

overview of the existing techniques

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Summary

- There are several techniques for estimating health state utility values (HSUVs), each of which presents pros and cons in rare diseases (RDs).
- Direct approaches such as standard gamble and time trade-off may be too demanding for certain patients with RDs (e.g. young children).
- The alternative is to use hypothetical 'vignettes' with proxy respondents, although their creation requires a clinical expertise that often lacks in RDs.
- The 'rule of rescue' is a promising approach in RDs, since it prioritizes identifiable patients with life-threatening conditions or evident disabilities.
- Multi-attribute utility instruments (MAUIs) are simpler to respond to, but may be not sensitive enough in capturing the specificities of RDs.
- Lastly, choosing one technique over another can have relevant implications for the assessment of new treatments in RDs.

Introduction

- HSUVs represent the preference weights for specific health states measured on a scale from zero ('death') to one ('perfect health'); when combined with survival, they generate quality-adjusted life years (QALYs).
- The incremental cost-effectiveness ratio (ICER), corresponding to the cost per QALY gained, is the main criterion used to inform reimbursement decisions in several Health Technology Assessment (HTA) systems.
- Two groups of techniques (i.e. direct and indirect) exist to estimate HSUVs [1].
- Their application to RDs may be challenging because of their small incidence, severity and heterogeneity.
- This paper discusses the pros and cons of each technique available to derive HSUVs in relation to the specificities of RDs (Table 1).

Results

Table 1. Overview of the available techniques and implications for RDs.

Group	Technique	Brief description	PROS (P)/CONS (C) in RDs	Comments relating to RDs	
Direct techniques	Visual analogue scale	Requires evaluating a given health state by drawing an X on scale of values spanning from 0 ('death') to 10 or 100 ('perfect health'), then converted into HSUVs by dividing the X score by 10 or 100	P	simple to administer, easily understood	up to 75% of RDs affect children, and many result in cognitive impairment
			C	is considered methodologically weak because does not require trade-offs	no specific comments, this limitation applies to all conditions
	Standard gamble	Requires choosing between two alternatives: (1) remaining in a given health state for the remaining lifespan and (2) returning to perfect health with probability <i>p</i> , or dying with probability (1- <i>p</i>); <i>p</i> is varied until the two alternatives are indifferent; the HSUV is equal to <i>p</i> .	C	both SG and TTO are demanding tasks	up to 75% of RDs affect children, and many result in cognitive impairment
	Time trade-off	Requires choosing between two alternatives: (1) remaining in a given health state for the remaining lifespan (e.g. 10 years) or (2) living in perfect health for a shorter period (X<10). X is varied until the two alternatives are indifferent; the HSUV is equal to X/10.	P/C	both SG and TTO tend to produce higher HSUVs, thus favouring allocation of resources to life-saving interventions	may favour treatments for life-threatening RDs (e.g. cystic fibrosis)
	Person trade-off	Estimates the 'social value' of healthcare interventions by asking people how many outcomes (X) of kind A they consider equivalent to outcomes (Y) of kind B. A disutility for health state B in relation to A is calculated as X/Y.	P	the public typically assigns greater value to treatments for severe diseases, irrespective of their effectiveness and cost	severity characterizes most RDs, and most treatments for RDs present an ICER above the accepted standards
			C	is quite demanding and requires a large number of respondents to minimize random measurement errors	large samples are difficult to recruit in RD studies due to the paucity of patients and/or physicians with knowledge of RDs
	DCE	Requires making a binary choice between hypothetical health states; HSUVs are derived through regression models	P	allows to easily value health states considered worse than death	useful for very severe RDs (e.g. amyotrophic lateral sclerosis)
	Rule of rescue	Relies on the principle that people feel a moral imperative to rescue identifiable individuals facing avoidable death (or severe illness). HSUVs are derived from a combination of SG/TTO and PTO.	P	prioritizes the severity of the disease over treatment effectiveness and costs	can favour treatments with high ICERs, which is often the case in RDs
			P	prioritizes life-saving interventions, but also interventions for highly visible physical deformities or disfigurements	can favour treatments for life-threatening (e.g. cystic fibrosis) or visibly disabling or disfiguring RDs (e.g. Antley-Bixler syndrome)
			P/C	gives absolute priority to identifiable patients and penalizes those unidentified, potentially causing ethical issues	RDs patients, and especially those with visible disabilities, are more likely to gain visibility through media/fundraising campaign
C			presents measurement problems (two-stage procedure)	no specific comments, this limitation applies to all conditions	
ALL		P/C	all direct tasks can be performed also by the public using 'vignettes', although patients are more likely to value their own health status correctly	useful in case of vulnerable patients and small samples, but creation of realistic 'vignettes' requires clinical expertise that often lacks in RDs	
Indirect techniques	MAUIs	Use of generic PROMs accompanied by a set of pre-calculated 'tariffs' to generate HSUVs	P	simple to administer, availability of children-specific tools (e.g. EQ-5D-Y)	up to 75% of diseases affect children
			C	may not be sensitive enough to capture some relevant health issues	heterogeneous symptoms not properly represented in generic PROMs
			P/C	tend to produce lower HSUVs, thus they might favour the allocation of resources to non-fatal, chronic conditions	may favour treatments improving symptomatology and quality of life in chronic RDs (e.g. cutaneous lymphomas)
	Mapping	Use or development of an algorithm relating non-preference-based measures (e.g. RD-specific PROMs) to MAUIs	P	allows to exploit a number of PROMs and clinical measures into HTA processes	studies in RDs tend to use disease-specific PROMs, which can be converted onto HSUVs using mapping
			C	there is scarce overlap between disease-specific measures and generic MAUIs	RD-specific PROMs include very specific symptoms that may not be captured in generic PROMs
		P/C	possibility to apply previously developed algorithms to derive HSUVs	several algorithms developed in common conditions (e.g. lung cancer) tend to overestimate HSUVs in their rare variants (e.g. pleural mesothelioma), which are usually more severe	

DCE: discrete choice experiment; EQ-5D-Y: EuroQol Five-Dimensional Questionnaire, Youth Version; HSUV: health state utility values; HTA: Health Technology Assessment; ICER: incremental cost-effectiveness ratio; MAUI: multi-attribute utility instrument; PROM: patient-reported outcome measure; PTO: person trade-off; RD: rare disease; SG: standard gamble; TTO: time trade-off.

Conclusions

- The estimation of HSUVs is a crucial area in RDs to assess the benefits of new treatments in terms of quality of life and QALY gains.
- There is no agreement on the most appropriate technique to derive HSUVs in RDs; it should be decided based on the individual condition. For example, in 75% of RDs affecting children, the use of children-specific (or proxy-reported) MAUIs is recommended.
- The use of less established approaches such as the PTO and the 'rule of rescue' requires more evidence on their advantages in RDs and acceptability by HTA bodies [2].
- Overall, the implications of using alternative approaches for reimbursement decisions in HTA should be carefully addressed.

References

[1] Arnold D, Girling A, Stevens A, Lilford R. Comparison of direct and indirect methods of estimating health state utilities for resource allocation: review and empirical analysis. *BMJ*. 2009; 339, b2688.
 [2] Silva EN, Sousa TR. Economic evaluation in the context of rare diseases: is it possible? *Cad Saude Publica*. 2015; 31(3), 496-506.

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