RESEARCH ON MODELING METHODS STUDIES

M01 REDUCING AND QUANTIFYING OVER-FITTING IN REGRESSION MODELS

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OBJECTIVES: Regression models are the multivariable analytical method of choice for epidemiologists and statisticians. It is widely recognized that these models may suffer from over-fitting where the sample estimates fail to generalize to other samples. Systematic approaches to minimize over-fitting are seldom adopted and there is a reluctance to hold data back for independent assessment of model performance. This study assesses penalized regressions for reducing over-fitting, cross-validation on training data for estimating over-fitting, and the extent to which over-fitting produces misleading conclusions. METHODS: Data were extracted from the IMS PharMetrics Plus US medical claims database for patients with Multiple Sclerosis receiving medications. Cohorts were matched using propensity scores producing 3,348 matched pairs. The probability of relapse and persistence were estimated using standard, stepwise and (LASSO) penalized logistic regressions. Over-fitting was measured as the difference between the Area Under Curve (AUC) for training and test data and additionally estimated using cross-validation on training data alone. RESULTS: Penalized logistic regressions greatly reduced over-fitting compared to standard and stepwise alternatives, irrespective of the choice of response variable and degrees of freedom: for example, modelling relapse with 50% of the data used for training and 50% used for testing showed overfitting of 9.9% with standard, 8.0% with stepwise and 3.9% with penalized logistic regression. Cross-validation, provided reasonable approximations for over-fitting, estimated over-fitting as 5.9% for standard logistic model and 10.4% for over-fitting inflated the estimated treatment effect by 25% (OR=2.03 vs. 1.64; standard logistic model vs. penalized model). CONCLUSIONS: Penalized logistic regression models had substantially lower over-fitting. Moreover, good estimates of over-fitting can be derived without withholding data. Both penalized regressions and cross-validation are straightforward to implement in most statistical packages and greater adoption of these methods is encouraged to ensure more reliable estimates of risk factors.

M02 A COMPARISON OF STATE TRANSITION AND Discrete EVENT MODELING APPROACHES FOR THE USE IN THE PREVENTION OF THROMBOTIC EVENTS AFTER Myocardial Infarction (MI)

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OBJECTIVES: A state transition model (STM) and a discrete event simulation (DES) were developed to evaluate the health outcomes associated with antithrombotic treat- ment for secondary prevention of thrombotic events for patients with a recent myocardial infarction (MI) in the UK. METHODS: The STM and DES were developed with similar assumptions about which events altered risk. In both models, results were compared between the vorapaxar plus standard care (VOR) and the standard care (SC) arms. Individual patient characteristics at baseline from the qualifying MI cohort of TRA 2°P-TIMI 50 trial were used to define patient profiles in both SC arm. The STM predicted 0.226 MIs, 0.132 strokes, and 0.417 CV-deaths per patient event per model cycle. While both approaches are valid, the DES technique offers advantages in being more likely to disseminate cost-effective findings than those using efficacy data when policy decisions are based on the type of “E” evidence used for CEA and appropriate interpretation.

M04 EXTRAPOLATING ALL-CAUSE MORTALITY ESTIMATES IN ECONOMIC EVALUATIONS: A SIMULATION ANALYSIS

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OBJECTIVES: A cost-effectiveness model can be populated using mortality rates from a period’s life-table or using extrapolations of mortality based on historical life-tables. Current decision models use the first method. This simulation study aims at identifying the impact of mortality methods used on cost effectiveness analyses. METHODS: A simulation study was based on a two-state Markov model (alive-death) that compared a hypothetical intervention against no intervention. The model was populated with age-specific, all-cause mortality probabilities from the estimation methods presented above. The mortality extrapolations were estimated using a smoothed Lee-Carter method. The model outcomes were incremental costs, life-years gained (LYG) and incremental net benefit (INB). The proportional difference (PD) of the model outcomes between the two mortality estimation methods was the outcome of each simulation. The following parameters were simultaneously varied: discounting rate (0% - 0.05), intervention effect (relative risk of mortality: 0.9-0.99), age at intervention (birth- 80 years old), duration of intervention effect (1/100/10 years/10/ lifetimes), duration of intervention administration. Simulations were conducted using Canadian life-tables. The impact of each parameter on the simulation outcomes was estimated using descriptive and graphical methods. RESULTS: The cohorts’ age and the intervention model had an important effect on the PD in all scenarios (cost and INB). The duration of intervention effect and administration were more influential on the effect of method on the PD of incremental costs and INB. Large variation was observed among the scenarios within parameter values, for the PD of all outcomes. Conclusions: Using mortality projection methods, substantial differences were observed in CEA model outcomes. Given that the magnitude and the direction of the impact of mortality estimation methods on the model outcomes is uncertain, no final decisions on mortality estimation method used in economic evaluations should be considered after conducting sensitivity analyses using both methods.

