Rare Diseases & Justice – Our Ethical Responsibility

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No conflict to declare

• This presentation reflects my personal view and should not be construed to represent any third party’s view or policy.
Introduction

• Definition of Rare diseases
• Are drugs for rare diseases essential?
• Distributive justice - Concept and theories
• Rare diseases and Essential drug list (EDL)
• LMICs context
• Way forward
Which diseases are rare?

- Definition
  - USA: 7.5:10 000 (< 200 000 patients)
  - Europe: <5:10 000
- Often underlying genetic abnormality
Are drugs for rare diseases essential?

- Is it ethical to allow benefit to one patient and no benefit to another patient based on prevalence of disease?
- What are the underlying ethical arguments?
Principle of Justice

- **Formal principle: Aristotle**
  - “Equals must be treated equally & unequals must be treated unequally”

- **Material principle**
  - To each person an equal share
  - *To each person according to need*
  - To each person according to effort
  - To each person according to contribution
  - To each person according to merit
  - To each person according to the free-market exchanges
Distributive justice definition

• “Fair, equitable and appropriate distribution by justified norms that structure the terms of social cooperation”
  
  Beauchamp and Childress

• Refers to the distribution of all rights and responsibilities in society
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<th>Utilitarian</th>
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<td>Maximize value</td>
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<td>May favour children – most years of benefit</td>
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## Theories of Justice

**(L Kopelman)**

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Resource allocation systems

• United Network for Organ Sharing
  • Sickest first
  • First come first served
  • Prognosis
  • *Disadvantage* – *No benefit maximizing or prognosis or youngest age*

• Quality adjusted life years (QALY)
  • Outcome measure – years
  • Maximizing assumption
  • *Disadvantage* – *Insufficient since person in wheelchair with impaired mobility may be very productive*

• Disability adjusted life years (DALY)
  • WHO: quality of life years
  • *Disadvantage: age as outcome measure*
Complete Lives System

- Five principles
  - Youngest first – not yet lived their lives
    - Can be modified – adolescents rather than infants
  - Prognosis
    - Poor prognosis – cannot live a complete life
  - Save the most lives
    - More persons to live a complete life
  - “Lottery”
    - Equal potential recipients
  - Instrumental value
    - Socio-economic active
  - Disadvantages – Older age discrimination

Persad G et al. Lancet 2009
Two approaches

- Essential Drug List (EDL)
- Orphan Drug list
Essential Drug List (EDL)

• WHO Essential drug list (EDL) – 1977

• Normative guideline
  • Save lives and improve health
  • Available, affordable, good quality and appropriately used
EDL Approach

- All drugs that are essential for a particular disease is included in the EDL

  - This is the case for both common and rare diseases with proven effective therapy

  - **Cost-effective analysis** prove high priority for a rare disease – included in EDL
Orphan Medicines Model

  - Prevalence
    - Rare disease
    - Chronic and debilitating
  - Effective treatment
  - Safety profile acceptable
  - Availability
  - Diagnosis feasible
  - Expertise infrastructure
<table>
<thead>
<tr>
<th>Aspect</th>
<th>EDL</th>
<th>Orphan Drugs</th>
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</thead>
<tbody>
<tr>
<td>Concrete policy</td>
<td>1977 Worldwide</td>
<td>1983 USA; 2000 EU</td>
</tr>
<tr>
<td>Primary focus</td>
<td>Public health</td>
<td>Individual patient</td>
</tr>
<tr>
<td>Developed by</td>
<td>WHO</td>
<td>USA, EU, Australia, Japan</td>
</tr>
<tr>
<td>Criteria</td>
<td>Drug driven: efficacious, safe, cost-effective, evidence-based</td>
<td>Disease driven – rare disease</td>
</tr>
<tr>
<td>Policies aim</td>
<td>Established medicines to patients</td>
<td>New medicines</td>
</tr>
<tr>
<td>Target populations</td>
<td>All countries especially low income countries</td>
<td>High income countries</td>
</tr>
<tr>
<td>Economics</td>
<td>Cost-effective, sustainable, affordable access</td>
<td>High price per individual patient</td>
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Adapted from Stolk P et al. *Bull World Health Org* 2006; 84: 745-751
What is the current status in LMICs?

