

regression analyses were conducted to compare the time to first antipsychotic drug dispensing between the rivastigmine and donepezil groups. **RESULTS:** A total of 532 patients receiving rivastigmine and 7,264 patients receiving donepezil were studied. The donepezil group was slightly older (81.1 vs. 79.9 years;  $p = 0.0044$ ) with a greater proportion of women (59.4% vs. 53.2%;  $p = 0.0053$ ). The Kaplan-Meier analysis showed that 30 (5.6%) rivastigmine and 589 (8.1%) donepezil patients received antipsychotic medications (Log-rank  $p = 0.0672$ ). Multivariate adjustment showed that rivastigmine was associated with a statistically significant reduction in emergent use of antipsychotic drugs by 34% relative to donepezil (hazard ratio: 0.66; 95% CI: 0.46–0.96;  $p = 0.0305$ ). Among other statistically significant covariates, older age, lower drug dose, baseline depression and neuropsychiatric symptoms, and admission to inpatient long-term care facilities were associated with an increased likelihood of antipsychotic drug use. **CONCLUSIONS:** Based on real-world data from a large cohort of antipsychotic-naïve patients with AD, rivastigmine was found to be associated with a significant reduction in the emergent use of antipsychotic drugs, compared to donepezil. Prospective studies are needed to verify these findings.

PND38

#### EMPIRICAL CLASSIFICATION OF EPILEPSY TYPES IN INSURANCE CLAIMS DATA

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**OBJECTIVES:** We have initiated a project to identify statistically independent dimensions of health services utilization in epilepsy. A desirable covariate for this analysis is the type of convulsive disorder. Here we report on the classification of epilepsy patients using insurance data. **METHODS:** We applied an iterative classification technique to patients' sequences of insurance claims for outpatient and inpatient services, diagnostic procedures and drugs. The target population included 122,850 US commercial insurance and Medicare supplement subscribers with a physician visit diagnosis of ICD-9 345xx. We classified persons into the ICD-9 coding scheme (or as "not epilepsy") by developing a family of rules corresponding to empirically observed claims patterns. We sampled patient histories in blocks of 50. Within each claims history, a neuroepidemiologist looked for diagnosis, procedure and treatment patterns that pointed to a clinical diagnosis, and added that pattern to the rule defining a diagnostic type. Removing classified patients, we sampled remaining claims histories and repeated the process of classification and removal and sampling until 50 claims histories suggested no new classification rules. Remaining patients were tagged as unclassifiable. Finally, we reviewed samples of the classified patients to identify disqualification criteria. **RESULTS:** The majority of patients are classifiable and the empirical classification rules "make sense" clinically (e.g. diagnostic changes are permitted immediately if they follow a diagnostic procedure). A significant minority of cases of epilepsy have only nonspecific treatment codes assigned. **CONCLUSIONS:** There are clear examples of patients with different clinical subtypes of epilepsy in claims data, and it will be possible to derive average utilization characteristics and drivers for different types of epilepsy. Analysis of the dimensions of health care utilization (combinations of drugs, procedures, physician and hospital) may yield further insight into currently unclassifiable cases and will provide sensitive measures of the cost impact of new therapies.

