previous pamidronate treatment (45.8%), were identified. CONCLUSIONS: Although regression coefficients are different, these risk factors proved significant in both multivariate models, further supporting that these factors are likely important in predicting the renal impairment associated with ZA use in.

Abstracts

Podium Session IV

Development and Application of Methods and Concepts in Statistics for Outcomes Research

MC5

ON EVALUATING COST ASSOCIATED WITH EVENT-CENSORED DATA: APPLICATION TO ALL-CAUSE GRAFT FAILURE FOLLOWING KIDNEY TRANSPLANTATION

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OBJECTIVES: Generation of population cost estimates for event-censored data requires a sophisticated approach to account for probability of incurring the event over time and different patient characteristics. We investigated Medicare costs specifically associated with all-cause graft failure following kidney transplantation. We were particularly interested in developing methods to study cost and see how these methods can inform decision makers. METHODS: A modified two-part econometric approach was used to determine Medicare claims attributable to all-cause graft failure (including deaths). The approach was accomplished in 3 steps: 1) Time was partitioned into discrete intervals whereby intervals were chosen to reflect changes in the relationship between cost and patient characteristics. Within each interval, we established the predictive relationship of the log-transformed costs with relevant factors based on those patients whose graft failed in the interval; 2) Probability of graft failure at the end of each interval was estimated using Cox hazards regression; and 3) Results of steps 1 and 2 were combined mathematically to obtain population-based estimate of cost. Data on adult, primary transplants from cadaveric donors between 1993 and 1998 were obtained from the United States Renal Data System. Covariates modeled included donor and recipient characteristics, and clinical variables including immunosuppression therapies. Costs among different risk groups were compared to evaluate their relative impact. RESULTS: Expected Medicare claims attributed to all-cause graft failure at 3-years post-transplant was highest among patients who experienced acute rejection by 6-months post transplant (AR: $62,749 vs. No AR: $47,787). CONCLUSIONS: For event-censored data, the estimation of cost associated with an event requires a sophisticated approach. The modified two-part model may provide more reliable estimates but the validity of this procedure requires further research. Specific to transplantation, these estimates may provide groundwork for further studies to address the potential cost-effectiveness of various treatments to delay or prevent graft failure.

MC6

PERFORMANCE OF THE DMM SIMULATION MODEL IN PREDICTING REAL WORLD CHANGES IN GLYCEMIC CONTROL FOLLOWING DIAGNOSIS OF DIABETES

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OBJECTIVES: Modeling approaches are used to estimate future consequences and costs of diabetes and its complications, since few studies provide data over a sufficient duration or for all costs, effects and populations. The Diabetes Mellitus Model (DMM) predicts 10-year outcomes for patients with Type 1 (T1DM) and Type 2 (T2DM) diabetes based on published clinical trials; these predictions mirror clinical trial outcomes. We compared the DMM against real world, population-based epidemiological data from the Diabetes Audit and Research in Tayside Scotland (DARTS) database. METHODS: We studied two cohorts of 931 T1DM (46% male) and 12,907 T2DM (53% male) patients, mean (±SD) age at diagnosis 21 (±14) and 61 (±13) years, respectively. Mean A1c for DARTS patients, diagnosed from 1 January 1993 to 31 December 2000, was derived as a function of time since, and age at, diagnosis. Cohorts were simulated using the DMM, and resulting A1c values were compared with DARTS cohorts. Goodness of fit was evaluated by assessing bias, i.e. the underlying difference between DMM and DARTS, and stochastic variation. RESULTS: For patients with T1DM, changes in A1c over time were not predicted well by the DMM; many of the differences between DARTS and DMM predicted A1c values were greater than 0.5% and the maximum bias was 0.9%. For patients with T2DM, the changes were well predicted for all ages and age bands; maximum bias was 0.5%. CONCLUSION: The DMM is successful in predicting real world changes in A1c for T2DM; further work is needed to reproduce real world changes in A1c for T1DM.

MC7

THE PHARMACOGENOMICS BIAS IN DECISION MODELS

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OBJECTIVES: To evaluate the direction and relative magnitude of a pharmacogenomics bias resulting from failure to adjust for genetic heterogeneity in both treatment response (HT) and heterogeneity in progression of disease (HP) in decision models extrapolating beyond short-term trial results. METHODS: We constructed two Markov models with three health states (early-stage, late-stage, dead), one adjusting and the other not adjusting for genetic heterogeneity. We compared life expectancy gains attributable to treatment resulting from both models and defined pharmacogenomics bias as percent deviation of treatment-related life expectancy gains in the unadjusted model (UAM) from those in the adjusted model (AM). We calculated the bias as a function of underlying model parameters to create generic results. We then applied our model to lipid-lowering therapy with pravastatin in patients with coronary atherosclerosis, incorporating the influence of two TaqIB polymorphism variants (B1 and B2) on progression and drug efficacy as reported in the DNA substudy of the REGRESS trial. RESULTS: Our generic simulation showed that a purely HT-related bias is negative (conservative) and a purely HP-related bias is positive (liberal). For many typical scenarios, the absolute bias is smaller than 10%. In case of joint HP and HT, the overall bias is likely triggered by the HP component and reaches positive values >100% if fractions of “fast progressors” and “strong treatment responders” are low. In the pravastatin example, the UAM overestimated the true life years gained (LYG) by 5.5% (1.07 LYG vs. 0.99 LYG for 55-year-old men). CONCLUSIONS: We have been able to predict the pharmacogenomics bias jointly caused by heterogeneity in progression of disease and heterogeneity in treatment response as a function of characteristics of patients, disease, and treatment. In the case of joint presence of both types of heterogeneity, models ignoring this heterogeneity may generate results that overestimate the treatment benefit.