specific to SJS/TEN and for related non-specific codes for erythema multiforme, drug dermatitis, and drug allergies. All records from 1/1/00-8/1/09 that were identified as potential cases were reviewed manually for confirmation and abstraction of suspected implicated drugs. In addition, we reviewed medical records of patients with two additional SSR: angioedema on ACE inhibitors, and drug hypersensitivity syndrome (DHSS). **Results:** Of 29 patients with codes specific for SJS/TEN, 23 (79%) were confirmed on chart review. Of 140 patients with non-specific SJS/TEN codes, 13 (9%) were confirmed. The most commonly implicated medications included amoxicillin, dilantin, trimethoprim and sulfamethoxazole, and isoniazid. Of 56 subjects with angioedema while on ACE inhibitors, 20 (36%) were confirmed. Of patients with DHSS, 1 of 29 (3%) that had inpatient codes plus abnormal lab values were confirmed on record review, while only 1 of 51 (2%) with inpatient DHSS codes and normal lab values were confirmed. **Conclusions:** We found that large linked electronic HMORN datasets efficiently identified highly probable cases of SJS/TEN. Searches for angioedema following ACE inhibitor exposure were also relatively successful. However, searches for DHSS were unsuccessful and only yielded 2 potential cases. These findings will be useful for planning the next study phase where patients will be recruited for genomic studies from a larger number of HMO sites.

Keywords: Serious skin rashes, Electronic datasets
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C-C5-01:

Drug Safety Data Mining with a Tree-Based Scan Statistic

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Background/Aims: Active post-marketing drug safety surveillance has traditionally focused on predefined drug-adverse event (AE) pairs. However, evaluating predefined pairs does not illuminate unsuspected potential AEs. Drug safety data mining is a surveillance approach that formally evaluates the relationship between medications and a very large number of AEs. We used varying specifications of the tree-based scan statistic data mining method (TreeScan) to search for adverse events among clozapine drug users. **Methods:** Electronic health records from three HMO Research Network health plans were assessed. We used TreeScan to evaluate a hierarchical clinical classification to identify signals of excess risk during prevalent drug exposure as compared to unexposed time. The test statistic – a Poisson based log likelihood ratio – is adjusted for multiple testing inherent in the many potential AEs evaluated. Four alternate specifications were incorporated: ramp-up periods of 180 and 400 days and outcome definitions using inpatient plus outpatient diagnoses and inpatient diagnoses only. For each drug and specification, we calculated expected and observed counts for each level of the hierarchical tree, adjusting for age, sex, and health plan. **Results:** We identified 242,000 to 580,000 exposed clozapine days and 150 to 345 exposed outcomes across the different specifications. Both ramp-up periods found 17 unique statistical signals using inpatient plus outpatient diagnoses. Of those, several represent confounding by indication (three signals in mental health, two for injury and poisoning) and others are known AEs (e.g., convulsions, hypotension, GI system). Limiting outcomes to the inpatient setting reduced the number of signals to 14 (180-day ramp-up) and 10 (400-day ramp-up). Overall, the inpatient-only AE signals were in the same clinical systems, with some exceptions. The inpatient specification signaled for circulatory events and diseases of the heart, but hypotension was no longer found. Genitourinary AEs signaled using inpatient plus outpatient diagnoses but were not identified using inpatient diagnoses only. **Conclusions:** Data mining using electronic health records is an important complement to other post-marketing drug safety research. Once specifications are finalized, TreeScan will be applied to assess the safety of over 100 oral outpatient medications.

Keywords: Data mining, TreeScan, Clozapine
doi:10.3121/cmr.2011.1020.c-c5-01

PS1-31:

Assessing the Potential for Research on Genetics of Drug Induced Liver Injury in the HMORN