PND39

#### ECONOMIC IMPACT OF GENERIC ENTRY OF TOPIRAMATE IN THE G4 EUROPEAN COUNTRIES

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**OBJECTIVES:** Generic substitution might produce economic impacts beyond the reduction in spending for new generic product, such as increased number of users, and utilization of health care resources. The current study forecasts the economic impact of generic entry of the antiepileptic drug (AED) topiramate into the settings of France, Germany, Italy, and the UK. **METHODS:** Health claims from Québec's provincial health plan (RAMQ) from January 2006 to September 2008, and IMS Health data on European AED sales between 1998 and 2008 were used. Patient-level health care utilization and costs in Canada were calculated during mutually-exclusive periods of brand versus generic use of topiramate (Topamax®). Annualized Canadian health care costs were projected for periods of branded and generic use in each country (€2007/person-year). Using market-level sales, branded and generic topiramate utilization were forecasted for 12 months following expected generic entry (September 2009–September 2010) using autoregressive and panel-data regression models. The economic impact of generic entry was projected for each country, stratified into its effect on market size, topiramate costs, and other health care costs. Budgetary consequences for individual, private, and government payers were assessed. **RESULTS:** Projected per-patient health care costs in G4 European countries, excluding topiramate, would be significantly higher during generic-use periods (adjusted cost differences per person-year: €706 to €815,  $p < 0.001$  for all comparisons) compared to brand-use periods. Assuming mandatory generic substitution for all patients, predicted system-wide increases in total adjusted health care costs would range from 3.5% (UK) to 24.4% (France) 1 year after generic entry. Increases in non-topiramate health care costs (+13.7% to +18.1%) would more than offset savings in topiramate costs (–6.3% to –13.8%) in France, Italy, and the UK. These impacts would be evenly distributed among payers of each country. **CONCLUSIONS:** Generic entry of topiramate in

Europe would represent a trade-off between reduced generic drug expenditures and increased health care costs.

PND40

#### EXPLORING THE IMPACT OF DISPENSING CHANNEL ON MEDICATION ADHERENCE AMONG MULTIPLE SCLEROSIS PATIENTS

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**OBJECTIVES:** To determine if dispensing channel (specialty pharmacy versus retail) impacts medication adherence for patients receiving therapy for Multiple Sclerosis (MS). **METHODS:** Retrospective pharmacy claims for MS patients were extracted for 2007–2008. Patients were followed for 12 months from the index claim. Adherence was measured using a Medication possession ratio (MPR), with patients considered adherent if  $MPR \geq 80\%$ . Propensity scoring was used in the sample selection. Differences of demographics were evaluated using the Wilcoxon signed-rank test for continuous variable and the chi-square test for the categorical variable. Generalize linear regression was used to calculate the adjusted mean adherence. **RESULTS:** From a study population of 31,593 MS patients, a matched sample of 19,742 was chosen (9,871 in the specialty and retail channel). There were no differences in demographics between the samples, with 76.19% female and mean age of 48.84. Overall comparison showed an average MPR of 89.94% for specialty and 84.08% for retail; with 81.52% of specialty patients adherent ( $MPR > 80\%$ ) vs. 71.18% of retail patients. The results were similar for each individual MS therapy. The following list the drug, and the percent of specialty and retail patients at least 80% adherent: Interferon beta-1a (Avonex) 87.49% vs. 78.13%, interferon beta-1a (Rebif) 80.97% vs. 75.50%, interferon beta-1b 79.16% vs. 66.48%, glatiramer acetate 78.26% vs. 63.81%. (Average MPRs for each drug available on the poster.) All comparisons were statistically significant ( $P < .05$ ). **CONCLUSIONS:** Patients who receive their MS medication from a specialty pharmacy are much more likely to be adherent than those who receive medication from a retail pharmacy. This is true across the broad category, as well as each individual therapy. Specialty pharmacy offers enhanced patient counseling and clinical services, which may explain differences in adherence. Follow up studies will explore the impact of improved adherence on clinical and economic outcomes.

PND41

#### DETECTION OF PROGRESSIVE MULTIFOCAL LEUKOENCEPHALOPATHY REPORTS ASSOCIATED WITH NATALIZUMAB PRE- AND POST-RISK MINIMIZATION ACTION PLAN FROM ADVERSE EVENT REPORTING SYSTEM DATABASE

