IDENTIFICATION OF DISEASES FOR EQ-5D BOLT-ON ITEM DEVELOPMENT: AN EMPIRICAL APPROACH
Solem CT1, Gu NY1, Pickard AS2
1Pharmrین North America, LLC, Bethesda, MD, USA, 2University of Illinois at Chicago, Chicago, IL, USA

OBJECTIVES: A perceived limitation of generic utility measures is lack of ability to capture change relevant to disease-specific areas or interventions. To test whether core EQ-5D items sufficiently measure variability in patients’ self-reported quality of life, we aimed to investigate whether the presence of a series of diseases could explain residual variability in EQ-5D visual analog scale (VAS) scores, beyond what is captured by EQ-5D items. METHODS: We utilized generalized linear models (GLM) with a gamma distribution and log link to predict VAS by the 5 EQ-5D items and the presence of 10 conditions (cancer, depression, glaucoma, heart disease, stroke, asthma, COPD/other respiratory, depression, anxiety disorder, osteoarthritis), controlling for age, gender, race/ethnicity and number of chronic conditions (i.e., as a proxy for comorbidities) using the 2000–2003 Medical Expenditure Panel Survey (MEPS) data. Coefficients for disease that were statistically significant (p-value < 0.05) and showed minimally important difference (MD: coefficient ≥0.03) served as criteria to support further investigation of condition-specific “bolt-on” items that extend the content of EQ-5D. RESULTS: Of 24,830 respondents, 45.7% were male, 77.2% were white non-Hispanic and had a mean age of 45.9 years (SD 17.1). Overall mean EQ-VAS was 79.7% at first measurement. Diabetes, stroke and depression significantly predicted VAS scores alongside the EQ-5D items and demographic characteristics (p-values<0.001) and met criteria. When concurrently controlling for all other conditions (i.e., as a proxy for co-morbidities) using the 2000–2003 Medical Expenditure Panel Survey (MEPS) data, controlling for age, gender, race/ethnicity and number of chronic conditions (i.e., as a proxy for comorbidities) using the 2000–2003 Medical Expenditure Panel Survey (MEPS) data. CONCLUSIONS: Findings suggest respondents with diabetes, stroke, and depression, potentially with cancer, CHD and COPD, had significant heterogeneity in their VAS valuation of their own health that was not explained alone by EQ-5D items or demographics. This study provides one approach to identifying potential chronic conditions where disease-specific “bolt-on” items may be considered for EQ-5D.

IMPROVING THE MEASUREMENT OF QUALITY OF LIFE BASED ON FUZZY SCALE
Chen PY1, Yao G2
1National Taiwan University, Taipei, Taiwan, 2National Taiwan University (Dept of Psychology), Taipei, Taiwan

OBJECTIVES: In past two decades, researchers have proposed to combine fuzzy theory into measurement in various areas. According to their studies, combining fuzzy theory could reduce the properties differences between measurement methods and human cognition, and the results collected by fuzzy scale were also explained residual variability in EQ-5D visual analog scale (VAS) scores, beyond what is captured by EQ-5D items. METHODS: We utilized generalized linear models (GLM) with a gamma distribution and log link to predict VAS by the 5 EQ-5D items and the presence of 10 conditions (cancer, depression, glaucoma, heart disease, stroke, asthma, COPD/other respiratory, depression, anxiety disorder, osteoarthritis), controlling for age, gender, race/ethnicity and number of chronic conditions (i.e., as a proxy for comorbidities) using the 2000–2003 Medical Expenditure Panel Survey (MEPS) data. Coefficients for disease that were statistically significant (p-value < 0.05) and showed minimally important difference (MD: coefficient ≥0.03) served as criteria to support further investigation of condition-specific “bolt-on” items that extend the content of EQ-5D. RESULTS: Of 24,830 respondents, 45.7% were male, 77.2% were white non-Hispanic and had a mean age of 45.9 years (SD 17.1). Overall mean EQ-VAS was 79.7% at first measurement. Diabetes, stroke and depression significantly predicted VAS scores alongside the EQ-5D items and demographic characteristics (p-values<0.001) and met criteria. When concurrently controlling for all other conditions (i.e., as a proxy for co-morbidities) using the 2000–2003 Medical Expenditure Panel Survey (MEPS) data, controlling for age, gender, race/ethnicity and number of chronic conditions (i.e., as a proxy for comorbidities) using the 2000–2003 Medical Expenditure Panel Survey (MEPS) data. CONCLUSIONS: Findings suggest respondents with diabetes, stroke, and depression, potentially with cancer, CHD and COPD, had significant heterogeneity in their VAS valuation of their own health that was not explained alone by EQ-5D items or demographics. This study provides one approach to identifying potential chronic conditions where disease-specific “bolt-on” items may be considered for EQ-5D.

