the framework is flexible enough to capture treatment effects that vary by line of therapy. We demonstrate how appropriate differentiation of treatment effects by line of therapy can still be made. We believe that the framework illustrated in this paper has wide applicability to sequencing models in many disease areas, most notably oncology and rheumatology where such sequencing models are common. We demonstrate the potential of the framework in the critical time dependent model incorporated at any sequence of the model without having to resort to individual patient simulation.

PRM139 A COMPREHENSIVE ECONOMIC AND PRICING MODELING FRAMEWORK FOR UNDERSTANDING ORPHAN DRUG DEVELOPMENT

Mallon P.T., Rizzo J.A., Irish W., Giese C.1
1S2 Statistical Solutions, Cincinnati, OH, USA, 2Stony Brook University, Port Jefferson, NY, USA, 3CTI Clinical Trial and Consulting Services, Raleigh, NC, USA, 4CTI Clinical Trial and Consulting Services, Cincinnati, OH, USA

Rare diseases provide a perplexing problem for reimbursement agencies. Orphan drug development is often incentivized by government entities. Despite these incentives, reimbursement at a viable level is not assured, and recent efforts by researchers highlight the reimbursement paradigm substantially. Value-based pricing agreements, which link the price of the drug to the value achieved, is one such effort. However, demonstrating value for an orphan drug remains challenging. To better understand the potential value and therefore pricing of orphan drugs, we developed a comprehensive model to evaluate the pricing, economics, reimbursement, and market strategy (FREMS) specifically for these drugs. The interactive simulation model was developed to combine evidence on development, commercialization, reimbursement pathways, improvements in quality of life, and market share. The FREMS model was designed to evolve alongside the drug development process, incorporating new parameters and data as they become available. Extensive sensitivity analyses are performed to highlight the substantial uncertainty in disease prevalence and costs of the diseases. An interactive interface is developed for users to examine how changes in model input values affect outcomes. In this presentation, we will describe the primary elements of the FREMS model, demonstrate how the results may vary across subpopulations and illustrate the potential value of new drugs. Concepts will be illustrated through the use of real-world examples such as graft-versus-host disease (GVHD); a major burden on patients due to adverse events associated with hematopoietic stem cell transplantation (HSCT). This will highlight the importance of differential uncertainty associated with each treatment option. We will present an example where the model is used to compare two proposed treatment strategies. The limitations of conducting a meta-analysis with a small number of trials should be understood regardless of the methodology used. In the special case of a star network with only one trial per treatment comparison, the differences between methods depend on effect sizes and sample sizes. If placebo effects were similar, the frequentist random-effects model was not able to estimate a random study effect and it was reduced to a fixed-effect model (similar to the AIC). CONCLUSIONS: The limitations of conducting a meta-analysis with a small number of trials should be understood regardless of the methodology used. In the special case of a star network with only one trial per treatment comparison, the differences between methods depend on the underlying evidence. The implications for interpretation will be discussed.

PRM141 MODELING ALL-CAUSE MORTALITY IN HEALTH ECONOMICS MODELS

Hernández J., Altimatá A, Pelligra C
Eli Lilly and Company, Indianapolis, IN, USA

The estimation of life-years is an important component of many health economic models and this outcome is often required by health technology assessment agencies. For instance, in the evaluation of health care technologies, life-years are often estimated by adjusting the country-, age-, and gender-specific all-cause mortality, which considers all deaths in a population regardless of the cause, to account for additional deaths due to a specific disease (i.e., the disease-specific mortality). Proper modeling of all-cause mortality and knowing the uncertainty associated with the estimates (if estimated) is therefore an important step in building a health economic model. The report of the International Society for Pharmacoconomics and Outcomes Research (ISPOR) Modeling Good Research Practices Task Force recommends modeling all-cause mortality non-parametrically based on life table data. This method uses the life table data directly to derive an empiric distribution of health utilities. Additionally, parametric survival analysis may be used to fit the life table data. This method may be more flexible, avoiding the need to look up mortality hazards directly from life tables, requiring fewer parameters, and possibly saving computation time. Typically, this method is carried out by linearizing specific parameters (i.e., the hazard regression) on the life table to obtain estimates for the parameters of the distribution. Although this type of analysis is fairly straightforward, the estimates of the uncertainty around the parameter estimates are inaccurate. This is because such an analysis involves simulating individual death times from the life table data and using maximum likelihood estimation to obtain the needed parameters, may be considered when modeling all-cause mortality. Utilizing the number of individuals at risk, this method provides more accurate estimates of parameters and their uncertainty. The implementation, appropriateness, challenges, advantages and disadvantages of these three techniques when modeling all-cause mortality in health economic models will be discussed.

PRM142 JOINT BAYESIAN NETWORK META-ANALYSIS FOR EVENT COUNTS AND TIME TO EVENT: A COMPARISON OF METHODS AND IMPLEMENTATIONS

Schmidt H., Nehmzow C
Boehringer Ingelheim Pharma GmbH & Co KG, Biberach, Germany

Networks of treatments summarize all available information about the relative effectiveness of several treatments, also if both direct and indirect evidence needs to be combined[1]. For clinical trials with survival results, some will have been reported based on numbers of patients with event, and some based on the hazard ratio. A common scale for mapping the observed effects has been proposed[2]. Treatment contrasts would then be estimated through Bayesian methodology based on Markov Chain Monte Carlo (MCMC) simulation. Similar problems arise for trials with binary outcomes, for example from pulmonary function studies. We compare two implementations of the MCMC method, WinBUGS and SAS® PROC MCMC. Moreover, we investigate a deterministic-numerical approximation to the distribution of treatment contrasts by implementing the Laplace approximation (LUA) method. Of particular interest here is the goodness of the approximation, as the example dataset includes only small numbers of trials, patients and events. We show how to condense graphically the complex pattern of multiple treatment comparisons. We conclude with remarks on model selection, goodness-of-fit and the Deviance Information Criterion (DIC).

PRM143 PRACTICAL ISSUES WHEN CONDUCTING NETWORK META-ANALYSIS WITH A LIMITED NUMBER OF STUDIES

O’Donn D., Chirla C., Sherrill B., Wang J
RTI Health Solutions, Research Triangle Park, NC, USA

OBJECTIVES: Meta-analysis is being conducted extensively in part due to requirements from health care decision-making agencies. Meta-analysis techniques continue to develop, and software now exists to model networks using Bayesian and frequentist approaches with study effects treated as fixed or random. The non-model based anchored indirect-treatment comparison (AIC) method is also suitable for making pairwise treatment comparisons. However, practical issues emerge particularly when the network is comprised of a limited number of studies. Of special interest is the situation where a star network contains only one trial for a given treatment comparison. Our goal was to investigate the performance and interpretable consequences of these methods as well as compare with available methods.

METHODS: Example star networks anchored by placebo were created for binary endpoints with varying proportions and sample sizes. Generalized linear mixed models were fitted using PROC GLIMMIX in SAS with a random study effect. Results were compared to the AIC method as well as a sensitivity analysis using the LUA method in WinBUGS. RESULTS: Estimated odds ratios were examined to identify patterns among methods. If placebo effects were largely different across individual trials, differences between methods varied depending on effect sizes and sample sizes. If placebo effects were similar, the frequentist random-effects model was not able to estimate a random study effect and it was reduced to a fixed-effect model (similar to the AIC). CONCLUSIONS: The limitations of conducting a meta-analysis with a small number of trials should be understood regardless of the methodology used. In the special case of a star network with only one trial per treatment comparison, the differences between methods depend on the underlying evidence. The implications for interpretation will be discussed.