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**OBJECTIVES:** To review postmarketing surveillance data in order to examine reports of progressive multifocal leukoencephalopathy (PML) in patients using natalizumab for multiple sclerosis (MS) before and after the implementation of a natalizumab Risk Minimization Action Plan (RiskMAP) in the United States (US). **METHODS:** The Adverse Event Reporting System (AERS) database was searched for reports of serious adverse events of PML associated with natalizumab in MS patients during the pre-(November 23, 2004–February 28, 2005) and post-RiskMAP (July 2006–June 2008) periods. AERS reports listing, 1) Tysabri or natalizumab as primary suspect drug; 2) events of PML; and 3) natalizumab-PML combination reports were extracted. Duplicate reports and drug redundancies were excluded; in the event of duplicate case reports, the report with the most recent date was used. Reports from foreign countries were excluded to focus the analysis on US-related events and to exclude variations due to different governmental requirements and national post-marketing surveillance systems. **RESULTS:** A total of 576,072 unduplicated reports were identified during the post-RiskMAP period in the US. A hands-on review of the reports of PML and tysabri/natalizumab identified 41 and 1221 unduplicated US reports respectively, during the post-RiskMAP period. There were two confirmed cases (from previous literature) of PML associated with natalizumab before RiskMAP implementation and eight reported cases following RiskMAP implementation. The mean age of reported natalizumab-PML cases post-RiskMAP was 50.6 years, and 7 of the cases (87.5%) were in females. **CONCLUSIONS:** The extracted reports from the AERS indicate continuing case reports for PML associated with natalizumab for MS during the post-RiskMAP period. Although AERS is incapable of detecting the true frequency of an adverse event associated with a drug or assessing the actual causal relationship, these reports of natalizumab-associated PML indicate that continued surveillance and further epidemiologic study is necessary.

PND42

#### BRAZILIAN NATIONAL GUIDELINE FOR MULTIPLE SCLEROSIS (MS): AN EXPLORATORY STUDY ABOUT THE IMPACT OF THE PATIENT'S ADHERENCE IN THE TREATMENT COSTS

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**OBJECTIVES:** To evaluate the impact of the patient's adherence to national guideline in the treatment costs. **METHODS:** A one-year (January 2007 to December 2007) retrospective database search was conducted to identify medication used, costs, patient adherence and provision. The source of data was the Ministry of Health public available database, called DATASUS. The study were conducted in four steps: 1) Determine the medicines codes in the public list; 2) Establish the relationships among drugs and

patients usage; 3) Analyze adherence pattern at country level, based on medication consumption; and 4) Estimate the impact of adherence in the treatment costs. **RESULTS:** Medication for MS was responsible by 12.9% of high cost medication supplied by Public Sector in Brazil. During the period of analysis an average of 34.4% of patients adhere to treatment from 10 to 12 months. Patients treated were distributed among therapeutics alternative as follow: 60.66% to interferon-1a (two brands), 20.5% to interferon-1b and 18.85 to glatiramer acetate. It was possible to detect an increase in drugs association. We found the following adherence per treatment: 36.9% to glatiramer acetate, 33.67% to interferon-1a (two brands) and 32.3% to interferon-1b. Due to these levels of adherence the annual costs per patient treated was USD 27,824 to glatiramer acetate, US\$42,151 to interferon-1a (two brands) and US\$34,038 to interferon-1b. Total treatment costs was higher than USD92 millions per year (R\$2.5 / USD1.0), the distribution of costs begins to diverge from patients distribution due to combination therapy. **CONCLUSIONS:** National guidelines standardize care, but the analysis of treatment patterns points to low treatment adherence. Due to actual levels of adherence the costs per patient treated was three times higher than the expected. Actions taken to change these levels will have a considerable impact to reduce the cost per patient treated.

