European Parliament and of the Council of 16 December 1999 on orphan medicinal products, 1999.
4. United States Government. Orphan Drug Act 2049-2066, 1983.
5. Orphanet. Orphadata. In: Orphanet, editor. 2019.