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A comparison of direct and indirect methods for the estimation of health utilities from clinical outcomes

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Introduction

- Mapping (or ‘cross-walking’) is used to estimate a utility score/index from a different outcome measure
 - clinical trials without a preference based measure
 - Within PROMS agenda as performance indicators
 - Essential element of VBP
- Mapping involves:
 - Estimating a relationship using a statistical model
 - Predicting using the estimated model
- **THIS IS ESSENTIALLY A STATISTICAL ISSUE!**

EQ-5D-3L UK-tariff

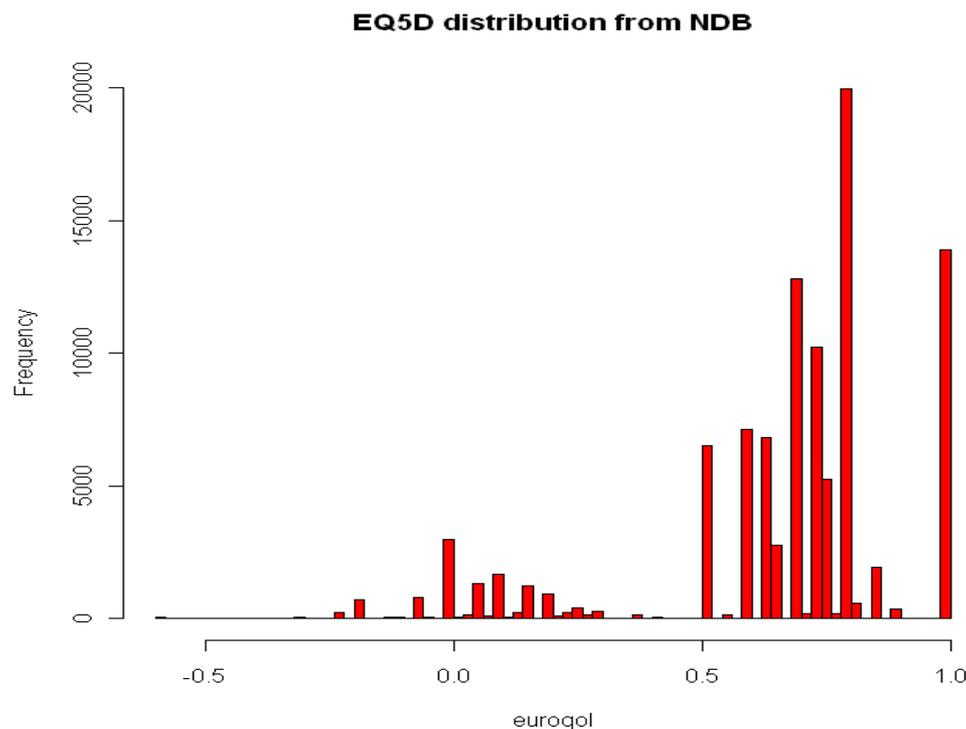
- Descriptive system 11111, 21123
 - 5 dimensions - mobility, self care, usual activities, pain, anxiety and depression
 - 3 levels in each dimension- no problems, some problems, extreme problems
 - 243 combinations
- Valuation (Dolan *et al* 1995) – utility scores
 - Analysis of preference data: 3000 individuals

Two general methods

- Direct: dependent variable – utility/index scores
 - 11213 -> 0.378
- Indirect: dependent variables – levels of descriptive system.
 - Expected index score is calculated as a second step
 - “Response mapping”

AIM: Estimate EQ-5D as a function of HAQ, Pain and other covariates – direct & indirect methods

- US not-for-profit database
- N=100,398 (16k patients)
- Adults with RA diagnosis
- Classic EQ-5D (UK tariff) distribution
- Multimodal
- Peak at 1
- Bounded top and bottom
- Gap between 1 and 0.883



Existing evidence

- Direct methods:

- Linear regression
- Tobit (often incorrectly applied!)
- CLAD
- Two-part models