#### URINARY/KIDNEY DISORDERS – Clinical Outcomes Studies

##### CHARACTERIZATION OF IMMUNOSUPPRESSIVE MEDICATION USE IN KIDNEY TRANSPLANTATIONS IN ACADEMIC MEDICAL CENTERS

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**OBJECTIVES:** The objective of the study was to characterize variance in the utilization of immunosuppressant agents among kidney transplant patients across academic medical centers (AMC), and to illustrate potential differences in clinical and economic outcome measures. **METHODS:** A retrospective database analysis, representing 48 AMCs participating in the University HealthSystem Consortium's (UHC) Clinical Resource Manager (CRM), was conducted on inpatients discharged between July 2007 and June 2008. Administrative data examined included total discharges for kidney transplants, source of renal allograft, cases with complications, immunosuppressant utilization, length of therapy (LOT), length of stay (LOS), days in intensive care unit (ICU), in-hospital mortality rate, estimated immunosuppressant cost, and estimated hospital costs. Descriptive statistics were used to evaluate data. **RESULTS:** The mean LOT and number of institutions utilizing particular agents varied. Cyclosporine was used in an average 16% of transplants. Tacrolimus and mycophenolate mofetil had a mean utilization of 83% (4% to 100%) and 92% (39% to 100%) respectively. Sirolimus and azathioprine were administered in an average 12% (1% to 75%) and 2% (<1% to 8%) respectively. Antithymocyte globulin, equine was dispensed in an average 28% (<1% to 91%) of cases. Antithymocyte globulin, rabbit was used in an average 53% (1% to 100%) of cases. Basiliximab and dactuzimab were utilized in an average 31% (1% to 96%) and 33% (1% to 89%). Thirty-three institutions utilized three or more agents in greater than 50% of their kidney transplants. Agents that contributed most significantly to immunosuppressant cost were antithymocyte globulin and basiliximab. The mean LOS index was 1.1 (0.6 to 1.7). The mean days spent in the ICU was 2.8 (1.6 to 8.0) days. The mean in-hospital mortality rate was 0.47%. The estimated average immunosuppressant cost per case was \$4249. **CONCLUSIONS:** Considerable variation exists among institutional utilization of immunosuppressive agents, LOT, and associated medication costs per case.

##### RESTRICTED ACCESS TO DRUGS IS ASSOCIATED WITH LESS OPTIMAL MINERAL METABOLISM CONTROL IN HEMODIALYSIS PATIENTS

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**OBJECTIVES:** Abnormalities in mineral metabolism (MM) are associated with increased morbidity and mortality in patients with chronic kidney disease (CKD). PhotoGraphTM software was designed to allow dialysis centres to track MM and assess treatment efficacy. Recent studies in other patient populations have suggested that restricted access to drugs was associated with poorer patient outcomes in the Canadian health care setting. The aim of this study was to compare MM management among dialysis patients who live in provinces with open vs. restricted access to expensive drugs. **METHODS:** A sample of 50 Canadian dialysis centres which used PhotoGraphTM were selected. Phosphorus (P), calcium (Ca), intact parathyroid hormone (iPTH) and calcium-phosphate product (CaXP) were measured and compared between provinces with open and restricted access. Data were analyzed by phosphate binder type. **RESULTS:** MM targets were more likely to be reached by patients residing in provinces with formularies allowing more open access to non-calcium based phosphate binders: P: 61.6% vs. 54.9%; Ca: 59% vs. 44.8%; iPTH: 31.1% vs. 27.3%; CaXP: 85.4% vs. 76.9%. Patients residing in provinces with more restrictive formularies were more likely to receive doses of calcium that exceed the

maximum recommended in treatment guidelines (i.e., >1.5 g/day) than those with more open listings (62% vs. 15%). In addition, patients residing in provinces with restricted access to sevelamer were less likely to receive this drug (16.2% vs. 42%). **CONCLUSIONS:** MM was better managed among patients in settings with more open access to non-calcium based phosphate binders. There is a reasonable expectation that this may translate to better outcomes and reduced mortality among hemodialysis patients.