DIRECT FROM THE PATIENTS – RESEARCH INTO WHAT PATIENTS WOULD LIKE TO IMPROVE IN THEIR ELECTRONIC DIARY EXPERIENCE
O’Gorman H1, Ross J2
1University of Strathclyde, Glasgow, UK, 2Almar Clinical Technologies, Souderton, PA, USA

OBJECTIVES: To illustrate patient needs and preferences for patient diaries in support of clinical trials and to identify what can be done to improve the electronic patient diary experience based on the patients’ recommendations. METHODS: Three hundred seventy two patients (45% female and 55% male) completed a 10-minute internet survey, fielded in December 2010. The age range of the patients was 19-77 years. This internet survey focused on patients’ perceived benefits and experience with current patient diaries and asked where improvements could be made. RESULTS: From the survey positive experiences reported by patients were ease of use (66%) and simple questions (60%). 48% found no unfavorable aspects in the diary keeping but 38% said that diary entries were too frequent. Patients were asked about the use of reminders and 80% stated that they would like to receive reminders via email and 55% via SMS text. With regard to the patient suggested improvements, 59% stated multiple options and more flexibility in keeping the diary would improve their experience and 58% said to shorten the time needed to make a diary entry. Further results will be presented. CONCLUSIONS: Simplicity came out as a key factor in patients’ use of electronic diaries and should be first improved when designing the diary. Patients would like to feel involved in the trial and the use of reminders when they need to complete an action was a patient preference. These factors should be considered when designing an ePRO system to be used in a clinical trial.

THE FIRST RESEARCH: ASSESSMENT OF THE WTP THRESHOLD FOR QALY BY CONGIDENT VALUATION METHOD IN RUSSIA
Zelenova O
Federal Research Institute for Health Care Organization and Information of the Ministry of Health and Social Development of Rus, Moscow, Russia

OBJECTIVES: To assess the WTP threshold for QALY in Russia. METHODS: We have held the opinion poll to define WTP for QALY of the 980 respondents. Questionnaire consists of demographic part: gender, age, education, hospitalization (within the last 5 years), hospitalization of any member of household (within the last 5 years) and occupation. The special part is a detailed categories of WTP. RESULTS: The results indicated that WTP was higher than estimated by the population sample. In Belgium the EQ-5D was mapped previously to the Visual Analog Score (VAS), hence patients in our study were also asked to indicate their actual perception of HR-QOL on a VAS only. EQ-SD profiles which were scored at least 10 times by different patients were considered for further evaluation. All profiles were mapped into VAS by multivariate regression. RESULTS: A total of 1348 questionnaires were distributed, of which 768 (57%) were completed. Male/female ratio was 41%/59%, with a mean age of 53.6. Right at the bottom of the profiles were females, at least 10 times, with a mean VAS of 0.64 (95% CI 0.63-0.66). The complete set of utilities obtained by multivariate regression was significantly different compared to the valuation by the Belgian population sample (p<0.0001). Especially in the profiles in which the patient indicates complete deficiencies in HR-QOL, value was increased by a higher number of patients as compared to the general population. CONCLUSIONS: Chronically ill patients perceive their HR-QOL, higher than estimated by the population sample. In order to evaluate health programs consequences of these findings should be considered.
obtained the similar results. CONCLUSIONS: The WTP for QALY in Russia is 63,000 rubles or $2,300 that is much lower than in other countries but WTP/VAI ratio is nearly the same as in the UK. There are WTP/VAI = WTPfam = WTPInc. Russia just like in Australia, the UK and the US.

PRM45 IMPORTANCE OF COLLABORATION WITH DEVELOPERS IN THE CLARIFICATION OF CONCEPTS: A CASE STUDY WITH THE UNIVERSITY OF CALIFORNIA, SAN DIEGO (UCSD) SOQ FOR BREATH QUESTIONNAIRE (SOBQ)

Ries AL,1 Kaschinski D,2 Montigny C

1University of California, San Diego, CA, USA, 2Boehringer Ingelheim GmbH, Ingelheim am Rhein, Germany, 3INRS Institute, Lyon, France

