**OBJECTIVES:** Updated risk equations are available for predicting outcome in people with type 2 diabetes (T2D): the UKPDS Outcomes Model (UKPDS 68). It is important to assess the validity of applying risk equations to populations other than those from which they were derived. The objective was to evaluate how well the UKPDS-68 equations predicted vascular morbidity and mortality in real-life data from Cardiff, UK, and compare estimates with the previous UKPDS Risk Engine equations (UKPDS-RE [from UKPDS publications 56 and 60]). **METHODS:** The equations were incorporated into a stochastic simulation model that estimated the incidence and prevalence of complications (DiabForecaster). Predicted results from the model were compared with population data from Cardiff for coronary heart disease (CHD), stroke and all cause mortality. The annual incidence of newly diagnosed T2D, baseline modifiable risk factors and demographic profiles were matched to the Cardiff data. **RESULTS:** Internal validation, using a baseline cohort matched to the UKPDS study, demonstrated that the model predicted 12-year cumulative incidence in line with previous UKPDS publications. Real life and predicted event rates for CHD were: 116, 153 and 137 events/1000 T2D patients/yr for the Cardiff data, UKPDS-RE and UKPDS-68, respectively. For stroke: 178, 153 and 128 events/1000 T2D patients/yr, respectively. For all cause mortality: 418, 430, and 475 events/1000 T2D patients/yr, respectively. **CONCLUSIONS:** All UKPDS equations demonstrated internal validity when compared with published UKPDS data, however both UKPDS-RE and UKPDS-68 equations over predicted the incidence of CHD and mortality and under predicted stroke. While all endpoints predicted were reasonably concordant with observational data discrepancies between UKPDS-68 and UKPDS-RE are worthy of further investigation.

**PDB24**

### EFFECTS OF INDUCING CORRELATION AMONG CHOLESTEROL PARAMETERS ON OUTCOMES IN SIMULATION OF PHARMACEUTICAL EFFECTIVENESS

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**OBJECTIVES:** To determine whether inducing correlation among triglyceride, HDL, and LDL levels in a pharmaceutical treatment Monte Carlo simulation affects parameters' means and variances; proportion with all parameters controlled; and summary statistics of estimated total cholesterol. **METHODS:** Means, standard deviations, and correlations among the cholesterol parameters were estimated from NHANES data for metabolic syndrome (MS) and diabetic patients with all parameters uncontrolled. For simulation, distributions were fit to the data. Analyses used 1000 replications of populations of 1000. Populations were generated without correlated parameters and with correlation induced in the uncorrelated data. Estimated changes with fenofibrate, statins, and a combination were taken from the literature. Total cholesterol was approximated using HDL, plus LDL, plus 20% of triglycerides. Differences in means and ratios of variances comparing uncorrelated and correlated results were calculated for each replication. Null hypotheses were rejected when the interval the middle 95% of replications spanned did not include zero for differences and one for ratios. **RESULTS:** Correlations were higher for diabetic than MS patients. Despite the data's and distribution's non-normality, induced correlations were close to NHANES correlations. Correlation did not affect the summary statistics of individual parameters or the propor-

tion with all parameters under control. Correlation affected results for total cholesterol, the sum of other parameters. For MS, variance of total cholesterol was less than 7% lower with uncorrelated data than with correlated data. For diabetic patients, variance of total cholesterol was more than 20% higher with uncorrelated data. Findings held for subpopulations with and without all parameters controlled after taking medication. Variance results were similar across treatments. Total cholesterol means differed primarily for MS subgroups. **CONCLUSIONS:** Summary statistics (particularly variance) for sums of parameters are affected by correlation in Monte Carlo simulations. Underestimated and overestimated variances increase the risk of Type I and II error respectively.

