Novel developments in HTA methodology

institute for Medical Technology Assessment

Leona Hakkaart, PhD

International Conference on Rare Diseases & Orphan drugs (ICORD) 2014

October 7th 2014, Ede

ERASMUS UNIVERSITEIT ROTTERDAM
iMTA

Content

- Setting the scene; availability of orphan drugs
- Health Technology Assessment
- Economic, societal and patient burden of orphan diseases
- Cost-effectiveness of orphan drugs
- HTA-study
- Future challenges for HTA

Number of orphan drugs

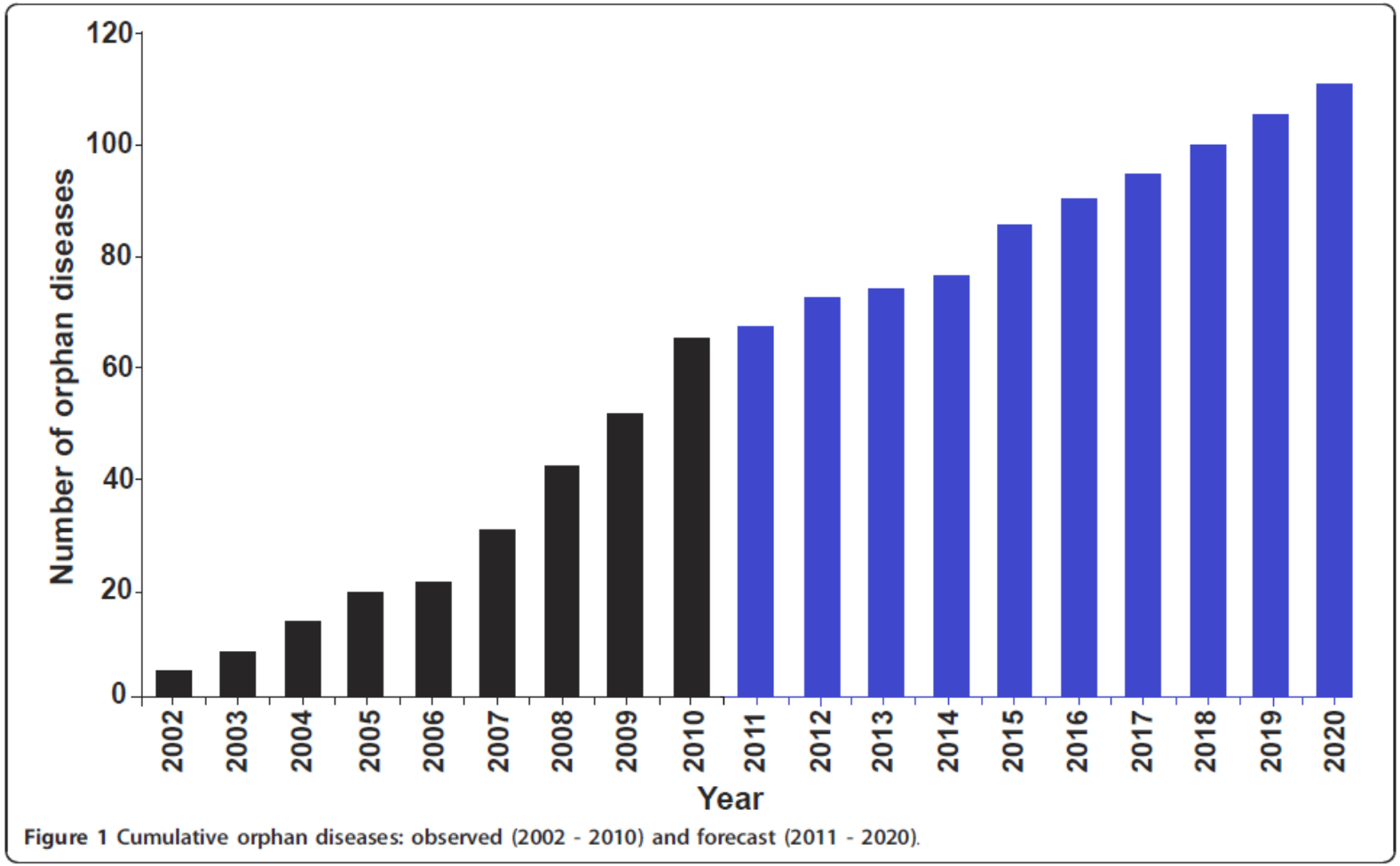
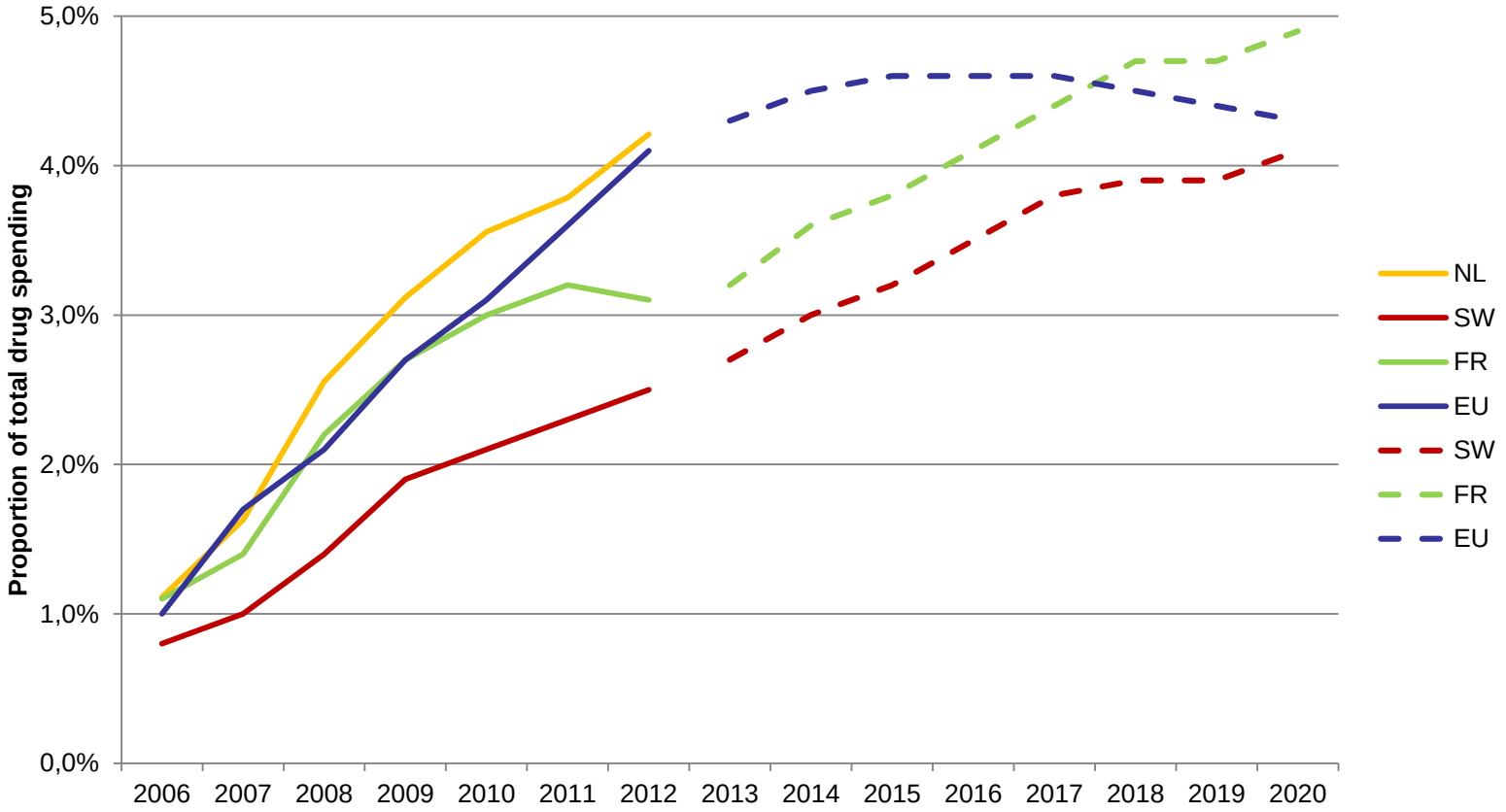


