derived from the five dimensions of the EQ-5D (mobility, self-care, usual activities, pain/discomfort, and anxiety/depression). A single utility score on an interval metric was provided by the application of health state evaluations. Individual differences in clinical outcome trajectories were modeled using latent curve models that captured linear and non-linear trends over time for SOHO participants. Model estimation used Maximum Likelihood methods in Mplus software and therefore enabled inclusion of missing data under a Missing At Random (MAR) assumption. RESULTS: EQ-5D utility scores could not be adequately summarised by simple linear models over two years. Instead models allowing for curvilinear trajectories were required. The fastest change in EQ-5D utility scores occurred in the six months after medication initiation or change. Some individuals with later relapses were also identified by turning points in their outcome trajectory. CONCLUSIONS: New statistical methods for latent growth modeling are useful tools for displaying and modeling individual variations in clinical and social outcomes, including self-rated quality of life, in schizophrenia patients. In future work we hope to relate these profiles to patterns of medication change.

PO2 DEVELOPMENT AND VALIDATION OF A QUESTIONNAIRE TO EVALUATE SEVERITY OF SYMPTOMS IN PATIENTS WITH IBS-C AND IBS-A

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OBJECTIVES: LOGIC (Longitudinal Outcomes Study of Gastrointestinal symptoms in Canada) and ILOS (Irritable bowel syndrome Longitudinal Outcomes Study) are two ongoing pharmacoepidemiologic studies of patients with irritable bowel syndrome with constipation or alternating constipation/diarrhea (IBS-C or IBS-A) across Canada and the US, respectively. The purpose was to develop and validate a self-report questionnaire that measures severity of IBS symptoms in patients with IBS-C and IBS-A. METHODS: The IBS patient’s symptoms questionnaire was a 15-item questionnaire that measured frequency, intensity, and distress/bother associated with the following IBS symptoms: constipation, gas, abdominal pain/discomfort, bloating, and diarrhea. All items were measured on a 0 to 5-point scale except for the frequency items from the ILOS study, which were measured on a 0 to 4-point scale. To explore the questionnaire items, a principal component analysis (PCA) was performed. Correlations between the baseline severity scores and the baseline IBS-QOL overall scores were calculated. RESULTS: To date, 1,537 subjects have provided the IBS severity of symptoms questionnaire at baseline for LOGIC. The PCA showed that three components provide a good summary of the data, with the 1st, 2nd, and 3rd components accounting for 37%, 20%, and 13% of the total variability in the data, respectively. Similar PCA results were observed for the 380 subjects who provided the ILOS questionnaire. For both studies, the first component approximates a simple average of scores for items of all symptoms excluding diarrhea. The resulting Severity Score significantly correlates with the IBS-QOL total score with r = -0.549 (p < 0.001) for LOGIC and r = -0.468 (p < 0.001) for ILOS. CONCLUSIONS: Although more extensive testing of the questionnaire is required, the IBS Severity questionnaire seems too efficiently and comprehensively measure patient severity of IBS symptoms. The Severity Score appears to be an effective measure of overall severity for subjects with IBS-C or IBS-A.

PO3 CLASSIFYING AND PREDICTING ANTIPSYCHOTIC ADHERENCE AMONG SCHIZOPHRENIA OUTPATIENTS IN EUROPE: A LATENT CLASS ANALYSIS

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OBJECTIVES: Interventions that increase compliance with medication may improve outcomes in schizophrenia, but need to be targeted on groups at high risk for non-adherence behaviours. The aims of this study were 1) to define latent adherence classes, one year after antipsychotic medication change or initiation, and 2) to examine predictors of class membership from clinical and treatment variables recorded one year earlier. METHODS: Latent class analysis was applied to indicators of compliance behaviour twelve months after new antipsychotic medication was initiated or existing medication changed. The sample comprised 1,736 patients with schizophrenia sampled from the seven drug cohorts participating in the Schizophrenia Outpatient Health Outcomes (SOHO) observational study of health outcomes of antipsychotic treatment (n = 10,218). RESULTS: Over three quarters of the SOHO sample were highly compliant with antipsychotic medication. 19% were identified by the model as non-adherent. In addition to treatment cohort, drug abuse (adj OR = 1.69, 95% CI 1.07–2.65), alcohol abuse (adj OR = 1.61, 95% CI 1.03–2.53) or hospital admission (adj OR = 1.97 95% CI 1.43–2.71) prior to study entry predicted non-adherence class membership one year later. CONCLUSIONS: Latent classification analyses identified a patient group at risk for poor medication compliance that could be targeted with interventions to increase adherence behaviours. Further refinements of this classification may identify a continuum of compliance behaviours.