Poor fit
Underestimate at top
Overestimate at
bottom

Biased estimates of treatment effect

Methods and models

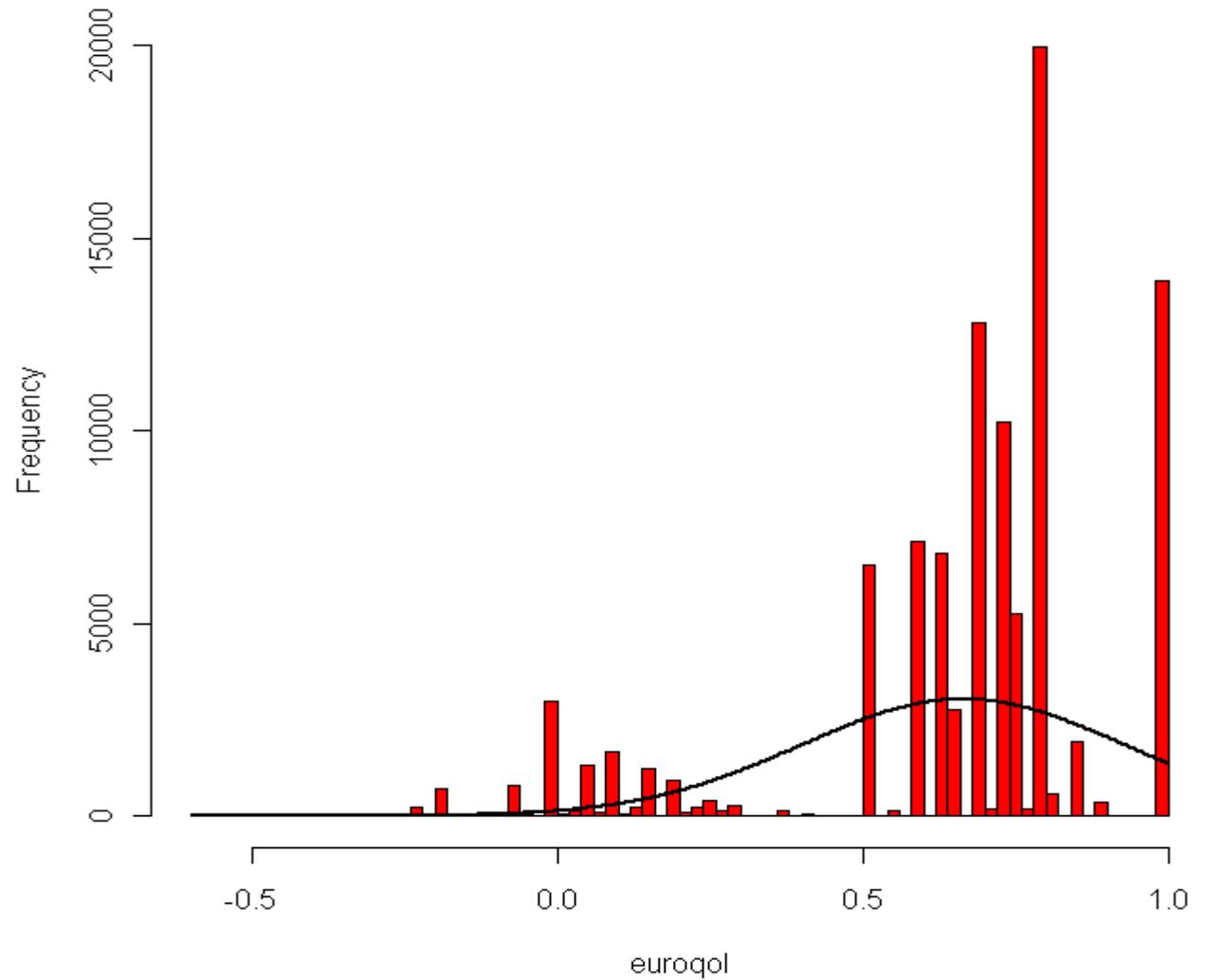
- Direct methods:
 - Adjusted Limited Dependent Variable Mixture Model
(development of Hernández Alava *et al* 2012)
 - RE linear regression
- Indirect method:
 - Set of Generalised Ordered Probits
(development of “Response Mapping” Gray *et al* 2006)

Direct method: Finite Mixture Modelling

- Useful where simple models don't fit complex data
- Model data as a finite mixture of component models (usually of the same type)
- Often used where interest is in identifying clusters of groups
- But here we are interested in approach because of flexibility
- Any continuous distribution can be approximated by a mixture of normals

