TO determine whether results from a diabetes progression model were bol (it is noteworthy) that the diabetes progression model used the electronic medical records of UK patients with suspected diabetes. METHODS: A data driven simulation was conducted using an existing stochastic model of diabetes progression. The model uses UKPDS equations to calculate annual transition probabilities to death and in five health dimensions (neuropathy, nephropathy, retinopathy, CHD, and stroke). Although equations in multiple dimensions may include the same factors (e.g., blood pressure, A1c), transitions in the various dimensions are calculated independently. The database consists of over 100 million encounters, patient or therapy records for 183,119 patients with suspected diabetes between 1982 and 2005. Initial validation was attempted by creating a cohort of patients from the database for whom gender, birth year, diagnosis date, A1c, and blood pressure were all available. Any diagnosis in the five health dimensions, prior to the diabetes diagnosis, was noted to assign non-zero levels to the simulated patients’ starting state. After initial poor fit, more rigorous cleaning was done, the time frame was limited, and A1c was imputed from blood glucose values when possible. RESULTS: Although the fit was adequate for most events in the health dimensions, the model predicted far more deaths than occurred in the cohort from the database. Compared to patients without A1c measurements in the database, those with A1c had 0.4 relative risk of death. The median birth year was eight years later for those with an A1c test. Moreover, the proportion of patients with an A1c was <6% through 1992, from 11% to 26% from 1993 to 1999, and 65% in 2001, and exceeding 90% the last two years. CONCLUSIONS: There are strong temporal interactions between year of birth diagnosis and A1c testing rate. Models should consider ISPOR task force reports on retrospective databases before assembling cohorts from longitudinal databases.

**CONCEPTUAL PAPERS & RESEARCH ON METHODS - Modeling Methods**

**PMc3**

**IMPACT OF IGNORING CORRELATION BETWEEN INPUT PARAMETERS ON VARIANCE OF COST-UTILITY RATIOS**

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Probabilistic sensitivity analysis in cost-utility (CU) study often makes draws from distributions of model input parameters assuming independence. It was pointed out (O’Brien et al, 1994) that correlation between cost and effectiveness measures affects variance of cost-effectiveness ratios. OBJECTIVES: This research shows variance of CU ratio may similarly be under or overestimated with potential correlation ignored. METHODS: The delta method was used to approximate variance of CU ratio. CU ratio was calculated as (Et – Ec)/(Et + Sc), where Et and Ec were effectiveness (utility) and cost for treatment (control) respectively. The sensitivity analysis involved changing parameters to examine the effects of correlation. RESULTS: Correlation between effectiveness and cost parameters, if of the same sign as (EtEc)/(EtSc), increases variance of CU ratio, and vice versa. It can be shown that under certain conditions, (EtEc)/(EtSc) is positive, and thus with positive correlation between effectiveness and cost (meaning better effectiveness associated with worse safety), variance of CU ratio would be underestimated if zero correlation is assumed. CONCLUSIONS: In CU analysis, especially those based on trial data, correlation between estimated parameters can impact uncertainty estimates around CU ratios.

**PMc4**

**TOO MUCH ADO ABOUT INSTRUMENTAL VARIABLE APPROACH: IS THE CURE WORSE THAN THE DISEASE?**

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OBJECTIVES: To review the efficacy of instrumental variable models in addressing a variety of assumption violations to ensure standard ordinary least squares estimates are robust. Instrumental variables may be used to minimize endogeneity in outcomes, because of their ability to consistently estimate the average causal effects even in the presence of unmeasured confounding. However, in order for this consistent estimation to be achieved several conditions must hold. In this paper, we provide an overview of the instrumental variable approach, examine possible tests to check the prerequisite conditions, and illustrate how weak instruments may produce inconsistent and inefficient results. METHODS: We use two instrumental variable models and apply Shea’s partial R-squared method, the Anderson canonical correlation, and Cragg-Donald tests to check for weak instruments. Hall-Pena tests are applied to see if any of these instruments are redundant in the analysis. RESULTS: Total 15,956 asthma patients from a private payer data set were examined in this study. We used controller-releaver copia ratio and physician/practice prescribing patterns as an instrument. We demonstrated that the former was a weak and redundant instrument producing inconsistent and inefficient estimates of the form of the effect of treatment. The results were worse than the results from standard regression analysis. CONCLUSIONS: Despite the obvious benefit of instrumental variable models, the method should not be used blindly. Several strong conditions are required for these models to work, and each of them should be tested. Otherwise, the results will be statistically worse than the results achieved by simply using standard ordinary least squares.