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Background/Aims: Drug Induced Liver Injury (DILI) is a major cause of liver failure in the US and the leading reason for failure of investigational drugs in clinical trials, lack of drug approval, and post-market withdrawal of approved drugs. Recent genome-wide association studies have identified variations within the major histocompatibility complex in Caucasians to be linked with flucloxacillin and lumiracoxib-related liver injury. The need for replication of these findings and extension of these investigations to other drug exposures and other ethnic groups will require substantial case numbers with supporting medical record documentation. With support from The Serious Adverse Event Consortium, an international consortium led by the pharmaceutical industry in conjunction with the FDA, we conducted a feasibility study to evaluate the potential for using electronic clinical and administrative data from two HMORN sites to identify provisional DILI cases. **Methods:** Building upon previous research, we developed data specifications for electronic searches of ICD-9 codes with time proximate laboratory results indicative of liver-related disease. Electronic criteria were used to 'rule out' other liver diseases and other co-morbid conditions indicative of systematic liver-related effects. For feasibility testing, two methods of population identification were incorporated: the VDW and EMR reporting. All records from 1/1/00-8/1/09 that were identified as 'potential DILI cases' were reviewed manually, and selected data were abstracted, including suspected implicated drug(s). **Results:** Records for 1,123,173 individuals were screened for potential case status; 29,893 records with one or more diagnoses of interest were identified. After application of the "rule out' exclusion criteria, 584 potential DILI cases were reviewed and 99 ultimately met provisional case status. Drugs commonly associated with provisional DILI cases were sulfa-containing antibiotics, anticonvulsants, isoniazid, and statins. Roughly one-half of provisional DILI cases were associated with a single implicated drug. **Conclusions:** Electronic infrastructures currently available within many highly integrated health care delivery systems can be efficiently leveraged to support identification of provisional DILI events. Systems that have comprehensive episodic, historic and post-event data, including lab, diagnostic, treatment, imaging, and medication records that can be accessed electronically should be considered primary systems for expanding DILI case accumulation efforts.

Keywords: Drug-induced liver injury, Research, Feasibility studies
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PS1-18:

A Feasibility Pilot to Determine the Practicality of Using the HMO Research Network to Research the Genetics of Drug-Induced Serious Adverse Events

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Background/Aims: The International Serious Adverse Events Consortium (iSAEC) is a pharmaceutical industry and FDA-led consortium focused on identifying DNA variants useful for predicting risk of drug-induced rare serious adverse events (SAEs). We assessed the feasibility of using electronic medical databases at six HMORN sites to identify provisional cases of three SAEs: drug-induced liver injury (DILI), serious skin rashes (SSR), including

Stevens-Johnson syndrome, toxic epidermal necrolysis, and angioedema, and extreme weight gain (EWG) among adults on atypical antipsychotics. **Methods:** Project work was divided among three teams. HealthPartners and Marshfield Clinic led the DILI team, Kaiser Permanente Hawaii and Kaiser Permanente Georgia led the SSR team and Group Health and Geisinger guided the EWG study. Teams met routinely via biweekly conference calls to coordinate their study efforts; monthly conference calls were conducted to coordinate the overall project, mark progress and discuss challenges and solutions. For each study, standardized case identification criteria were developed with input from iSAEC, expert panels, and medical literature. Potential cases were identified through electronic data searches using diagnoses, medication histories, laboratory test results, and other clinical data elements indicative of DILI and SSR during 2000-2009, or EWG from 2004-2009. Potential cases of DILI and SSR were abstracted to assess provisional case status and determine implicated drugs. Weight trajectories of suspected EWG cases were visually inspected to confirm EWG during atypical antipsychotic treatment period. **Results:** A total of 99 provisional cases of DILI, 41 cases of SJS/TEN and 56 provisional cases of angioedema were identified from the electronic records of the participating HMOs. For EWG, 249 cases were confirmed and an additional 341 were categorized as "possible" cases, with additional chart review and patient interview required for confirmation. Confirmation rates varied from 17% for DILI to 2-79% for SSR and 23-30% for EWG. **Conclusions:** The SAEC and HMORN study sites identified well-phenotyped cases with the targeted drug-induced SAEs of interest. The relative success of these efforts has been critical in the planning of a larger second study that will include analyses of genetic factors associated with provisional case SAEs.

