

Whose perspective? Implications on cost-effectiveness modelling of differences between country value sets (a case study)

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How do decision makers decide which healthcare interventions to fund?

- Incremental cost-effectiveness ratio (ICER) =

$$\frac{\Delta cost}{\Delta effectiveness} = \frac{(cost_{treatment} - cost_{control})}{(effectiveness_{treatment} - effectiveness_{control})}$$

- A means of standardising health benefits
 - across endpoints
 - across therapy areas
- Often measured in Quality-Adjusted Life Years (QALYs)

QALY

- To calculate QALYs, we multiply the **length of life** expected to be gained by the new treatment or invention by the **quality of life** a patient can expect to have.
- Quality of life is measured on a scale of 0 to 1. This score or 'weight' represents the **value** of different levels of health.
- **How do we find the 'Q' in QALY?**
 1. We need to describe the health state that is going to be valued
 2. We need a way to value the health state that we have described
 3. We need a group of people to provide the values

1. How to describe the health states?

- Objective vs. subjective measures
- Condition specific (AQL-5D for asthma) vs. generic measures (SF-36, EQ-5D)
- Clinician (or proxy) vs. patient reported measures
- Health related quality of life vs. overall well-being measures

Example: EQ-5D-3L

- A generic PROM which has 5 domains.
- Each domain has a single question which has 3 severity levels.
- A health state is formed from the responses to each question.
- Total of 243 possible health states

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

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

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

Pain/Discomfort

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

Anxiety/Depression

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

2. Method to value the health benefit?

- There are different techniques that can be used. The most common ones are
 - time trade-off, which asks individuals **how much time** they would be willing to give up in order to avoid poor health states
 - standard gamble, which asks individuals **how much risk** they are willing to take in order to avoid poor health states.

Example of Time trade-off (TTO) method:



Value of health state = 6 / 10

Choice A (6 years)

- Full Health

=

Choice B (10 year)

- I have no problems in walking about
- I have no problems with self-care
- I have some problems with performing my usual activities
- I have extreme pain or discomfort
- I am moderately anxious or depressed

Time trade-off (TTO) method

- To find out the value an individual places on this health state,
 - vary the time lived in the full health state until the respondent is indifferent
 - divide the years in perfect health by the years in the health state
- **We all value health states differently.**
- The different preferences that we have mean that we place different values on health states. This can be due to our own experiences of ill health or simply our views on what we think matters in health.

3. Who should value health?


- General population
- Patients
- Clinicians

Case study

- Daigl M, Bennett I, McDougall F, Singh Jhuti G, *Impact of Disease Activity Measures on Health Utilities in Primary Progressive Multiple Sclerosis*, 20th Annual European Congress (ISPOR-EU); 4–8 November 2017; Glasgow, UK, https://www.ispor.org/research_pdfs/57/pdf/files/PND59.pdf

Impact of Disease Activity Measures on Health Utilities in Primary Progressive Multiple Sclerosis

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INTRODUCTION

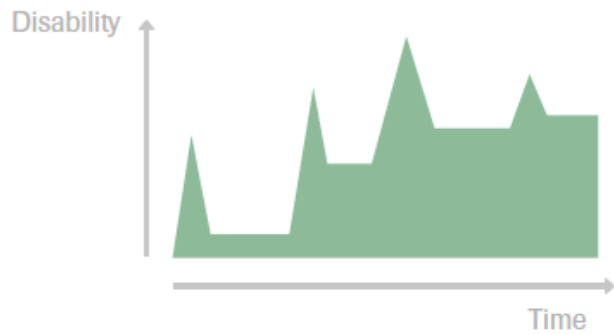
- Multiple sclerosis (MS) is a chronic demyelinating disease of the central nervous system that affects mainly young and middle-aged adults, and may lead to significant disability that can impact patients' health-related quality of life (HRQL)
 - Primary progressive MS (PPMS) is characterized by a gradual progression of clinical symptoms from disease onset
- The Expanded Disability Status Scale (EDSS) is a widely used tool for quantifying disability in MS; scores range from 0 (normal neurological assessment) to 10 (death due to MS) in 0.5 unit increments²
- A previous study demonstrated a relationship between EDSS scores and health utilities based on the 5-dimension EuroQol questionnaire (EQ-5D) for relapsing forms of MS (RMS)³ however, the relationships between health utilities and measures of disease activity for PPMS are poorly understood
- In addition to using the EDSS, other outcomes measures used to quantify disease activity in patients with PPMS include:
 - the 9-hole peg test (9HPT), which measures upper limb function by testing both dominant and non-dominant hands⁴
 - the Modified Fatigue Impact Scale (MFIS), which measures the impact of fatigue in terms of physical, cognitive and psychosocial functioning⁵
- The objective of this analysis was to evaluate the impact of disease activity measures on health utilities in PPMS. Country-specific health utilities are reported for Australia, Belgium, Canada, France, Italy, the Netherlands, Portugal, Sweden, the UK and the USA

