Challenges and Possible Solutions to access to treatment for Rare Diseases in Developing Countries

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Conflict of Interest

- Owner and CEO of FYMCA Medical Ltd
- I am a non prescribing physician since retirement
- FYMCA Medical provide services to all sectors of the rare disease field and most of the pharmaceutical companies working in this field
- Medical advisor to multiple patient organizations and regulators
- Thank you Dr Ramswami for slides
Rare Diseases

* Globally around 6000 to 8000 rare diseases exist with new rare diseases.
* 80% of all rare disease patients are affected by approximately 350 rare diseases.
* Individually rare, collectively they affect a considerable proportion of the population in any country - between 6% and 8%.
* Rare diseases include genetic diseases, rare cancers, infectious tropical diseases and degenerative diseases.
* 80% of rare diseases are genetic in origin and hence disproportionately impact children.
Rare Diseases

* In the EU, a rare disease is one which affects fewer than 5 people per 10 000

* Collectively, there are approximately 36 million people living with a rare disease in Europe (3.5 million in the UK)
## Prevalence of Rare Diseases

And Africa best estimate 0.0005/10 000

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<thead>
<tr>
<th>S No.</th>
<th>Country</th>
<th>Per 10,000 population</th>
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</thead>
<tbody>
<tr>
<td>1</td>
<td>USA</td>
<td>6.4</td>
</tr>
<tr>
<td>2</td>
<td>Europe</td>
<td>5.0</td>
</tr>
<tr>
<td>3</td>
<td>Canada</td>
<td>5.0</td>
</tr>
<tr>
<td>3</td>
<td>Japan</td>
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<tr>
<td>4</td>
<td>South Korea</td>
<td>4.0</td>
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<tr>
<td>5</td>
<td>Australia</td>
<td>1.0</td>
</tr>
<tr>
<td>6</td>
<td>Taiwan</td>
<td>1.0</td>
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</tbody>
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National policy for treatment of rare diseases; Ministry of health and family welfare, Government of India; 2017

Courtesy adapted from Ramaswami
Many rare disorders are life threatening or chronically debilitating.

Rare Diseases reduce quality of life; affecting potential for “normal” living, education and learning.

Rare Diseases impact patients, families, friends, caregivers, physicians, fund holders, and society as a whole.

Loss of income and expertise.
Parent:
“Our son's condition is ultra rare so you HAVE to educate yourself on the topic, no doctor has time/inclination to research orphan syndromes for you.”

Information, combined with the right support, is the key to better care, better outcomes and reduced cost.
Rare Disease Impact on Patient and Families

* Rare diseases, in most cases, serious, chronic, debilitating and life limiting
* Affects primarily children unless treated.
* Limits achievements of whole family.
* Require long-term and specialist treatments/management.
* Significant impact on quality of life and cognition
Rare Diseases Policy India document 2017:

Disproportionately impact children:

* 50% of new cases are in children and are responsible for 35% of deaths before the age of 1 year
* 10% between the ages of 1 and 5 years
* 12% between 5 and 15 years.
* The impact on families is often catastrophic in terms of emotional as well as financial drain, as the cost of treatment is prohibitively high.
The European Union is committed to equality of care, stressing the “paramount” need for “equity and solidarity” of care between orphan and common diseases, as well as requiring “delivery of high-quality, accessible and cost-effective healthcare” for those suffering from rare diseases.


Courtesy Ramaswami
Legislation for Rare Diseases

- Disability legislation
- National and health system constitutions
- Judicial review
- Tort law “it is the doctor’s duty to provide a treatment that he considers to be in the interests of the patient and that the patient is prepared to accept
- Human rights legislation


Courtesy Ramaswami
Challenges

* Rare diseases are Rare - delayed or misdiagnosis
* Lack of adequate resources for patients/ caregivers to deal with the emotional impact of rare diseases
* Poor data collection and epidemiology
* Poor record keeping
* More research required to expand the current rare disease body of knowledge
* Lack of Co-ordinated services and value for health care costs in the health care models
* Lack of Country specific rare disease policies
Resulting in a diagnostic delay

- Based on a systematic review\(^1\)
  - Median age at symptom onset: **2.0 years** (range -0.3 – 42)
  - Median age at diagnosis: **5.7 years** (range 0 – 51)

Lack of Awareness – Missed or Delayed Diagnosis of Rare Diseases

- 25% of people reported waiting between 5 and 30 years from the time of first symptoms to a confirmatory diagnosis of their disease.

- 25% of people had to travel to a different region to obtain a diagnosis and 2% had to travel to a different country.

- In 33% of cases, the diagnosis was announced in unsatisfactory terms or conditions.