OBJECTIVES: The UCSD SOBQ, a 24-item instrument developed in US English, assesses self-reported shortness of breath while performing a variety of daily living activities. The objective of this report is to underline the importance of collaboration with the developers to clarify concepts and ensure their correct interpretation while maintaining the item independence in different languages. Methods: The execution of interactive interviews with the developers of the SOBQ was undertaken to formalize a concept list that would: 1) Explain and clarify the conceptual notions underlying each item in simple language so they would be accurately reflected in each language version produced, and 2) Provide acceptable approved translation alternatives. RESULTS: The concept list was revised five times and widely expanded with definitions and alternate translations validated by the developers. Through questions raised during the linguistic validation process, collaboration with the developers highlighted items initially considered as unambiguous but which required additional information to be faithfully rendered in all languages. Among the 24 items of the SOBQ, four items proved to be unclear (e.g., “dressing” was clarified as “putting on and taking off clothes” and “picking up and straightening” as “picking things up and tidying them up”). Three other items appeared as culturally inappropriate and, therefore, needed to be adapted to be suitable to the countries for which these activities were not relevant (e.g., “washing car or any other vehicle” was one of the accepted alternatives for “washing car” and “watering flowers” for “watering the lawn”). CONCLUSIONS: It is essential to involve the developers in the clarification of the concept list during each item. Collaboration is required to allow their correct interpretation in other languages and cultures. This step is crucial to ensure comparable content validity between different language versions. This example with the SOBQ shows that the involvement of developers is a dynamic and necessary process.

PRM46 LINGUISTIC VALIDATION AND EPRO – VALUE OF COLLABORATION

Zarzar KM1,2,3,4 Daveno K

1TransPerfect, Durham, NC, USA, 2TransPerfect, Atlanta, GA, USA

OBJECTIVES: As the use of clinical outcomes assessments in global studies continues to rise, and the diversity of methods of administration proliferate, collaboration between EPRO and linguistic validation providers becomes critical to the success of global initiatives. This cooperation enables the incorporation of the electronic mode of administration into the cognitive interviewing stage of linguistic validation, allowing respondents to view the context in context. Collaboration between EPRO and linguistic validation providers also yields time and cost efficiencies to the sponsor. METHODS: A review of prior collaboration with four ePRO providers was conducted to provide insight into key areas for efficiency prior to initiation of a large-scale linguistic validation project involving EPRO. Prior to project initiation, a detailed kick-off meeting was held. The meeting included a review of the most relevant ePRO file formats, processes and milestones were developed with input from the linguistic validation provider, the ePRO provider, and the sponsor to ensure deadlines were met. RESULTS: Reviews of prior projects revealed early collaboration was common. A requirement for the development of the ePRO platform often initiates on different timelines than linguistic validation process. Common reasons include differing contracting timelines from the sponsor for each service, and addition of countries or languages after ePRO contract execution. By building a collaborative project workflow ahead of project initiation, the EPRO and linguistic validation partners can identify cost and timeline efficiencies in 1) the source content, 2) uploading the translated language directly into ePRO platforms, 3) use of EPRO mode in cognitive interviews, 4) post-localization testing of fonts and characters, and 5) proofreading of the final screenshots. CONCLUSIONS: Timeline restrictions resulting from study deadlines and contracting processes can limit the benefit to be achieved by collaboration between EPRO and linguistic validation partners. Early planning, and contracting of each provider with the expectation of collaboration will enable cost and timeline efficiencies, and process improvements.

PRM47 REVIEW OF CLINICIAN AND OBSERVER REPORTED OUTCOMES MEASURES

Zarzar KM

TransPerfect, Durham, NC, USA

OBJECTIVES: Since the publication of the FDA PRO Guidance in 2009, focus has largely been dedicated to patient-reported outcomes measures. Other commonly used clinical outcomes assessments including clinician-reported outcomes (Clin-RO) and observer-reported outcomes (Obs-RO) warrant attention, as the expectation is that clinical trial outcomes assessments will be expected to follow the properties of the PRO guidelines. It can be inferred that the same expectations for translation and cultural adaptation of these measures will also apply, and discussion surrounding translation methodologies for these outcomes measures is necessary. METHODS: A review of Clin-RO and Obs-RO measure translation methodologies was conducted. Linguistic feedback resulting from each stage was reviewed for relevance and impact on language changes. RESULTS: Past translation methodologies involved concept definition, dual forward translation, reconciliation of forward translations, back translation, resolution of back translation and forward translation, and clinician or expert review for all clinical outcomes assessments. An additional stage specific to observer-reported outcomes assessments included cognitive interviewing with the relevant respondent population, such as caregivers, parents, etc. Clin-RO measures involve review by native-speaking clinicians in the relevant area of interest. Cognitive interviews with clinicians were not found to be a common practice. CONCLUSIONS: The results of this review and feedback analysis suggest observer-reported outcomes measures are best suited to follow the same methodology as PRO measures, with the cognitive interviews conducted with the relevant observer population. Clinician-reported outcomes measures should also follow the same guidelines as PRO measures for translation, loss, and interpretation. Further research into the methodology for execution of the review stage is required to assess if clinician reviews, focus groups with clinicians, cognitive interviews with clinicians, or an alternative will yield the best results for this particular clinical outcomes assessment.

