Mapping non-preference onto preference-based PROMs

Patient-reported outcomes measures (PROMs) in health economics

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RSS Primary Health Care Special Interest Group
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Outline of seminar

- What is meant by “Mapping”?
- Mapping studies in the literature and usage in health technology assessment
- Statistical methods to map non-preference to preference-based PROMs
  - Statistical modelling (direct vs indirect mapping)
  - Three case empirical mapping studies
- The MAPS reporting statement
What is meant by “Mapping”?

Non preference-based PROMs
(e.g. disease specific or generic questionnaire)

Preference-based PROMs
(e.g. EQ-5D-3L, EQ-5D-5L)

Source measure

Target measure

Algorithm: statistical association or more complex series of operations

- Searches conducted from 1996-2007
- Identified 30 studies.
- Most common target measure was the EQ-5D-3L.
- Comparisons across studies limited.
Mapping in the published literature


[Bar chart showing the number of papers reporting new mapping models by year from 2000 to 2013.]

Identified 90 studies reporting 121 mapping algorithms
The use of mapping in NICE technology appraisals


<table>
<thead>
<tr>
<th>Time Period</th>
<th>Submissions</th>
<th>Using Mapping</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>2004-2010</td>
<td>90</td>
<td>23</td>
<td>25%</td>
</tr>
<tr>
<td>2004-2008</td>
<td>46</td>
<td>19</td>
<td>41%</td>
</tr>
<tr>
<td>2008-2010</td>
<td>44</td>
<td>4</td>
<td>9%</td>
</tr>
</tbody>
</table>
Steps to develop mapping algorithms

1. Rationale for the mapping study
2. Identification of source and target measures
3. Identification of estimation and external validation sample
4. Exploratory data analysis
5. Statistical modelling
6. Estimation of predicted scores or utilities
7. Validation methods
8. Measures of model performance
9. Dealing with uncertainty
Statistical Modelling

Direct mapping
Indirect or response mapping
Statistical Modelling

Direct mapping

- Dependent variable using a preference-based score
  - EQ-5D-3L index has been widely used in direct mapping studies
Statistical Modelling
Direct mapping

\[ Y = X\beta + \epsilon \]

**Dependent variable**
Vector of observations:
Overall score (e.g. EQ-5D-3L index)

**Vector of parameters to be estimated**

**Matrix of predictor variables:**
- Condition-specific measures
- Generic measures
- Clinical measures
- Sociodemographic variables
- Other relevant data

**Vector of errors**
Distribution of EQ-5D-3L values

Asthma (n=2,935)

Chest pain (n=679)

Cronic obstructive pulmonary disease (n=185)

Clodronate (n=320)

Hormone replacement therapy (n=755)

Irritable bowel syndrome (n=374)

Statistical Modelling
Indirect or response mapping

- Dependent variable using response variables rather than overall index
  - EQ-5D-3L responses have been widely used in response mapping
- Ordered and multinomial logit/probit models
Statistical Modelling
Indirect mapping (multinomial logit)

\[ \Pr(y_i = m/x_i) = \frac{\exp(x_i\beta_m)}{\sum_{j=1}^{J} \exp(x_i\beta_j)} \]

- **Dependent variable**: Categorical variable (e.g. EQ-5D-3L responses)
- **Predictor variables**: Vector of parameters to be estimated
- **Individual participant**: Outcome of dependent variable (e.g. 1, 2 and 3 for the EQ-5D-3L)
- **Levels of dependent variable**: (e.g. 1, 2 and 3 for the EQ-5D-3L)
Statistical Modelling
Indirect or response mapping

- Dependent variable using response variables rather than overall index
  - EQ-5D-3L responses have been widely used in response mapping

- Ordered and multinomial logit models

- Probabilistic model and different methods available to calculate utility predictions:
  - Higher or most-likely probability - biased and not recommended
  - Expected value (equivalent to using an infinite number of Monte Carlo draws) – unbiased and recommended
3 case studies

Comparison of direct and indirect methods:
1. Mapping from Health Assessment Questionnaire (HAQ) to EQ-5D-3L
2. Mapping from Parkinson’s Disease Questionnaire (PDQ-39) to EQ-5D-3L
3. Mapping from Oxford Hip Score (OHS) to EQ-5D-3L

What will be presented?
1. Mean (SD) of actual EQ-5D-3L in estimation and external validation dataset (if available)
2. Measures of prediction accuracy: mean squared error (MSE) or root mean squared error (RMSE)
**HAQ to EQ-5D-3L**

