PRM68

CALIBRATING AN INTEGRATED PHARMACOECONOMIC-PHARMACOMETRIC MODEL OF COPD TREATMENT: WHAT A DIFFERENCE THE VARIANCE MAKES

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OBJECTIVES: The objective was to calibrate a pharmacometric-pharmacoeconomic 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 in the treatment group. Costs and utilities were derived from the literature and applied to 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 numbers 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 may substantially misrepresent true 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 some 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 fits for an HPV type 6/11 agent-based model. **METHODS:** We developed an agent-based HPV model of HPV 6/11 infections and disease (warts) to explore the effect 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 reported in surveys and has the biggest impact on the infection spread, and that durations of short-term partnerships, along with risk group 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 achieving 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 positive 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 was used to model current SOC for NSCLC, no test and first-line platinum-based doublet chemotherapy versus the proposed intervention, EGFR mutation test and gefitinib treatment for EGFR M+ patients and SOC for EGFR M- and EGFR unknown patients. The IPASS Study (NCT00322452) confirmed the benefit of TKIs in EGFR M+ patients, but also the potential harm to EGFR M- patients in the first-line setting. Data were thus available for EGFR M+ and EGFR M- patients treated with both gefitinib and SOC. This information was critical to development of a screening module and survival curves. **RESULTS:** EGFR testing regimens to target TKI treatment at various points in the patient's life from diagnosis through to palliative care were compared. The results were most sensitive to choice of comparator such as: inclusion of switch maintenance following doublet chemotherapy; proportion of patients receiving second-line therapies including targeted TKI; and use of subsequent untargeted TKI. EGFR testing+gefitinib was a dominant economic strategy when compared to commonly used treatment alternatives. Assuming the most conservative comparator strategies, EGFR+gefitinib remained cost-effective. Decreasing the specificity of EGFR testing (false positive rate) or including a mortality benefit to TKI worsened the ICER. **CONCLUSIONS:** Simultaneous reimbursement of the EGFR test and gefitinib for first-line treatment of EGFR M+ aNSCLC was a cost-effective alternative to no testing and chemotherapy.

PRM71

PROGRESSION OF VISION LOSS IN PATIENTS WITH GEOGRAPHIC ATROPHY- A DISEASE MODEL

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OBJECTIVES: Geographic Atrophy (GA) affects eight million people worldwide, limits visual acuity (VA) resulting in blindness. Our aim was to forecast the long term impact of GA on visual loss and blindness, and the expected benefits of early treatment. **METHODS:** The model was developed using Excel Visual Basic Application (VBA) with the following inputs: 1) population characteristics (gender, age at GA diagnosis, baseline VA, one eye versus two eyes involvement), 2) health states by VA (no visual impairment, visual impairment, blindness and death), 3) rate of VA decline. Data of natural progression of GA from Age-Related Eye Disease Study (AREDS) was used as the main input for this model. The key outputs of the model under no intervention/hypothetical intervention are: 1) time to loss of functional vision (VA>20/40), visual impairment (VA<20/80), and blindness (VA≤20/200), and 2) time to event curves for visual disability and blindness. **RESULTS:** In a simulated cohort of 500 patients diagnosed with GA (with a mean age of 70 years and VA= 20/60), the model estimated that 60% of them would develop blindness in the affected eye over their lifetime without intervention. On average, they experience four years with visual impairment and eight years with blindness. The model also showed that GA patients with younger age and worse VA at diagnosis, and faster rate of VA decline are at increased risk of attaining blindness. A hypothetical intervention with 25% and 50% efficacy avoided 1 and 3 years of blindness, respectively. Sensitivity analysis showed that treatment efficacy when compared to starting age, starting VA, and rate of VA loss, had the highest impact in reducing time spent in blindness. **CONCLUSIONS:** The simulation model based on natural history of GA progression showed that effective treatment started early at diagnosis can reduce the burden of vision loss among GA patients.

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 analyses of retrospective or observational data. Several approaches have been developed 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:** Medline and PubMed databases were used to perform a targeted 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 pooling (NP); 4) Simple single-level modeling (SSLM); 5) "Two stage" modeling (TSM); and 6) "Dummy" modeling (DM). CP ignores potential clustering in the data and is the most commonly used approach. SSLM 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 cluster and matches prior to pooling. The PP 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 PS model that account for clustering, 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 and the sample size in each cluster. A thorough investigation of data should be undertaken before selecting an approach to use PSM in studies with multi-level data.

PRM73

CONTRASTING THE RELATIVE RISK REDUCTION OF CARDIOVASCULAR EVENTS IN THE CORE DIABETES MODEL ASSOCIATED WITH SINGLE RISK FACTOR CHANGES ACROSS ALTERNATIVE RISK ENGINES: UKPDS68, UKPDS82 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-CORE-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 250 mg/dl, HDL 50 mg/dl and LDL 170 mg/dl). The relative risk (RR) 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-lipoprotein (HDL) (+5 mg/dl) and low-density-lipoprotein (LDL) (-10 mg/dl). **RESULTS:** The RR of CV endpoints associated with risk factor changes