Research On Methods – Statistical Methods

PRM48 A MODEL FOR PATIENTS ACCRUAL IN MULTI-SITE OBSERVATIONAL STUDIES: A SURVIVAL ANALYSIS APPROACH

Longagnani C1, Bagnardi V2, Zanolli L1, Simon L1

1Medical aT Medena, Italy, 2University of Milano-Bicocca, Milano, Italy

OBJECTIVES: The allocation of sufficient time for participant recruitment is one of the fundamental aspects in planning a clinical trial (Carter, 2004): the study of patient accrual is of great interest not only in clinical trials but also in observational studies. In this work we developed a time-to-event (i.e. survival) model aimed to explain the course of patients, according to site and study characteristics. METHODS: Seventeen observational, retrospective studies (106,123 patients) managed by Medidata from 2002 to 2009 were included in the analysis. Time to patient enrolment was calculated as the percentage of time elapsed from the first-patient-in to the enrolment of the patient out of the study planned duration. Individuals enrolled after this period were considered as censored. Site and study characteristics were included in a Cox Proportional Hazard regression model. Hazard Ratios were estimated. RESULTS: The course of patients was significantly associated with year of the study (2008 vs. <2008: Hazard Ratio 2.37), number of planned sites (≤25 vs. >25: 0.63), study design (cross- sectional vs. longitudinal: 0.71), site initiation visit (yes vs. no: 0.38), electronic vs. paper data capture (2.87), start-up and investigator meeting execution (yes vs. no: 2.27 and 0.45 respectively), single patient fee vs. other (1.78), top-enrol list communication (yes vs. no: 0.71), competitive enrolment (yes vs. no: 0.47), site initiation visit (yes vs. no: 0.38), protocol amendment with possible effects on enrolment (yes vs. no: 4.21), type of site (academic private hospital/ university/private outpatient clinic vs community hospital: 0.86) and median monthly number of phone calls/site (1.15). CONCLUSIONS: In our analysis, the most interesting factors influencing patient accrual in the setting of observational studies managed by an Italian CRO appeared to be the number of planned sites, cross- sectional study design, electronic data capture, start-up and investigator meeting execution, top-enrol list communication, and competitive enrolment. Further analyses are ongoing as regards a predictive model.

PRM49 EVALUATION OF BIVARIATE META-ANALYSIS METHODS TO SYNTHESISE RESULTS OF SEVERAL STUDIES WITH TWO CORRELATED ENDPOINTS

Abillea SB1, Vataire AL2, Neize ME3, Le coroller G4, Tombi M5

1CREATIV-CEUTICAL, Paris, France, 2CReatiV-Ceutical, Paris, France, 3University Claude Bernard Lyon1, Lyon, France

OBJECTIVES: Clinical studies generally include several endpoints to compare the effects of alternative interventions. Meta-analyses are usually performed on different endpoints separately. We investigated advantages of bivariate meta-analysis models, accounting for the correlation between endpoints, compared to univariate meta-analyses. METHODS: Alternative meta-analysis approaches were applied and compared using simulated datasets of logarithms of odds ratios (OR) for two endpoints. Several datasets of 20 studies were simulated, with different correlations between endpoints, and with or without missing values. Simulations were based on a bivariate normal distribution with mean log ORs of -0.5, corresponding to ORs of 0.61, and variances of 0.25 for both endpoints. The models used were: 1) random-effects univariate models for each endpoint separately; 2) two-stage approach using univariate model for studies with one endpoint and bivariate model for studies with two endpoints; and 3) bivariate model with prior imputation of the variance of second endpoint for studies with one endpoint only, based on the correlation between variances for the two endpoints. All the models were estimated in a Bayesian framework, using WinBugs. RESULTS: Results of different models were fairly similar in absence of missing data. In a situation with one endpoint missing at random for 10 studies, and a correlation of 0.8, the bias around estimated OR for that endpoint was 0.12, 0.03, and 0.04 with models 1, 2 and 3 respectively, when an informative prior was used for the correlation. The bias was not reduced with uninformative prior. Variance estimates also differed between models, and were very large with model 2 for some simulations. CONCLUSIONS: Bivariate meta-analysis can improve treatment effect estimates when information is collected for two correlated endpoints, especially for an endpoint which is not