

# Health Technology Assessment and Orphan Drugs

Keith Tolley, Director, Tolley Health Economics Ltd

European Haemophilia Consortium Conference

Budapest, 7<sup>th</sup> October 2011

# Healthcare payers

National payers



Local payers

# Pressures on the payers...

- Drug expenditures continue to rise
  - New drugs are rarely cost saving
  - New drugs for previously untreated conditions
  - Ageing, obesity, alcohol abuse
  - Growing patient awareness
- Budgets for health care becoming even more constrained
  - Always been constrained
  - Economic crises meaning becoming even more constrained

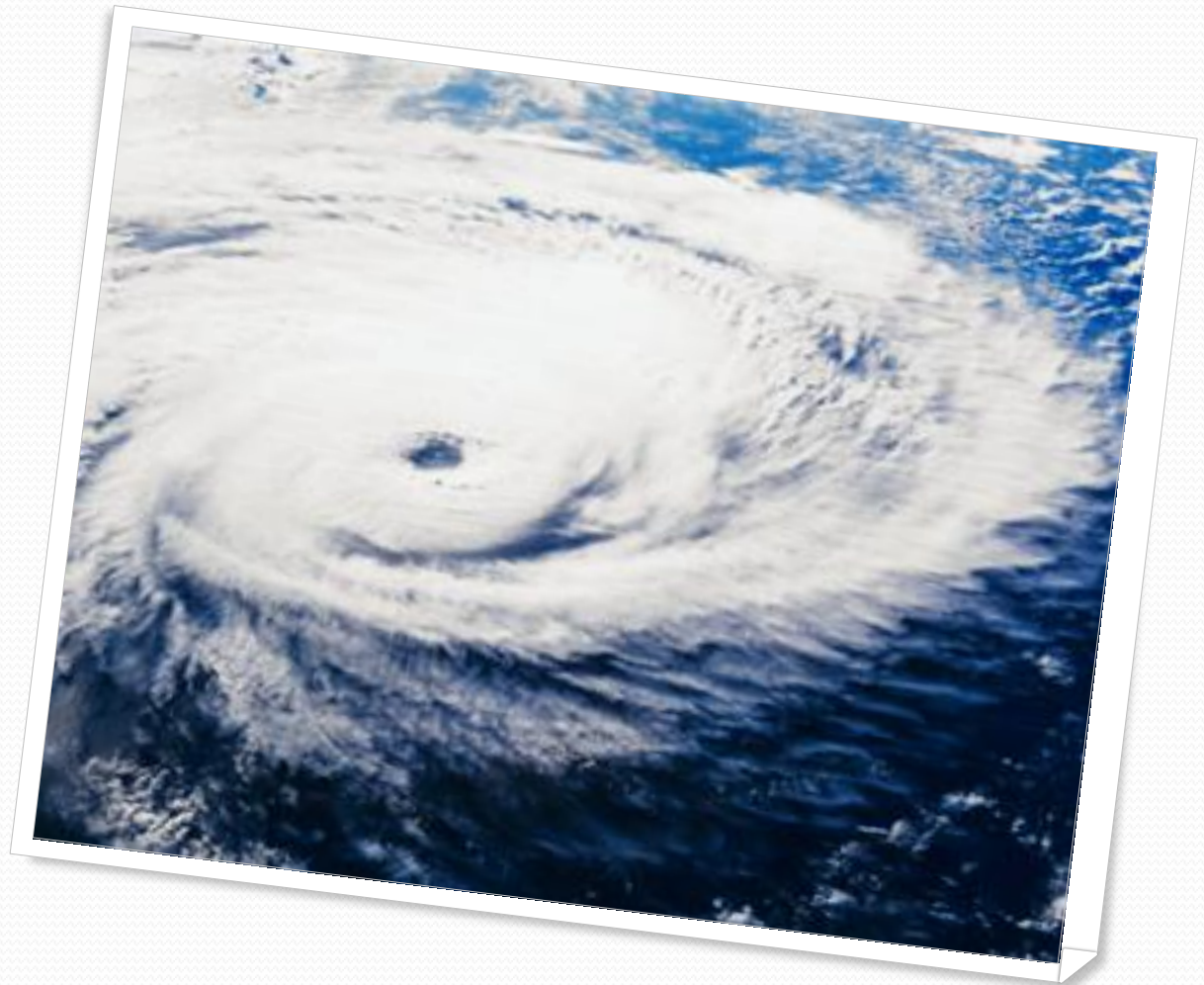
# Climate change in haemophilia

Previously little  
Funding  
restriction

But growth in  
use and cost of  
factor VIII  
(prophylaxis)

