identified for study inclusion. Sildenafil was the most common initial treatment (n = 455 patients), followed by bosentan (n = 251 patients) and ambrisentan (n = 21 patients). On average, ambrisentan patients received one pill/day with a daily dose of 7 mg, bosentan patients received 2 pills/day with a daily dose of 222 mg, and sildenafil patients received 2.3 pills/day with a daily dose of 61 mg. Approximately 44% of ambrisentan, 35% of bosentan, and 25% of sildenafil patients experienced a dose increase ($p = 0.013$) during the follow-up period. PAH-related inpatient and emergency department utilization were similar among the groups, while ambulatory visits differed among the groups, with average monthly counts of 1.2, 0.8, and 0.5 visits for ambrisentan, bosentan, and sildenafil patients ($p < 0.001$). Follow-up total PAH-related costs were significantly different among the groups, with average monthly costs of $6820, $5332, and $3632 for ambrisentan, bosentan, and sildenafil patients ($p = 0.020$). Cost differences were primarily driven by PAH-related pharmacy costs, which were significantly lower in sildenafil patients ($p < 0.001$). **CONCLUSIONS:** Of the three oral PAH treatments studied, sildenafil was the most frequently prescribed, and was associated with lower pharmacy and overall costs than either ambrisentan or bosentan.

CARDIOVASCULAR DISORDERS – Conceptual Papers & Research on Methods

PCV153

FAILURE OF THE BLAND-ALTMAN METHOD TO IDENTIFY CLINICALLY IMPORTANT DISAGREEMENT BETWEEN MEASURES OF THE INTERNATIONAL NORMALIZED RATIO

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OBJECTIVES: The Bland-Altman method is often upheld as the optimal method to assess agreement between alternate measures of the same clinical parameter. However, recent research by our group demonstrates the Bland-Altman method does not report agreement in a clinically meaningful way. The objective was to determine if the Bland-Altman method distinguished between two point-of-care (POC) INR devices. These devices were previously shown to have significantly different levels of agreement with our core laboratory. **METHODS:** In a previous experiment, 170 patients provided three separate INR measures at the same clinic visit—two by POC (Avosure™ and ProTime™ devices) and one venous sample analyzed at our core laboratory (considered the standard measure). Agreement was achieved when the POC and lab INR values led to the same clinical decision. Differences in agreement between the POC devices and laboratory were assessed by McNemar's test. In the current study, we applied the Bland-Altman method to determine if inferences regarding agreement between the POCs and laboratory were identical to the previous experiment where clinical decisions defined agreement. **RESULTS:** The Avosure device was significantly more likely to lead to the same clinical decision as the laboratory versus the ProTime device (80% vs. 66%, respectively, $p < 0.001$). However, the Bland-Altman method produced virtually identical mean bias (0.4 and 0.5 INR units, respectively) and did not distinguish between the devices. Statistical analysis of the Bland-Altman method produced the same findings for each device: significantly different standard deviations between the POC and the laboratory ($p < 0.001$), significant bias in each device ($p < 0.001$), and high correlations between the POCs and the laboratory (0.925 and 0.926, respectively). **CONCLUSIONS:** The Bland-Altman method did not detect clinically important differences between the POC INR devices. Clinically meaningful agreement between measures of INR is optimally assessed by a method that directly observes or explicitly estimates clinical decisions.

PCV154

USING DIFFERENT MEASURES TO DETERMINE TIME IN THERAPEUTIC INR RANGE AMONG WARFARIN-TREATED PATIENTS FOLLOWING TOTAL HIP OR KNEE REPLACEMENT

