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HEIDELBERG

Interventions for Ultra-Rare Disorders and the Logic of Cost Effectiveness

or

The Need for Alternative Methods to Evaluate Medical Interventions for Ultra-Rare Disorders

Michael Schlander,
Silvio Garattini, Sören Holm, Peter Kolominsky, Erik Nord,
Ulf Persson, Maarten Postma, Jeffrey Richardson, Steven Simoens,
Oriol de Solá-Morales, Keith Tolley, and Mondher Toumi

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INNOVAL HC
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The 5 Most Expensive Drugs in the World[1]

1. **Soliris (Alexion)**
   paroxysmal nocturnal hemoglobinuria (PNH), atypical hemolytic uremic syndrome (aHUS); average annual cost: **US-$ 409,500**
2. **Elaprase (Shire)**
   Hunter syndrome (ERT); **US-$ 375,000** p.a.
3. **Naglazyme (BioMarin)**
   mucopolysaccharidosis (MPS) VI (ERT); **US-$ 365,000** p.a.
4. **Cinryze (ViroPharma)**
   hereditary angioedema (HAE); **US-$ 350,000** p.a.
5. **Myozyme (Sanofi / Genzyme)**
   Pompe disease (ERT); **US-$ 300,000** p.a.

[1]S. Williams, The Motley Fool, June 29, 2013. http://www.fool.com/investing/general...

Key Challenges for URDs

- **Establishing "Value for Money" (Efficiency)**
  - international heterogeneity in institutional arrangements and established methodologies to determine "value for money";
  - the still prevailing "logic of cost-effectiveness", relying on cost per QALY benchmarks, in applied health economics;
  - the broadly held assumption that the social desirability of an intervention would be inversely related to its associated incremental cost per QALY gained;
  - the adoption of "efficiency-first" instead of "fairness-first" evaluation approaches in a number of jurisdictions;
  - the high fixed (i.e., volume-independent) cost of R&D and the need to recoup this investment from a small number of patients during limited periods of market exclusivity;
  - …

Adopting the Logic of Cost Effectiveness

… using Incremental Cost-per-QALY-Gained Benchmarks …

… would have the potential

to necessarily and inevitably deprive many patients

with URDs from any chance to ever get access

to innovative, effective interventions.

Orphan drugs and the NHS: should we value rarity?

Christopher McCabe, Karl Claxton, Aki Tsuchiya

The growing number and costs of drugs for rare diseases are straining healthcare budgets. Decisions on funding these treatments need to be made on a sound basis

[…]

The justification for special status for rare diseases must rest on the question: should we value the health gain to two individuals differently because one individual has a common disorder and the other has a rare disorder?

[…]

While orphan drugs were rare, healthcare systems were able to deal with them in an ad hoc manner. But there are now over 6000 orphan diseases with over 200 treatments approved by the US Food and Drugs Administration and 64 trials currently sponsored by the US Office of Orphan Products Development. […] Genomics is expected to disaggregate currently prevalent diseases into many genetically defined distinct conditions. Orphan status is thus likely to become increasingly common.

[…]

Special status for orphan drugs in resource allocation will avoid difficult and unpopular decisions, but it may impose substantial and increasing costs on the healthcare system. The costs will be borne by other, unknown patients, with more common diseases who will be unable to access effective and cost effective treatment as a result.

British Medical Journal 2005, 331: 1016-1019

Orphan drugs policies: a suitable case for treatment

Michael Drummond, Adrian Towse

A starting point for designing any health policy is to clarify society's views and objectives in relation to the issues concerned.

Although there is scant evidence on what the general public in different countries expect from their health care system, **the utilitarian perspective of maximising the total benefits to the population as a whole is a reasonable starting point**, particularly in jurisdictions where public financing of health care predominates.

This notion also underpins most of the assessments of value for money conducted in those jurisdictions where these are explicitly required. Namely, the implicit or explicit objective is to maximise the total health gain from the use of health care resources, although the methods for measuring health gain v ary from jurisdiction to jurisdiction.