**PDB25**

### MARGINAL STRUCTURAL MODELS—AN EXPLANATION AND ILLUSTRATION

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**OBJECTIVES:** 1) Provide a concise explanation of "inverse probability of treatment weights" (IPTWs) for estimating marginal structural models (MSM), pointing out its advantages and disadvantages to alternative methods of adjusting for covariates in observational studies, and 2) illustrate use of MSM for comparing impact of drug use on medical costs. **METHODS:** Confounding can be controlled by stratification or with covariates in regression. When there are many confounders adjustment using propensity scores is sometimes used but these are 1) not easily generalized with more than two comparison groups, and 2) may result in residual confounding when matching is used, and is not helpful with time dependent covariates affected by the exposures being compared. An alternative is based on modeling the "marginal" distribution of counterfactuals associated with each group (as described by Robins, Hernan, and Brumback [2000]). This is accomplished using weights related to propensity scores. A MSM will be illustrated by comparing outpatient medical costs for patients taking diabetic drug treatments, adjusting for both baseline and subsequent time dependent diagnoses and lab data. A multinomial logit model is used to estimate each subject's conditional probability of receiving TZD, sulfonylurea, or metformin given their history of baseline and time dependent covariates. **RESULTS:** These predicted probabilities are basis for IPTWs used to estimate mean marginal outpatient costs for each drug group. **CONCLUSIONS:** Effects of confounders are broken when their associations with drug treatment groups are broken, and this can be done using MSM where the data is reweighted such that confounders have similar distributions within drug comparison groups.

**PDB26**

### ANTIPSYCHOTIC UTILIZATION AND TREATMENT-EMERGENT DIABETES—A METHODOLOGICAL COMPARISON USING A CLAIMS DATABASE

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**OBJECTIVE:** To evaluate the robustness of the relationship between antipsychotic utilization and treatment-emergent diabetes among patients newly initiated on therapy, when methodologies were varied while controlling for covariates. **METHODS:** Seven models were created based on the following methodological variations: 1) study designs (retrospective cohort and case-control); 2) treatment exposure assignment (intent-to-treat (ITT) and as-treated (AT)); and 3) statistical approaches

(propensity scoring, standard and conditional logistic regression, and Cox proportional hazards function). Control variables included: demographics (age, gender, race, and region), general health comorbidities (hypertension and dyslipidemia), mental health comorbidities (bipolar disorder, depression, post-traumatic stress disorder, schizophrenia, and substance abuse), antipsychotic drug utilization patterns (monotherapy, switching, and combination therapy), treatment duration, medication re-exposure, and treatment initiation year. Claims databases from the Veterans Administration North Texas Health Care System and the South Texas Veterans Health Care System (1995–2004) were used. **RESULTS:** Of the eligible patients (N = 8949), regardless of variations in methodologies of the seven models, there were no significant differences in diabetes risk among patients who were: 1) initiated on the second generation antipsychotics (SGAs) compared to those on the first generation antipsychotics (FGAs); 2) initiated on olanzapine compared to those on risperidone; and 3) exposed to olanzapine or quetiapine compared to those exposed to FGAs. Inconsistent results among the models were observed when comparisons were made between: 1) patients initiated on quetiapine (increased risk vs. no difference) compared to those on risperidone, and 2) patients exposed to risperidone (decreased risk vs. no difference) compared to those exposed to FGAs. Differences occurred among the following. **METHODS:** ITT retrospective cohort and ITT case-control; and AT retrospective cohort and AT case-control. **CONCLUSIONS:** With respect to antipsychotic utilization, results of the various models using different methodologies were largely consistent. Advantages and disadvantages of the seven models will be presented.