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OBJECTIVES: To determine the proportion of the post-surgery prophylaxis period that warfarin-treated patients undergoing total hip or total knee replacement (THR/TKR) spent in the American College of Chest Physicians (ACCP)-recommended therapeutic international normalized ratio (INR) range using two methods: within-patient proportion and Rosendaal linear interpolation. **METHODS:** Using an electronic database, patients undergoing total THR/TKR between January 1, 2004 and January 31, 2009 who received warfarin within 3 days after surgery were identified and followed for up to 90 days. Analysis focused on Day 5 onward since warfarin takes several days to reach therapeutic effect and on patients with at least 2 measured INR levels during this period. INR results were categorized based on ACCP guidelines: in range (2–3), below range (<2), or above range (>3). The proportion of INR levels within each range was determined for each patient, and the distribution of these within-patient proportions computed. Time within each range was imputed using the Rosendaal method, which assumes a linear interpolation between observed measurements, applying an INR level to each treatment day. **RESULTS:** A total of 653 THR and 871 TKR patients were identified; both groups had a median of 5 INR measurements from Day 5. Median within-patient percentages of in-range INR values were 33% for the average THR patient and 29% for the average TKR patient. Using the Rosendaal method, THR patients spent a median 29% and TKR patients a median 28% of within-patient proportion of time within the INR 2–3 range. **CONCLUSIONS:** The within-patient proportion of actual INR values and the proportion of imputed days spent in the ACCP-recommended therapeutic range (2–3) were similar in this post-surgical cohort of THR/TKR patients. Regardless of the method, the majority of INR values among all patients were outside of the ACCP-recommended INR therapeutic range.

PCV155

LINKING CLAIMS AND ELECTRONIC MEDICAL RECORD (EMR) DATA FOR A HYPERTENSION STUDY

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OBJECTIVES: To develop a methodology to link patients from two de-identified databases and leverage unique data from both to measure the impact of blood pressure and clinical findings on total costs. **METHODS:** Hypertensive patients (ICD-9 diagnosis 401.xx-405.xx) were identified from the MarketScan Commercial and Medicare Supplemental administrative claims databases (MarketScan) and the GE Centricity Electronic Medical Record (EMR) database (Centricity) for the years 2004–2008. A hybrid approach of deterministic and probabilistic matches was developed to identify common patients. Patients were included if they matched on zip code, gender and month of birth, and had at least three matching office visit dates at a rate of 75% or higher. Patients were followed for 12 months after the initial diagnosis. MarketScan provided data on enrollment, all reimbursed services (medical and drug) and costs, and Centricity provided clinical and biometric details, such as body mass index (BMI) and blood pressure. **RESULTS:** Among the 3 million MarketScan and 1.5 million Centricity patients with hypertension, 31,786 met the matching criteria. Mean age was 58 and 54% were female. The demographic and clinical characteristics of these patients did not vary substantially from those of the two data sources. Among the 31,786 patients, 84% received drug treatment, 56% had a BMI over 30 and mean systolic and diastolic values were 134 and 81, respectively. Mean unadjusted costs were $9,338 for patients with consistently controlled (first and last systolic <140 and diastolic < 90) hypertension and $8,773 for patients not consistently controlled. **CONCLUSIONS:** A combined probabilistic and deterministic approach of linking patients yielded a sample size large enough to conduct a study and leverage the strengths of administrative and EMR data. Initial findings suggest that controlled patients incur higher costs, however, adjustments have not been made for additional demographic, clinical, and treatment characteristics.