Figure 1 Cumulative orphan diseases: observed (2002 - 2010) and forecast (2011 - 2020).

Schey et al. (2011) Estimating the budget impact of orphan medicines in Europe: 2010-2020. *Orphanet J Rare Dis* 6: 62

Orphan drug expenditures in Europe



EUR: Schey et al. (2011) Estimating the budget impact of orphan medicines in Europe: 2010-2020. *Orphanet J Rare Dis* 6: 62

SW & FR: Hutchings et al. (2014) Estimating the budget impact of orphan drugs in Sweden and France 2013-2020. *Orphanet J Rare Dis* 9: 22

NL: Kanters et al. (2014) Orphan drugs expenditure in the Netherlands in the period 2006-2012, *Accepted for publication*

Disease severity

- Some examples of orphan diseases (untreated)

	QoI (utility)	Survival (age at death)
Pompe adults	0.72	Less than NL pop
Pompe infants	0.62	<1 year
Fabry	0.77	60-75 years
Gaucher type I	0.36-0.93	~60 years
Morquio	0.50	25-30 years
Hunter	0.51	25-60+ years
Hemophilia	0.66	65-70 years

Health technology assessment (HTA)

"The systematic evaluation of the properties and effects of a health technology, addressing the direct and intended effects of this technology, as well as its indirect and unintended consequences, and aimed mainly at informing decision making regarding health technologies."

HTAGlossary.net (2014)

Cost-effectiveness

- Cost-effectiveness is used to distribute a specific health care most efficiently

- Cost-effectiveness is often expressed as cost per QALY (Quality Adjusted Life Year)

Assessment of orphan drugs

- Several factors play a role any reimbursement decision
  - Effectiveness
  - Cost-effectiveness
  - Necessity
  - Feasibility

- For orphan drugs, other factors might be included, or might replace ‘common’ factors
  - Rarity
  - Target population
  - Equity

Cost-effectiveness (some examples)

- High treatment costs often lead to high cost/QALY ratios
- Remarkable differences between countries

Product	Indication	UK: ICER (£/QALY)[1]	NL: ICER (€/QALY)
Iloprost (Ventavis)	Primary Pulmonary Hypertension	23,324	
Miglustat (Zavesca)	Gaucher (I)	116,800	
Nonacog alfa	Haemiphilia B	172,500	
Agalsidase beta (Fabrazyme)	Fabry	203,009	3.3 Million [2]
Laronidase (Aldurazyme)	MPS I	334,880	
Imiglucerase (Ceredase)	Gaucher (I & II)	391,244	0.9 Million [3]
Alglucosidase alfa (Myozyme)	Pompe (infantile)		1.0 Million [4]

[1] National Institute for Health and Care Excellence. Appraising orphan drugs (DRAFT). 2006
[2] Rombach et al. (2013) Cost-effectiveness of enzyme replacement therapy for Fabry disease
[3] Van Dussen et al. (2014) Cost-effectiveness of enzyme replacement therapy for type 1 Gaucher disease
[4] Kanters et al. (2014) Cost-effectiveness of enzyme replacement therapy with alglucosidase alfa in classic-infantile patients with Pompe disease

Reimbursement of orphan drugs

- Reimbursement of orphan drugs is often black box
- Differences both within and between jurisdictions

