Optimizing Regression Models for Patient-Level Utility Scores: A Case Study on Addressing Ceiling Effects in EQ-5D Data from the MYR301 Clinical Trial

MSR23

MYR301

Shubhram Pandey[1], Barinder Singh[2], Akanksha Sharma[1], Marvin Rock[3], Chong Kim[3]

[1]Pharmacoevidence, Mohali, India; [2]Pharmacoevidence, London, UK; [3]Gilead Sciences, Inc., Foster City, CA, USA

Conclusion

- Tobit around the median exhibited the highest performance, particularly in managing heavy ceiling effects, followed by the mean-centered Tobit and the log-transformed two-part model (TPM) with median
- In the presence of a ceiling effect in the EuroQol 5 Dimension (EQ-5D) index scores, Tobit analysis provides most accurate and robust results by accounting for censoring in the regression models
- From the perspective of health technology assessment submissions, a detailed assessment of regression models should be considered to select the most appropriate model that accurately describes the utility gain/loss thus allowing for a reliable and robust assessment of the impact of treatments on health-related quality of life

Plain Language Summary

- A noticeable ceiling effect was observed in the MYR301 EQ-5D data, where close to 50% of participants attained the highest health score
- This study explored various statistical models to analyze EQ-5D data for addressing the ceiling effect challenge
- The predictive accuracy of the models was assessed using pseudo-R-squared, where higher values signify better prediction
- The study concluded that Tobit around the median was the most effective, followed by Tobit around the mean and log-transformed TPM with the median model
- The Tobit models provided most accurate and robust results, compared to other regression models (e.g., beta regression), when dealing with the ceiling effect in EQ-5D scores

References: **1.** Gusi N, et al. *Handbook of Disease Burdens and Quality of Life Measures*. 2010; 87-99.

2. Huang I, et al. *Health Serv Res*. 2008; 43; 327-39.

3. Wedemeyer H, et al. *N Engl J Med*. 2023; 389; 22-32.

4. Hardin, J. W., Hilbe, J. M. (2007). Generalized linear models and extensions. USA: Taylor & Francis. Page 60, Google Books

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Correspondence: Barinder Singh, barinder.singh@pharmacoevidence.com

Introduction

- The EQ-5D index is the preferable and widely used instrument that could serve as the basis for summarizing and comparing health outcomes to assess preference-based health status[1]
- EQ-5D index measures the degree to which individuals prefer certain health states on a scale from 0 to 1, with 0 representing death and 1 representing optimal health[2]
- Patient-level utility scores derived using regression models may exhibit suboptimal performance when confronted with the ceiling effect

Objective

- This study aimed to identify the most suitable model for addressing the ceiling effect in EQ-5D scores from the MYR301 clinical trial[3]

Methodology

- MYR301 was a Phase 3 trial designed to assess the long-term efficacy and safety of bulevirtide in Hepatitis D patients by comparing daily doses of 2 mg and 10 mg bulevirtide to delayed treatment
- EQ-5D health state profile at the patient level was transformed into an index score (utility) by applying the United Kingdom general population preference weights to each level in every dimension
- Various regression models were employed to analyze EQ-5D scores and generate coefficients linked to covariates. The models' predictive accuracy was evaluated using McFadden's pseudo-R-squared; where higher values signify better prediction
- McFadden's Pseudo R-Squared[4] is calculated as :

$$Pseudo\ R^2 = 1 - \frac{\ln LL\ (Mfull)}{\ln LL\ (Mintercept)}$$

Where, the numerator is the log likelihood of the model with intercept and covariates and the denominator is the log likelihood with intercept only

Results

- The analysis of EQ-5D index scores from MYR 301 indicated a noticeable leftward skew in the distribution, with approximately 45-50% of subjects achieving the highest score of 1
- This observation strongly suggested the presence of a ceiling effect in the data, characterized by a substantial proportion of subjects i.e. approximately 50%, attaining maximum scores (greater than 0.9 to 1) at week 48
- **Figure 1** depicts the distribution of utility scores across 100 subjects and **Figure 2** represents accuracy measure of regression models

