PRM68
CALIBRATING AN INTEGRATED PHARMACO-ECONOMIC-PHARMACOMETRIC MODEL OF COPD TREATMENT: WHAT A DIFFERENCE THE VARIANCE MAKES
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OBJECTIVES: This study was to calibrate a genetic and pharmacometric microsimulation model of COPD to ensure that variation resulting from model estimates was consistent with the underlying trial data, thereby providing more accurate estimates of the probability of the clinical and economic "success" of drug development options based on this model.
METHODS: A Markov microsimulation model was developed to estimate monthly changes in key COPD severity metrics (FEV1 and exacerbations) in order to compare a hypothetical FEV1-increasing drug to placebo. The pharmacometric model, based on a model-based meta-analysis of COPD trials, was used to predict the exacerbation rate (ER) in a group of actual trial patients, given their known baseline FEV1. The hypothetical drug increased FEV1 and thereby decreased the ER. The model was then run in silico and used to develop treatment- and monthly model outcomes. The variance in exacerbations generated by this model was calibrated to the variance in the trials underlying the pharmacometric model. Model results were compared to those generated by a Markov model without such calibration. A common random number assumption for non-COPD mortality was tested for its effect on variation in health economic outcomes.
RESULTS: In the reference case, relative to the uncalibrated model, the calibrated model resulted in similar outcome means but 15-17 times larger standard deviations (SDs) for exacerbations, 6-7 times larger SDs for 1-year costs, and three times larger SDs for QALYs. This led to more elliptical ICER scatterplots and flatter cost-effectiveness acceptability curves in the calibrated model. Use of common random numbers did not make a significant difference in these results. CONCLUSIONS: Integration of pharmacometric and pharmacoeconomic models provides a basis for outcomes variance calibration with actual data. Without calibration, variation induced within a typical Markov model resulted in suboptimally misrepresent the clinical variation and lead to inaccurate probabilities of success versus clinical and economic thresholds.

PRM69
INFORMING UNCERTAIN MODEL PARAMETERS THROUGH MODEL CALIBRATION: HUMAN PAPILLOMAVIRUS (HPV) MODEL CASE STUDY
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OBJECTIVES: Numerous HPV models have been developed to evaluate the cost-effectiveness of HPV vaccination. However, uncertainty remains in many key model parameters such as the risk of transmission and partner formation and dissolution rates. We attempted to identify those parameters that influenced most calibration for an HPV type 6/11 agent-based model. METHODS: We developed an agent-based model of HPV 6/11 infections in the USA. Several key model parameters of partnership formation and natural history parameters on how well the model output fit observed data on HPV 6/11 infections and disease. Our heuristic model describes the population in terms of the three groups by individuals’ sexual activity level. The activity level is positively correlated with the risk of infection transmission or acquisition. Persons belonging to the low and medium risk groups tend to have long-lasting relationships with low probability of forming concurrent partnerships, whereas those in the highest risk (most active) group tend to engage in short and often concurrent partnerships.
RESULTS: We found that the most sexually active group of people is responsible for forming a power-law tail in the partnership statistics relevant to infection spread, and that durations of short-term partnerships, along with group risk and age mixing patterns, have the biggest impact on the model fit. In combination, these factors also determine the characteristic shapes of the warts age-specific incidence curves with the peak occurring in the female population approximately five years earlier than in the male population.
CONCLUSIONS: The transmission dynamics of HPV 6/11 infection and disease depend greatly on the short-living partnership networks. Accounting for the formation of such partnerships is critical to developing acceptable model fits. Further research is necessary to explore how accounting for partnership formation affects cost-effectiveness analyses of HPV vaccination strategies.

PRM70
PRACTICAL ISSUES IN DEVELOPING ECONOMIC MODELS FOR TARGETED TREATMENTS
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OBJECTIVES: A reimbursement process for targeted therapies was introduced in 2011 requiring joint economic assessment of both the new treatment and associated diagnostic test. Thus the emphasis of the evaluation was no longer simply on the effectiveness of the new treatment in targeted patients but also in patients inappropriately treated due to false negative test results. A submission for subsidy of EGFR mutation testing to determine eligibility for first-line gefitinib treatment of patients with advanced NSCLC was undertaken. METHODS: An individual patient simulation (IPS) model was used to model the cost of gefitinib versus placebo in a hypothetical cohort of patients with NSCLC, estimated using data from the AVAPERL trial (NCT00322540) and published sources. A Markov model was used to model the health states of the patients and the lifetime duration of health states.
RESULTS: The results of a probabilistic sensitivity analysis (PSA) showed the cost effectiveness of gefitinib was dependent on the number of clusters and the sample size in each cluster. A thorough review.

