sources may be integrated in order implement prospective observational research studies that answer complex research questions.

RESEARCH ON METHODS – Conceptual Papers

PRM132
WHAT ARE THE ROLES OF HEALTH ECONOMIC MODELS IN PRODUCT DEVELOPMENT?

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OBJECTIVES: Health economic models are widely used for drug evaluation during the post-approval and reimbursement process. However, similar models can also be used to inform objectives, decisions and designs earlier in the drug development process with the idea to optimize the potential future value to payers. This project assesses how an economic heart failure (HF) model can facilitate the decision making process during the early stages of drug development. **METHODS:** A discrete event simulation is developed to track the events associated with disease progression of HF patients over 5 years. Patients are initially categorized into one of three health states based on their HF status: in-hospital, 30 days post-discharge and > 30 days post-discharge. To capture movement in the model, the time to hospital discharge, re-hospitalization and death are generated based on each patient's current health state and the event rates taken from available literature. The model is used to identify baseline levels of risk, a range of potential prices or the required drug efficacy that the drug candidate needs to meet in order to be cost-effective compared to standard care. **RESULTS:** By way of illustration, we considered a patient with baseline mortality risk of 0.1% and a 0.2% readmission rate per day. If treatment costing $1 /day is provided to patients outside of hospital, a mortality reduction of at least 12% is needed to meet a $25,000/QALY threshold. For a higher risk population, the treatment can remain cost-effective at either a higher price or lower clinical efficacy. **CONCLUSIONS:** This study demonstrates that health economic models are useful to determine the acceptable ranges of baseline risk, efficacy, and price to assess the potential value of future drug candidates.

PRM133
USING SURROGATE ENDPOINTS FOR HEATH ECONOMIC ANALYSIS: WHAT IS THE ROLE OF STATISTICAL VALIDATION?

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OBJECTIVES: To explore the appropriate use of surrogates within an economic modeling framework, compared to the statistical approaches of validating surrogates. **METHODS:** We reviewed the statistical literature on validating surrogate endpoints. Published statistical approached to validating surrogate endpoints include those described by Prentice and Buyse. We explore the use of these statistical approaches to validation in the context of health economic models where surrogates are used (a) predict final outcomes, and (b) as endpoints for stopping rules and patient access schemes. **RESULTS:** Given regulatory trials powered on surrogate endpoints, economic modeling often requires the use of surrogate endpoints to estimate the impact of treatment on final health outcomes of interest to reimbursement agencies. This requirement occurs even when there is no statistical validation of the surrogacy relationship, or when the surrogate fails a formal statistical validation. As a consequence we argue that the appropriate focus for economic modeling is on the appropriate propagation of uncertainty in the estimates of the effect of the surrogate on final health outcome and the avoidance of bias due to multiple testing rather than the formal testing of validity. This includes the use of stopping rules that are designed to improve cost-effectiveness estimates for patient access. **CONCLUSIONS:** The approach to surrogacy in reimbursement is necessarily different to that in a regulatory environment. We outline a general estimation approach based on appropriately characterizing uncertainty in the surrogacy relationship rather than the formal statistical testing of surrogate validity as the appropriate focus of reimbursement models.

PRM134
STANDARDIZING CRITERIA FOR COGNITIVE ASSESSMENT OF PAPER-TO-ELECTRONIC EQUIVALENCE OF PROS

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AIMS: Use of electronically administered outcome measures is increasing in clinical trial data collection. The 2009 ISPOR ePRO Task Force Report recommends cognitive assessment as sufficient evidence of equivalence when only minor changes have been made to the measure. No consensus exists, however, for how cognitive assessment results should be evaluated to determine if equivalence has been established. **METHODS:** Existing literature around equivalence assessment for PROs was combined with firsthand experience in conducting over 500 cognitive interviews aimed at assessing paper and electronic equivalence of 55 different PRO instruments. Using these two resources, we developed suggested criteria to cognitively assess equivalence between the two modes, and present a practical process for meeting these criteria. **RESULTS:** The criteria for determining equivalence between paper and ePRO formats should focus primarily on whether or not the ePRO is likely to produce data substantially different if administered via one method versus the other. To determine whether such a risk to ePRO data exists, we propose a three-step process for interpreting cognitive interview responses. 1) Determine whether a patient perceives a cognitive difference between paper PRO and ePRO, and whether that difference represents a variation in the understanding of the item or simply a recognition of different appearance; 2) Determine whether any difference in patient understanding has a meaningful impact on their response to the item, and 3) determine whether or not that difference presents a significant risk to the data that justifies modification of the ePRO. **CONCLUSIONS:** In the years since the ISPOR ePRO Task Force issued their recommendations, data capture technology has continued to develop while clarity on methods to evaluate the cognitive impact of this technology have lagged. The steps we present provide a standardized system for ensuring that ePROs measure what is intended and the risk to research data is minimized.