Table 1. Impact of EDSS score-derived health state, clinically significant upper limb dysfunction and clinically significant fatigue on average health utilities in each of the 10 countries

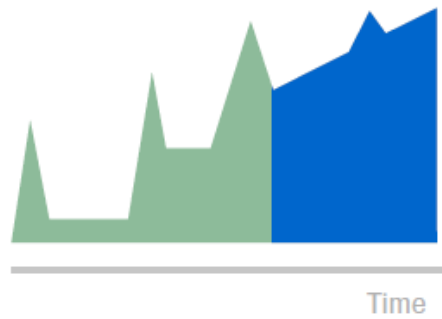
	Assessments/ patients	Impact on utility (95% CI)									
		Australia ^a	Belgium ^a	Canada ^a	France ^a	Italy ^a	Netherlands ^a	Portugal ^a	Sweden ^a	UK ^a	USA ^a
EDSS 1.5 (1–2.5) ^b	71/51	0.78 (0.74, 0.82)	0.74 (0.70, 0.78)	0.80 (0.77, 0.83)	0.73 (0.68, 0.78)	0.88 (0.85, 0.91)	0.82 (0.78, 0.87)	0.84 (0.80, 0.88)	0.84 (0.82, 0.86)	0.79 (0.74, 0.84)	0.83 (0.80, 0.87)
EDSS 3 (3–3.5) ^b	381/230	0.73 (0.71, 0.75)	0.69 (0.67, 0.71)	0.76 (0.75, 0.78)	0.67 (0.65, 0.70)	0.86 (0.84, 0.87)	0.78 (0.75, 0.80)	0.59 (0.57, 0.61)	0.82 (0.81, 0.83)	0.74 (0.71, 0.77)	0.80 (0.78, 0.82)
EDSS 4 (4–4.5) ^b	385/231	0.68 (0.66, 0.71)	0.63 (0.61, 0.66)	0.73 (0.71, 0.74)	0.59 (0.56, 0.62)	0.82 (0.81, 0.84)	0.73 (0.70, 0.75)	0.52 (0.50, 0.55)	0.79 (0.78, 0.80)	0.68 (0.65, 0.71)	0.75 (0.74, 0.77)
EDSS 5 (5–5.5) ^b	173/129	0.68 (0.65, 0.70)	0.62 (0.59, 0.65)	0.72 (0.70, 0.74)	0.55 (0.51, 0.59)	0.82 (0.80, 0.84)	0.72 (0.69, 0.76)	0.49 (0.46, 0.52)	0.78 (0.76, 0.79)	0.66 (0.63, 0.70)	0.74 (0.72, 0.77)
EDSS 6 (6–6.5) ^b	525/283	0.63 (0.61, 0.65)	0.58 (0.55, 0.60)	0.68 (0.66, 0.70)	0.49 (0.46, 0.51)	0.78 (0.76, 0.80)	0.67 (0.64, 0.70)	0.44 (0.42, 0.46)	0.76 (0.75, 0.77)	0.60 (0.58, 0.63)	0.70 (0.68, 0.72)
EDSS 7.5 (7–8.5) ^{b,c}	31/26	0.48 (0.42, 0.54)	0.45 (0.38, 0.51)	0.55 (0.50, 0.60)	0.31 (0.23, 0.39)	0.60 (0.55, 0.65)	0.54 (0.46, 0.61)	0.27 (0.20, 0.33)	0.71 (0.68, 0.74)	0.43 (0.35, 0.51)	0.57 (0.51, 0.62)
Impact of clinically significant upper limb dysfunction ^d	N/A	-0.05 (-0.09, -0.01)	-0.04 (-0.08, 0.00)	-0.04 (-0.08, -0.01)	-0.07 (-0.12, -0.02)	-0.06 (-0.09, -0.03)	-0.05 (-0.09, 0.00)	-0.06 (-0.10, -0.02)	-0.02 (-0.04, 0.00)	-0.06 (-0.11, -0.01)	-0.05 (-0.08, -0.02)
Impact of	N/A	-0.12	-0.13	-0.10	-0.18	-0.09	-0.14	-0.13	-0.07	-0.15	-0.11