Figure 1. Distribution of utility scores at week 48

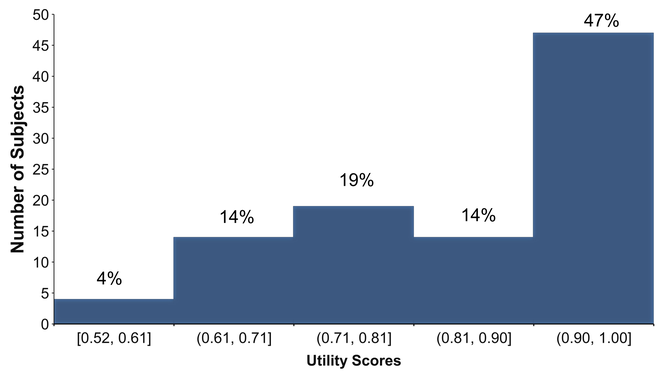
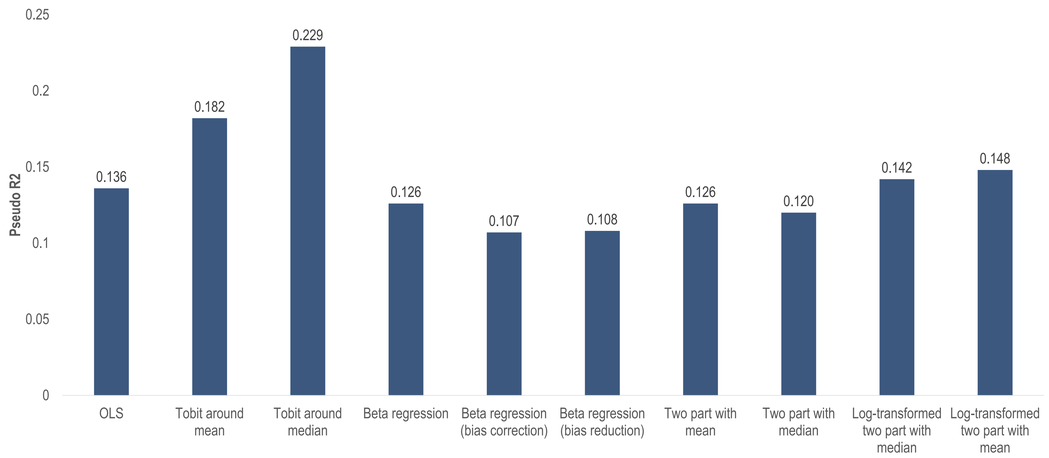


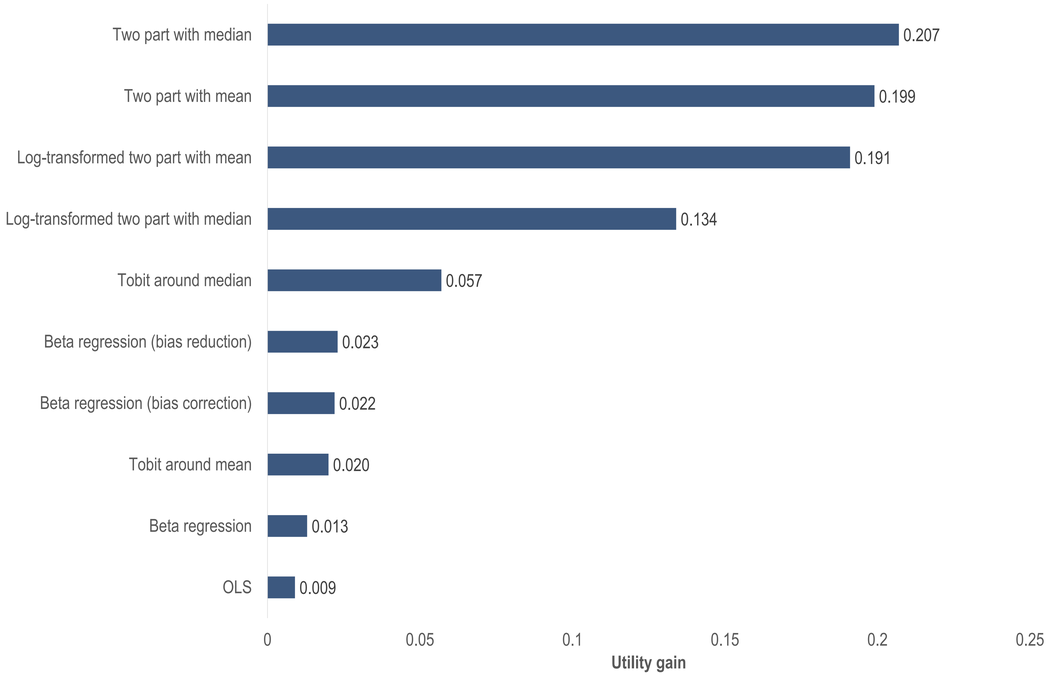
Figure 2: Regression models depicting pseudo R^2



Results (Contd.)

- According to Pseudo R^2 values, the Tobit model around the median showed the highest accuracy followed by Tobit around the mean
- The highest utility gain for composite responders was reported (**Figure 3**) for the TPM with median (0.207) followed by the TPM with mean (0.199)

Figure 3: Composite Responder Utility Gain



Limitations

- The data for missing values of EQ-5D scores were not imputed
- TPM may suffer from the problem of multicollinearity between explanatory variables and the probability correction variables