A novel mapping approach for estimating utilities in non-dystrophic myotonia

PRO119

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BACKGROUND

Objective

- Non-dystrophic myotonic (NDM) disease marked by the inability to relax muscles following voluntary contraction.
- This is a disabling condition which affects many aspects and quality of a patient's life
- NaMuscla® (mexiletine) was recently approved in Europe for the symptomatic treatment of myotonia in adults with non-dystrophic myotonic disorders.
- Patient outcomes in NDM are typically assessed using the disease specific, Individualised Neuromuscular Quality Of Life Questionnaire (INQoL) INQoL (Rose et al 2006, Vincent et al 2007).
- The INQoL assesses the severity of symptoms and functional problems that people experience and their impact on a person's day to day quality of life.
- This research was designed to elicit utility weights for the INQoL measure so that the data could be used in cost-effectiveness modelling.
- Using the INQoL to estimate utilities would allow utilities to be estimated at the individual patient level, obtained through a preference-based valuation.

Table 1: The INQoL items chosen to match the EQ-5D items

EQ-5D	INQoL
Mobility	How much weakness would you say you have in the muscles affected by your condition? How much muscle locking would you say you have at the moment?
Self care (washing & dressing)	At the moment does your muscle condition affect your ability to do daily activities e.g. washing, dressing & housework?
Usual activities (leisure, work, social activities)	At the moment does your muscle condition affect your ability to do leisure activities?
Pain/ discomfort	How much pain would you say you have at the moment? How much tiredness/ fatigue would you say you have at the moment
Anxiety/ depression	At the moment does your muscle condition make you feel anxious/ worried? At the moment does your muscle condition make you feel depressed?

Table 2: Demographic characteristics of DCE sample

Characteristic	N=508
Mean age (SD)	48.5 (16.3)
Female	N=256 (50.4%)
Ethnicity, n (%)	
White Caucasian	458 (90.2)
Black British/ Black African	4 (0.8%)
Asian Indian/ Pakistani/ Bangladeshi/ Other	21 (4.2%)
Chinese	7 (1.4)
Mixed Race/ Other	18 (3.6%)
Education, n (%)	
No formal qualifications	19 (3.7)
Left school at 16	127 (25)
Left school at 18	114 (22.4)
University degree	208 (40.9)
Other	37 (7.3)
Main activity, n (%)	
Paid employment	268 (52.8)
Looking after family/home	44 (8.7)
Retired	112 (22.1)
Seeking work, unemployed	24 (4.7)
Not working, health problems	46 (9.1)
In education or training	10 (2.0)

RESULTS

Preference data

- All INQoL items were significant predictors of choice in the DCE indicating that they were all independently important
- Some minor logical inconsistencies emerged in the preference weights.
  - *E.g. A moderate amount* was preferred to *Some* (but by the scale structure it should be less preferred). This may just reflect how people interpret these labels - in reality *A moderate amount* is not logically better or worse than *Some*.
- Where logical inconsistencies have occurred the inconsistent value (disutility) in the scoring algorithm was changed to be the same as the better level. So the value for *A moderate amount* would be the same as *Some*. This was considered a conservative approach.
- Logical inconsistencies also occurred whereby people preferred *Some* or *Slight* problems to the upper anchor (i.e. Very little/ Not at all). Where this has occurred those disutilities were changed to 0 for these labels, again as a conservative approach.
- Weights from the DCE were only available for 4 response options (INQoL items have 6 or 7 response levels). To generate weights for the remaining response levels linear interpolation was used.
- Sensitivity analyses explored weighting the instrument using different EQ-5D anchor states (33333, 23233, 22233).

