

one state to another. Depending on the purpose, the color of the parallelograms indicates the categories of a chosen cycle or could refer to additional attributes of the patients like age or sex. **RESULTS:** State probability and survival curves merely show specific aggregates of the data while classic Markov trace visualizations with for example bubble diagrams do not visualize data in a sense that would facilitate a detection of proportions and trends. Applying Parallel Sets to analyze Markov models provides an interactive visualization technique where changing the reference Markov cycle is as easy as highlighting particular dimensions, thus enabling the exploration of the progress of patient cohorts with certain characteristics through the model. **CONCLUSIONS:** Model development always requires thorough analysis of its structure, behavior and results. Parallel Sets enable an intuitive and efficient visualization technique for presentation purposes as well as exploratory analysis.

#### PRM76

##### A TREATMENT SEQUENCE APPROACH FOR MODELLING CROHN'S DISEASE

Lee D<sup>1</sup>, Gladwell D<sup>1</sup>, Batty A<sup>1</sup>, Berry P<sup>2</sup>, Smith HT<sup>3</sup>  
<sup>1</sup>BresMed, Sheffield, UK, <sup>2</sup>GSK, King of Prussia, PA, USA, <sup>3</sup>GSK, Brentford, UK

**OBJECTIVES:** Crohn's disease (CD) is a relapsing remitting inflammatory disease affecting the gastrointestinal tract. Previous economic evaluations in CD have focussed on single treatment comparisons within the treatment pathway. This project aimed to develop a model capturing lifetime costs and utilities throughout the entire treatment pathway. **METHODS:** A treatment sequence model was adapted from an earlier CD model by including the option to change treatments as patients stop responding. A Markov structure was used with five health-states: full-, partial- and no-response, surgery and death. Transition probabilities and survival rates were derived from previous analyses with separate transition matrices used for standard care and anti-TNF- $\alpha$ s. The model allows for  $\leq 11$  treatment stages (each with induction and maintenance phases) to be evaluated. Patients failing in induction progress to the next stage, if failing in maintenance they return to the induction treatment from that stage unless it is the same as the maintenance treatment. Surgery can be included as a separate treatment stage, although patients can receive surgery at any time. Costs were taken from published sources, and utilities from previous analyses. Limitations of available contemporary data and reporting of modelling methods posed challenges for model development; in particular the lack of data on the efficacy of combination treatment and probabilities of sustained response on anti-TNF- $\alpha$  therapies. **RESULTS:** In a patient cohort (mean age 35), lifetime costs and QALYs (LYs) were £169,560 and 14.85 (20.97) for a treatment pathway where patients initiated therapy with steroids + azathioprine followed by azathioprine maintenance, progressed through more intensive steroid induction, available anti-TNF- $\alpha$ s and surgery, ultimately becoming treatment refractory. **CONCLUSIONS:** This model represents an advance in economic evaluation of CD, allowing lifetime evaluation of treatment strategies in a complex treatment area. Further research into the natural history of CD would improve the potential for robust economic evaluation.

#### PRM77

##### MAPPING THE MEANINGS OF WORDS PATIENTS USE TO DESCRIBE THEIR PAIN

Scanlon M<sup>1</sup>, Martin ML<sup>2</sup>, Mccarrier KP<sup>2</sup>, Wolfe M<sup>1</sup>, Bushnell DM<sup>1</sup>  
<sup>1</sup>Health Research Associates, Inc., Mountlake Terrace, WA, USA, <sup>2</sup>Health Research Associates, Inc., Seattle, WA, USA

**OBJECTIVES:** To identify the meaning of descriptors patients use to describe the quality and severity of their pain by mapping word clusters that patients identify as synonyms for the same pain sensation. **METHODS:** Subjects were recruited by web posting and telephone screening. Those self-reporting active treatment for Migraine or Low Back Pain (LBP) were scheduled for in-person interviews using card sort exercises with 93 different pain descriptors to identify those each subject commonly used to describe the pain associated with their condition, and to identify pairs of descriptors that describe the same pain. Network maps that diagrammed patient identified equivalences between descriptors were created for each condition using Netdraw (Borgatti 2002) and then compared. **RESULTS:** Subjects ranged between 19 and 70 years (mean age of 41). The majority (73%) was female, 65% were working full or part time, and 59% were Caucasian. Migraine patients identified more descriptive synonyms to describe their pain (10% of all identified synonym pairs) than the LBP group (6%). For the Migraine group, most words used synonymously formed a single large cluster of connections. For the LBP group two main clusters of descriptors emerged, differentiating low-intensity and high-intensity pain. Patients in both groups tended to identify STIFFNESS-TIGHT, ACHING-HURTING, RADIATING-SHOOTING and PULSATING-PULSING-THROBBING as synonymous. LBP patients also associated RADIATING with movement (SPREADING/PENETRATING) and thermal (HOT) descriptors, while Migraine patients tended to use it interchangeably with PIERCING. Migraine patients described TIGHT as equivalent with SQUEEZING/CRUSHING, while LBP patients associated it with PULLING/TENSION. For LBP patients, SPREADING was closely associated with PENETRATING/RADIATING/SHOOTING, while for Migraine patients it was linked closely to THROBBING/GNAWING/FLASHING. **CONCLUSIONS:** While some descriptors were used to convey a more consistent meaning across groups, other descriptors demonstrated condition-specific meaning. These findings emphasize the importance of context of use when using pain as a study endpoint.

