MULTI-NATIONAL CHART REVIEW STUDIES IN EUROPE: OPPORTUNITIES AND CHALLENGES

Papke KA1, Wassai R2, Stain D3, Chancellor J4
1United BioSource Corporation, Danville, PA, USA; 2United BioSource Corporation, London, UK; 3Chancellor Health Economics Ltd, Beaconsfield, Buckinghamshire, UK

OBJECTIVES: In support of European pricing and reimbursement submissions, country-specific health economic evidence is required. In the absence of patient-level databases, multi-national, retrospective chart review studies can provide data relevant to real-world patient characteristics, patterns of care, clinical outcomes and the natural history of disease. METHODS: A critical review and qualitative analysis of six recent multi-national chart review case studies designed to inform health economic questions was performed. The characteristics common research aims, objectives, and design parameters, and to delineate main methodological, operational and analytic challenges. RESULTS: Design challenges include defining an eligibility period sufficiently long to obtain enough cases while accessing patterns of care that are current, sample size determination and balancing the need for stable estimates of resource utilization with the need to contain study costs, and delineating sampling frame methodology to mini- mize chart selection bias. Detailed treatment and clinical outcome data must be weighed in the context of abstraction burden, and data collection methods should be considered separately from data interpretation. A common case report form for multi-national studies should allow local area treatment variation while maintaining consist- tency in data collection across health care settings. Operationally, knowledge of country-specific ethics and privacy protection regulations for retrospective studies is paramount as requirements are diverse and impact timelines differently. Data collection and study execution is also dependent on the ability to rapidly identify and recruit clinical sites representative of a broad range of clinical practice that also can provide sufficient geographical coverage. CONCLUSIONS: Despite significant challenges, practical, efficient, and scientifically sound approaches to the design and conduct of multi- national chart review studies in support of health economic analyses are possible. Main methodological and operational challenges can be identified across studies, thus can be anticipated and planned for.

CONCEPTUAL PAPERS & RESEARCH ON METHODS – Modeling Methods

THE THRESHOLD PRICING MODEL: NOT JUST ANOTHER COST-EFFECTIVENESS MODEL

Mudin Q1, Earnshaw S2, Aziz-Hashim Renoux N3, Keith M55
1RTI Health Solutions, Research Triangle Park, NC, USA; 2Shire Pharmaceuticals, Wayne, PA, USA

BACKGROUND: Threshold analysis as it is typically applied to cost-effectiveness models is an extension of sensitivity analysis in which the threshold analysis may be used to demonstrate the maximum price given different levels of health outcomes resulting in cost-effectiveness. In these instances, the ICER is the primary result of the model, and threshold analysis aids interpretation. As a result, the model is restricted to evaluating one health outcome, indication, population, line of therapy, reflecting less development decisions that have already been made. In contrast, a threshold pricing model, which is developed early in a drug’s development, is not attempting to evaluate the drug’s cost-effectiveness. Instead, it is built to inform the development plan, pricing strategy, and go/no-go investment decisions. OBJECTIVES: To outline the differences in the underlying mathematical structure, inputs, and outputs of a threshold pricing model compared with a traditional cost-effectiveness model, and to demonstrate its application. METHODS: We present the algebraic manipulations required to convert a decision-analytic model into one used for threshold pricing analysis. Using a hypo- thetical new pharmaceutical possessing two versions of a product profile, we demon- strate application of the threshold pricing model by generating a table of potential value-based pricing estimates corresponding to the unique combinations of indication, subpopulation, line of therapy, and comparator. We provide graphical depictions of the lost value-based pricing opportunity (reflecting the lost opportunity for the new product to address a greater unmet need) of development strategies that are not value- driven. CONCLUSIONS: A threshold pricing model is a powerful tool for helping to construct a value-driven development plan and a value-based pricing strategy. Con- structed appropriately, threshold pricing models can be used to prioritize among possible indications, identify target subpopulations, select the appropriate line of therapy, and choose and clarify required performance against comparators.

THE OPTIMAL NUMBER OF MONTE CARLO SIMULATIONS TO BE PERFORMED IN PROBABILISTIC SENSITIVITY ANALYSIS: EMPIRICAL EVIDENCE FROM ECONOMIC MODELS CONSTRUCTED FOR SUBMISSION TO THE NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

Batty AJ1, Paudlon M2
1Battet Health Solutions, Sheffield, UK; 2University of Toronto, Toronto, ON, Canada