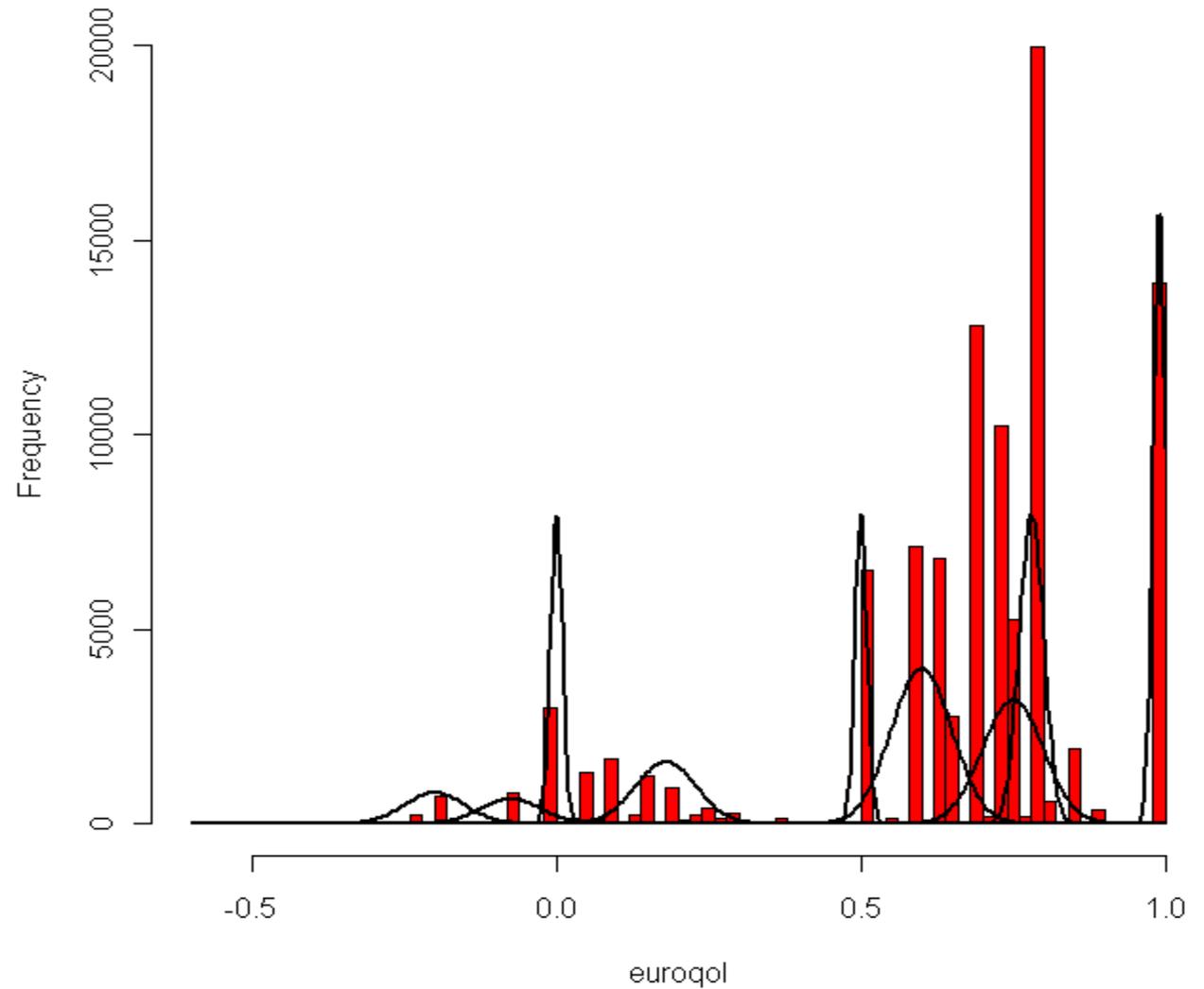


Mixture model example - 1 component

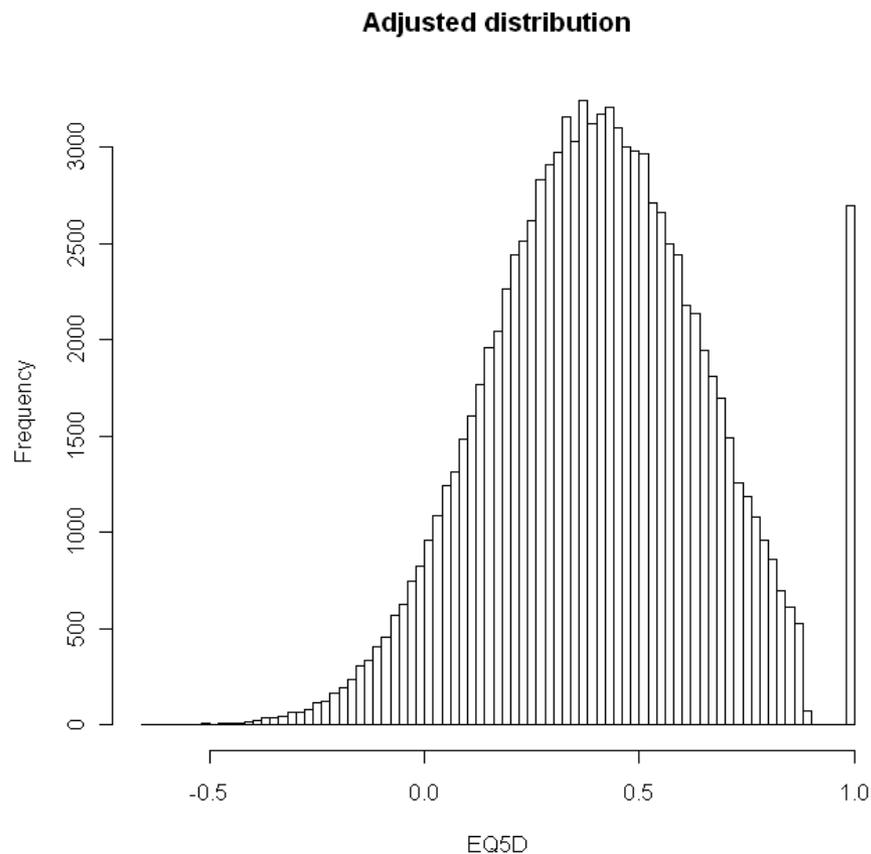




Mixture model example - more components



- Don't need to use normal distributions
- More appropriate bespoke distribution
- Each component reflects EQ-5D properties
- Overcomes need for a class of "1"s
- Combination of:
 - a) Adjusted dist
 - AND
 - b) Mixture framework



Indirect method: Random Effects Generalised Ordered Probit

- 3 point ordered discrete dependent variable for each of the five dimensions of EQ-5D
- (RE) Ordered Probit – implicit parallel regression assumption too restrictive
- Multinomial logit model BUT ignores ordinality of the dependent variable



Indirect method: Random Effects Generalised Ordered Probits

- q_{it}^s discrete dependent variables for $s=\{\text{mobility, self care, usual activities, pain, anxiety and depression}\}$