METHODS

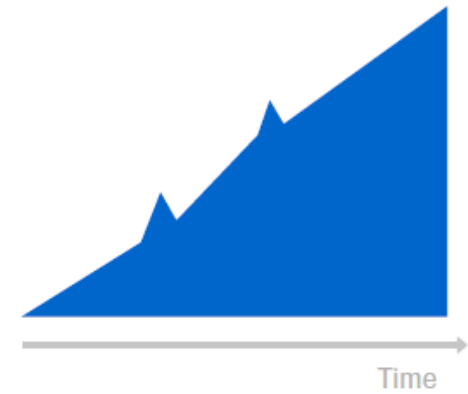
Multiple sclerosis



RRMS
Relapsing-remitting MS

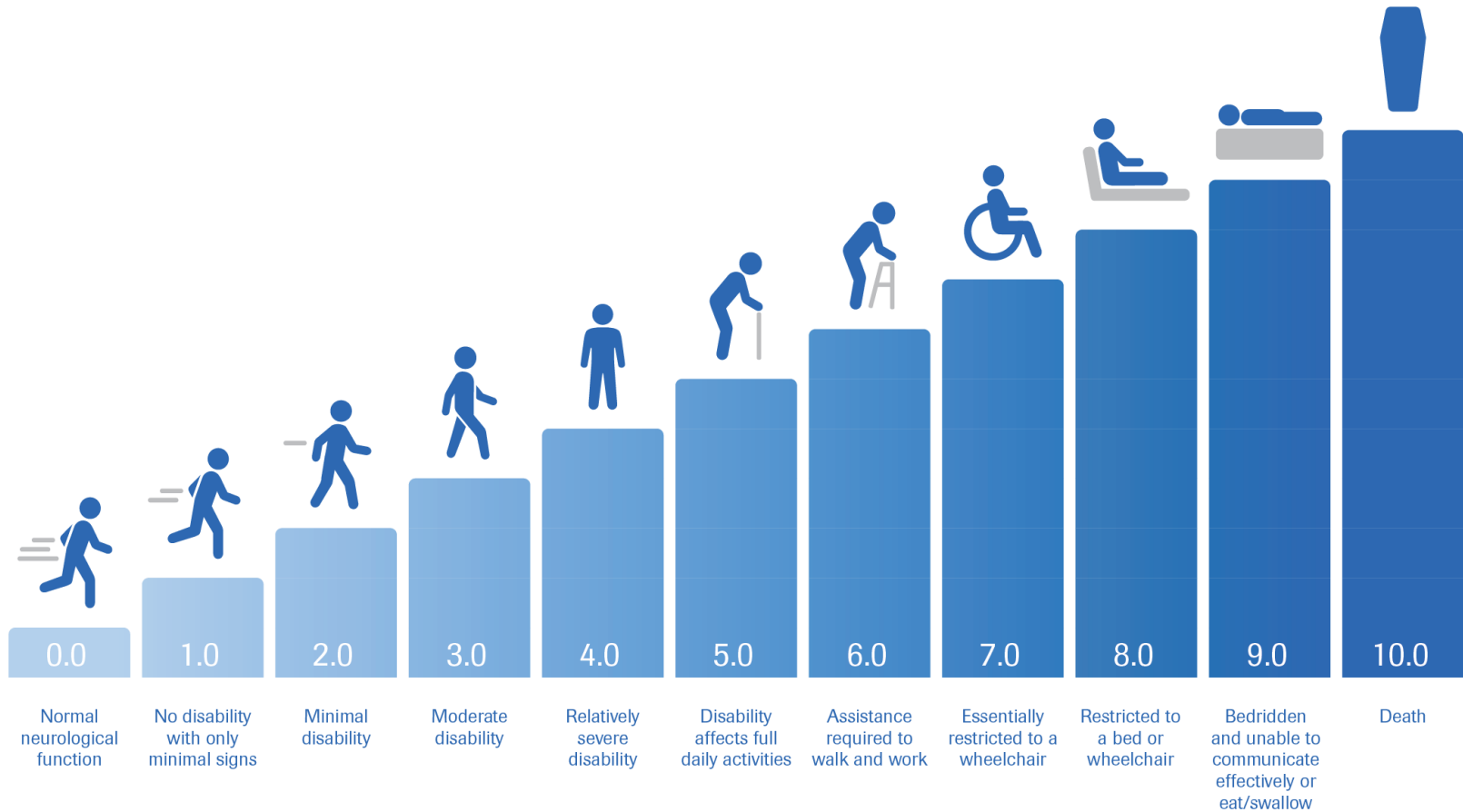