EurordisCare survey, 2004

Courtesy Ramswami
Lack of Awareness – Missed or Delayed Diagnosis of Rare Diseases

• The genetic nature of the disease was not communicated to the patient or family in 25% of cases (despite most rare diseases having a genetic component)

• Genetic counseling was only provided in 50% of cases

EurordisCare survey, 2004
Challenges: Rare Diseases – Developing Countries

- Lack of epidemiological data
- Difficult to ascertain natural history and disease progression
- Health care system differences – private and public
- National health priorities
- National policies in general – Health not priority
- Diagnostic costs and expertise issues resulting in diagnostic odysseys and delay/missed/misdiagnoses
- Cost implications or misinterpretation of cost impact

Speaker’s Opinion and adapted from Ramaswami; National policy for treatment of rare diseases; Ministry of health and family welfare, Government of India; 2017
Challenges:
Rare Diseases – Developing Countries

- Lack of rare disease research and development investment
- Limited tertiary level management involving long term care and rehabilitation
- Lack of facilities to support patients
- Not least: Unavailability, lack of licensing and prohibitive high cost of disease modifying therapies
- Perception – Task is too big so easier to ignore

*Speaker’s Opinion and adapted from Ramaswami; National policy for treatment of rare diseases; Ministry of health and family welfare, Government of India; 2017*
* Quality of Life Measures to monitor health impact
* Patient Reported Outcome Measures
* Liaising with patients/family/carer & patient organisations
* Care Co-ordinators
* Holistic care pathway development
* Transition - Adolescent wards and clinics
* Newer technologies: E.g. Telemedicine, Video clinics
• Global Multinational Clinical Trials

• Lack of diagnostics means participants not identified

• Regulatory bodies (E.g. NICE, UK) evaluation of newer treatments – champion robust tools to measure health outcomes of treatments for rare diseases

• Many tools not appropriate for Africa

• Partnerships with Industry and other Health Care enterprises

• Champion and participate in disease specific registries National and International, Electronic Rare Disease networks
On the one hand, health problems of a much larger number of persons can be addressed by allocating a relatively smaller amount.

On the other, much greater resources will be required for addressing health problems of a relatively smaller number of persons.
Rare Diseases Challenges in South Africa

- Total population about 57 million - 45 million black ethnic groups, 5 million mixed race, 4 million white, 2.5 million foreigners and 1.5 million Indian.
- 11 official categories and 12 official languages including sign language.
- Approximately 40% of population have no permanent work yielding a living wage.
- Approximately 20% has access to private health which is better than U.K. but NHS service in UK is much better resourced with formal rare disease policy and expert centers in place.
- Rare disease drugs are limited in funding and rest depends on area.
- Some areas have very good state health like Pretoria and Cape Town and rest poorly resourced and staffed.

Speakers interpretation
http://www.statssa.gov.za/?p=11129
Rare Diseases Challenges in South Africa

- Metabolic test is very limited with only a few tests available and not funded in general.
- Limited rare disease knowledge outside Pretoria, Johannesburg and Cape Town.
- There are only expert centers for common disorders like heart surgery but none for rare disease.
- 80% of all care is delivered by GPs (GPs multitask – including doing surgery and most procedures).

Speakers opinion
Rare Diseases Challenges in South Africa

• Tb and HIV dominates all health care and costs; predicted at least 50% is positive and malnutrition is common.
• Very poor infrastructure so electricity and water is not easily available everywhere.
• Even large cities have electricity blackouts for days.
• Lack of money spent on health care
• Corruption
• Lack of knowledge regarding rare diseases
Rare Diseases Challenges in South Africa

- Poor education system; many reaching universities struggle to attain grades - variable levels of medical trainees finishing
- Public system overwhelmed and very poorly funded
- Very strict ethics making trials near impossible
- Very difficult to get samples sent out of country
- No postal system as it has collapsed
Immediate Measures

• Patient registry for rare diseases housed in Indian Council of Medical Research (ICMR)

• Arriving at a definition of rare diseases suited to India

• Developing materials for generating awareness in the general public, patients and their families and health care providers.