$$P(q_{it}^s = 1|x_{it}, u_i^s) = 1 - \Phi(x_{it}\beta_1^s + u_i^s)$$

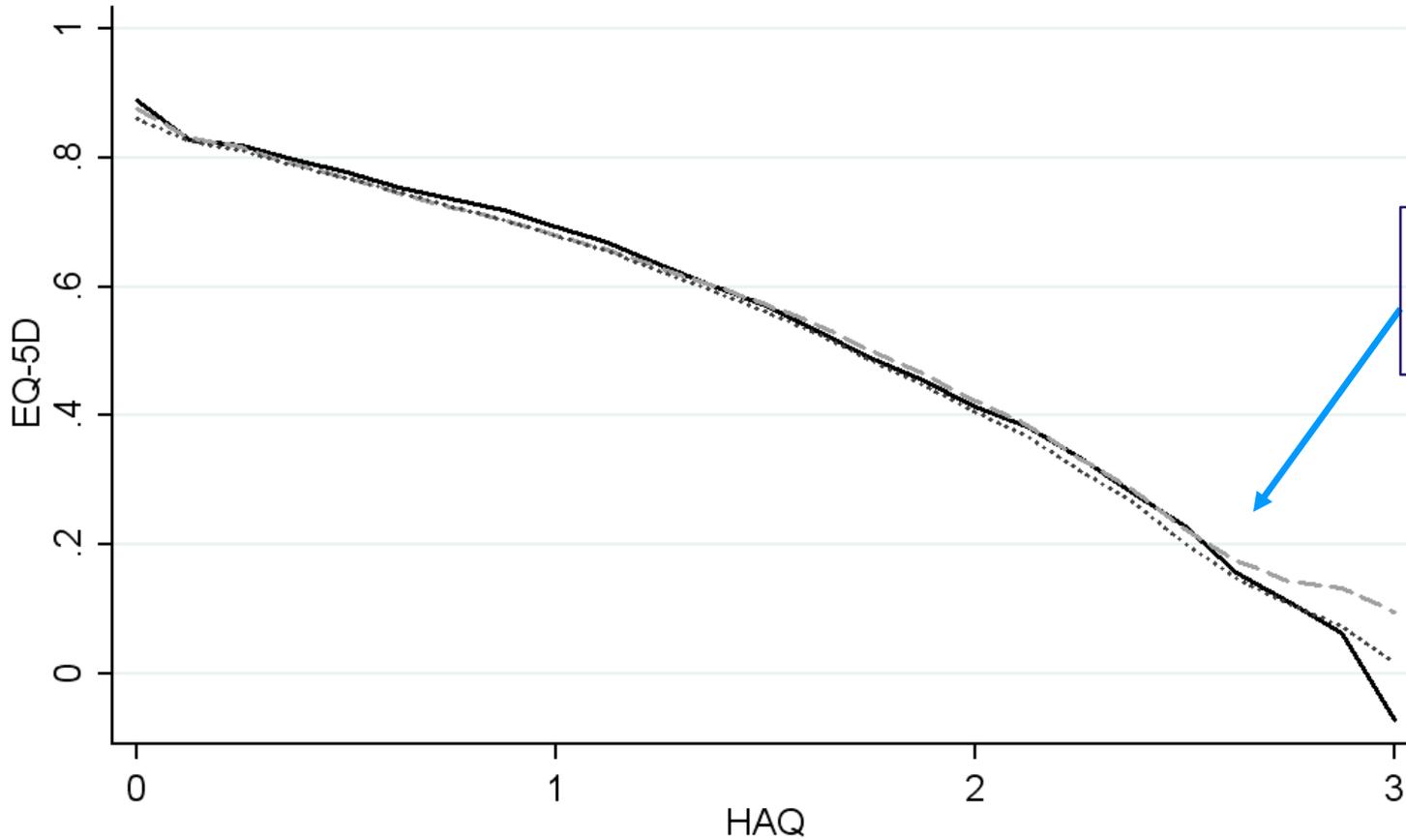
$$P(q_{it}^s = 2|x_{it}, u_i^s) = \Phi(x_{it}\beta_1^s + u_i^s) - \Phi(x_{it}\beta_2^s + u_i^s)$$

$$P(q_{it}^s = 3|x_{it}, u_i^s) = \Phi(x_{it}\beta_2^s + u_i^s)$$

- Expected value calculated mathematically – average of all 243 utility values weighted by their estimated probabilities