PRM71
PROGRESSION OF VISION LOSS IN PATIENTS WITH GEOPATHY ATROPHY: A DISEASE MODEL
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OBJECTIVES: Geographic Atrophy (GA) affects eight million people worldwide, limiting its visual acuity (VA) resulting in blindness. Our aim was to forecast the long-term impacts of GA, in terms of visual loss, on daily activities, and the expected treatment.
METHODS: The model was developed using Excel Visual Basic Application (VBA) with the following inputs: 1) population characteristics (gender, age at diagnosis, baseline VA, one eye versus two eyes involvement), 2) health states by VA (no Medline and PubMed databases were used to target a literature review to identify studies that use PSM methodologies in multi-level data. The following search terms were used: ‘Propensity score’, ‘Multi-level data’, ‘Hierarchical model’ and ‘Propensity score matching’. Methodologies that specifically considered the challenges of performing PSM with hierarchical data were included in the final review.
RESULTS: Six strategies were identified in the literature to perform PSM in multi-level data. These included 1) Complete pooling (CP), 2) Partial pooling (PP), 3) No PSM, 4) Simple random modeling (SRM), 5) Two-stage modeling (TSM), and 6) Dummy modeling (DM). CP ignores potential clustering in the data and is the most commonly used approach. SLM differs from CP in that it matches patients only within a given cluster. In contrast, the NP method generates separate propensity scores (PS) for each patient, regardless of the cluster to which they belong. The method uses random intercept models to generate PS and patients are matched across all clusters. The TSM approach first estimates random errors separately and applies them in a subsequent step to the patient-level PS, after which patients are matched as in the PP method. The DM method simply includes the cluster identifier as a fixed effect in the PS model.
CONCLUSIONS: Performance of each approach is dependent on the number of clusters, number of patients, and the propensity score of patients should be calculated, after which patients are matched as in the PP method. The DM method simply includes the cluster identifier as a fixed effect in the PS model.

PRM72
REVIEW OF METHODOLOGICAL APPROACHES TO GENERATE PROPENSITY SCORES IN MULTILEVEL DATA
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OBJECTIVES: Propensity score matching (PSM) techniques are frequently used in analytical studies. However, there is a lack of consensus on how to handle multi-level data. Several multi-level modeling level approaches to account for the hierarchical structure of data in PSM analyses. The aim of this study is to identify and review existing multi-level PSM methodologies.
METHODS: Six strategies were identified in the literature to perform PSM in multi-level data. These included 1) Complete pooling (CP), 2) Partial pooling (PP), 3) No PSM, 4) Simple random modeling (SRM), 5) Two-stage modeling (TSM), and 6) Dummy modeling (DM). CP ignores potential clustering in the data and is the most commonly used approach. SLM differs from CP in that it matches patients only within a given cluster. In contrast, the NP method generates separate propensity scores (PS) for each patient, regardless of the cluster to which they belong. The method uses random intercept models to generate PS and patients are matched across all clusters. The TSM approach first estimates random errors separately and applies them in a subsequent step to the patient-level PS, after which patients are matched as in the PP method. The DM method simply includes the cluster identifier as a fixed effect in the PS model.
CONCLUSIONS: Performance of each approach is dependent on the number of clusters, number of patients, and the propensity score of patients should be calculated, after which patients are matched as in the PP method. The DM method simply includes the cluster identifier as a fixed effect in the PS model.

