

# Development of methods for the mapping of utilities using mixture models: Mapping the AQLQ-S to EQ-5D-5L and HUI3 in patients with Asthma

**Laura A Gray<sup>†</sup>, Monica Hernandez Alava<sup>†</sup> & Allan J Wailoo<sup>†</sup>**

<sup>†</sup> - The University of Sheffield  
**Jornadas AES, Barcelona**

6th September, 2017

# Introduction

## Background

- PBMs are needed to calculate QALYs for use in cost-effectiveness analysis.
- Many RCTs and clinical effectiveness studies do not record PBMs.
- Clinical measures - usually disease specific.
- Mapping estimates PBMs.
- PBMs have a number of unusual characteristics.

# Introduction

## Previous Mapping Studies

- Beta regressions - multi-modal. (Basu & Manca (2012))
- Limited dependent variable (0,1) found to be inappropriate (Young et al. (2015))
- Some studies have censored the data at 0. (Kaambwa et al. (2016), Khan & Morris (2014))
- Transforming values onto (0,1). (Smithson & Verkuilen (2006), Kent et al. (2015), Khan et al. (2016))
- Mixture models are flexible and capture the multi-modality.
- Mixtures of normal distributions.(Hernandez Alava et al. (2012, 2013, 2014), Hernandez & Wailoo (2015))
- Mixtures of beta distributions.(Kent et al. (2015), Gray et al. (2017))

# Data

- Multi Instrument Comparison (MIC) data.
  - 7933 observations
  - Australia, Canada, Germany, Norway, UK, US
  - 856 self-report asthma, 852 after observations removed
- EQ5D-5L [-0.281, 0.951] & 1
- HUI3 [-0.36, 0.97258] & 1
- AQLQ-S, 20 questions, 4 domains, [0, 4]
- Also include age, age squared and sex.

# Econometric Analysis

## ALDVMM

- Adjusted Limited Dependent Variable Mixture Model (ALDVMM)
- User-written Stata command -aldvmm- (Hernandez Alava & Wailoo, 2015)
- Allows upper and lower limits of PBMs as well as the 'truncation point'.
- Mixture of normal distributions allows for the multi-modality
- Truncation at the second best feasible health state
- Large number of observations at 1 estimated using a single component with very small variance.

# Econometric Analysis

## Beta-based mixture model

- Beta-based mixture model
- User-written Stata command -betamix- (Gray & Hernandez Alava, 2017)
- Generalisation of a truncated inflated beta regression (Pereira et al. 2012)
- Two-part Model
  - Multi-nomial logit model
  - Beta mixture model
- Not constrained to  $(0,1)$ , we transform to the appropriate interval.

# Econometric Analysis

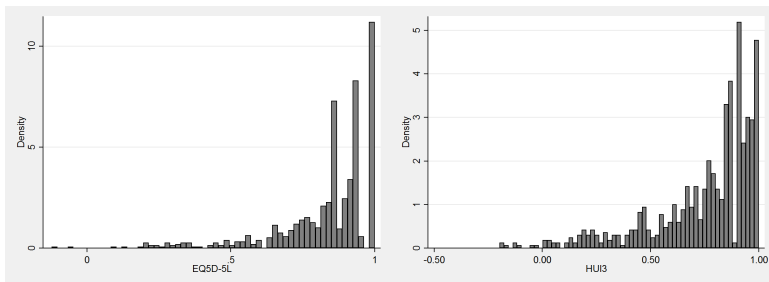
## Mixture models

- We estimate multiple models for each technique
  - Different number of components
  - With and without a gap between full health and the next feasible state
  - Different probability masses - betamix only
- Model selection using AIC, BIC, RMSE, MAE
- Conditional distribution function and mean predicted vs mean observed

# Results

## Summary

- 62.3% female, 18-89 years
- AQLQ-S spans full range [0,4]
- PBMs do not span full range





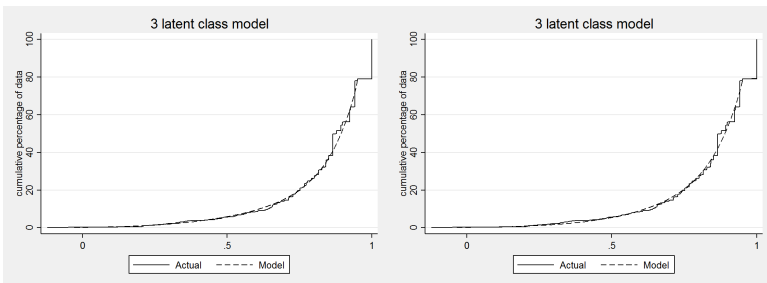
# Results

## Summary

- Directly estimating the gap improves the models.
- Gap previously shown to be important when estimating EQ5D-3L (Hernandez et al, 2012)
- Still important when gap is smaller in EQ5D-5L & HUI3

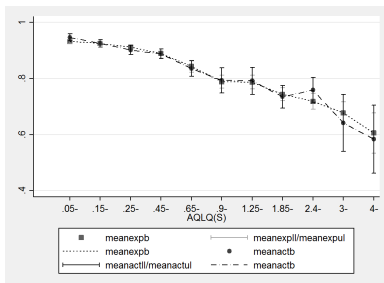
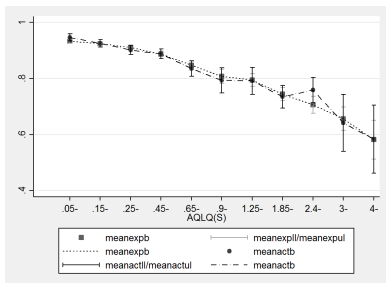
# Results

## Summary



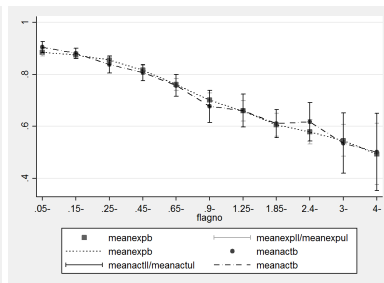
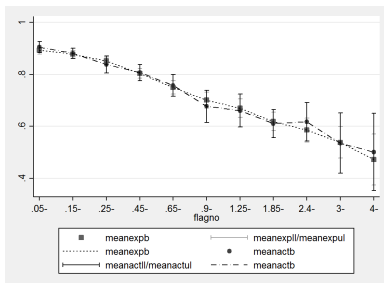
# Results

## Summary



# Results

## Summary



## Preferred models for EQ5D-5L:

- 3 component beta-based model with mass at full health
- 3 component ALDVMM

## Preferred models for HUI3:

- 4 component beta-based model with mass at full health and next feasible state
- 4 component ALDVMM

## Discussion

- Betamix models have better fit than ALDVMMs.
- Betamix include probability masses - more artificial.
- Over-fitting the data - identification problems
- Proportion of observations at the truncation point
- Multimodality
- Theoretical justification is required for probability masses.

# Discussion

- Important to consider the distribution:
  - Comparison to OLS and other non-mixture models (Kaambwa et al, 2016)
  - Mixture models do not suffer from a lot of the problems other models do.
  - Estimate very closely at all parts of the distribution.
  - Restrict estimation to the feasible range.
  - Ensure a global maximum.

- Mixture models fit the data well.
- Beta models outperformed ALDVMM, but might over fit the data.
- Important to directly estimate the gap between full health and the rest of the distribution.
- Skilled judgment required
- Global maximum
- Results do not suffer from bias



## Conclusions

Thank you

# Thank you