Interview data

The clinical experts agreed that extreme problems with muscle weakness and locking may equate to extreme problems on EQ-5D mobility. One expert said that '*some problems*' may be more accurate.
Our utility expert commented that

- The response levels may well not be linearly spaced and that how people interpreted the response labels in the DCE may be different to the context of questionnaire.
- He suggested that sensitivity analyses should be undertaken to explore different assumptions regarding the value for the INQoL worst health state.
- We assume best state on the INQoL has a value of 1.0 which may need to be tested

Figure 1: An example choice question from the DCE

	Treatment A	Treatment B
How much muscle weakness you would have	An extreme amount	Very little
How much 'locking' (seizing up) of your muscles you have	An extreme amount	Very little
Your muscle condition affects your ability to do daily activities e.g. washing, dressing & housework	Moderately	Extremely
Your muscle condition affects your ability to do leisure activities	Moderately	Extremely
How much pain you have	An extreme amount	Very little
How much tiredness or fatigue you have	A moderate amount	An extreme amount
Your muscle condition makes you feel anxious	Slightly	Moderately
Your muscle condition makes you feel depressed	Extremely	Not at all
Which treatment is best? Please tick A or B	**A ❑**	**B ❑**

STUDY METHODOLOGY

- The INQoL measure (version 1.2) includes 52 questions which assess different areas of HRQL [Rose et al 2006].
- Questions assess how patients are affected in different areas of function or symptoms.
- The instrument is disease specific and includes items which assess:
  - muscle weakness and muscle locking.
  - usual activities (washing & dressing, leisure activities and work);
  - psychological health (anxiety, depression); social relationships
  - pain, tiredness and fatigue.
- An item reduction process was undertaken to simplify the measure. The following criteria were used:
  - Items were selected to align with the content of the EQ-5D as closely as possible in terms of the descriptive system of the EQ-5D, the most frequently used preference-based measure for assessing or estimating utilities in cost-effectiveness analysis.
  - Items which were designed to rate the *severity* of each specific problem were selected. Items which explored the *impact* of these issues were not included.
- The INQoL has been independently developed and validated and we have assumed that all items have content and construct validity [Rose et al 2006].
- INQoL items include 6 or 7 response choices. For this exercise it was decided to simplify the response choices to just 4. Response options were chosen which most closely matched the response options in the EQ-5D-5L.
- Disease specific Items describing fatigue and muscle locking were included (on clinical advice). Three clinical experts in NDM reviewed the process of selecting items and response levels and provided feedback.
- An expert on utilities reviewed the proposed approach and analyses and provided feedback.
- The eight questions in the INQoL were then combined with response choices using a published orthogonal design (http://neilsloane.com/oadir/). The orthogonal design was folded over to produce statistically efficient pairs of choices (Street et al., 2005). The order of questions was randomised and half of the participants completed questions 1-16 and half 17-32. An example choice question is in Figure 1.
- The survey was hosted online and a sample of the general public was recruited. Quota sampling was used to balance geographic distribution, gender, and ethnicity.
- Choice data were analysed using the conditional logit model to estimate a linear function. The resulting coefficient weights were then rescaled so that the maximum score was 1 and the minimum score was -0.594 (in line with the UK valuation weights for EQ-5D-3L). Linear interpolation was used for the three missing response levels.
- The discrete choice experiment (DCE) is a quantitative method that contains a number of attributes and levels that are presented as scenarios for an individual to select their preferred option. This method is increasingly used in healthcare to elicit preferences indirectly by enabling the development and assessment of preference-based value sets
- The DCE tells us the importance of each INQoL item that is included, with respect to the other items in the measure. In order to 'map' it to the EQ-5D we made the following assumptions:
  - *Given the conceptual match of the two sets of items we have assumed that the best state defined by INQoL is equivalent to the best state defined by EQ-5D-3L and so can be given a value of 1.0.*
  - *Equally we have assumed that the worst health state defined by the two measures is equivalent and so can be given a value of -0.594*
  - *Sensitivity analyses also explored using state 23233 (-0.291) and 22233 (-0.181) as worst health states*
  - *We assume that the preference data can be described in terms of linear function with no interaction effects.*
- The weights from the DCE will then be used to rescale the items onto the 1 to -0.594 range using the simple function below

$$U_{tot} = 1 + U_{weak} + U_{lock} + U_{pain} + U_{tired} + U_{wash} + U_{leis} + U_{anx} + U_{dep}$$

- Where U_{tot} is the individual's utility score, and U_{weak} through to U_{dep} are the disutilities for each item in the INQoL included in the exercise.

