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 in the UK. There are WTPs: WTPsel = WTPfam = WTPprot 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) SHORTNESS OF BREATH QUESTIONNAIRE (SOBQ) Ries AL1, Kaschinski D2, Montigny C3

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 translating the SOBQ into other languages and cultures. The discussion 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., “washing car or any other vehicle” was one of the accepted items proved to be unclear (e.g., “dressing” was clarified as “putting on and taking off clothes” while translating the original version into other languages. Three other items appeared as culturally inappropriate and, therefore, needed to be adapted to be suitable for 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 during the cognitive interviewing step, and in shaping 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 Zarar KM1, Dowmany K2

OBJECTIVES: As the use of clinical outcomes assessments in global studies continues to rise, and the variety of modes 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 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, item-by-item analysis was conducted, a review of past 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 commonly achieved by developing each item in a questionnaire to allow their correct interpretation in various 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.

PRM47

REVIEW OF CLINICIAN AND OBSERVER REPORTED OUTCOMES MEASURES TRANSLATION METHODOLOGIES Zarar KM

TRANSLATION METHODS

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 expectations in both clinician-level 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 past Clin-RO and Obs-RO measure translation methodologies was conducted. Linguisitc 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. Lack of 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, Zanoli L1, Simoni L1

OBJECTIVES: The allocation of patients in 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: We used the Cox Proportional Hazard model (Cox PH model) to estimate effects of several variables on survival processes. The survival model was estimated using the 913 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 planned duration. Individuals enrolled after this period were considered as censored. Site and study characteristics were included in the model in a Cox Proportional Hazard regression model. Hazard Ratios were estimated. RESULTS: The course of patients was significantly associated with the 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: 0.58), type of site (academic private hospital/ university/private outpatient clinic vs clinical hospital: 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, post- enrolment site communication and competing 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 Abillea S1, Vataire AL2, Neine ME3, Le croqo GF, Toumi M4

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
three groups were identified: High-SES (n=398), Medium-SES (n=889), Low-SES (n=567). Key patterns are: High-SES: mean 35.9 years-old, 90% of working age, most married, technical or university level, only 2.7% with ethnic background. Medium-SES: mean 33 years-old, >60% technical education, mixed cluster. Low-SES: mean 25 years-old, >60% women, 8% ethnic background, up to high-school only, 2 poorest income quintiles. CONCLUSIONS: Immigrants in Chile are a very heterogeneous group. Hierarchical clustering does not provide an appropriate method to group immigrants according to their socio-economic characteristics and, consequently, to provide clear patterns of SES vulnerability within the total immigrant population. Immigrants living in the Low-SES cluster are a vulnerable group that needs further attention in Chile.

OBJECTIVES:

Comparing multiple propensity score adjustment and traditional regression analysis to assess the exposure-outcome association using retrospective claims data

METHODS: Researchers have suggested that, propensity score (PS) adjustment provides similar results as traditional regression analysis in observational studies. This has been attributed to the inappropriate implementation of PS, like inclusion of both PS and baseline covariates, and absence of covariate balance verification after PS adjustment. The present study employed a multiple PS adjustment model to evaluate the risk of falls/fractures in older adults using atypical antipsychotics, performed a balance check of covariates after PS adjustment and compared the results to the traditional regression analysis.

RESULTS: Differences between cluster and IPR designs found that under sampling in IPR formulas vary from 5-15% and are largest when effect sizes are smallest. The IPR samples were smaller than cluster samples for the same effect size and power. Sample size using the cluster formula was smallest when ICC was small (0.15), at 80 percent power and cluster size of 5 patients per group. Cluster sample size was largest when ICC was large (0.25). The percent power and cluster size of 20. CONCLUSIONS: In the research environment where prospective observational methods are used to gather “real world” data, studies that are conducted using cluster sampling, but powered with IPR formulas, are underpowered by as much as 15%. Ethical implications of this should be considered in prospective studies. The study is underpowered. If the prospective study involves risk the equipoise argument may be violated and place patients at risk (assuming there is a study treatment regimen), as the study may not be conclusive because of low power.

METHODS: Data were collected from routine medical visits in primary care settings over a period of 12 months. Adverse events were assessed using a standardized questionnaire. The study population included patients aged 18 years or older with a diagnosis of non-insulin-dependent diabetes mellitus (NIDDM). The study was conducted in a community health center in a city with a population of approximately 250,000. The study was approved by the institutional review board.

RESULTS: The study found that the PS adjustment model overestimated the risk of falls/fractures. The traditional model included only 7 baseline covariates which were used to calculate the PS. The PS model included the two PS adjustment methods which were used to calculate the PS. The results showed that the PS adjustment method was more conservative, leading to better balanced covariates across treatment groups. This suggests that PS adjustment is more appropriate for reducing confounding bias than traditional regression analysis.