##### CALCIUM-BASED PHOSPHATE BINDERS LEAD TO INCREASED PROGRESSION OF VASCULAR CALCIFICATION IN CHRONIC KIDNEY DISEASE

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**OBJECTIVES:** Cardiovascular disease is the leading cause of death among patients with chronic kidney disease (CKD). Vascular calcification (VC) is a common feature of CKD that predicts mortality and may contribute to future outcomes. CKD treatment guidelines recommend that calcium-based phosphate binders (CBBs) be restricted to doses of 1.5 g/day elemental calcium, however a previous study showed that this dose was associated with VC in CKD. Similarly, the use of calcium (<1.5 g/day) has been associated with poorer cardiovascular outcomes in other patient populations (e.g., postmenopausal women). The aim of this review was to compare the prevalence of VC among CKD patients treated with CBBs and sevelamer. **METHODS:** A literature search using Medline was conducted using the following terms: CBB, calcium carbonate, calcium acetate, non-CBB, sevelamer, lanthanum, vascular calcification, coronary and aorta. Studies reporting mean changes from baseline (%) in VC scores in CBB and sevelamer groups were used for data extraction. **RESULTS:** Increased progression of coronary calcification was observed in CBB groups as compared to sevelamer: 13.4% to 50.8% vs. -8.0% to 23.4% (n = 6 studies). Sevelamer was associated with regression of aortic calcification compared to CBBs: -71.3% to -13.4% vs. 5.7% to 135% (n = 3 studies). Average doses of calcium ranged from 1.39 to 2.3 g/day. **CONCLUSIONS:** Although the doses of elemental calcium used in these studies approached those recommended by treatment guidelines, CBBs were associated with increased progression of VC. CBBs are associated with increased VC, a predictor for mortality, even when calcium doses concur with current standards of practice. More research on the impact of CBBs on VC and future outcomes is required.

##### THE EFFECTS OF CALCIUM-BASED VS. NON CALCIUM-BASED PHOSPHATE BINDERS ON OUTCOMES AMONG PATIENTS WITH CHRONIC KIDNEY DISEASE: A META-ANALYSIS

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**OBJECTIVES:** Two-thirds of patients with Chronic Kidney Disease (CKD) will die of cardiovascular disease (CVD). In addition, 30 year old dialysis patients have a 500-fold increased mortality risk vs. an age-matched general population. Coronary artery calcification (CAC) is a major risk factor for CVD in CKD patients. Increased serum calcium accelerates this process, which suggests that calcium-based phosphate binders (CBBs) may accelerate CAC and increase mortality. The aim of this systematic review was to determine the effect of CBBs vs. non-CBBs on all-cause mortality and CAC among patients with CKD. **METHODS:** We conducted a detailed search of several electronic databases (e.g., MEDLINE, EMBASE, CINAHL) using the following terms: kidney disease, phosphate binders, calcium dialysis, phosphate levels, CV events and mortality. Standard Cochrane methods for study selection and data abstraction were followed. We included nine studies which compared CBBs to non-CBBs. **RESULTS:** Fifty-seven articles were retrieved for detailed evaluation. Sevelamer was the only non-CBB noted in the nine trials which met the inclusion criteria. Sevelamer was associated with a trend towards reduction in all-cause mortality (RR 0.81; 95% CI 0.65-1.02), p = 0.07 vs. CBBs. Overall difference in change of CAC scores among those taking sevelamer vs. CBBs was -76.35 (95% CI -158.25 - 5.55), p = 0.07. **CONCLUSIONS:** Compared to CBBs, sevelamer is associated with a non-significant trend toward reduced all-cause mortality. This is concordant with the trend toward a modest reduction in CAC progression with sevelamer. Since CBBs are used frequently in CKD patients, this systematic review highlights the need to further evaluate the safety of CBBs in this high-risk population.

##### COMPARISON OF LIFE EXPECTANCY, EXPECTED YEARS OF LIFE LOST AND SURVIVAL BETWEEN HEMODIALYSIS AND PERITONEAL DIALYSIS PATIENTS

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**OBJECTIVES:** This study aimed to compare the life expectancy, expected years of life lost (EYLL) and survival between patients under hemodialysis (HD) and peritoneal dialysis (PD). **METHODS:** Adult patients who underwent maintenance dialysis at National Taiwan University Hospital from 1995 to 2006 were followed-up until the