#### PRM78

##### MAPPING OF THE NATIONAL EYE INSTITUTE 25-ITEM VISUAL FUNCTIONING QUESTIONNAIRE (VFQ-25) TO EQ-5D UTILITY SCORES

Kay S<sup>1</sup>, Ferreira A<sup>2</sup>  
<sup>1</sup>Adelphi Real World, Bollington, UK, <sup>2</sup>Novartis Pharma AG, Basel, Switzerland

**OBJECTIVES:** The purpose of this analysis was to develop a mapping algorithm to

estimate EQ-5D utilities based on the 25-item National Eye Institute Visual Functioning Questionnaire (VFQ-25), a patient-reported outcome measure developed to evaluate vision-specific functioning. **METHODS:** The dataset comprised 951 paired EQ-5D/VFQ-25 observations from 344 patients in RESTORE, a 12-month, randomized, double-masked trial in patients with visual impairment due to diabetic macular edema. EQ-5D index scores were calculated based on the UK tariff. We evaluated 11 models and 4 separate predictor lists of VFQ-25 subscales to estimate utility as a function of VFQ-25 score, based on 4 models: Tobit, CLAD (Censored Least Absolute Deviation), GEE (Generalized Estimating Equation) and reverse two-part GEE models (which address the strong ceiling effect and left-skewed distribution of the EQ-5D). Model performance was assessed by ten-fold cross-validation comparing root mean squared error (RMSE), mean absolute error (MAE) and correlation with EQ-5D score (Spearman R-squared). **RESULTS:** Mapping results were similar across all techniques and predictor lists. The reverse two-part GEE model had the best predictive performance (RMSE 0.199, MAE 0.140) and used fewest predictors, but correlated relatively weakly with the original EQ-5D results (Spearman R-squared 0.34). **CONCLUSIONS:** Mapping VFQ-25 scores to EQ-5D utilities results in low predictive power independent of the modelling methodology applied. The difficulties in this mapping exercise are likely the result of the inability of the EQ-5D to discriminate vision-related activities.

#### PRM79

##### INTEGRATING PATIENT PREFERENCES AND CLINICAL TRIAL DATA IN A BAYESIAN MODEL FOR QUANTITATIVE RISK-BENEFIT ASSESSMENT

Broekhuizen H<sup>1</sup>, Ijzerman Mj<sup>1</sup>, Groothuis-Oudshoorn KG<sup>1</sup>, Hauber AB<sup>2</sup>  
<sup>1</sup>University of Twente, Enschede, The Netherlands, <sup>2</sup>RTI Health Solutions, Research Triangle Park, NC, USA

**OBJECTIVES:** Regulatory agencies show a growing interest in quantitative models for risk-benefit assessments to increase decision transparency. Regulators increasingly incorporate patients' view on benefit-risk tradeoffs but little is known on how to integrate elicited preferences into the quantitative models. There is little knowledge on how to integrate these preferences with clinical performance data and how to use knowledge about the uncertainty surrounding both types of parameters (preference and performance). The objective of this study was to demonstrate how patient preferences can be integrated in a Bayesian framework for quantitative benefit-risk assessment. **METHODS:** An MCDA model was developed that integrates clinical trial data, elicited patient preferences and uncertainty surrounding these estimates. Stochastic characteristics of preference and drug performance parameters can be approximated from stated preference studies and performance data from systematic reviews or RCT's. Risk and benefit scores of drugs are then simulated with Monte Carlo methods using approximated distributions. The acceptability (runs where weighted benefits > weighted risks) is calculated. A 'benefit-risk factsheet' with acceptability graphs is provided, to facilitate decision makers in their appraisal. **RESULTS:** The model was applied to an anti-depressants case. We included two benefit and one risk criteria. Preference data was derived from an expert panel and the performance data (pooled odds ratio's compared to placebo) were derived from a systematic review. The simulations show all drugs have high ( $\approx 1$ ) acceptabilities. The problem is more sensitive to performance information than to preference information and most sensitive to the adverse events performance criterion. **CONCLUSIONS:** Using this MCDA model it is possible to include patient preference in a quantitative risk-benefit assessment model. The model allows integration of stochastic uncertainty concerning preference and performance. It demonstrates that comprehensive presentation of data is possible. We are currently working on applying the model to a case on advanced renal cell carcinoma.

#### PRM80

##### PROPORTIONAL HAZARDS ASSUMPTION AND ITS IMPACT ON RESULTS OF COST-EFFECTIVENESS ANALYSIS

Pochopien M, Zerda I, Gwiosda B, Plisko R  
 HTA Consulting, Krakow, Poland

**OBJECTIVES:** If proportional hazards assumption holds, Cox regression allows for estimation of treatment effect in the form of hazard ratio. The common practice is to fit parametric model to control arm, then to apply hazard ratio to predict treatment arm. However proportional hazards assumption is rarely verified. Our aim was to estimate how proportional hazards assumption may impact cost-effectiveness. **METHODS:** Markov model was developed to describe cancer patients treatment. Health states distinguished in the model were: progression-free, progression and death. Time to progression and death were obtained from clinical trials for breast and renal cell cancer and implemented into the model on the basis of Weibull curves, fitted to data from clinical studies. Calculations were carried out separately with or without using given hazard parameters. It was assumed that compared interventions differ only in terms of time to progression or death. All the other parameters were the same for both arms. **RESULTS:** In case of renal cell carcinoma bisphosphonates combined with sunitinib were compared with sunitinib alone. When time to progression differs between interventions the average time spent by patient in progression-free state was 1.39 vs 0.72 and 2.01 vs 0.72 years with and without proportional hazards assumption, what lead to differences in QALY of 0.20 and 0.39 respectively. When time to death differs between interventions the average survival was 5.17 vs 2.65 years and 5.41 vs 2.65 years with and without proportional hazards assumption and that resulted in differences in QALY of 1.01 and 1.11. **CONCLUSIONS:** These results indicate that, taking costs into account, proportional hazard assumption may have large impact on cost-effectiveness. Proportional hazards assumption should be always checked and its impact on obtained results should be estimated in sensitivity analysis.