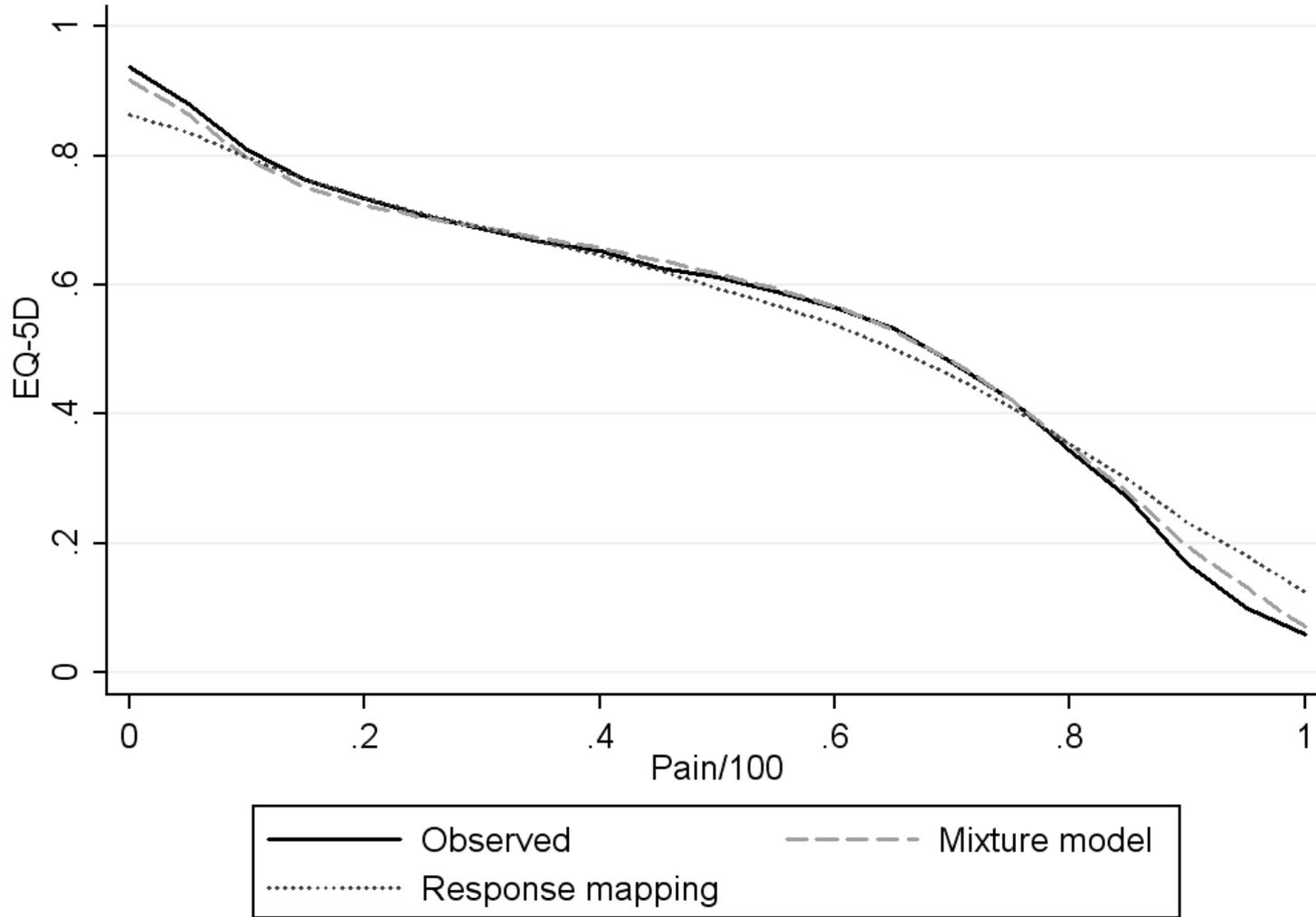
Model selection and comparisons

- Explanatory variables:
HAQ, HAQ², pain, gender, age and age²
- BIC to choose number of mixture components –
4
- MAE & RMSE (insensitive but widely used)
- Monte Carlo simulation to generate data from
models and compare to observed data