Name	Indication	AUS	BEL	CAN	ENG	NZE	SCO	WAL	Total reimbursed (%)
laronidase	Mucopolysaccharidosis I	YES	YES	NO	YES	NO	NO	YES	57
alglucosidase alfa	Pompe disease (adults)	NO	YES	NO	YES	NO	NO	NO	29
alglucosidase alfa	Pompe disease (infants)	YES	YES	YES	YES	NO	NO	YES	71
agalsidase alfa	Fabry disease	YES	YES	NO	YES	NO	-	YES	57
agalsidase beta	Fabry disease	NO	YES	NO	YES	NO	-	YES	43
galsulfase	Mucopolysaccharidosis VI	YES	YES	-	YES	NO	-	-	43
idursulfase	Mucopolysaccharidosis II	YES	YES	NO	YES	NO	NO	NO	43
clofarabine	Acute lymphatic leukemia	-	YES	-	-	-	NO	YES	29
eculizumab	Paroxysmal nocturnal hemoglobinuria	YES	-	NO	-	NO	NO	YES	29
trabectedin	Soft tissue sarcoma	-	-	-	YES	-	NO	NO	14
canakunimab	Cryopyrin-associated periodic syndromes	-	-	NO	-	-	NO	NO	0
ofatumumab	Chronic lymphatic leukemia	-	-	-	NO	-	NO	NO	0
Proportion reimbursed (%)		6/8 (75%)	8/8 (100%)	1/8 (13%)	8/9 (89%)	0/8 (0%)	0/9 (0%)	6/11 (55%)	

Kanters et al. (20XX) Factors affecting reimbursement decisions on 11 high-priced inpatient orphan drugs, *Forthcoming publication*

Challenges

- Increasing number of Orphan Drugs
- Increasing Expenditures
- No transparancy in reimbursement procedure
- Unsatifactory from all perspectives
- Negative advice/Positive reimbursement
- HTA

Assessment of orphan drugs (interviews)

- Same criteria apply to orphan drugs
  - Necessity
  - Effectiveness
  - Cost-effectiveness
  - Feasibility

- Other aspects play a role in the assessment
  - Alternative treatments
  - Age of target population
  - Impact for the patient
  - Stimulating science and knowledge development

Assessment of orphan drugs (interviews)

- Not necessarily different from non-orphan drugs
  - Same requirements for clinical evidence
  - Same guidelines for cost-effectiveness analyses
  - Same guidelines for budget impact analyses

- In practice, assessment is different for some aspects
  - Smaller studies, less clinical evidence
  - Irrelevance of some guidelines

Recommendations for assessment of orphan drugs (interviews)

- Provide clarity on reimbursement criteria

- Determine outcome parameters upfront
  - Relevant outcome parameters
  - Relevant thresholds
  - Appropriate time lines
  - In collaboration with clinical experts and patients

- International collaboration is crucial

Multi Criteria Decision Analyses

- Multi Criteria Decision Analyses (MCDA):
  - proposed as alternative instrument for reimbursement decision making
  - uses explicit criteria and weights
  - transparent and systematic way of decision making

Multi Criteria Decision Analyses

- Remaining questions:
  - What criteria should be assessed?
  - How to determine weights?
  - Who's weights should be used?
  - Are decision makers willing to cooperate?
  - …

Future HTA-challenges Orphan Drugs

- Society´s values
- Priority setting and incentives for research

Cost containment during other phases of drug cycle

- ‘Salami slicing’
  - Only genuine orphan drugs should be reimbursed (reduce the number of orphan drugs)
- Stimulation of generics
  - (reduce the prices of orphan drugs)
- Price/volume arrangements
  - (reduce the costs of orphan drugs)

institute for Medical Technology Assessment

Thank you very much for your attention

ERASMUS UNIVERSITEIT ROTTERDAM
iMTA