Assessing the Societal Value in Rare Diseases: A Stated Preference Discrete Choice Experiment in Patients with rare diseases in Italy

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INTRODUCTION: The multicriteria decision analysis (MCDA) approach provides opportunities for evaluation of process effects and non-health outcomes additional to traditional QALY analysis. One MCDA technique, the discrete choice experiment (DCE) has received attention and is a technique for investigating individual preferences. A specific DCE questionnaire online was elaborated to collect information from patients with cystic fibrosis and haemophilia in Italy about the societal values for orphan drugs with a view to further elicit preferences.

METHODS: The DCE survey in this study was conducted replicating the methods used by an already published by Green and Gerard (2009). **Attributes and levels**: A systematic review of the empirical literature on distributive preferences informed the attribute selection (2). The aim of the literature review was to identify attributes for the design of a DCE for rare diseases, in order to develop and validate a framework to support decision-making (see Table 1). **Experimental design**: the design used an orthogonal approach, including 36 pairs of scenarios distributed into two blocks of 18 pairs each. Each scenario described a combination of attribute and levels. **Different scenarios**: respondents were asked to make a series of choices involving two alternative healthcare scenarios (pair comparisons). **Data collection**: a patients DCE survey was conducted, using online questionnaire, in order to explore the preferences of patients with cystic fibrosis and haemophilia from Registries in Italy. **Data analysis**: As the data are binary choice data – '1' represents the option being chosen, with '0' where not chosen – the conditional logit/probit models are used for modelling. A series of utility models were fitted. Means and standard errors were used for continuous variables and proportions for dichotomous variables. All statistical analyses were performed on STATA MP.

RESULTS: A total of 54 questionnaires (80% of all questionnaires sent out) were completed by and collected from patients with cystic fibrosis and haemophilia. Of these, 8 were excluded from the study following the exclusion criteria. Therefore, the valid sample totalled 46 patients. The feedback from respondents in the pilot survey and the main survey was that they were enthusiastic to participate in the survey, they had few problems completing the survey and they accept the fact that choices were difficult. "Improvements in health", "the cost of treatment" and "value for money" are the attributes receiving greatest attention from patients with rare diseases, while less important for patients with rare diseases are "severity of the diseases" and available of other treatment" (see Table 2).

Table 1: Discrete choice experiment: attributes and levels

Attribute	Description (summary)	Levels
Severity of the disease	Refers to the pre-treatment health state of patients	Moderate
		Severe
Improvement in health	Refers to the benefits that the patient feels following treatment	Large
		Moderate
		Small
		Very small
Waiting times	Refers to the time a patient must wait for treatment.	Short
		Moderate
		Long
Availability of other treatments	Refers to the existence of alternative treatments for the same disease	Yes
		No
Side effects	Refers to the undesired effects caused by the treatment. Any medical treatment carries risks	Few
		Moderate
		Many
Value for money	Refers to how efficiently resources are used	Very good
		Fairly good
		Fairly poor
		Very poor
Beginning of life	Refers to the age patients are diagnosed with this disease, referring to situations in which the patients are younger than 10 years (children)	Yes
		No
Cost of treatment	Refers to the resources that must be mobilized to ensure the financing of the treatment	Zero
		Lower
		Moderate
		High

Table 2:Logit/probit models coefficients

	Levels	Model framework	
		Logit	Probit
Importance of the disease	Severe disease	0.005	0.003
Improvement in health	Moderate	-0.425	-0.266
	Small	-0.369	-0.230
	Very small	-0.070	-0.044
Waiting times	Moderate	-0.102	-0.063
	Long	0.020	0.013
Availability of other treatment	No	-0.008	-0.005
Side effects	Moderate	-0.079	-0.050
	Many	-0.002	-0.002
Value for money	Fairly good	-0.285	-0.178
	Fairly poor	-0.042	-0.026
	Very poor	-0.301	-0.188
Beginning of life	No	0.158	0.098
Cost of treatment (Measured by tax increase / copayments)	Low	0.396	0.248
	Moderate	0.361	0.225
	High	0.112	0.070

DISCUSSION: The findings presented in this document provide evidence about how patients with cystic fibrosis and haemophilia think that decision should be made in Italy when considering which health technology scenarios are more appropriate to receive funding. The DCE approach is an instrument that allows to measure the preferences of patients about all kinds of health care interventions. DCE data can be used to consider the strength of preference over alternative scenarios in a priority-setting context. **Limitations.** This study has a number of limitations. The experimental design is not complex, with a small orthogonal design being used, and the results presented here are based on a simple analytical framework, using the conditional logistic/probit model. The study is open to a certain level of criticism over the presentation and contextual approach adopted. However, the results are useful and indicative of what may be possible in future research of this type. Future research could address many of the limitations highlighted; for example, using interviewers and qualitative methods to investigate the interpretation of attributes and the considerations when respondents make their choices.

CONCLUSIONS: Our results suggest that a "beyond Cost-QALY" framework could be created by using the DCE method. Specifically, the results suggest that such a "new" framework would be potentially beneficial for rare diseases in terms of "fair play" in the decision-making process. This evidence could be useful for future research designs following a similar approach.

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