• Developing and conducting training programmes of health care providers on rare diseases

• Rare Diseases Cell within MoHFW, ICMR and DoP in Ministry of Chemicals and Fertilizers respectively to be the ‘nodal’ on rare diseases in their respective ministries and departments
Long term measures: The below mentioned measures are of a continuing nature that ought to be initiated now with deliberate, concrete steps towards their scale up and progressive realization:

* Systems in place for reporting and data collection
* Conduct epidemiological studies to estimate prevalence of rare diseases
* Take measures to improve research and development for treatment, diagnostic modalities, care and support including assistive devices, drug development for rare diseases etc.
* Measures, legislative or otherwise, for encouraging local manufacturing of drugs for rare diseases
India: Rare Diseases Policy 2017

Long term measures: The below mentioned measures are of a continuing nature that ought to be initiated now with deliberate, concrete steps towards their scale up and progressive realization

* Take legal and other measures to control the prices of drugs for rare diseases to ensure its affordability and health system sustainability
* Encourage funding support from Public Sector Undertakings (PSUs) and corporate sector and exploring other options for sustainable funding for the corpus
* Ensure insurance coverage for rare genetic disorders
* Allow import of Enzyme Replacement Therapies (ERTs) and remove import duty on them as well as on assistive devices

National policy for treatment of rare diseases; Ministry of health and family welfare, Government of India; 2017  Courtesy Ramaswami
Long term measures: The below mentioned measures are of a continuing nature that ought to be initiated now with deliberate, concrete steps towards their scale up and progressive realization -

* Piloting, and rolling out testing for rare genetic diseases in newborns, in tandem with development and standardization of diagnostic modalities and availability of treatment
* Develop **standardized protocols for diagnosis and treatment/management of rare diseases**, to be revised in conformity with evolving diagnosis and treatment landscape
* **Strengthen laboratory networks** for diagnosis of rare diseases
India: Rare Diseases Policy 2017

Long term measures: The below mentioned measures are of a continuing nature that ought to be initiated now with deliberate, concrete steps towards their scale up and progressive realization -

* Develop and accredit **Centres of Excellence (CoE)** over a period of time, in a phased manner
* As a preventive strategy, explore feasibility for **providing and progressively scaling up pre-conception and antenatal genetic counseling and screening in a targeted manner**, or otherwise, to provide option to parents to prevent conception or birth of a child with a rare genetic disease
* **Drug Controller General of India (DCGI)** to consider feasibility of amending Drugs and Cosmetics Act or otherwise taking measures under it, to include appropriate provisions on drugs for rare diseases, including provisions to **facilitate clinical trials and import of ERTs**.
<table>
<thead>
<tr>
<th>Categories</th>
<th>Recommendations</th>
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</table>
| 1 Disorders amenable to one time treatment    | Prioritise funding category:  
• One time treatment cost 5-20 lacs Indian Rupees  
• Treatment outcome good  
• Private and public sector access with good expertise and outcomes  
• Funding for follow up included  
• Ceiling on existing funding limits made flexible |
| 2 Disorders requiring long term therapy / life long therapy | • Cost for these disorders mostly prohibitive  
• Documented treatment outcomes (E.g. Gaucher Type I)  
• Objective Inclusion/exit criteria  
• Identify institutes with expertise and manpower |
| 3 Disorders with no known therapy             | • Supportive care                                                               |
Context: high cost therapies Vs Public Health priorities
Lysosomal disorders as an example

• The annual recurring cost of one patient with Enzyme Replacement Therapy could range from 1.8 – 17.0 lakhs Indian Rupees per kg of body weight.
• I.e. child weighing 10 kgs, the cost would be between 18 lakhs to 1 crore! This is a huge cost in a resource constrained public health system.
• This amount could treat:
  400 TB or 400 HIV patients in a year.
  10-100 patients with Type 1 diabetes (annual cost estimated at Rs. 18,000/- based on a study in South India in 2011)
  Potentially prevent 10,000 malaria cases a year
  Prevent almost 600 under five children from being hospitalized with pneumonia annually.

Laurence Y.V. et al, Pharmacoeconomics, 2015; 33(9):939-955;
IC Verma Report, Rare Diseases Policy, India, 2017 Courtesy Ramaswami
• Government Policies and Centralised funding to address Rare Diseases – Needs ‘buy in’ from governments
  (Indian Rare Diseases Policy 2017 is a step in the right direction)
• Country specific rare disease policies
• Education and Training Initiatives at primary, secondary and tertiary care
• Educational Networks/Forums – national, international – Webased/Telecommunications/face to face –
• New genetic techniques – Next Generation Sequencing, Array Comparative Genomic Hybridisation

Courtesy Ramaswami
• Screening: Selective; New-born screening
• Accessible diagnostics – affordable and results obtained in a timely manner
• Centres of Excellence for Treating Rare Diseases
• Governments, Ethics Reviews, Academic Institutions, Health care professionals engaged and facilitating research – epidemiology and therapies
• Local drug manufacturing – biosimilars, generics
• High Cost drug review for existing therapies with country specific discounted costs as appropriate
• Legislations for Rare Diseases

Courtesy Ramaswami
Owl - stay awake when the rest of the world is asleep