PCV156

MODELING TRANSFORMED HEALTH CARE COSTS WITH UNKNOWN HETEROSKEDASTICITY

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OBJECTIVES: Log models are widely used to deal with skewed outcomes, such as health care costs. They improve precision of estimates and diminish the influence of outliers. Smearing estimation suggested in literature only works with homoskedastic or heteroskedastic errors due to categorical variables. Generalized linear models (GLM) have been proposed as an alternative to deal with any kind of heteroskedasticity but recent literature shows that log models are superior to GLM under certain conditions. We present a method using log transformation that accounts for any kind of heteroskedasticity in the estimation of health care cost **METHODS:** Assume there is a population represented by the random vector of explanatory variables (ex. patient and clinical characteristics) and with the scalar response variable (ex. health care costs) and we want to estimate unknown parameters. Assume that error terms are in function of explanatory variables, and therefore heteroskedasticity exists. By modeling heteroskedasticity separately, we created a weight function and using this weight in an outcomes model, we corrected the heteroskedasticity in the log transformed model. Retransformation was done by adjusting for heteroskedasticity. **RESULTS:** As a case study, we calculated the burden of illness of venous thromboembolism (VTE). The difference between the cost of VTE and non-VTE patients is estimated to be $6,345 and $8,239 depending on whether the proposed or a GLM model is used. The standard errors changed significantly depending on the model. The difference was significant with the log transformed model with heteroskedasticity-adjusted standard errors and the GLM model. However, the difference was insignificant when the adjustment was not done. **CONCLUSIONS:** Log transformation provides more efficient estimators than GLM models under certain conditions (ex. if there is excess kurtosis) and heteroskedasticity can be adjusted even if its form is unknown.

PCV157

ACCOUNTING FOR TRIAL-EXCLUDED MEDICAL CONDITIONS WHEN SIMULATING MORTALTIY IN CLINICAL TRIAL POPULATIONS

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BACKGROUND: Clinical trials frequently exclude patients likely to die within the trial timeframe. Thus, these highly-selected patients have lower initial mortality probabilities relative to the age- and gender-matched general population. **OBJECTIVES:** To capture the effect that clinical trial exclusion criteria have on intermediate-term (i.e., one- to five-year) death probabilities in study subjects with substantial asymptomatic carotid artery stenosis. **METHODS:** We "phased-in" certain relevant death probabilities in a microsimulation model using data from the Asymptomatic Carotid Atherosclerosis Study (ACAS). The phase-in process initially eliminates or greatly reduces the mortality probability from a condition (reflecting patients excluded with

that condition) and increases the mortality probability as time progresses (reflecting patients that entered the trial with less severe and undetected cases of the condition or who developed the condition during the trial). Mortality was phased-in for four conditions reflective of their high prevalence and consistency with exclusion criteria: CHD, malignant neoplasms, chronic lower respiratory disease, and liver disease. **RESULTS:** To statistically compare the ACAS simulated versus actual mortality survival curves, we calculated the absolute differences between the curves and performed a standard equality of probabilities test on the curves at 12, 24, 36, 48, and 60 months. For the ACAS curve without mortality phase-in, at all times t before 60 months the simulated and actual curves had a statistically significant difference ($0 < p < 0.04$). With mortality phase-in, there was no evidence at any time t that the simulated and actual curves had a statistically significant difference ($0.62 < p < 0.95$). **CONCLUSIONS:** Phasing in mortality probabilities for trial-excluded conditions can simulate mortality survival curves that reflect the control arms of clinical trials.

PCV158

RARE EVENT BIAS IN RETROSPECTIVE ANALYSIS OF OUTCOMES MEASURES

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OBJECTIVES: It is well documented that standard logit regressions are biased in rare events. We wanted to illustrate how to analyze rare events in observational analysis using Medicare claims data. In particular, we compared the operational mortality for patients who underwent hip fracture surgery and suffered venous thromboembolism (VTE). **METHODS**: We applied two correction methods to address possible rare event bias. The first method involved obtaining information about the fraction of those in the population and the observed fraction of those in the sample. We estimated the adjusted constant coefficient in the logit model. In the second method, we weighted the proportion of ones and zeros in the sample to equal the true proportion in the population. We tested for differences in predicted probabilities using a non-parametric test. The Mann-Whitney U test and Kolmogorov-Smirnov two sample test can both be used on predicted probabilities of logit regression to see whether differences exist. **RESULTS**: To apply the methodology, we constructed a retrospective cohort study comparing the operational death rate between patients who underwent hip replacement surgery who suffered VTE and patients who did not suffer VTE. 60,245 patients with hip fracture surgery were identified from the 100% Medicare Inpatient dataset. Mortality was rare (0.81% vs. 3.34% for patients with non-VTE vs. VTE). Using Monte Carlo simulation, the unadjusted rate was 0.97% for non-VTE patients and 4.36% for VTE patients. The odds ratio was 3.98 for the standard model, 3.98 for the prior correction method, and 4.37 for the weighted mechanism. The predicted event probabilities were significantly different. **CONCLUSIONS**: Standard logit regression is proven to underestimate probabilities with rare events. We examined two correction methods. The predicted event probabilities adjusted for rare event bias were significantly different from the unadjusted ones.