OBJECTIVES: Probabilistic Sensitivity Analysis (PSA) is a common technique to assess uncertainty in economic models, with the majority of economic model publications now containing some form of PSA. Historically the number of simulations performed has been set at arbitrary levels (e.g. 1,000 simulations), however the aim of this research is to rationalise the number of simulations performed, minimizing both wasted computational time and the risk of incorrect conclusions being drawn. METHODS: The analysis investigates the number of simulations required in order for a Cost-Effectiveness Acceptability Curve (CEAC) to remain stable at the periphery. Secondary analyses focused on the number of simulations required to give reliable estimates of the mean values in (non-linear) models. The Institute for Health and Clinical Excellence (NICE) require manufacturers to submit PSA as part of the Single Technology Appraisal (STA) process. Models from different contract research agencies that have been constructed in Microsoft Excel, for submission to NICE, were then used to generate 50,000 simulations per model. This data was retrospectively analyzed to determine the number of simulations required such that a cost-effectiveness acceptability curve would remain stable at the periphery (5th and 95th percentiles). Secondary analyses focused on the number of simulations required to give reliable estimates of the mean values in (non-linear) models. RESULTS: Preliminary analyses suggest that conventional numbers of simulations are sufficient to estimate the CEAC at low levels of precision at the 5% and 95% limits and generate the mean value. However this is not the case if high levels of precision are required. CONCLUSIONS: Research is to the optimum number of Monte Carlo Simulations allows analysts to ground the number performed in empirical data, and suggests that accuracy can be achieved without spurious precision, wasted computing time, or worse, unreliable/unstable conclusions.

USING GROWTH IN THE COST-EFFECTIVENESS THRESHOLD TO INFORM THE DIFFERENTIAL BETWEEN THE DISCOUNT RATES ON COSTS AND HEALTH EFFECTS: REASON TO BE CAUTIOUS!

O’Mahony J
1Erasmus University Medical Center, Rotterdam, The Netherlands

BACKGROUND: Differential discounting of the costs and effects of health care interventions has been extensively debated. Proponents argue that a rising valuation of health as incomes grow justifies discounting health effects at a lower rate than costs. However, despite that fact that the impact of differential discounting is highly sensitive to the difference between the two rates, little attention has been paid what the appro- priate differential should be. The existing justification for the differential rests on the income and health elasticities of utility and income and health growth rates, all of which are uncertain: estimates of the appropriate differential are speculative at best. The discount differentials recommended by cost-effectiveness analysis advisory bodies vary, being 1.5 percentage points in Belgium, 2.5 in The Netherlands and 4.5 in the UK prior to 2004. What has not been widely recognized is that the discount rate should approximate the annual rate of growth in the cost-effectiveness threshold: this has been shown in a simple model published in the literature in which decision makers use a cost-effectiveness threshold in their reimbursement decision rule. ANALYSIS: This link to threshold growth provides a more immediate alternative by which empirically determine the appropriate differential compared to the current estimates. While cost-effectiveness thresholds are often not made explicit, there is no strong evidence that they have risen in recent years. Indeed, there are reasons to expect thresholds to remain constant or even decline, even if income growth is positive. CONCLUSION: This consideration of the plausible discounting differential complements current theo- retical debate over differential discounting. Growth in cost-effectiveness thresholds provides an alternative basis for justifying the discount differential. Existing evidence and expectations of threshold growth leads to conservative estimates of the discount- differential of at or near zero.

REVENUE OPTIMIZATION MODEL TO OPTIMIZE POSITION AND INDICATION OF NEW LAUNCHES

Mukku S1, McCorkley D2
1Double Helix Consulting Group, London, UK

OBJECTIVES: To assess the impact on revenues from a new drug in different indica- tions and at different positions within a treatment pathway. METHODS: The model was developed by price modeling experts at Double Helix Consulting using a logical flow developed over years. The model is tested by internal and external experts with different products. RESULTS: Drugs that reach to market very rarely are released in only a single indication, especially in chronic disease areas where there may be several different illnesses with a related etiology but different presentation. This is exemplified in the field of immunology and rheumatology, where several different drugs with a similar MOA are being used to treat many conditions that are pathophysiologically related. To explore the impact that multiple indications or use in different lines has or will have on the pricing of a new therapeutic agent, Double Helix Consulting gener- ated a revenue optimization model that can be used to establish the most likely price point for a new drug given several different scenarios. This model will help in optimiz- ing the best position and or indication for long term revenues from the drug. The model uses EPI data, prevalence, incidence, number of competitors, prices of compara- tors, line of treatment and other inputs. The outputs include NPV over a chosen period of time that can be sorted by line of treatment and indication. CONCLUSIONS: While it is desirable for a drug to be indicated in the largest patient pool possible, such actions can have serious negative consequences for the price at which payers are willing to pay for the treatment. A larger patient pool makes the burden on the health care provider smaller if the drug is too expensive, and as a result can lead to sig- nificant price erosion or HTA rejection.