New 'expensive'  
recombinant  
products

Payers concern  
to control costs



# Growth in Health Technology Assessment around the globe

Organisations  
assessing clinical  
and cost-  
effectiveness of  
new medicines

To aid decisions  
about  
reimbursement  
and funding



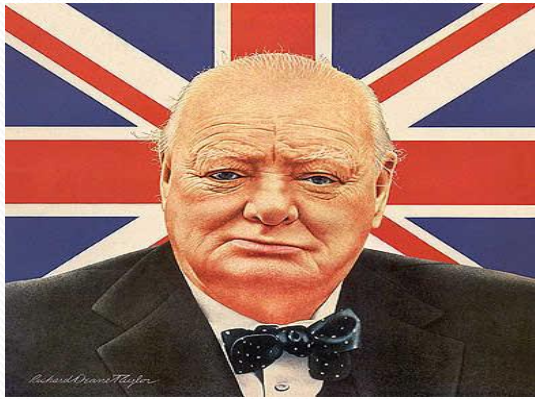
# GETTING MARKETING AUTHORISATION



# GETTING MARKET ACCESS



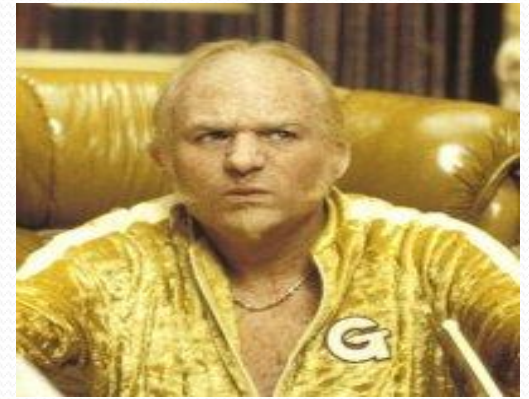
# Where is Health Technology Assessment used for drug reimbursement?