However, since orphan drugs are never as cost-effective as drugs for more prevalent diseases, **departures from a strict utilitarian perspective would have to be justified** if they were to be funded. That is, society would have to be willing to give up some of the health gain to the population as a whole.

European Journal of Health Economics 2014, 15: 335-340

Social Preferences: Non-Selfish Motives

A person exhibits social preferences if the person not only cares about the material resources allocated to her but also cares about the material resources allocated to relevant referehce agents.[1]

In addition to material self-interest, these are

- **Reciprocity or Reciprocal Fairness**
  with fairness being determined by the equitability pf the payoff distribution (relatiuve to the set of feasible payoff distributions)
- **Inequity Aversion**
  resulting in altruism or envy towards other people
- **Pure Altruism**
  a form of unconditional kindness
- **Spiteful or Envious Preferences**
  always valuing a material payoff of relevant reference agents negatively

Heterogeneity of motives at the individual level.

[1]cf. E. Fehr and U. Fischbacher (2002)

Empirical Ethics

The "Sharing Perspective":

A Broad Range of Social Preferences

- **severity** of the initial health state,
  i.e., a stable preference to prioritize health care for the worse off;
- **urgency** of the initial health problem,
  especially if life-threatening, i.e., the so called "rule of rescue";
- **capacity to benefit** of relatively lower importance,
  i.e., people appear to value additional health gains lower
  once a certain minimum effect has been achieved;
- certain **patient attributes** (such as [younger] age,
  parent or caregiver status, [non] smoker);
- a strong dislike for "**all-or-nothing**" resource allocation decisions;
- **rights**-based considerations (such as nondiscrimination).

Potential Ways Forward

Perspectives on Cost:

- From a **decision-makers**' perspective, overall budgetary impact should be more relevant than incremental cost effectiveness ratios.
- If a **social value** perspective (instead of an almost exclusive focus on individual utility) was adopted, the social opportunity cost (or [social] value foregone) of adopting a program would be reflected by its net budgetary impact. This would move the focus from cost per patient to cost on the program level.
- Likewise, a **pragmatic approach** would reflect the commercial realities and the basic cost structure of the research-based biopharmaceutical industry, which incidentally is showing signs of a strategic shift from price maximization to **life cycle revenue management** (in order to "extract" maximum value).

Potential Ways Forward

Valuation Principles:

- **Alternative** economic (e)valuation principles – that promise to reflect normative concerns and capture social preferences better than the conventional logic of cost effectiveness – should be rigorously assessed for their potential to complement of replace the currently predominant standard.
- The most promising **candidates** include (but are not limited to)
  1. a **multicriteria decision analysis (MCDA)** framework, which, in principle, might incorporate cost utility analysis with benchmarks adjusted to multiple contextual variables, as a short-term or "quick" fix;
  2. **cost value analysis**, using the person-trade off (PTO) or the relative social willingness-to-pay (RS-WTP) method, as a mid- to long-term solution better capturing **social value**.

How to Evaluate Evaluation Methods:

How well do they capture

- **Normative Premises**, in particular
  - Links to Moral Theory
  - Links to Economic Theory
- **Empirical Preferences** related to
  - Attributes of the Health Condition
  - Attributes of the Persons Afflicted
- **Pragmatic Aspects / Practical Experience** regarding
  - Feasibility
  - Implementation

Thank You for Your Attention!

Professor Michael Schlander, M.D., Ph.D., M.B.A.

Contact

www.innoval-hc.com
www.michaelschlander.com

michael.schlander@innoval-hc.com
michael.schlander@medma.uni-heidelberg.de

INNOVAL HC
Institute for Innovation & Valuation in Health Care

Address

An der Ringkirche 4
D-65197 Wiesbaden / Germany

The *URD Consensus Documents* are available at the Institute's website **www.innoval-hc.com**