ing will drive up the quality and efficiency of pharmacoepidemiological database studies.

PRM51
APPLICATION OF SURVIVAL ANALYSIS TO ADULT PNEUMOCOCCAL VACCINATION RATE IN THE UNITED STATES
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**OBJECTIVES:** Using observational databases to calculate vaccination rate is challenging because of limited continuous enrollment and loss to follow-up. The objective of this study was to apply the concept of survival analysis in estimating rate of pneumococcal vaccination among adults with the high-risk medical conditions included in the ACIP (Advisory Committee on Immunization Practices) recommendations. **METHODS:** This was a retrospective cohort study using a large administrative claims database. The study cohort was 19-64 years old adults with newly diagnosed high-risk conditions (HIV/AIDS, diabetes, asplenia, chronic lung disease, chronic renal disease, chronic heart disease, organ transplant, cochlear implant, cancer, chronic liver disease and alcoholism) during 2007 to 2010 and had at least three years of continuous enrollment. Subjects were followed from the initial diagnosis date to the end of enrollment or 2011. Cox proportional hazard model was used to analyze the association of high-risk medical conditions with pneumococcal vaccination after controlling potential confounders. Survival curves were estimated from the Cox model. **RESULTS:** A total of 946,898 eligible subjects were followed for a total of 2,358,563 person-years, of which, 71,298 subjects received pneumococcal vaccine. The overall pneumococcal vaccination rate was 3.023/100 person years (95%CI=3.001, 3.045). Pneumococcal vaccination rate was the highest in HIV/AIDS patients (16.499/100 person years, 95%CI=(15.374,17.683)) followed by diabetes patients (4.520/100 person years, 95%CI=(4.466,4.574)) and was the lowest in alcoholism patients (1.042/100 person years, 95%CI=(0.953,1.137)). After controlling potential confounders, high-risk conditions had a significant association with pneumococcal vaccination. Compared to patients with alcoholism, HIV/AIDS patients were 11 times more likely to receive pneumococcal vaccination (HR=11.964, 95%CI=(10.696,13.382), p<0.0001). **CONCLUSIONS:** Pneumococcal vaccination rate was more accurately analyzed by applying survival analysis because a larger and more representative sample was constructed and loss to follow-up was taken into account. Study suggests pneumococcal vaccination rate was low in adults with newly diagnosed high-risk conditions.

PRM52
FROM PRIVATE SITES TO BIG DATA WITHOUT COMPROMISING PRIVACY: A CASE OF NEUROIMAGING DATA CLASSIFICATION
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**OBJECTIVES:** Open data sharing for large-scale studies is an expensive and resource-wasteful approach that does not scale well with participating sites. Critically, some data simply cannot be shared due to privacy concerns and/or risk of re-identification. We pursue distributed computation that only shares data derivatives, such as statistical summaries, as a notable alternative allowing data holders to maintain control over data access. Privacy protection, if implemented via the *differential privacy* framework, can quantify and controllably reduce the risk of sharing the results of computations on private data. Unfortunately, it can impair the quality of statistical estimates at a single site. Using structural MRI data we present a distributed differentially private classifier that greatly improves the accuracy. **METHODS:** We used a combined MRI dataset from four separate schizophrenia studies conducted at Johns Hopkins University (JHU), the Maryland Psychiatric Research Center (MPRC), the Institute of Psychiatry, London, UK (IOP), and the Western Psychiatric Institute and Clinic at the University of Pittsburgh (WPIC). The sample comprised 198 schizophrenia patients and 191 matched healthy controls. We trained differentially private classifiers on these data using a method that minimizes a perturbed version of the SVM classifier. The outputs of these classifiers were used to train a logistic regression classifier. A combined SMVs plus logistic regression classifier was tested for accuracy. **RESULTS:** Using 100 random splits of data into 70% training and 30% validation groups followed by splitting the training set into 11 sites of 24/25 subjects each, we assessed classification accuracy at each site and of combination per split. Average site-accuracy was below 78%, while our combined classifier averaged to 96%: substantial and significant improvement with Bonferroni-corrected p-values below 1.8e-33. **CONCLUSIONS:** Our approach provides a way to enable use of distributed big data while still providing privacy and thus a much larger effective sample size.