NICE, SMC, AWMSG



AMNOG/IQWiG



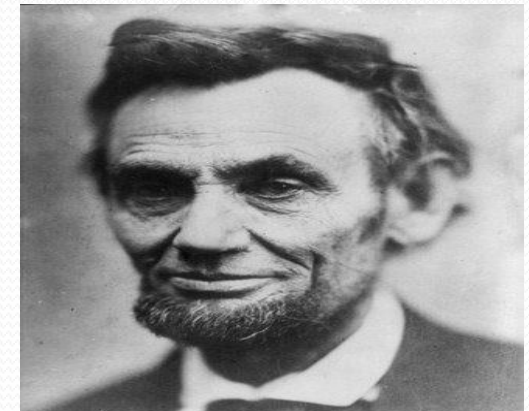
CVZ



TLV

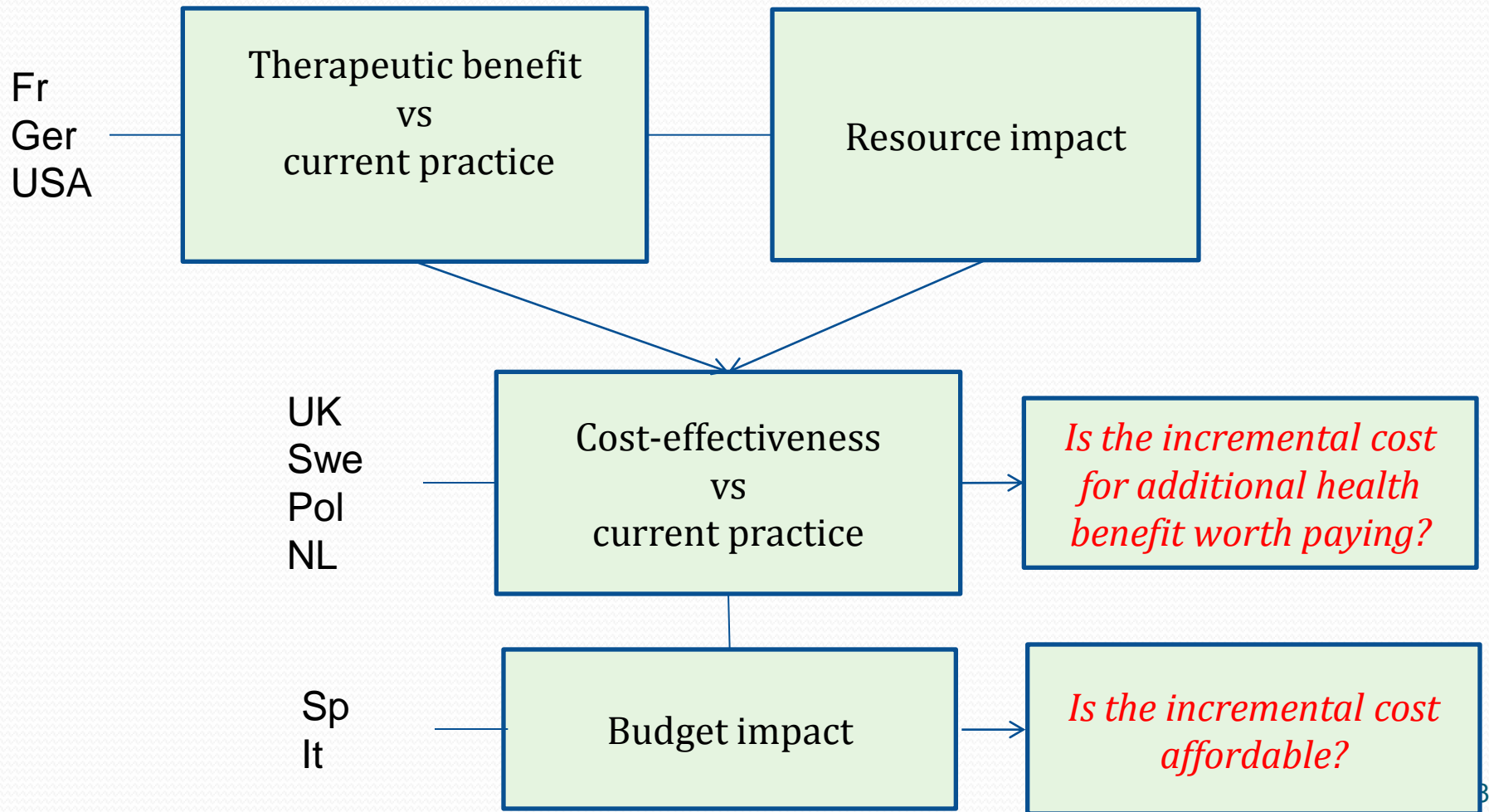


AHTAPol



AHQR

# 'Added value' of a new pharmaceutical based on evidence .....



# Demonstrating value – what data?

- In HTA driven systems such as UK the added clinical benefits need to be translated into long run health benefits (over patient lifetime or course of disease).
  - Bleeds prevented
  - Quality Adjusted Life Years (QALYs)

Condition	Short and medium term clinical measures			Long run Outcome measure	Resource benefits
<b>Type 2 Diabetes:</b>	HbA1c reduction →	Reduced CV events →	Reduced mortality, improved QoL →	QALY gain	Less CV event costs
<b>Cancer:</b>	Progression free survival →		Improved survival →	QALY gain	None usually
<b>Haemophilia:</b>	Bleeds prevented →		Improved HRQoL →	QALY gain	Reduced surgery

# Orphan and 'ultra-orphan'

- Orphan defined as life threatening or chronically debilitating diseases with prevalence  $\leq 5$  out of 10,000 cases
  - Ultra-orphan: no 'official' definition, although NICE have specified prevalence of 1 per 50,000.
- Drugs benefit from an EU wide orphan drug designation
  - Protocol assistance, EMA central procedure access, 10 yr market exclusivity, financial incentives
  - Growth in orphan designations: from 22 marketing authorisations in 2005 to 61 by 2011
- However, HTA is applied to orphan drugs at the national level and varies in stringency across countries:
  - No so stringent in NL, Ger. More so in UK, Sweden

# UK is a tough market for orphans

- Require a 'standard' health economic evaluation for UK HTA
  - Assessment of incremental cost per QALY gained over current practice
  - (Surprisingly maybe) - tougher in Scotland (SMC) than in England (NICE)
- To January 2009 51% of orphan drug submissions received a positive SMC recommendation, compared to 95% receiving reimbursement in the Netherlands (Vegter et al, *Clin Ther.* 2010).
- In addition, only one of 38 NL submissions for orphan drugs involved a cost/QALY analysis, compared to 24/37 submissions to SMC (Vegter et al, 2010).