Table 3: INQoL preference weights from DCE, rescaled against EQ-5D-3L UK scores for different worse health states

		Worst health anchor	Very little	Some	A fair amount	A moderate amount	A considerable amount	A lot	An extreme amount
Q1a	How much weakness would you say you have in the muscles affected by your condition?	33333	0	-0.005	-0.010	-0.015	-0.049	-0.082	-0.116
		23233	0	-0.004	-0.008	-0.012	-0.040	-0.067	-0.094
		22233	0	-0.004	-0.007	-0.011	-0.036	-0.061	-0.086
Q2a	How much muscle 'locking' would you say you have at the moment?	33333	0	-0.009	-0.019	-0.028	-0.069	-0.110	-0.151
		23233	0	-0.008	-0.015	-0.023	-0.056	-0.089	-0.122
		22233	0	-0.007	-0.014	-0.021	-0.051	-0.082	-0.112
Q3a	How much pain would you say you have at the moment?	33333	0	-0.068	-0.136	-0.204	-0.299	-0.393	-0.487
		23233	0	-0.055	-0.110	-0.166	-0.242	-0.318	-0.394
		22233	0	-0.050	-0.101	-0.151	-0.221	-0.291	-0.361
Q4a	How much tiredness would you say you have at the moment?	33333	0	0	0	0.008	-0.049	-0.099	-0.148
		23233	0	0	0	-0.006	-0.044	-0.082	-0.120
		22233	0	0	0	-0.006	-0.041	-0.075	-0.110
Q5a	Daily activities e.g. washing, dressing & housework	33333	0	0	0	0	-0.052	-0.104	-0.156
		23233	0	0	0	0	-0.042	-0.084	-0.127
		22233	0	0	0	0	-0.039	-0.077	-0.116
Q5b	Leisure activities	33333	0	-0.043	-0.043	-0.043	-0.06	-0.079	-0.097
		23233	0	-0.035	-0.035	-0.035	-0.026	-0.052	-0.078
		22233	0	-0.032	-0.032	-0.032	-0.045	-0.059	-0.072
Q8a I	At the moment, does your muscle condition make you feel anxious?	33333	0	-0.016	-0.028	-0.039	-0.070	-0.101	-0.132
		23233	0	-0.013	-0.022	-0.032	-0.057	-0.082	-0.107
		22233	0	-0.012	-0.021	-0.029	-0.052	-0.075	-0.098
Q8a II	At the moment, does your muscle condition make you feel depressed?	33333	0	0	-0.038	-0.077	-0.154	-0.231	-0.307
		23233	0	0	-0.0311	-0.062	-0.125	-0.187	-0.249
		22233	0	0	-0.0355	-0.057	-0.114	-0.171	-0.228

DISCUSSION

Points

- We describe the estimation of a preference-based mapping function between the INQoL and the EQ-5D using a discrete choice experiment.
- DCE methods elicited the importance of each item. These weights were then rescaled onto the same range as the EQ-5D-3L UK weights.
- This approach allows us to map a PRO measure to the EQ-5D without having access to large datasets to generate statistical associations.
- We believe this approach is suited to the rare disease context where data are often limited

Limitations

- 8 from 52 INQoL items were selected to determine our scoring weights. The selection of these items was based on perceived conceptual overlap rather than statistical methods and guided by expert opinion.
- The selected items are not generic in the same way that EQ-5D items are because they refer to problems that patients experienced as a result of their NMD.
- Muscle locking and fatigue were included from the INQoL on the advice of the clinical experts but are not specifically questions in the EQ-5D.
- Linear interpolation was used for the simplified response choices
- Logical inconsistencies in the data meant that not all response options have unique scoring weights, however a conservative approach was used to facilitate any such inconsistencies. (see results)

CONCLUSIONS

- This preference driven mapping approach provides a mechanism for estimating QALY weights from a measure in a clinical trial where other approaches to capturing utilities are not available due to lack of data in this rare disease
- The resulting utilities are driven by patient derived data and so we believe represent a better approach than using vignette type studies.
- The method is transparent.
- We are keen to test how closely the resulting scores match EQ-5D scores which will help us to identify ways to improve the approach.

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