PCV159

COMPARATIVE EFFECTIVENESS INDEX: A CONCEPTUAL APPROACH TO COMPARATIVE EFFECTIVENESS RESEARCH

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OBJECTIVES: The Comparative Effectiveness Index (CEI) provides a quantitative method of transforming efficacy data into effectiveness indices. In lieu of head-to-head randomized controlled trials, the CEI uses efficacy, adherence, and safety data to facilitate the drug evaluation process by providing a single value index for each therapeutic alternative. **METHODS:** Efficacy data from clinical trials serve as surrogate markers of effectiveness. In analyzing two hypothetical anti-hypertensive drugs, A and B, the efficacy of each drug is ranked on a nominal scale based on the literature: A = 10 and B = 8. The drug with the highest nominal value is the most efficacious. However, this value needs to be moderated by adherence and safety data. Adherence rates, calculated from claims databases for example, are: A = 60% and B = 90%. The formula for calculating the Modified Efficacy Score (MES) of each drug is the (adherence rate*efficacy score)/100: A = 6 and B = 7.2. Adverse events (AE) reported in the clinical trials are ranked based on severity, the scale is anchored at 0 and 100 where 0 = No AE and 100 = Death. Each AE is assigned a value depending on its severity then multiplied by the probability of its incidence. This is repeated for each AE and summed. The inverse of the sum, the Adverse Events Score (AES), is used in the final computation so that both MES and AES modifiers have a direct relationship with the CEI. The AES for the drugs are: A = 3.33 and B = 5.00. The MES is multiplied by the AES to calculate the CEI. Consequently, the CEI would be: A = 19.98 and B = 36.00. Although drug A was more efficacious, drug B is more effective. **CONCLUSIONS:** The CEI provides health care decision-makers with valuable comparisons between therapeutic alternatives, but it requires further development and validation. Incorporating measures of dispersion for efficacy and compliance in a sensitivity analysis can generate more comprehensive indices.

INDIVIDUAL'S HEALTH – Clinical Outcomes Studies

PIH1

THE NATIONAL BURDEN OF PEDIATRIC ADVERSE DRUG EVENTS: A CASE-CONTROL STUDY USING THE 2006 KIDS' INPATIENT DATABASE

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OBJECTIVES: Pediatric adverse drug events (ADEs) lead to substantial burden on patients, caregivers, and payers. The objective of the current study was to quantify the extent of the national pediatric ADE burden by determining (1 the frequency of ADE occurrence; (2 excess length of stay (LOS) and excess cost associated with hospitalization; and (3 the hospital, patient, and ADE characteristics that predict excess LOS and excess cost. **METHODS:** Using the 2006 Kids' Inpatient Database, ADEs were identified using ICD-9 and supplemental Ecodes; ADE frequencies were computed. A hospitalization with an ADE was matched with 1 hospital visit without an ADE; matching criteria included the All Patient Refined-Diagnosis Related Group, which accounts for severity of illness and risk of mortality, and gender and age. Excess LOS and excess cost (totals and means) were calculated for case-control pairs. An ordinary-least-squares regression was run, with the case-control pairs as observations, to determine significant predictors of excess LOS and excess cost. **RESULTS:** In 2006, 118,779 ADEs occurred in 99,320 visits out of 7,558,812 total pediatric hospitalizations. The mean excess LOS was 0.98 days ($p < 0.0001$), while the mean excess cost was \$2,252 ($p < 0.0001$). Adverse effects from benzodiazepine-based tranquilizers, certain anticonvulsants, adrenal corticosteroids, and various antibiotics led to the highest excesses (all with $p < 0.0001$). The mean excess LOS and excess cost, respectively, for neonates aged 0–7 days were 6.4 days ($p < 0.0001$) and \$26,417 ($p < 0.0001$). Statistically significant predictors included age, hospital region, insurance coverage, hospital size, urban versus rural hospital location, major diagnostic category for hospital admission, and severity of illness. **CONCLUSIONS:** A substantial share of the pediatric ADE burden is accounted by adverse effects rather than accidental poisoning. Variation across regions, drug classes, and diagnoses suggests that efforts to reduce the ADE burden can be targeted to have the greatest impact.

