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/AAI ratio is nearly the same as in the UK. There are WTPml=WTPhl=WTP1ml=WTP2ml in 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) SOBQ OF BREATH QUESTIONNAIRE (SOBQ)

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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 adapting the SOBQ into different languages. Methods: In-depth discussions 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 concepts and in validating each item in a questionnaire 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

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OBJECTIVES: As the use of clinical outcomes assessments in global studies continues to rise, and the number of modes of software administration proliferate, collaboration between ePRO and linguistic validation providers become 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 content 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 workflow was outlined, a review of relevant ePRO file formats was conducted, and 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 critical to defining each item in a questionnaire to allow their correct interpretation in other languages and cultures. 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 content 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 TRANSLATION METHODOLOGIES

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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 clin RO clinician assessments will be expected to follow the proprieties 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 past 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, as long as 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

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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: A total of 1514 observational retrospective and prospective (129, 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 planed duration. Individuals enrolled after this period were considered as censored. Site and study characteristics were included in a Cox Proportional Hazard 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: 0.27), number of paper vs. paperless sites (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-entroller site 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 out-patient 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-entroller site communication and competitive enrolment. Further analyses are ongoing as regards a predictive model.

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

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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: We compared different meta-analysis approaches and 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