Keywords: Drug-induced liver injury, Serious skin rashes, Extreme weight gain

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PS1-23:

The Incidence and Epidemiology of Inpatient and Outpatient *Clostridium difficile* Infections at Kaiser Permanente

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Background/Aims: *Clostridium difficile* is the most common cause of healthcare-associated infectious diarrhea in the United States. However, few population-based epidemiologic studies of *C. difficile* infection (CDI) exist. Our aims were to: 1) describe the epidemiology of CDI among HMO members from two geographical regions; 2) extrapolate the incidence of CDI from these health plans to the U.S. population; and, 3) identify patient characteristics that predict inpatient versus outpatient identification of CDIs. **Methods:** We conducted a population-based, dynamic, retrospective cohort study among Kaiser Permanente Colorado (KPCO) and Northwest (KPNW) enrollees between June 1, 2005 and September 30, 2008. We identified incident CDIs and categorized infections based on identification in the inpatient or outpatient setting. We calculated incidence rates and extrapolated our estimates to the 2007 U.S. population. KPNW and KPCO regional electronic databases provided data on membership, pharmacy dispensings, demographics, clinical measures, and healthcare utilization. Logistic regression determined how strongly patient characteristics predicted inpatient versus outpatient identification of CDIs. **Results:** We identified 2,879 incident CDIs; 55% were identified in the outpatient setting. In 2007, our total population incidence rate was 13.5 CDI cases per 10,000 person-years; incidence increased with age. Extrapolated to the U.S. white-only population, we estimate that 220,000 cases of CDI occurred among persons 20 years or older in 2007. Baseline characteristics and healthcare utilization prior to identification of CDI in both settings were similar, although individuals with CDI identified in the inpatient setting were older and had greater comorbidity than individuals with outpatient-identified CDI. We identified few strong and independent predictors of setting, although risk for CDI identification in the inpatient setting was associated with an estimated glomerular filtration rate <15 (OR: 4.96; 95% CI: 2.73, 9.02), inflammatory bowel disease (OR: 2.41; 95% CI: 1.45, 4.02), an outpatient antimicrobial dispensing in the previous 180 days (OR: 2.67; 95% CI: 2.13, 3.35), and malignancy (OR: 2.08; 95% CI: 1.60, 2.72). **Conclusion:** The incidence of CDI among this population is substantial (13.5/10,000 person-years). Because the incidence of and risk for CDIs increases with age, the U.S. burden of CDIs will continue to rise as the proportion of older individuals in the U.S. population rises.

Keywords: *Clostridium difficile*, Incidence, Epidemiology

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PS1-11:

Feasibility of Prospective Surveillance for Adverse Drug Events – Lessons Learned from a 12-Month Pilot Study

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Background/Aims: When new medications are introduced, safety data are often sparse. Health plan data may be useful for active surveillance for adverse events. We conducted a 12-month pilot study to demonstrate the feasibility of prospective active surveillance using data from several large health insurers. This presentation will summarize logistical challenges and lessons learned. **Methods:** We studied the safety of generic divalproex sodium, an antiepileptic drug introduced in July 2008, compared to the branded drug. We performed monthly surveillance using the maximized sequential probability ratio test, comparing observed outcomes in new users of the generic drug to expected counts based on new users of the branded drug from January 2002 - June 2008. Programmers at four HMO Research Network sites extracted data monthly, ran quality control (QC) programs, and returned summary tables to the lead site. Medication exposure was identified from outpatient pharmacy dispensings. Outcomes identified from health plan utilization data included potential adverse effects (e.g. pancreatitis and liver disease) and efficacy outcomes (e.g. hospital or emergency department visits for seizures.) **Results:** We will discuss lessons learned related to data sharing and HIPAA compliance, timing and synchronization of data pulls, and QC activities. Obtaining IRB approval took 3.5 months, and protocol development took 7 months. Developing the analytic program required two rounds of corrections, one leading to meaningful changes in results. QC programs identified substantial differences in monthly extracts across sites. Some QC flags required only understanding differences across sites, but others revealed data problems requiring resolution at the site level. Overall, 14% (4/28) of monthly extracts across the four sites could not be used due to underlying data problems or lack of analyst availability for timely extracts. **Conclusions:** Prospective drug safety surveillance is feasible, but future projects should anticipate the need for longer timelines and multiple revisions to data pulls and analytic programs. They should develop approaches to handling missing data, because some data pulls will not be usable. QC activities should continue throughout study implementation. A knowledgeable, engaged lead at each site is vital to ensure accuracy and appropriate interpretation of each site's data.

Keywords: Antiepileptic medications, Drug safety, Prospective surveillance

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C-C5-05:

Genetic Risk Factors: Idiopathic Thrombocytopenic Purpura following the First Dose of Measles-Mumps-Rubella Vaccination in Children

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