- **Public Health**
  - Utilitarian approach
  - WHO EDL

- **Private Health**
  - To a certain extent similar to public health
  - Allow egalitarian approach with equal opportunity in proven therapy for rare diseases
Convention on the rights of children

- **Article 1**
  - The best interest of the child shall be the primary consideration

- **Article 3**
  - Ensure the existence of institutions, services and facilities for adequate health care

- **Article 6**
  - Every child has the inherent right to life
  - To ensure to the maximum extent possible, the survival and development of the child
Causes of Death in children < 5 years

Causes of deaths in children under 5 years
(over 8 million/year)

- Diarrhoea: 14%
- Pneumonia: 14%
- Other infections: 9%
- Malaria: 8%
- Noncommunicable diseases: 4%
- Preterm: 12%
- Asphyxia: 9%
- Sepsis: 6%
- Other neonatal: 5%
- Pneumonia, neonatal: 4%
- Congenital: 3%
- Tetanus: 1%
- Diarrhoea, neonatal: 1%

Children: 59%
Newborns: 41%
How do we decide?

- Original position: “veil of ignorance
- General concept:
  - All social primary goods must be distributed equally unless an unequal distribution of any or all goods are to the advantage of the least favoured.
- Two principles: (Rawls, 1971)
  - The Difference Principle: addresses “social and economic inequalities”, which must be arranged in such a manner that they are to everyone’s advantage under all circumstances and must result in the greatest benefit to the most disadvantaged.
Tools

- **Need**
  - Acute
  - Aggressive
  - Technological advanced
  - *Negative impact on chronic and palliative care*
- **Age**
  - Younger population
  - *Negative impact on chronic and palliative care, as well as elderly*
- **Opportunity**
  - Private health care - *You can buy your health care according to your own contribution*
- **Cost effective**
  - Total cost compared to effectiveness – cost effective ratio
Proposal for rare diseases Step 1

Biomedical consideration
Will health improve?
- Yes

Ethical consideration
- Principle of non-abandonment

Budgetary insulation

W Pinxten et al. JME 2011
Proposal for rare diseases Step 2

How can we do this fairly?

Is the opportunity cost of orphan drug acceptable?

Yes
- Certainty for some
  - Severity
    - Life-threatening
  - Health gain
- Possibility for all
  - Real chance of adoption

NO
- Individual welfare erode common interest of social health care

W Pinxten et al. JME 2011
# SIOP – PODC MODIFIED GUIDELINES

<table>
<thead>
<tr>
<th></th>
<th>Setting 1 Low Income</th>
<th>Setting 2 Moderate Income</th>
<th>Setting 3 High Income</th>
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</thead>
<tbody>
<tr>
<td>Imaging</td>
<td>None or CT only</td>
<td>CT and/or MRI</td>
<td>MRI</td>
</tr>
<tr>
<td>Access to treatment</td>
<td>Minimal</td>
<td>Moderate access</td>
<td>Moderate to high access</td>
</tr>
<tr>
<td>Surgery</td>
<td>Minimal only conservative</td>
<td>Moderate surgical skills</td>
<td>Full spectrum</td>
</tr>
<tr>
<td>Pathology</td>
<td>Minimal</td>
<td>Limited risk assessment</td>
<td>Excellent</td>
</tr>
<tr>
<td>Genetic</td>
<td>None</td>
<td>None</td>
<td>Limited availability</td>
</tr>
<tr>
<td>Criteria for reclassification</td>
<td>Improved treatment, pathol,</td>
<td>Improved treatment, pathol,</td>
<td></td>
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<tr>
<td>Advocacy for rare diseases</td>
<td>Probably none except</td>
<td>Initiate for some if drugs in EDL</td>
<td>Advocacy for all</td>
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Way forward

- Distributive justice argument – Aristotle, Rawls
  - Proper distribution of benefits and burdens
- Is it ethical to allow benefit to one patient and no benefit to another patient based on prevalence of disease?
  - Address question through cost-effective analysis – Cost-effective ratio
  - If proven cost-effective and safe – include in EDL as essential for the disease
Way forward

• Use Convention on the rights of children since this is “basic health care”

• Ensure budget insulation for rare diseases with guaranteed access for some and possible access for all (Pinxten et al. 2011)

• Ensure publishing all evidences of effective treatment even if only case reports to generate evidence

• Advocate for rare diseases in the face of an existing therapy is our ethical responsibility
Thank you for the invitation