PRM73
CONTRASTING THE RELATIVE RISK REDUCTION OF CARDIOVASCULAR EVENTS IN THE CORE DIABETES MODEL ASSOCIATED WITH SINGLE RISK FACTORS ACROSS ALTERNATIVE RISK ENGINEERS: UKPDS2 and SWEDISH NATIONAL DIABETES REGISTRY EQUATIONS
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OBJECTIVES: The degree to which predefined risk factor (RF) changes alter life time benefits and costs in projections with the IMS Diabetes-Model (CDM) has been previously reported. The objective of this study was to contrast the relative risk reduction of cardiovascular events by individual RF changes using alternative risk equations (RE), specifically: UKPDS-68 (UK68-RE), UKPDS-82 (UK82-RE) and the Swedish National Diabetes Registry (SNDR-RE).
METHODS: The CDM was applied to estimate annual probabilities for 1st myocardial infarction (MI), 1st stroke, ischemic heart disease (IHD) and heart failure (HF) for an intermediate risk type 2 diabetes individual (age 55 years, HbA1c 8%, SBP 140 mm-Hg, BMI 30 kg/m2, TC 150 mg/dL, HDL-C 45 mg/dL). The risk of RF (RA) in association with unit RF changes was determined for HbA1c (-1%), body-mass-index (BMI) (-1 kg/m2), systolic-blood-pressure (SBP) (-10 mmHg), total-cholesterol (TC) (-10 mg/ dL), (high-density-cholesterol (HDL) (+5 mg/dL) and low-density-cholesterol (LDL) (+5 mg/dL).
RESULTS: The RR of CV endpoints associated with risk factor changes
for HbA1C, SBP, BMI, TC, HDL and LDL was predicted as follows: MI: 0.89, 0.90, 1.00 (UK68-RE), 0.95, 1.00, 1.00 (UK82-RE) and 0.92, 0.93, 1.00 (UK82-RE); 0.91, 0.94, 1.00 (UK82-RE) and 0.95, 1.00, 1.00, 0.97 (UK82-RE) and 0.85, 0.94, 1.00, 0.99, 1.18, 1.00 (SNDR); HD: 0.85, 0.89, 0.94, 1.00, 1.00 (UK82-RE) and 0.90, 1.00, 1.00, 0.98, 1.00, 1.00 (UK82-RE) and 0.83, 0.89, 0.94, 1.19, 1.00 (SNDR). CONCLUSIONS: The degree to which RF modification influences CV risk is only dependent on RE selected. The choice of equation within a model may influence the predicted health economic benefit associated with CV risk factor modification.

PM74

EVALUATING THE RELATIVE CONTRIBUTION TO CHANGES IN QUALITY- ADJUSTED LIFE EXPECTANCY ASSOCIATED WITH HBA1C, WEIGHT AND HYPOGLYCÆMIA IN THE UK DIABETES MELLITUS MULTIPLE RISK EQUATIONS WITH THE CORE DIABETES MODEL (CDM)

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OBJECTIVES: The cost-effectiveness type 2 diabetes mellitus (T2DM) therapies are often driven by changes in HbA1C, weight and hypoglycaemia rates. There are a number of risk equations available for modeling diabetes complications. The objective of this study was to attribute the predicted gain in quality adjusted life years (QALYs) to HbA1C, weight and hypoglycaemia change for each of the UKPDS-68 risk equations (UK-68-RE), the UKPDS-59 risk equations (UK-59-RE), the Swedish National Diabetes register risk equations (S-NDR) and the ADVANCE RE (A-Re). METHODS: Published data on T2DM switching to insulin degludec from either insulin glargine or detemir were used. Mean (± SD) baseline profiles were age 62.8 years (±14.7), diabetes duration 16.2 years (±5.0), HbA1c 9.4% (±1.1), weight 102.8 kg (±23.0) and 1.0 hypoglycaemia events per week (±1.4). Mean 1-year change in clinical variables was HbA1c -0.7% (±0.3), weight -1.3kg (±1.1) and hypoglycaemia events/week -1.0 (±1.3). The functionality was assessed by changes in weight and hypoglycaemia frequency as it is as important as justifying choice of risk equations used.

PM75

META-ANALYSIS FOR THE EVALUATION OF MULTIPLE SURROGATE ENDPOINTS

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OBJECTIVES: In health technology assessment (HTA), decision-makers face increased pressures to make earlier decisions. However, in early stages of drug development, data on the clinical effectiveness of new health technologies is measured by the final outcome is often limited, especially when measuring the effectiveness of new interventions requires long follow-up time. Therefore, shorter-term surrogate endpoints play an important role. Candidate surrogate endpoints data provide proof of concept. When, however, more than one of such endpoints exists, they may jointly fully mediate the treatment effect on the final outcome. This study presents methodology for evaluation of multiple surrogate endpoints as predictors of the treatment effect on the final outcome.

PM76

EVALUATING THE VARIABLES AFFECTING THE COMPLETION OF A COMPLIANCE MONITORING PROGRAM (CMP) FOR NURSES UNDERGOING SUBSTANCE ABUSE TREATMENT

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OBJECTIVES: This study is a retrospective analysis to determine the factors which best predict the completion of a nurse substance abuse monitoring program. METHODS: A retrospective cross sectional analysis was conducted in a state database (Florida) of 65,030 nurses enrolled in CMP. The entire database and the subset of 10,000 were used for analysis. The outcome variable was the status of CMP program. The predictors included demographics, treatment type and length, drug usage, healthcare training and experience, status of treatment, aftercare treatment, and nursing specialty. Missing data was not considered in the study. After checking for all the assumptions, univariate analysis using chi-square test was performed on the entire data as well as the subset. All features with significant relationships in the univariate analysis were included in the forward, backward and stepwise multiple logistic models to predict the completion of contract by the nurses. All tests were conducted at 5% level of significance. RESULTS: All independent variables had a CV risk, dependent on RE selected. The choice of equation within a model may influence the predicted health economic benefit associated with CV risk factor modification.