## RESEARCH ON METHODS – Modeling Methods

PRM53
THE IMPACT OF ALTERNATIVE ESTIMATES OF DISUTILITIES ASSOCIATED WITH HYPOGLYCEMIA ON NET QALYS: CANAGLIFLOZIN VERSUS SITAGLIPTIN AS ADD-ON THERAPY IN INDIVIDUALS WITH TYPE 2 DIABETES MELLITUS (T2DM) INADEQUATELY CONTROLLED ON A BACKGROUND OF METFORMIN (MET) PLUS SULFONYLUREA (SU) IN THE CANADIAN SETTING
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**OBJECTIVES:** Differences in the frequency and severity of hypoglycemic episodes associated with alternative treatments often contribute significantly to differences in QALYs (the denominator of the cost-effectiveness ratio). The 2013 T2DM CADTH report examining third-line therapy used disutility values from studies conducted before 2009 based on small samples. A new study with over 1,600 individuals with T2DM (including Canadian respondents) found disutility estimates that were meaningfully greater (e.g. 0.005 versus 0.000004767 per non-severe hypoglycemic event). This analysis examined the impact of these alternative estimates on QALYs in an evaluation of canagliflozin 300mg versus sitagliptin 100mg in patients inadequately controlled on MET+SU. **METHODS:** Two 40-year simulations were performed using a validated economic model (ECHO-T2DM), differing only in the hypoglycemia disutility weights: (A) CADTH and (B) new estimates. Disutilities for T2DM-related complications and other adverse events were sourced from the literature. Data for patient characteristics, treatment effects (i.e. A1C, SBP, BMI, and cholesterol), and rates of adverse events were obtained from a previously reported 52-week trial, where canagliflozin 300mg demonstrated statistically superior A1C-lowering, as well as reductions in blood pressure and weight versus sitagliptin 100mg. Hypoglycemic event rates were similar. In the simulations, insulin (which has an excess risk of hypoglycemia) was added and titrated as necessary to maintain A1C < 7.0%. **RESULTS:** Discounted QALYs for canagliflozin and sitagliptin were (A) 8.4 and 8.32; (B) 7.91 and 7.81. The higher QALYs associated with canagliflozin versus sitagliptin are largely attributable to the delay in the need for insulin for canagliflozin-treated patients. The contribution of hypoglycemic events to these total QALY differences was greater in scenario B (20.8%) than scenario A (2.3%). **CONCLUSIONS:** These results illustrate the need to carefully consider downstream assumptions in economic evaluations. Using the older values yielded 20% fewer net QALYs, implying that the corresponding ICER would be approximately 25% greater.

PRM54
RISK HETEROGENEITY IN CLINICAL TRIALS: AN EVALUATION OF 25 LARGE CLINICAL TRIALS USING INDIVIDUAL PATIENT DATA
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**OBJECTIVES:** Risk of the outcome is a mathematical determinant of the absolute treatment benefit of an intervention. While substantial risk heterogeneity can lead to clinically important differences in treatment effect, the degree to which risk varies within randomized clinical trials (RCTs) is largely unknown. **METHODS:** We selected all RCTs that had greater than ~1000 enrollees and clinical outcomes from several sources (NHLBI, NIDDK, Trials journal). We derived Cox or logistic regression models using established risk factors blinded to treatment assignment. Risk heterogeneity was evaluated using the extreme quartile risk ratio (EQRR, the ratio of outcome rates in the lowest risk quartile to that in the highest). Skewness was evaluated with median to mean risk ratio (MMRR, the ratio of risk in the median risk patient to the average). **RESULTS:** We describe the distributions of 34 unique risk analyses from 25 heterogeneous large trials. Overall event rates across studies ranged from 3% to 63% (median=15%, interquartile range [IQR] 10% to 23%). The number of established risk factors included in each risk model ranged from 4 to 32 (median=9, IQR 7 to 11); events per variable ranged from 13 to 1515 (median=46, IQR 32 to 66). Models had estimated C-statistics of 0.58 to 0.81 (median 0.69, IQR 0.65 to 0.73). EQRR ranged from 1.8 to 21.6 (median=4.1, IQR 3.0 to 5.5). The MMRR ranged from 0.5 to 1.0 (median=0.87, IQR 0.80 to 0.89). The model C-statistic and the outcome rate of the trial determined the EQRR (r-squared=0.87) and the MMRR (r-square=0.81). **CONCLUSIONS:** Clinically significant risk heterogeneity is common even in phase 3 "efficacy" trials. The typical patient is generally at lower risk than reflected by the trial summary results. A risk stratified approach to trial analysis is feasible and may be most clinically informative where the outcome is predictable and uncommon.

PRM55
DEALING WITH COMPETING RISKS IN DIABETES MELLITUS: COMPARISON OF RESULTS USING A MARKOV VERSUS A MICRO-MARKOV SIMULATION MODEL
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**OBJECTIVES:** To present an efficient new methodology to calculate cost and effects of alternative interventions for Diabetes Mellitus (DM), and to validate this approach by comparing cost-effectiveness results when identical interventions for DM are simulated by this Markov model (DELTA) or by a well-known Micro-Markov model (CARDIFF). **METHODS:** The Markov model (DELTA) deals with multiple competing events; complications are modeled as individual Markov chains. By creating a dynamic link between the life table and the subdiseases, any change in the individual Markov chains is propagated throughout the entire model. Advantage of this approach is a considerable decrease in computational time. In order to test the validity of the DELTA model and its applicability in modeling interventions and treatment sequences in T2DM, cost-effectiveness results were compared with published outcomes predicted by the CARDIFF model. Similar treatment sequences were applied as well as identical key data sources for predicting the occurrence of diabetes related events (equations UKPDS Outcomes model), quality of life effects attached to BMI changes and hypoglycemia, and inputs related to drug- and health care costs. **RESULTS:** Incremental life-years gained (LYG), discounted incremental costs, incremental QALYs and ICUR in the Cardiff and DELTA models are 0.050 LYG, £1,246, 0.467 QALY, £2,671/QALY, and 0.031 LYG, £1,021, 0.555 QALY, £1,841/QALY, respectively. Differences between model outcomes may be explained by the underlying independency assumptions of the DELTA model. **CONCLUSIONS:** The point estimates obtained by both models using similar scenarios seem to resonate quite well. However, further research is needed to substantiate the observed differences in outcomes. Additional insight can be provided by comparing the confidence intervals around the estimates, which will be incorporated shortly. It seems the DELTA approach offers a flexible way to model multiple diseases simultaneously. The loss of subtlety and necessary assumptions may outweigh the gains in clarity and computational speed.

PRM56
OPTIMAL INFORMATION ACQUISITION POLICIES: APPLICATION TO HEPATITIS C SCREENING
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