SPMS
Secondary progressive MS



PPMS
Primary progressive MS

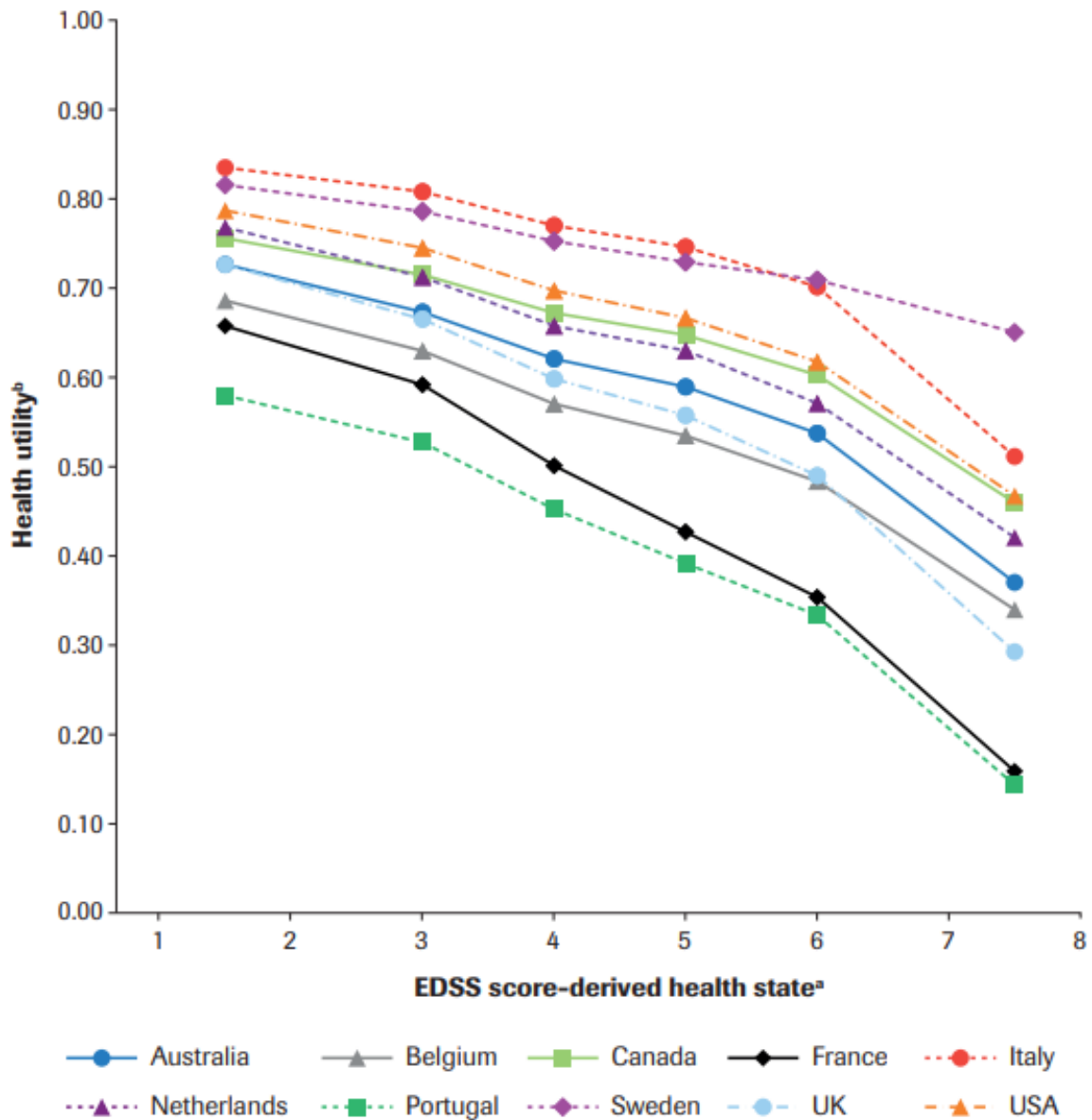
Expanded Disability Status Scale (EDSS)