PM77

A BAYESIAN FRAMEWORK TO ESTIMATE THE COST OF CARE FOR RENAL DISEASE PATIENTS WITH AND WITHOUT A USUAL SOURCE OF CARE PROVIDER

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OBJECTIVES: To model total health costs of end-stage renal disease adult patients with and without an usual source of care provider and to evaluate whether these costs differ between dialysis and transplant patients. METHODS: Retrospective cohort study was conducted on data from 197 unique adult patients was collected for years 2002 to 2011 using the Medical Expenditure Panel Survey conducted on American households. Total cost for renal disease patients was modeled using the probability distributions and estimated utilities associated with changes in weight and hypoglycaemia rate. Total cost comprised of total costs for office based expenditures, prescription drugs, home health care, inpatient care, outpatient care, emergency room visits and costs associated with equipment and care nurses. RESULTS: Among the 197 end-stage renal adult patients, 43% underwent dialysis and 22% underwent transplantation. Overall for the end-stage renal disease adults, the mean annual costs of care for a patient with an usual source of care provider vs. without an usual source of provider was $28,857 vs. $20,851. In comparison, the mean annual cost of care for a transplant patient without a usual source of care was $19,464 and for a dialysis patient was $92,326. Transplant patients with a source of care provider can potentially save 23% in annual total costs in comparison to patients without an usual source of care. Patients can save 56% of total cost annually. CONCLUSIONS: Transplant and dialysis patients having an usual source of care provider incurred less health expenditures. In renal disease patients, having an usual source of provider has possibly large implications for health care cost savings.

PM78

THE USE OF BOOTSTRAP MODEL AVERAGING WHEN ESTIMATING SURVIVAL CURVES

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OBJECTIVES: To explore the use of bootstrap model averaging (BOOT) for estimating survival curves when conducting parametric survival analysis. METHODS: A set of four clinical trials as advanced hypertension were selected and published (www.rctreview.org). Individual patient data for overall survival were estimated from digitised Kaplan-Meier curves using a published algorithm. A range of parametric survival models (exponential, Weibull, Gompertz, lognormal, log-logistic, Gamma and Generalised Gamma) were fitted for each study. One thousand bootstrap samples of the IBD for each study were taken. The model which minimised the Bayesian Information Criterion (BIC) was selected for each sample. The proportions of bootstrap samples within which each model was selected were used as the weights for the BOOT estimate. These were applied to the mean survival estimates obtained from each candidate model applied to the original data set to obtain the weighted average BOOT estimate of mean survival for each treatment. RESULTS: Estimates of mean survival varied markedly according to the choice of functional form for the parametric survival model. There was also considerable uncertainty in the selection of an optimal functional form based on the BIC (the bootstrap estimation for the probability that the optimal functional form was selected varied between 16% and 43% across studies). Using the results from the BOOT analysis rather than selecting a single functional form reduced the estimated variance in mean survival in all studies. CONCLUSIONS: BOOT can reduce the variance in mean survival estimates and avoids the need for selecting a single functional form for a parametric survival model. Given the considered uncertainty in selecting a functional form and the influence of this process on mean survival estimates, BOOT could act as a useful method for addressing uncertainty in functional form selection and hence in cost-effectiveness analyses.

PM79

DEVELOPMENT AND VALIDATION OF THE HEMOPHILIA-SPECIFIC BURDEN SCALE FOR CAREGIVERS OF CHILDREN WITH HEMOPHILIA IN THE US – THE HEMOPHILIA ASSOCIATED CAREGIVER BURDEN SCALE (HACBS)

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OBJECTIVES: The objective of this research was to determine the factors which best predict the completion of a nurse substance abuse monitoring program. METHODS: A retrospective cross sectional analysis was conducted in a state database (Florida) of 65,030 nurses enrolled in CMP. The entire database and the subset of 10,000 were used for analysis. The outcome variable was the status of CMP program. The predictors included demographics, treatment type and length, drug usage, healthcare training and experience, status of treatment, aftercare treatment, and nursing specialty. Missing data was not considered in the study. After checking for all the assumptions, univariate analysis using chi-square test was performed on the entire data as well as the subset. All features with significant relationships in the univariate analysis were included in the forward, backward and stepwise multiple logistic models to predict the completion of contract by the nurses. All tests were conducted at 5% level of significance. RESULTS: All independent variables had a CV risk, dependent on RE selected. The choice of equation within a model may influence the predicted health economic benefit associated with CV risk factor modification.

RESEARCH ON METHODS – Patient-Reported Outcomes Studies