# SMC acceptance rate for full submissions\*

	Accepted for use (no restrictions)	Accepted for use (with restrictions)	Not recommended
All submissions	29%	44%	26%
Orphan drug submissions	20%	41%	39%

\*From 2002 to August 2011

# Why does the acceptance rate for orphan drugs appear low?

- Rarity per se is not a factor in the decision, nor is directly the 'severity' of the condition
- Factors that are taken into account are:
  - Life threatening and drug substantially increases life and/or quality of life
  - Reverses rather than just stabilises condition
  - Bridges to a cure
- Incremental cost per QALY gained is typically very high (i.e. very poor cost-effectiveness)
  - From a healthcare perspective (not societal)

# Examples of Orphan drugs at SMC

Drug	Annual Cost	Approx numbers (Scot)	Cost per QALY gained	Recommendation
<b>Mifurmatide:</b> <i>Osteosarcoma</i>	£114K	5	£48K	Recommended (2011) <i>(with patient access scheme)</i>
<b>Eculizumab:</b> <i>Paroxysmal nocturnal haemoglobinuria</i>	~£252,000	9	>£500K	Not recommended (2010)
<b>Nelarabine:</b> <i>Refractory T-cell acute lymphoblastic leukaemia &amp; lymphoma</i>	~£22,000 (3 cycles)	?	£52-£103K	Restricted recommended <i>(if used to bridge to curative treatment)</i> (2008)
<b>Idursulfase:</b> <i>Hunter syndrome</i>	~£310,000	5	£560K -£1.2 mn	Not recommended (2008)
<b>Clofarabine:</b> <i>Refractory acute lymphoblastic leukaemic (ALL) in paediatric patients</i>	~£72,000 (3 cycles)	5	£22K – £3.6 mn	Restricted recommended <i>(if used to bridge to curative treatment)</i> (2007)
<b>Alglucosidase alfa :</b> <i>Pompe disease</i>	£38-£240K	4	£244K-£318K	Not recommended (2007)