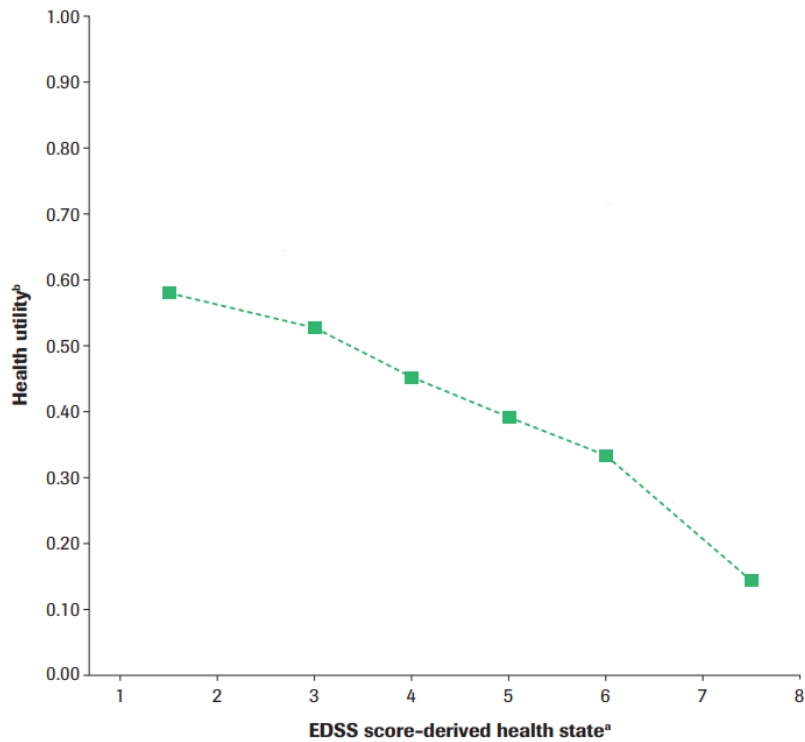
Methods

- ORATORIO, a double-blind, placebo-controlled trial, evaluated the efficacy and safety of ocrelizumab patients with PPMS
- Disease activity was assessed using the EDSS, the 9HPT and the MFIS at baseline, and at 48 weeks and 120 weeks after treatment initiation
- Patients also completed the 3-level EQ-5D (EQ-5D-3L) at the same time points to determine the impact of PPMS on HRQoL by EDSS score-derived health states
 - EQ-5D-3L value sets from 10 countries were used to derive country-specific health utilities for each of the EDSS score derived health states
- A repeated-measures linear model was used to regress health utilities on EDSS score-derived health states, clinically significant upper limb dysfunction, clinically significant fatigue, sex, age and region of the world using the UK value set
- The value sets from each of the 9 other countries were applied to this model

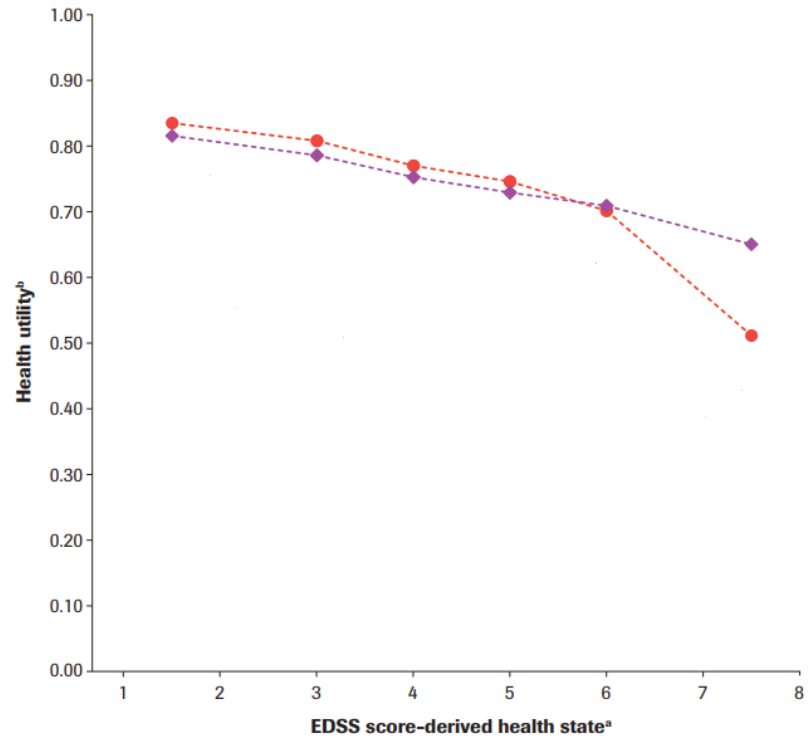
Results



Implications for decision making?