PIH2

THE PREVALENCE AND USE OF POTENTIALLY INAPPROPRIATE MEDICATION IN ELDERLY POPULATION USING NATIONAL NURSING HOME SURVEY

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OBJECTIVES: The aim of the study is to determine the prevalence and use of potentially inappropriate medication in elderly population according to the Beer's criteria. **METHODS:** Data for the present study was obtained from National Nursing Home Survey (NNHS) 2004. Patients of the age 65 and above were taken as sample. The use of potentially inappropriate medication was assessed by ranking the rate of usage of the 48 medications listed in the Beer's criteria that should be avoided in elderly patients and assessing the medication usage across demographics like gender and age. Descriptive statistics were carried out using SPSS 17. **RESULTS:** The total number of cases of the age 65 and above using the potentially inappropriate medication was 2209. The top five most used drugs were ferrous sulfate (54.33%), Clonidine (7.8%), Lorazepam (6.9%), Biscodyl (6.9%) and Amioderone (5.7%). Other more used drugs were Nifedipine (2.6%), Amitryptyline (2.5%), Alprazolam (2.2%), Fluoxetine (1.6%), Naprozen (1.4%), Temezepam (1.1%), Diazepam (0.95%) and Nitrofurointoin (0.90%). The usage was more in female (73.7%) as compared to male (26.3%), it was more in the age group 85 to 100 (43.1%) compared to 65 to 74 (17.9%) and 75 to 84 (39.1%). There were 2208 (91.8%) elders using at least one of the 48 medications and 181(8.1%) elders using two of these 48 medications. **CONCLUSIONS:** The use of potentially inappropriate medication listed under Beer's criteria is highly prevalent among the elderly. There is more usage in females compared to males and more in the age group 85 to 100. Among the top 12 drugs used, accept for Ferrous sulfate and Clonidine which has the low Beer's severity rating, all other drugs have a high Beer's severity rating and causes Adverse Drug Events.

PIH3

RISK OF WEIGHT GAIN WITH THE USE OF SELECTIVE SEROTONIN REUPTAKE INHIBITORS (SSRI) AND ATYPICAL ANTIPSYCHOTICS (SGA) COMBINATION TREATMENT IN CHILDREN AND ADOLESCENTS

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OBJECTIVES: To estimate the risks of gaining weight, with the use of selective serotonin reuptake inhibitors (SSRI) and atypical antipsychotics (SGA) in combination among children and adolescents. **METHODS:** A retrospective cohort study was conducted using 2003–2005 Medicaid Analytic eXtract (MAX) data from four U.S. states. Combination pharmacotherapy was operationalized as the concurrent prescribing of SSRI and SGA, where at least 14 days of treatment overlap occurred. Long term combination use is defined as an overlap beyond 60 days. Children and adolescents aged 6–18 years, and enrolled in Medicaid during 3 months prior and 1 year post the treatment initiation were selected. Multivariable logistic regression models were employed to estimate the risks of gaining weight during the one year follow up period. **RESULTS:** Among 118,126 children and adolescents received SSRI or SGA, 56,091(12.5%) were on combination treatment and of which approximately 80% were on long-term therapy (>60 days). Vast majority (63%) of these recipients were