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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Background: Immune thrombocytopenic purpura (ITP) is a rare though well recognized adverse event following measles, mumps, and rubella (MMR) vaccine. Identification of individuals at high risk for these and other vaccine adverse events might inform pre-vaccination screening options for the future. Working in close collaboration with the FDA, we seek to identify genetic differences underlying the susceptibility to ITP following MMR or MMR and varicella (MMRV) vaccination. We will compare the genetic make-up of these cases to ITP occurring after medication exposure and to idiopathic cases of ITP. **Methods:** We plan to recruit 450 persons with ITP. These will include 150 cases with ITP following vaccination from the FDA's Vaccine Adverse Events Reporting System (VAERS) and the Intercontinental Cooperative ITP Study Group (ICIS) and 300 cases (150 with ITP related to prescribed medications, and 150 cases of idiopathic ITP) recruited from ICIS, Kaiser Permanente Georgia, and Kaiser Permanente Southern California. To identify novel candidate genes or pathways, we will perform whole exome resequencing for (at least) six unrelated individuals with a Mendelian form of ITP. Polymorphism frequencies within these candidate genes will be examined and their proportions compared with control data available from the 1000 Genomes Project. The identified polymorphisms will inform the genome-wide association study (GWAS) phase, which will also include a copy number variation (CNV) component. **Results:** To date, we have identified 232 potential cases of ITP following MMR/MMRV vaccination reported to VAERS during 2000-2009. Of these potential cases, 214 have been abstracted and 156 (73%) have been confirmed. Recruitment is set to begin in November 2010. In addition, we have identified six participants from families with congenital thrombocytopenia for exome resequencing. Supplemental funding was obtained to support recruitment efforts and additional sequencing. **Conclusions:** This study involves a unique collaboration between the FDA and the HMORN, leveraging HMORN experience in pharmacogenomics and vaccine adverse event research. The ultimate goal of this project will be to use new resequencing strategies, combined with GWAS and CNV, to identify variants which may enable the prediction of risk, at the individual level, of developing ITP after vaccination.

Keywords: ITP, MMR/MMRV, Vaccine safety

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Virtual Data Warehouse

PS1-33:

CESR Proof-of-Concept Projects: Lessons Learned from the DCC Perspective

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Background/Aims: Two multi-site proof-of-concept projects were initiated to demonstrate the viability and sustainability of the newly created Kaiser Permanente (KP) Center for Effectiveness and Safety Research (CESR). This presentation highlights lessons learned from the Data Coordinating Center (DCC) perspective as both projects conclude. **Methods:** Each proof-of-concept project, charged with finishing within one year of start-up, assembled teams, including investigators and programmers from each KP site. CESR's DCC supplied an overall project manager as well as consultation services on Institutional Review Board (IRB) issues, Data Use and Sharing Agreements(DUSA) and secure transfer of collected data. Other DCC services included SAS multi-site extraction programs for Virtual Data Warehouse (VDW) data and other non-VDW data. When non-VDW data was requested, the DCC also defined specifications for these tables. Cleaning of, Quality Assurance (QA) of and final combination of data from multiple sites was performed at the DCC. **Results:** The proof-of-concept projects helped to refine CESR processes for future projects. Lessons learned include 1) consult a VDW specialist early in the planning process, including before IRB submission; 2) describe data to be extracted and outlined in IRB applications and DUSAs broadly enough to include related variables to minimize the number of time-consuming modifications (e.g., ask for newborn statistics, not head circumference or agpar5); 3) create and use templates for extraction programs, for programs which combine multi-site data and simple statistical processes; 4) date stamp programs and returning datasets and related output; 5) develop one location to allow investigators and programmers to access project related information and documents; 6) develop documents for tracking programs (including modifications) and datasets flowing between multiple sites and data coordinating center; and 7) invest time to create, update and communicate data flow diagrams (DFD) for each SAS program sent to sites. **Conclusions:** Documenting and analyzing the processes involved in proof-of-concept projects can help inform and contribute to efficiencies in future projects.

Keywords: Project management, Organization

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C-B1-04:

Piloting Use of the HMO Research Network Virtual Data Warehouse for Pelvic Inflammatory Disease Surveillance and Research

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Background/Aims: National surveillance for pelvic inflammatory disease (PID) has been problematic for some time, as treatment and practice patterns have shifted away from inpatient settings and surgical procedures. Research and surveillance may be enhanced by use of automated data now available in many health plans. We evaluated the use of the HMO Research Network (HMORN) Virtual Data Warehouse (VDW) at two sites (GH and KPCO) to compare rates and 9-year trends in PID. As part of these evaluations, we explored the feasibility of using the VDW to obtain related chlamydia testing and infection information. **Methods:** Using standard ICD-9 codes for PID, we identified all cases occurring among GH women aged 15-44 years during 2000-2008. We then modified these programs for use by other HMORN sites by applying the VDW data dictionary standard variable naming conventions. We piloted these programs at KPCO. We calculated annual PID rates per 100,000 person years by 5-year age groups. We also sought information on chlamydia testing and test result within 7 days of the coded PID diagnosis date. The VDW includes relevant CPT codes for chlamydia testing, but microbiology test results are currently unavailable. Therefore, each site accessed their respective lab databases and used agreed-upon text strings to extract test result data. **Results:** PID rates were lower at KPCO than at GH. From 2000-2008, there were no significant PID linear trends at either plan. At GH, the rate was 562/100,000 person-years in 2000 and 526/100,000 in 2008; at KPCO, rates were 532/100,000 in 2000 and 485/100,000 in 2008. PID rates declined significantly only in the 20-24 year-old age group at KPCO. The proportion of cases receiving inpatient treatment was low (8%-16%). At both sites, approximately one-half of PID cases had evidence of chlamydia testing within 7 days. **Conclusions:** Given the national surveillance challenges for PID, the HMORN VDW is a potentially valuable resource that can add to PID surveillance and research by providing standardized data from multiple health plans across the U.S. With some expansion, the VDW could include additional information on characteristics of infection and aspects of care that have not previously been widely available.

Keywords: Surveillance, Automated data, Infectious disease

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PS1-12:

Load I2B2 with VDW Data

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The Virtual Data Warehouse (VDW) and Informatics for Integrating Biology & the Bedside (I2B2) are important components of our population-based health research collaboration efforts. Much hard work is put into cleaning and standardizing a health care institution's data for inclusion in the VDW. The I2B2 tool offers slick drag and drop, point and click query access to health care data. A method for leveraging the VDW for populating a Microsoft SQL Server version of the I2B2 database was developed using a