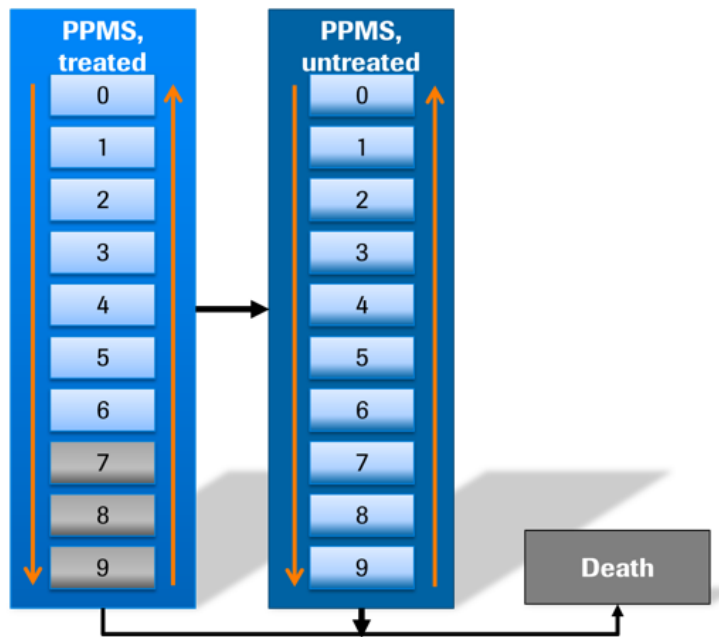
---■--- Portugal



---◆--- Sweden

---●--- Italy

Implications for decision making?



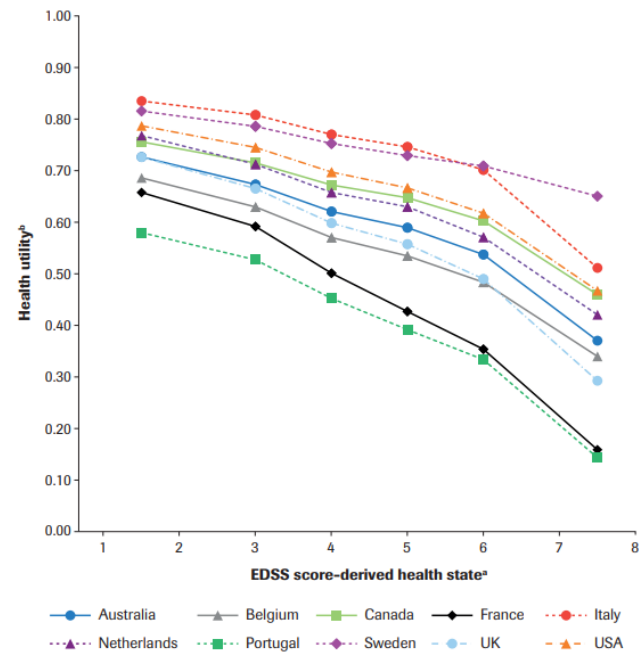
Orange arrows = show the direction in which patients may move along the EDSS scale.

Grey boxes in 'PPMS treated' = these indicate the stages at which treatment is discontinued

Country	Incremental QALYs (as a proportion of ref case)
UK (reference)	1
Portugal	0.87
Portugal (extrapolated)	0.60
Sweden	0.97
Sweden (extrapolated)	0.42

Implications for statistics?

- Role of statistics in extrapolating patient preferences?
 - missing states (EDSS 0, EDSS 9, EDSS 10)
 - missing countries
 - complex models required



In sum

- Relationships exist between health utilities derived from the EQ-5D-3L and EDSS score-derived health states in PPMS; varying across countries
- Data collection required, as predicting preferences is challenging
- Complicated modelling methods to be run, but also communicated to non-analysts
- There may be different decisions coming out of different countries that otherwise share a same decision framework due to differences in valuation of different levels of health

Acknowledgments

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- Iain Bennett

Thank you for your attention!

- What questions do you have?



Doing now what patients need next