RESEARCH PODIUM PRESENTATIONS - SESSION II

CANCER OUTCOMES RESEARCH STUDIES

C01 THE IMPACT OF CHRONIC CONDITIONS ON THE ECONOMIC BURDEN OF CANCER SURVIVORSHIP IN THE UNITED STATES

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OBJECTIVES: The objective of this study is to examine the prevalence of chronic conditions and their impact on the economic burden among cancer survivors in the United States. METHODS: Using National Health Interview Survey data from 2012 and 2013 Medical Expenditure Panel Survey (MEPS) we identified 8,617 cancer survivors and 111,695 individuals without a history of cancer. Adjusted predictive margins from multivariable regression were used to examine the prevalence of chronic conditions. Direct medical costs were measured using annual health care expenditures and adjusted means were estimated using a two-part model. Indirect morbidity costs were calculated from the lost productivity due to employment disability, missed work days, and lost household productivity and adjusted means were estimated using multivariable logistic regression and negative binomial regression modelling. Separate models were used to evaluate the impact of each chronic condition and the impact of MCCs. RESULTS: Cancer survivors were more likely to have MCCs, with 12.4% reporting ≥4 chronic conditions compared to 9.3% of individuals without a history of cancer. Medical expenditures for cancer survivors with other chronic conditions, particularly those with MCCs were higher than among cancer survivors without any of the chronic conditions studied. The largest increase in medical expenditures was associated with heart disease ($4,287) and stroke ($4,210). Having ≥4 chronic conditions was associated with increased expenditures of $9,082 per cancer survivor. Lost productivity was greater among cancer survivors with other chronic conditions. The largest increase in lost productivity was associated with stroke ($4,164) and arthritis ($3,420). Having ≥4 chronic conditions was associated with increased lost productivity of $9,245 per cancer survivor. CONCLUSIONS: Chronic conditions, especially the presence of MCCs, are associated with higher medical expenditures and lost productivity among cancer survivors. Efforts to reduce the health and economic burden caused by chronic conditions among cancer survivors are important given their substantial impact on medical expenditures and lost productivity.

C02 A COMPARATIVE COST UTILITY ANALYSIS FOR FIRST LINE TREATMENT OF METASTATIC NON-SMALL CELL LUNG CANCER (NSCLC) PATIENTS WITH EGFR EXON 19 DELETIONS OR EXON 21 (L858R) SUBSTITUTION MUTATIONS

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OBJECTIVES: This study used a Markov model to compare the lifetime health costs and utilities for 17 CEA’s were done: 13 CEA’s were from pragmatic trials, and another 4 studies (23.5%) from observational studies. The aim was to determine the incremental cost-effectiveness ratio for these studies. The incremental cost-effectiveness ratio for these studies was higher than among cancer survivors without any of the chronic conditions studied. The largest increase in medical expenditures was associated with heart disease ($4,287) and stroke ($4,210). Having ≥4 chronic conditions was associated with increased expenditures of $9,082 per cancer survivor. Lost productivity was greater among cancer survivors with other chronic conditions. The largest increase in lost productivity was associated with stroke ($4,164) and arthritis ($3,420). Having ≥4 chronic conditions was associated with increased lost productivity of $9,245 per cancer survivor. CONCLUSIONS: Chronic conditions, especially the presence of MCCs, are associated with higher medical expenditures and lost productivity among cancer survivors. Efforts to reduce the health and economic burden caused by chronic conditions among cancer survivors are important given their substantial impact on medical expenditures and lost productivity.