# Miners et al 2009 results for prophylaxis v on-demand in the UK

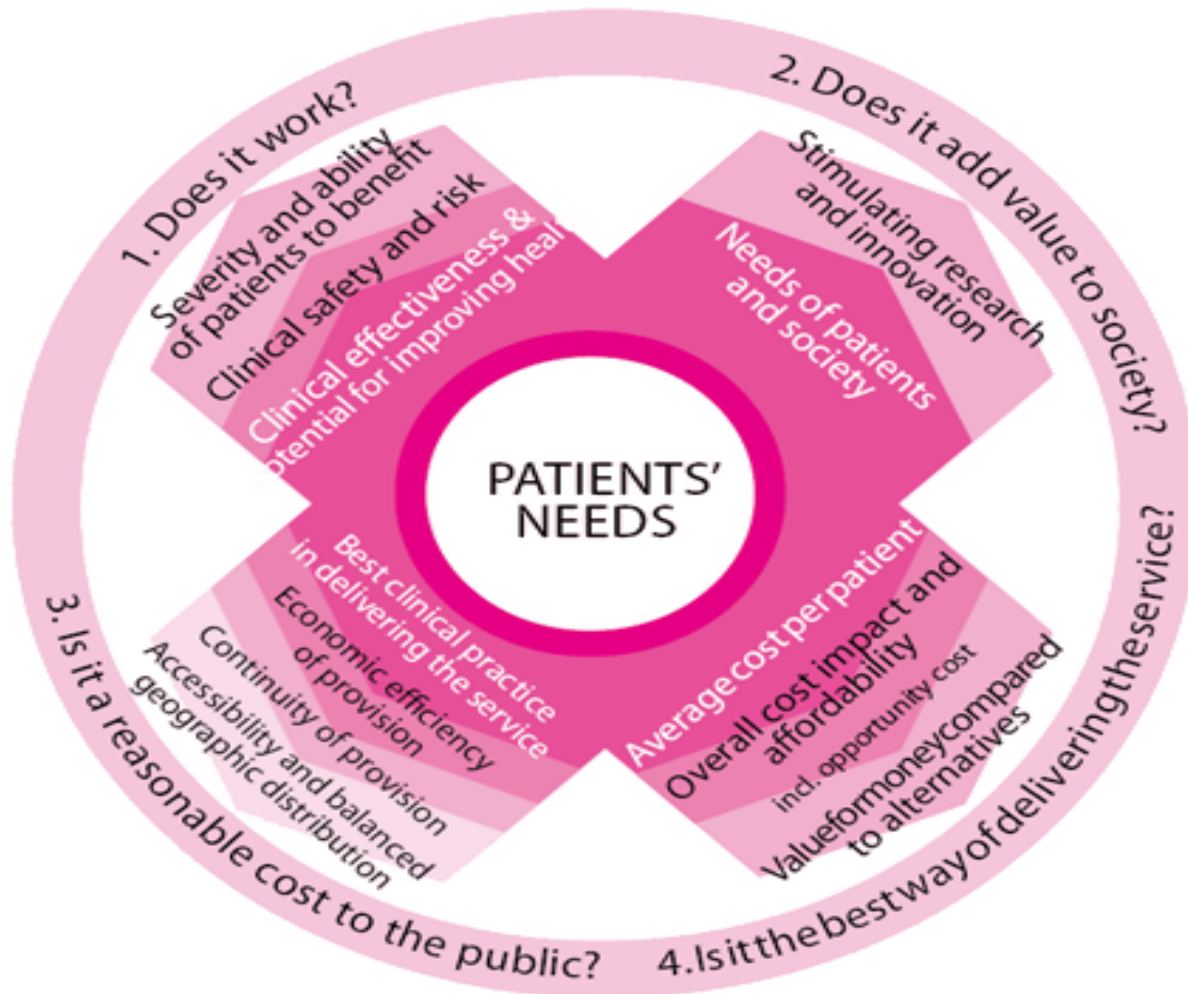
- Base case result of **£38,000 per additional QALY**:
  - On-demand mean lifetime cost of £644,000 for 14 QALYs
  - Prophylaxis mean lifetime cost of £858,000 for 19.5 QALYs
- There is **uncertainty** in the cost/QALY results
  - Miners found there was only a 13% chance that prophylaxis could achieve a cost/QALY <£30K with the current evidence base

# Haemophilia cost-effectiveness studies

Study	Treatment/patients considered	Cost/QALY Result Prophylaxis superior effectiveness but.....
Miners et al 2009	Lifetime treatment with prophylaxis vs on-demand for severe haemophilia	~€44 thousand per QALY gained for prophylaxis
Risebrough, 2008	Treatment of children up to 6 years with standard prophylaxis, escalating dose prophylaxis	~€320 thousand for escalating dose prophylaxis
Lippert et al, 2005	Treatment of adults with severe haemophilia with prophylaxis vs on-demand over one year time horizon	>€1 million for prophylaxis in each country

# HTA for orphan drugs – revised approaches

Advisory Group for National Specialised Services (AGNSS)



## AGNSS aims:

- To assess submissions for interventions for rare and complex diseases
- Determine eligibility for national funding and centralised service provision

# What can the haemophilia and rare disease community do?

- More payer attention on value for money of orphan drugs (including on haemophilia) can be expected
- So best to understand the language of HTA and QALYs
- Promote wider notions of value: societal, carers, innovation etc

# Any questions?



# BACK-UP

# About Keith Tolley

- Director of Tolley Health Economics Ltd
- Health economist (previous positions at York and Nottingham Universities, Pfizer, GSK and J&J)
- Economic Assessor at New Drugs Committee (NDC), Scottish Medicines Consortium (SMC) (previously industry representative on NDC)

# Patient-reported health status and quality of life

By placing a tick in one box in each group below, please indicate which statements best describe your own health state today.

