SESSION II

METHODOLOGY ISSUES—Clinical Outcomes

Study Issues

PMD 1
THE NEW METHOD FOR TIME ADJUSTMENT OF THE NUMBER NEEDED TO TREAT AND ITS APPLICATION TO PHARMACOECONOMICS ANALYSIS
Aino H, Yanagisawa S, Kamae I
Kobe University, Kobe, Japan

The number needed to treat (NNT) is a benchmark invented in evidence-based medicine to describe the incremental effect between two medical treatments. Although it is potentially useful on pharmacoeconomics, the estimate is limited to be valid at a certain endpoint of a clinical trial. OBJECTIVE: To overcome such time-constraint, we developed a new method that can standardize the NNT to ex/intrapolate over the time axis. METHOD: We reviewed a linear approximation model in which the absolute risk reduction (ARR), the reciprocal of the NNT, is directly proportional to the duration of the clinical trial. Then, we extended the linear model into a more complex model using exponential function to ex/interpolate the NNT, and also developed mathematically how to calculate the incremental cost-effectiveness ratio according to the standardized NNT. RESULTS: We found the linear model has a fatal disadvantage that the time-adjusted ARR can be larger than 1 (i.e., the time-adjusted NNT can become impractically smaller than 1) under the assumption of constant relative risk reduction and constant event rate over time. On the other hand, the exponential model was able to overcome such a disadvantage in consistency with practical assumptions. CONCLUSION: The exponential model is practically better than linear model to standardize the NNT. The method we developed is applicable to estimate the incremental cost-effectiveness introducing the ratio of incremental cost per person responded to a treatment.

PMD 2
THE USE OF DISCRETE CHOICE MODELLING IN THE DESIGN OF CLINICAL TRIALS
Backhouse ME
Research Triangle Institute, Manchester; United Kingdom

OBJECTIVE: Discrete choice modelling (DCM) applied to data generated by stated preference (SP) experiments is being used increasingly by health economists as a method for valuing process and outcome characteristics of health interventions in utility or monetary terms. The purpose of this paper is to illustrate how sponsors of randomised controlled trials (RCTs) could use DCM to assist with the planning of their studies. The approach is illustrated using a case study of the design of trials to evaluate the use of adjuvant bisphosphonates in the management of patients with primary operable breast cancer. METHODS: A stated preference experiment was conducted amongst UK specialists involved in the management of patients with primary operable breast cancer. Respondents were asked to choose 1 bisphosphonate regimen from each of 16 binary choice scenarios. Each regimen was characterised in terms of the following trial design attributes: 1) Primary endpoint; 2) Effect size demonstrated; 3) Uncertainty surrounding demonstrated effect; 4) Duration of observation; 5) Study population; and 6) Cost of the treatment alternatives. The survey was performed using a telephone-mail-telephone approach. Probit analysis was used to estimate a binary choice model of drug prescribing behaviour. RESULTS: 54 specialists fully completed the survey questionnaire providing a sample of 864 discrete choice responses. In qualitative terms, the signs on the coefficients were in line with prior expectations and all coefficients were statistically significant at conventional levels. The marginal and average effects were used to determine the relative importance of the attributes and to rank alternative designs in terms of the ex ante probabilities of product adoption. CONCLUSIONS: DCM could be used by sponsors of RCTs to incorporate decision-maker preferences into their designs. It could also be used to estimate product uptake contingent upon different designs. Results from this study suggest that the approach is both feasible and valid.

PMD 3
RELEVANCE OF PATIENT REPORTED OUTCOMES FOR CHRONIC PAIN PATIENTS: THE ROLE OF SATISFACTION WITH ANALGESIC MEDICATION AND APPLICATION FORM
Anderson-Hillemacher A1, Hastedt C1, Pösl M2
1Gruenenthal GmbH, Aachen, Germany; 2Institute for Medical Psychology, University of Munich, München, Germany

OBJECTIVES: Patient satisfaction is a multi-facet construct and an important parameter of patient reported outcomes (PRO). In order to be able to measure chronic pain patient’s satisfaction, the relevance of different dimensions were identified, with a focus on the role of analgesic medication. METHOD: First, a literature review was conducted to summarise the current instruments of PRO measures. To identify relevant dimensions of patient’s satisfaction, 4 focus groups were held (10 patients with tumour pain, 10 with non-tumour pain). In semi-standardised interviews, patients’ personal pain experience and articulation were explored, including their satisfaction with analgesics in different dosage forms (oral, transdermal). RESULTS: Besides HRQoL and other parameters, the PRO referred to the literature also include a reference to the importance of data relating to patient satisfaction. To date, instruments used to survey patient satisfaction have three dimensions: 1) Satisfaction with
clinical care (doctor-patient relationship, competence of nursing staff, etc.); 2) Satisfaction with physical surroundings (medical facilities, organisational structure, etc.); 3) Satisfaction with clinical outcomes (result of treatment, impairment due to side effects, etc.) In the focus groups patients reported that analgesics and their application forms have an impact on acceptance, compliance, and on several areas of life such as sleep and life style. CONCLUSIONS: The results of the focus groups support the assumption, that at least one further dimension of patient’s satisfaction exists: satisfaction with medical treatment. This aspect has not yet been taken up by theoretical or empirical research. Due to this, world wide there is no instrument for recording this dimension today. The need to develop a new questionnaire to establish patients level of acceptance and satisfaction with their medication was specified and suggestions for a 4-dimensional model of patient’s satisfaction were made.