PO4 ESTIMATING QUALITY-ADJUSTED TIME WITHOUT SYMPTOMS OR TOXICITY USING A MULTIVARIATE FAILURE TIME REGRESSION MODEL

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OBJECTIVE: The Q-TWiST (Quality-Adjusted Time Without Symptoms or Toxicity) method compares treatments for time spent in clinically different health states that vary by patient utility (toxicity, symptom-free period and disease relapse). Kaplan-Meier or Cox model-based estimators of transition times between states are generated separately to account for censoring and loss to follow-up. Q-TWiST is then calculated as a weighted sum of mean health state durations and its variance is calculated using the bootstrap method. The methodology is well-accepted in oncology research, but has been used infrequently in other therapeutic areas. Application is restricted to time-sensitive outcomes and to well-controlled clinical trials. METHODS: We present a new approach to calculate Q-TWiST and its variance using a repeated measures framework in a multivariate failure time regression model (Wei, Lin, Weissfeld, 1989). First, a single likelihood function that incorporates multiple events is derived and event-specific parameters are then estimated simultaneously by maximizing the likelihood function. Once the parameter estimates are obtained, the robust variance-covariance matrix is easily computed, incorporating within-patient correlations of event times. The utility-weighted Q-TWiST and its variance are derived by the delta method utilizing the estimated parameters.
and the variance-covariance matrix from the model. RESULTS: The advantages of this new approach over the traditional methods are two-fold: 1) The variance of Q-TWiST can be estimated directly, and 2) It is possible to restrict or to compare parameters across different health states. CONCLUSION: Q-TWiST represents a unique quantitative method to simultaneously evaluate the risks and benefits of treatment on successive health states. We present a single survival model that addresses data censoring, covariate adjustment and variance estimation. This new approach provides opportunities for expanded use of the Q-TWiST method beyond the clinical trial such that application to observational studies is possible.

Health Related Quality of Life Based Patient Reported Outcomes: Session I

**QL1**

**DETERMINING THE MINIMALLY IMPORTANT DIFFERENCE OF THE OVERACTIVE BLADDER QUESTIONNAIRE (OAB-Q)**

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OBJECTIVE: The Overactive Bladder Questionnaire (OAB-q) assesses symptom bother and health-related quality of life (HRQL) among patients with overactive bladder (OAB) and has been shown to be robust, valid, and responsive. The purpose of this analysis was to establish the instrument’s minimally important difference (MID), which is the smallest difference in score that patients perceive as beneficial. METHODS: Data were from four clinical trials (1 US, 3 international), totaling 3426 patients. All trials involved 12 weeks of tolerodine treatment. Distribution-based (eg, effect size, standard error of measurement (SEM), and half-standard deviation) and anchor-based approaches were used. RESULTS: The mean age of the 4 trial samples ranged from 58.7 to 61.3 years. Patients were predominantly female (65.0%) and Caucasian (87.8%). At baseline, half-standard deviation of the OAB-q Symptom Bother subscale ranged from 9.4 to 9.9, and SEM ranged from 7.0 to 7.28. Half-standard deviation of the HRQL subscales (Coping, Concern, Sleep, and Social Interaction) ranged from 9.8 to 13.6, with SEM ranging from 6.8 to 8.3. The OAB-q subscales had moderate to large effect sizes in all trials, with Symptom Bother having the largest effect sizes (range = −0.61 to −1.23). Anchor-based analyses found significantly greater OAB-q change scores were associated with greater patient perceived treatment benefit and satisfaction. The difference between change scores of patients perceiving “no benefit” and “little benefit” ranged from 6.9 to 16.8 for all scales except Social Interaction (4.3 to 7.8), with the majority of differences greater than 10 points (possible subscale scores range from 0 to 100). Greater OAB-q change scores were associated with greater improvements in micturition diary variables. CONCLUSIONS: Multiple methodologies provide strong justification for recommendation of a 10-point MID for all OAB-q subscales. This MID may be conservative for some subscales, however a uniform MID is recommended to facilitate instrument use and interpretation.