PRM135
RISKS, IMPACTS, AND MITIGATION OF MISSING EPRO DATA ON CLINICAL TRIALS

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OBJECTIVES: Although missing and incomplete responses in ePROs can be minimized through risk assessment and mitigation plans, missing data can have varying implications on clinical trials. This conceptual paper assesses the impact of missing ePRO data to the trial, taking into account the phase of the trial and intended use of the data. **METHODS:** Common uses for data gathered via ePRO instruments and diaries are reviewed. An assessment of the impact of different levels of missing data and associated risks with analyzing data is also performed. **RESULTS:** Data gathered via ePRO are frequently used to support primary/secondary trial endpoints. They are also commonly used for exploratory purposes, allowing sponsors to gather preliminary information to guide the planning of future trials. Types of data collected may include study medication usage for study drug reconciliation reasons, symptom presence or severity to determine eligibility for trial participation, and responses over time to indicate improvement or worsening of the symptom/disease. Each data use is assessed for risks to the analyzability of the data associated with different levels of missing data. For example, in projects with ePRO responses used to support primary/secondary endpoints overall project risk is low when compliance rates are high (e.g. 90-100%). As compliance rates drop to <80%, bias introduced in the results increases, quality of the data decreases, and risks that the data may not be able to be used in the analysis rises. Impacts could include a need to recruit additional patients or that the trial may need to be re-run. **CONCLUSIONS:** Impacts of missing data on clinical trial analysis vary depending on the intended use of the data. It is important to understand the impact of missing data to the project so that an appropriate plan can be decided upon and included in the protocol.

PRM136
METHODOLOGICAL AND OPERATIONAL CONSIDERATIONS IN CONDUCTING RETROSPECTIVE MEDICAL CHART REVIEW STUDIES IN HOSPITALS AND MEDICAL CENTERS IN EMERGING MARKETS

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OBJECTIVES: Retrospective medical chart reviews are an increasingly valuable source of data for clinical, treatment patterns, and outcomes research, particularly in emerging markets where availability of databases for secondary analysis is limited. This abstract aims to describe methodological and operational considerations that sponsors and researchers should be aware of prior to and during the undertaking of chart review studies in these markets. **METHODS:** Key considerations for executing chart review studies in hospitals and major medical centers from study conception through the completion and quality review of data collection were identified and summarized. **RESULTS:** After identification of research objectives and target countries/markets for research, thoughtful consideration of site selection (single or multi-site/country, local investigator interest and availability), data availability (nature, comprehensiveness, and quality of existing medical records), and patient selection (sampling design, specificity of inclusion/exclusion criteria) form the basis for implementing a successful chart review. Study design steps may be taken to optimize performance, for example: careful consideration of how inclusion/exclusion criteria will impact patient recruitment given the rarity of the study condition (data on this may be limited); assessing feasibility of data collection instrument completion via piloting and prior local experience; standardization of terms and definitions to ensure cross-site comparability. Additional operational considerations include meeting varied requirements for obtaining national/state and local ethics approval in multi-country studies, use of electronic data capture given variation in information technology infrastructure across study sites, and impact of workday/cultural traditions on recruitment/ timelines. **CONCLUSIONS:** To maximize the opportunity for successful medical chart review studies in emerging markets, review and assessment of operational feasibilities in the target research areas, appropriate tailoring of study objectives, engagement of local investigators and site staff, and continuous oversight of data collection and quality control processes are essential.

PRM138
A FRAMEWORK FOR ANALYSING TREATMENT SEQUENCES: INCORPORATING TIME DEPENDENT TRANSITIONS THROUGH PARTITIONED SURVIVAL ANALYSIS

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It is often the case that cost-effectiveness models need to consider the sequence of treatments in a treatment algorithm. Since traditional state transition Markov models have an inherent memoryless property, time dependency in time to event analysis cannot be incorporated in this modelling framework. This has been used as a rationale for moving to individual level simulation models to handle treatment sequences. However, individual simulation models increase the computational burden of a model, particularly when it comes to undertaking real-time probabilistic sensitivity analysis to characterize uncertainty. Therefore, adifferent approach to modeling treatment sequencing should be examined. In this paper, we discuss a novel approach to analyzing sequencing models that allow time dependency in the time to event analysis within a cohort model framework,thus avoiding the disadvantages of resorting to individual simulation. Typically parametric survival models can be used to characterize time to event. This may be time to overall survival or time to progression in cancer modelling, or time to treatment failure / treatment switching in oncology. We illustrate the approach using parametricWeibull models, although in principle any parametric survival model could be used. We show how