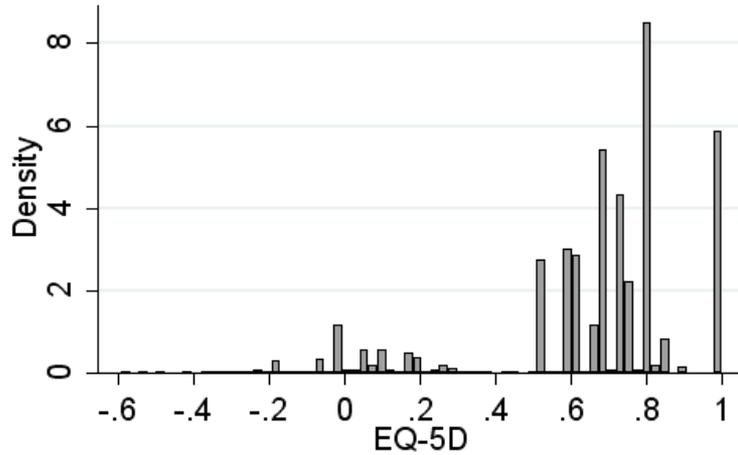
• Only 1% with HAQ > 2.5



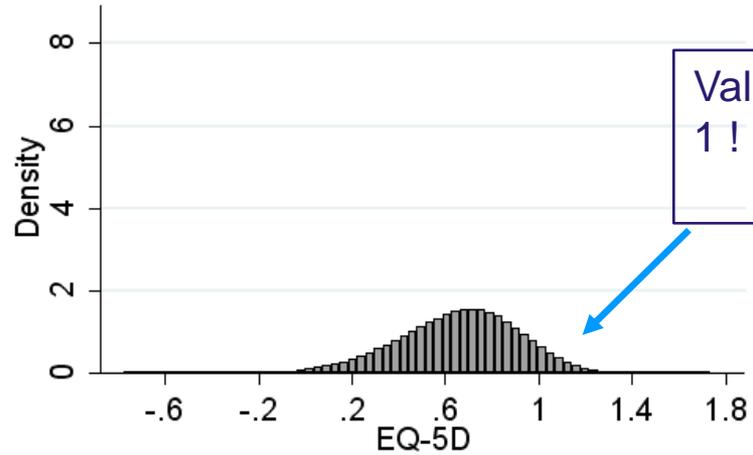




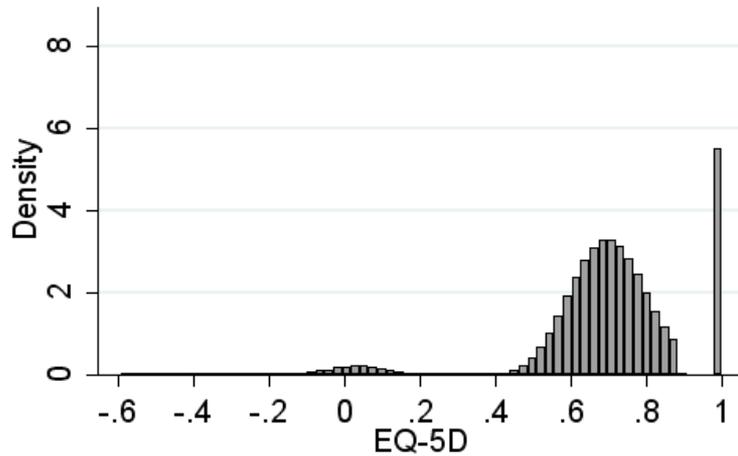
a - Data



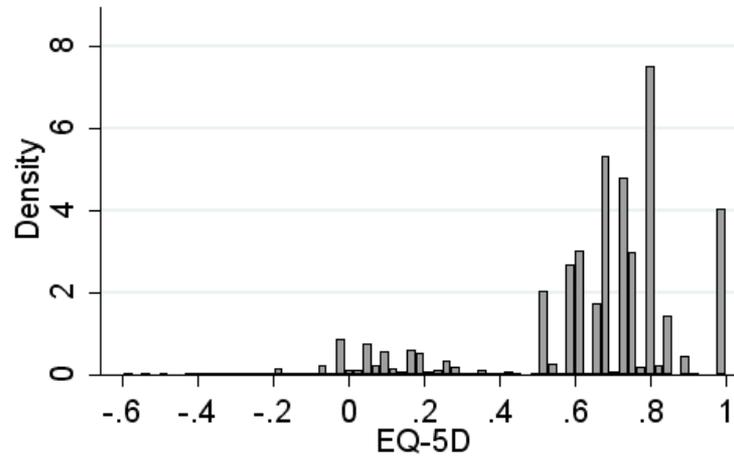
b - Linear model



c - Mixture model



d - Response mapping



Conclusion/Discussion

- Linear models are not appropriate for mapping
 - Response mapping and mixture model approaches substantially better in all regards
 - ...and it matters!
- Generalized ordered probit can be used for response mapping
 - Respects ordered nature of data

Conclusion/Discussion

- Bespoke mixture model performs best overall in this example
- Further work
 - Develop response mapping (correlations, more flexible functional forms)
 - Compare methods in other datasets/simulation/outcomes
 - How will it work with EQ-5D-5L?
 - Depends how valuations are modelled



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