**QL2**

**TESTING THE CROSS-WALK: SALVAGING CANCER SPECIFIC MEASURES FOR USE IN ECONOMIC EVALUATION**

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OBJECTIVES: Clinical trials often include condition-specific measures that lack the attributes required for economic evaluation. This study reports on the investigation of models for estimating EQ-5Dindex (a generic, utility-weighted index of health status) from FACT-G and QLQ-C30 (two widely used cancer-specific measures.) METHODS: As part of an observational study in colorectal cancer FACT-G, QLQ-C30 and EQ-5D were administered to 223 patients in an NHS hospital one week after discharge following surgery. Alternative models for estimating EQ-5Dindex from the items of both cancer-specific questionnaires were evaluated. Items were treated as both continuous data or were dichotomised. These were entered as independent variables in a series of stepwise linear regression analyses with EQ-5Dindex as the dependent variable. Criteria for comparing model performance were pre-specified and included explained variance (r²), Pearson correlation co-efficient (r) and mean absolute difference. RESULTS: More than 55% of the variance was explained by the model which employed continuous items and the estimated EQ-5Dindex correlated well with actual scores (r > 0.65). Items from FACT-G and QLQ-C30 performed equally well in this model. Less variance was explained by the model using dichotomised items (r² > 0.40) and the correlation between estimated and actual EQ-5Dindex was less pronounced (r > 0.45). Items from QLQ-C30 performed better than those from FACT-G in this model, but altering the cut-point to dichotomise the items had an appreciable effect on explained variance. Despite moderate to good correlation between actual and estimated EQ-5Dindex in both models, the mean absolute difference between these scores gave some cause for concern. CONCLUSIONS: Despite differences in item content, both QLQ-C30 and FACT-G generate viable estimates of EQ-5D. This is an important finding that allows for the conversion of data from studies where direct comparison is otherwise impossible. However, the technique requires further refinement so as to improve its performance.

**QL3**

"FAMILIDAL STUDY": ANALYSIS OF THE DIFFERENCES BETWEEN DIALYSIS PATIENTS AND THEIR CAREGIVERS (FAMILY CARERS, NURSES AND DOCTORS) ON DIALYSIS PATIENTS’ HRQOL AND OF THE FAMILY CAREGIVERS’ HRQOL AND BURDEN

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OBJECTIVE: To assess the agreement between patients and careers (Familiar-FAM, Nurse-NUR and Physician-PH) on patients’ HRQoL and to evaluate HRQoL and burden of FAM. METHODS: 221 patient-carrier pairs stratified by age and gender were randomly selected from 14 dialysis units: 132 hemodialysis–69 peritoneal dialysis. Patients’ HRQoL was evaluated by patient and FAM, NUR and PH using EQ-5D (dimensions and Visual Analogue Scale-VAS). Patients and FAM answered the SF-36 (PCS-MCS) and Duke-UNK Functional Social Support (FSS). FAM also answered Caregiver Burden Interview of Zarit (ZS); PH, the co-morbidity Index of patients; and NUR, patient’s dependence in daily activities using the EQ-5Dindex in both models, the mean absolute difference between these scores gave some cause for concern. CONCLUSIONS: Despite differences in item content, both QLQ-C30 and FACT-G generate viable estimates of EQ-5D. This is an important finding that allows for the conversion of data from studies where direct comparison is otherwise impossible. However, the technique requires further refinement so as to improve its performance.