urinary flow rate. Physician’s diagnosis according to their experience, was recorded after each step. A descriptive analysis was conducted and validity and concordance were measured between strategies. RESULTS: A total of 356 patients, mean age (SD) of 65.2 (8.4) years, with suspected BPH participated in the study. Sensitivity, specificity, positive predictive value and negative predictive value were 91%, 65%, 95% and 50%, respectively. Percentage of agreement and kappa index between initial and final diagnosis were 87.9% and 0.5, respectively. CONCLUSIONS: Concordance between initial diagnosis based on medical history, I-PSS questionnaire, DRE and PSA with final diagnosis of BPH was high. This group of diagnostic procedures may be recommended for BPH initial diagnosis in daily practice.

CO2

EARLY GLYCEMIC CONTROL IMPROVES HEALTH AND ECONOMIC BENEFITS IN TYPE 2 DIABETES: A MODEL BASED ANALYSIS

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OBJECTIVES: Despite current diabetes guidelines recommending increasingly stringent HbA1c targets, in the US approximately 60% of subjects are not controlled to target HbA1c < 7%, with a typical 5-year delay. The purpose of this analysis was to evaluate the effect of early achievement of glycemic control on diabetes-related complications and costs.

METHODS: The Archimedes model was used to conduct a simulated clinical trial using patient-specific US NHANES data to determine patient characteristics, current levels of glycemic control and other CAD risk factors in people with diabetes. Subjects with HbA1c > 7% were randomly assigned to four management strategies: status quo (SQ: maintaining current levels of HbA1c but good compliance to guidelines for other CAD risk factors), and reaching mean HbA1c < 7% within 6 months (MO), 12MO, or 24MO. The analysis focused on microvascular outcomes. RESULTS: The model predicted that reducing HbA1c to <7% in currently uncontrolled subjects would reduce the risk of microvascular disease compared with SQ. Reaching HbA1c < 7% within 6MO would reduce the 20-year risks of proteinuria (52%), ESRD (44%, approximately 20,000 US cases prevented p.a.), eye surgery (73%) and blindness (73%, approximately 17,500 cases prevented) compared with SQ. However, compared with reaching HbA1c < 7% within 6MO, delaying to 24MO increases these risks by 15%, 16%, 41% and 47%, respectively, resulting in 3900 and 3000 more cases of ESRD and blindness, respectively. Reaching target within 6MO would save approximately $2.3 billion p.a. compared with SQ. Delaying reaching HbA1c < 7% to 24MO decreases these savings by approximately $430 million. Benefits were greater in patients with mean baseline HbA1c > 9%. CONCLUSIONS: The Archimedes model predicts that in uncontrolled patients, achieving HbA1c < 7% within 6MO would have important effects on microvascular outcomes and costs. Delaying control to 24MO would reduce the amount of benefit gained. Bringing currently uncontrolled people into control is important and should be achieved as rapidly as clinically feasible.

CO3

META-REGRESSION ASSESSMENT OF ATOMOXETINE EFFICACY USING RANDOMIZED CONTROLLED ADHD TRIALS

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OBJECTIVES: Several trials of atomoxetine for the treatment of attention deficit hyperactivity disorder (ADHD) have employed an active comparator arm of methylphenidate (MPH). This study estimated efficacy of atomoxetine and MPH in treating children and adolescent with ADHD using combined patient-level data from multiple trials. METHODS: Five randomized atomoxetine trials contained an active comparator arm of MPH. Pooling of all available data resulted in total 1078 patients, with 562 on atomoxetine, 327 on MPH, and 189 on placebo. Because trials excluded known non-responders to stimulant, stimulant exposed patients may have a bias in favor of MPH. Subgroup analyses were performed by stimulant history. The meta-regression is set up as logistic regression for response. Response was defined as a ≥25% reduction in ADHD Rating Scale. In addition to treatments, patient age, sex, duration of therapy, and trial effects were controlled for. Random effect model was also estimated, but fixed effect was chosen. RESULTS: Response rates for stimulant naive patients were: 70.51% for atomoxetine, 77.27% for MPH, and 41.46% for placebo. Response rate for each active treatment was significant, and significantly different from placebo (p < 0.001). However, the two treatments were not statistically different by difference in means test (p = 0.069). In the exposed group, response rates were: 62.17% for atomoxetine, 70.03% for MPH, and 29.42% for placebo. Response rate for each active treatment was significant, and significantly different from placebo (p < 0.001). Difference between the two treatments, yet again, was not statistically significant (p = 0.214). CONCLUSION: To improve power and precision in the estimate, this study pooled all available patient-level data from five randomized trials, and estimated response rate using the meta-regression method. Efficacy of atomoxetine and MPH were significantly different from placebo. While response rate was higher for MPH, response rates of the two active treatments were not statistically different from each other.

CO4

A COMPARISON OF LOGISTIC REGRESSION AND COX PROPORTIONAL HAZARDS MODELS FOR IDENTIFICATION OF RISK FACTORS FOR RENAL IMPAIRMENT IN HORMONE REFRACTORY PROSTATE CANCER (HRPC) PATIENTS WITH BONE METASTASES (BM) TREATED WITH ZOLEDRONIC ACID (ZA)

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OBJECTIVE: To identify independent risk factors for renal impairment in HRPC patients receiving ZA, we compared logistic regression and Cox proportional hazards models. METHODS: A comprehensive medical record review was performed, using electronic databases and paper records, in a large tertiary oncology center. Inclusion criteria: ≥18 years, actively treated, HRPC with BM, at least one ZA infusion (from 12/1999 to 4/2005), and at least one creatinine reading before and after first ZA infusion. Renal impairment was defined as an increase of ≥0.5mg/dL and ≥1.0mg/dL over baseline serum creatinine if baseline was <1.4mg/dL and ≥1.4mg/dL, respectively; or any doubling of baseline creatinine. Risk factor analysis was by logistic regression with time adjustment, and by Cox model for time-related binary outcome data. RESULTS: Among the 122 eligible patients (mean age = 70.1), mean ZA treatment lasted 367.2 days (mean 10.7 infusions per patient). About 39% of patients discontinued ZA; 21% due to renal complications. Twenty-nine patients (23.8%, 95% CI: 16.2–31.3%) had renal impairment during treatment; this is higher than previously reported in clinical trials. Renal risk increased with extended ZA therapy (<6 months: 22.5%; ≥12 months: 23.5%; ≥24 months: 31.3%) and
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.

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). CCONCLUSIONS: 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 56-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.