**WHEN CAN MISSING DATA BE CONSIDERED MISSING AT RANDOM (MAR) IN SUBSTANCE ABUSE TREATMENT OUTCOMES RESEARCH?**

_Ciesla JR, Spear SF_

_Northern Illinois University, DeKalb, IL, USA_

**OBJECTIVES:** A lot of attention is focused on the outcome effectiveness of substance abuse treatment. The usual method of assessing outcomes is by contacting clients after treatment and querying them on recovery-related behaviors and on drug/alcohol use. Since researchers are not always able to contact every client after treatment, the issue of response bias is important. Missing data is MAR, and thus ignorable, if differences between respondents and nonrespondents can be characterized by variables that are measured for both groups. The objective of this research is to illuminate this issue by using data collected from a U.S. treatment population and to discuss statistical methods for correcting response bias. **METHODS:** The data were collected from treatment records and follow-up interviews of clients completing substance abuse treatment at a facility in the U.S. Appropriate consent was obtained. Each client contacted was administered a questionnaire. Eighty-eight (44.9%) completed the questionnaire; 102 (52.4%) could not be contacted. Since the treatment records for the responders and nonresponders were available, information was extracted on variables related to treatment outcomes so that statistical analysis could be conducted. **RESULTS:** No differences were found between responders and nonresponders for most variables. Variables measuring demographics, family support/structure, criminality/truancy, psychological comorbidities, treatment attributes, and drug use were not different. Variables with statistically significant differences were: “number of months at current residence” (t = 2.12 p = .037) and the proportion “holding a job” (difference in proportions = .182; 95% CI = .043 to .321). **CONCLUSIONS:** Missing data are not MAR, and thus not ignorable, when missing variables are the same as or related to variables that determine outcomes. In this case “number of months at current residence” and “holding a job” may predict treatment success. If this is true, some method of control must be used. Weighting adjustments such as post-stratification and likelihood-based methods are considered. Since the variables that predict treatment outcomes are not fully understood, it is difficult to be certain MAR criteria are met.

**METHODOLOGY ISSUES—Economic Study Issues**

**PMD5**

**VALUATION OF NEW DRUG APPLICATIONS OF PHARMACEUTICAL COMPANIES USING COMPOUND OPTION MODELS**

_Cassimon D, Engelen Pj, Thomassen L, Van Wouwe M_

_University of Antwerp, Antwerpen, Belgium_

**OBJECTIVES:** This paper presents a model based on real option analysis for the valuation of R&D in the pharmaceutical sector both for start-up ventures as well as big conglomerates. We derive a formal compound option model to value New Drug Applications (NDA) and show the valuable contribution of real option analysis compared to conventional DCF-analysis. **METHODS:** The key understanding is that R&D projects of NDAs can be seen as compound options. The growth option framework looks at pharmaceutical investment projects as a sequence of options, which differs from a conventional DCF-analysis by incorporating the possibility to stop the project when a subsequent phase is not valuable (abandon the option), and only continues with the project (exercising the option) when it is valuable. Traditional valuation techniques as DCF-analysis fail in valuing innovative companies because most of the value of R&D projects is embedded in unexercised real options whose future value is uncertain at this moment. If one considers a company as a portfolio of real options, one can value the projects or the company based on a compound option model. **RESULTS:** The compound option model reveals that real option analysis can better incorporate the value of a NDA than conventional DCF-analysis would reveal. Real option analysis will better reflect the fundamental value of the project or of the company, which cannot be captured by DCF-analysis. **CONCLUSION:** The paper presents a new methodology for valuing R&D of pharmaceutical companies based on compound option models.

**PMD6**

**MODIFYING COST-EFFECTIVENESS RATIOS TO BE MAXIMALLY COMPARABLE ACROSS MULTIPLE DISEASES: AN APPLICATION OF MANIFOLD THEORY**

_Gold K, Botteman M, Pashos C_

_Abt Associates Inc, Cambridge, MA, USA_

**OBJECTIVE:** Develop methodology to create a more globally informative, CE-based “valuation” that is useful