## Mobility

- I have no problems in walking about
- I have some problems in walking about
- I am confined to bed

Mobility

## Self-Care

- I have no problems with self-care
- I have some problems washing or dressing myself
- I am unable to wash or dress myself

Self-Care

## Usual Activities (e.g. work, study, housework, family or leisure activities)

- I have no problems with performing my usual activities
- I have some problems with performing my usual activities
- I am unable to perform my usual activities

Usual activities



## Pain/Discomfort

- I have no pain or discomfort
- I have moderate pain or discomfort
- I have extreme pain or discomfort

Pain/Discomfort

## Anxiety/Depression

- I am not anxious or depressed
- I am moderately anxious or depressed
- I am extremely anxious or depressed

Anxiety/Depression

100 = best assessment

Your own health state today

100mm Visual analogue scale

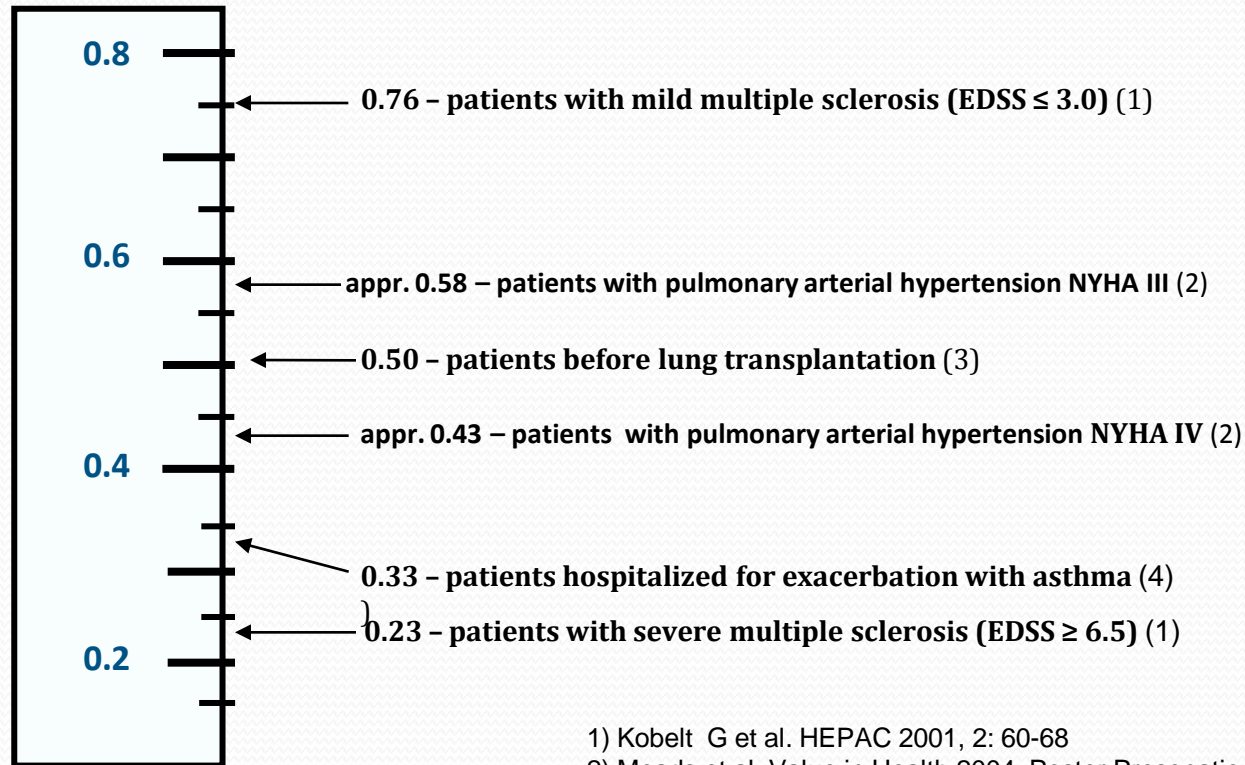


0 = worst assessment

# Patient-reported health status and quality of life

## EQ-5D - utility values

1,00 – best health status



0,00 - death

1) Kobelt G et al. HEPAC 2001, 2: 60-68

2) Meads et al. Value in Health 2004; Poster Presentation at ISPOR 2004

3) Groen et al. Am J Transplantation 2004; 4:1155-1162

4) Lloyd A et al. Primary Care Respiratory J 2007, 22-27