**ANTIPSYCHOTIC UTILIZATION AND TREATMENT-EMERGENT DIABETES—COMPARISON OF RESULTS WITH AND WITHOUT PROPENSITY SCORING**

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**OBJECTIVE:** To examine whether the relationship between antipsychotic utilization and treatment-emergent diabetes among patients newly initiated on therapy varied, when propensity scoring was (Model I) and was not (Model II) used. **METHODS:** Claims databases from the Veterans Administration North Texas Health Care System and the South Texas Veterans Health Care System (1995–2004) were used. Both Models I and II utilized a retrospective cohort design and an intent-to-treat method to assign treatment exposure. Covariates included demographics (age, gender, race, and region), general health comorbidities (hypertension and dyslipidemia), mental health comorbidities (bipolar disorder, depression, post-traumatic stress disorder, schizophrenia, and substance abuse), antipsychotic drug utilization patterns (monotherapy, switching and combination therapy), treatment duration, medication re-exposure, and treatment initiation year. Logistic regression was used to analyze data. **RESULTS:** Eligible patients (N = 8949) had a 6.0% annual diabetes incidence rate. No significant difference was found in diabetes risk between patients treated with the first generation antipsychotics (FGAs) and the generation antipsychotics (SGAs). Findings were consistent among most covariates. In both models, when compared to monotherapy, antipsychotic combination therapy increased diabetes risk, while switching did not. Antipsychotic re-exposure, early treatment initiation years, and a shorter treatment duration were associated with an increased diabetes risk. Results varied with the following two variables: nonwhites

were associated with an increased risk in Model I, while there was no association in Model II; depression was associated with an increased risk in Model II, while there was no association in Model I. All other variables were not significant and were consistent between the two models. **CONCLUSIONS:** SGAs were not associated with an increased diabetes risk when compared to FGAs. Including propensity scoring in a retrospective cohort design may alter the results of some covariates; however, it did not change the results regarding the class of antipsychotics utilized and risk of diabetes mellitus.

**DEVELOPMENT OF NEW INDICES OF GLYCEMIC CONTROL IN PATIENTS WITH DIABETES USING DIGITAL SIGNAL PROCESSING**

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**OBJECTIVES:** The objective is to examine the performance of a variety of filters used in digital signal processing and evaluate the filter coefficients as potential indices of glycemic control. Digital signal processing has played an extensive role in separating signal from noise in biological signals for decades. Cascaded adaptive filters, high pass filters, Kalman filters as well as discrete Fourier transforms have been used to produce clean signals and obtain the frequency spectrum for ECG signals. With the rapid advances in Continuous Glucose Monitoring (CGM) sensors, a nearly continuous stream of glucose levels is made available with wavelike postprandial excursions. Extraction of key information beyond descriptive statistics from the mass of glucose data has been illusive. This is no clean classification as in the case of cardiac arrhythmias. Little prior work in the medical literature exists except a Kalman filter simulation using a sinusoidal function to represent a postprandial excursion (Palerm, 2005), and a brief note by Knobbe (2005) discussing Kalman filters in CGM. **METHODS:** The mathematical form of each filter is presented along with identification of associated formulas for each of their filter coefficients, a table of characteristic filter coefficients, coefficient ranges, stability and evidence of substantive interpretability. Archetype postprandial excursions are represented by truncated Taylor series. **RESULTS:** Characteristics compared include: stability of filter coefficient under trivial curve variation representing the post-prandial excursion waveform, range of values, sensitivity to substantial variation in the waveform, usefulness in combination with other statistics and sensitivity and specificity in predicting hypoglycemic events. **CONCLUSIONS:** Several signal processing filters appear to be effective for extraction of information from CGM series, and some of these appear promising as a basis for new indices of glycemic control and for classification of patients and effects of medications such as rapidly acting insulin analogs that blunt the post-prandial excursions.

**DIABETES—Patient Reported Outcomes**

**IMPACT OF TYPE OF PHARMACY (CHAIN VERSUS INDEPENDENT) ON MEDICATION ADHERENCE IN PATIENTS WITH TYPE 2 DIABETES: A RETROSPECTIVE DATABASE ANALYSIS**

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**OBJECTIVE:** Studies have indicated that independent pharmacies outperform chain pharmacies in one-on-one personal attention and quality of patient counseling. However, there are no studies examining whether these benefits translate into outcomes