Hernandez-Alava et al 2014

<table>
<thead>
<tr>
<th></th>
<th>Estimation dataset (n = 100,398)</th>
<th>External validation dataset (n=n/a)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean</td>
<td>Mean</td>
</tr>
<tr>
<td>Actual EQ-5D-3L index</td>
<td>0.665</td>
<td>n/a</td>
</tr>
<tr>
<td></td>
<td>RMSE</td>
<td>RMSE</td>
</tr>
<tr>
<td>Direct mapping</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Simple linear regression</td>
<td>0.175</td>
<td>n/a</td>
</tr>
<tr>
<td>Adjusted limited mixture models</td>
<td>0.169</td>
<td>n/a</td>
</tr>
<tr>
<td>Indirect mapping</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Generalised ordered probit</td>
<td>0.171</td>
<td>n/a</td>
</tr>
</tbody>
</table>

n/a: not available

### PDQ-39 to EQ-5D-3L

**Kent et al 2015**

<table>
<thead>
<tr>
<th></th>
<th>Estimation dataset (n = 9,123)</th>
<th>External validation dataset (n=719)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Actual EQ-5D-3L index</strong></td>
<td>Mean (SD)</td>
<td>Mean (SD)</td>
</tr>
<tr>
<td>PDQ-39</td>
<td>0.60 (0.27)</td>
<td>0.51 (0.27)</td>
</tr>
</tbody>
</table>

| **MSE**                |                               |                                     |
| Direct mapping         |                               |                                     |
| Simple linear regression | 0.031                         | 0.045                               |
| Adjusted limited mixture models | 0.031                        | 0.044                               |

| **Indirect mapping**   |                               |                                     |
| Multinomial logit model | 0.030                         | 0.044                               |

# OHS to EQ-5D-3L

## Work-in-progress (Oxford team)

<table>
<thead>
<tr>
<th></th>
<th>Estimation dataset</th>
<th>External validation dataset</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(n = 51,800)</td>
<td>(n = 75,322)</td>
</tr>
<tr>
<td><strong>Actual EQ-5D-3L index</strong></td>
<td>Mean (SD)</td>
<td>Mean (SD)</td>
</tr>
<tr>
<td></td>
<td>0.558 (0.356)</td>
<td>0.561 (0.355)</td>
</tr>
<tr>
<td><strong>MSE</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Direct mapping</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Simple linear regression</td>
<td>0.033</td>
<td>0.033</td>
</tr>
<tr>
<td>Two-part model</td>
<td>0.033</td>
<td>0.032</td>
</tr>
<tr>
<td>Adjusted limited mixture models</td>
<td>0.024</td>
<td>0.035</td>
</tr>
<tr>
<td>Indirect mapping</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Multinomial logit model</td>
<td>0.032</td>
<td>0.032</td>
</tr>
</tbody>
</table>
Direct versus indirect mapping

- There is no consensus about which method is preferable
- Evidence seems to suggest that overall both approaches are similar in terms of prediction accuracy
  - Differences observed favouring one method cannot be generalised to all instrument and patient populations
- Indirect mapping has some attractive properties:
  - Preserves logic of utility instruments such as EQ-5D
  - Provides more descriptive information than direct mapping
  - Compatible with different country-specific tariff sets
Additional statistical challenges ahead

- Performance of methods deteriorates as health states decline
- Does using more complex models (e.g. mixture models, Bayesian networks) improve performance of both direct and indirect methods?
- Need of better methods to deal with uncertainty
- Guidance on appropriate validation of mapping algorithms in practice

Overall we need to improve the reporting of these studies
MAPS reporting statement

- **MAPS statement:** MApping onto Preference-based measures reporting Standards

- **Objective:** to develop a checklist to promote complete and transparent reporting by researchers

- **Methods:** two-round Delphi survey with 48 representatives from academia, consultancy, HTA, and journal editors

- **Results:** a set of 23 essential reporting items was developed
MAPS reporting statement

**Title and abstract**
- Item 1: Title
- Item 2: Abstract

**Introduction**
- Item 3: Study Rationale
- Item 4: Study Objective

**Methods**
- Item 5: Estimation Sample
- Item 6: External Validation Sample
- Item 7: Source and Target Measures
- Item 8: Exploratory Data Analysis
- Item 9: Missing Data
- Item 10: Modelling Approaches
- Item 11: Estimation of Predicted Scores or Utilities
- Item 12: Validation Methods
- Item 13: Measures of Model Performance

**Results**
- Item 14: Final Sample Size(s)
- Item 15: Descriptive Information
- Item 16: Model Selection
- Item 17: Model Coefficients
- Item 18: Uncertainty
- Item 19: Model Performance and Face Validity

**Discussion**
- Item 20: Comparisons with Previous Studies
- Item 21: Study Limitations
- Item 22: Scope of Applications

**Other**
- Item 23: Additional Information

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**MAPS working group**
- Stavros Petrou, Warwick University
- Oliver Rivero-Arias, Oxford University
- Helen Dakin, Oxford University
- Louise Longworth, Brunel University
- Mark Oppe, EuroQol Research Foundation
- Robert Froud, Warwick University
- Alastair Gray, Oxford University

For each item examples of good reporting practice, an explanation and the rationale and relevant evidence is provided.
Conclusions

- Mapping algorithms to translate non preference onto preference-based PROMs are available
  - HOWEVER, collection of primary data with the preferred utility instrument is desirable (mapping as second-best)

- Statistical methods have been evaluated to understand direct and indirect methods
  - No consensus in the literature
  - Additional statistical challenges ahead

- The development of the MAPS statement should improve the reporting (and quality?) of this studies in the future