years) who started antipsychotic treatment during July 1, 2001 and December 31, 2003. Antipsychotic users were followed for up to six months using an intent-to-treat approach. Extended Cox proportional hazard regression model stratified on matched pairs based on the propensity score was used to evaluate the comparative risk of death among users of typical and atypical antipsychotic agents. **RESULTS:** There were 84, 162 (42, 081 atypical and 42, 081 typical) users of antipsychotic agents in the final matched cohort. The unadjusted mortality rate was 11.12% (4, 682) for atypical users and 15.01% (6, 318) for typical users. Results of Cox regression suggest that, typical users were more likely to die compared to atypical users [Hazard Ratio (HR) 1.59, 95% Confidence Interval (CI) 1.52-1.66]. The extended Cox model revealed that the risk of death was greater with typical use during the initial 40 days of treatment [<40days: HR 2.00, 1.86-2.15]. The difference in risk persisted after 40 days of typical antipsychotic use [40-180 days: HR, 1.40, 1.32-1.47]. **CONCLUSIONS:** The use of typical antipsychotic agents was associated with short-term and long-term risks of mortality among elderly dual eligible beneficiaries compared to atypical use. Given the underlying poor health status of dual eligible beneficiaries, the study findings suggest that the use of typical agents needs to be optimized in the vulnerable elderly population.

RM4

A SYSTEMATIC REVIEW OF COSTS ASSOCIATED WITH PRESCRIPTION OPIOID RISKS

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OBJECTIVES: The US Food and Drug Administration (FDA) requires drug manufacturers to implement Risk Evaluation and Mitigation Strategies (REMS) to ensure drug benefits outweigh their risks. REMS for opioids target abuse, misuse, addiction, and overdose deaths. This study aims to identify which among these REMS-designated risk categories contribute most to societal burden, where burden is the product of prevalence (or rate for death) and per-event cost. This study also examines opioid diversion risk as a non-REMS secondary outcome. **METHODS:** Based on systematic review and meta-analysis, we estimated opioid-related mortality and prevalence for other outcomes. For outcomes other than death, we estimated health care costs per occurrence as documented by the Healthcare Cost and Utilization Project (HCUP) dataset. We focused on the value people place on avoiding death, rather than on the health care resources consumed. As such, we estimated the cost of each death using the Environmental Protection Agency's value of a statistical life (VSL), which reflects willingness to pay to avoid mortality risks. **RESULTS:** Excluding populations at high-risk for adverse behaviors, prevalence rates were 6% to 38% for misuse, 6% to 15% for abuse, 0.3% to 0.4% for addiction, and 9% to 20% for diversion. Mortality varied widely, ranging from 1 to 108 per 100,000 person years. Treatment costs per occurrence were $8,300 for abuse, $7,400 for addiction, and $10,000 for diversion. Misuse had no documented treatment costs. EPA's VSL is $7.9 million. **CONCLUSIONS:** Based on prevalence and per occurrence health care costs, abuse and diversion pose the greatest societal burden, but these findings require verification due in part to design differences across studies and differences among populations investigated.

PODIUM SESSION I: IMPORTANCE OF SELECTION BIAS IN HEALTH CARE RESEARCH

SB1

COMPARISON OF MEDICAL CARE CONSUMPTION BETWEEN DULOXETINE INITIATORS AND PREGABALIN INITIATORS AMONG FIBROMYALGIA PATIENTS

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OBJECTIVES: To compare medical care consumption between duloxetine initiators and pregabalin initiators among fibromyalgia patients. **METHODS:** We conducted a retrospective cohort study based on a US national commercial claims database (2006~2009). Fibromyalgia patients who initiated duloxetine or pregabalin in 2008, age 18 to 64, and maintained continuous health insurance coverage one year before and one year after initiation were assigned to duloxetine or pregabalin cohorts based on their initiated agent. Patients with pill coverage of the agents over last 90 pre-initiation days, with less than 30 supply days of the agents in the follow-up year, or with a diagnosis of depression, anxiety, DPNP, epilepsy or post-herpetic-neuralgia before the initiation were excluded. Fibromyalgia-related medical care consumption (inpatient, outpatient, medication utilization) was compared between the two cohorts. Bootstrapping and propensity score stratification methods were used to adjust for distribution bias as well as cross-cohort differences in demographics, pre-index clinical and economic characteristics, and medication history. **RESULTS:** Compared to pregabalin initiators (n=4,838), duloxetine initiators (n = 3033) had a similar mean initiation age (49 years), female percentage (89%), percentages of patients using inpatient care (11.6% vs. 11.4%), outpatient care (100%) and medications (92.7% vs. 92.8%) in the pre-initiation year. During the post-initiation year, duloxetine initiators had fewer patients using fibromyalgia-related inpatient care (2.1% vs. 3.0%, $p<0.05$), fibromyalgia-related outpatient care (54.0% vs. 64.3%, $p<0.05$), specialty outpatient care (83.7% vs. 89.4%, $p<0.05$), opioids (73.5% vs. 77.1%, $p<0.05$), and non-steroidal anti-inflammatory drugs (38.8% vs. 41.1%, $p<0.05$) than pregabalin initiators did. They also had fewer inpatient admissions (0.2 vs. 0.3, $p<0.05$), fibromyalgia-related outpatient claims (4.7 vs. 8.3, $p<0.05$), specialty outpatient claims (26.1 vs. 30.4, $p<0.05$), and opioid claims (6.0 vs. 7.4, $p<0.05$). **CONCLUSIONS:** Among fibromyalgia patients, duloxetine initiators consumed less fibromyalgia-related inpatient, outpatient, and specialty outpatient care, and had fewer post-initiation claims for opioids.

SB2

COMPARATIVE EFFECTIVENESS OF ON-PUMP AND OFF-PUMP CORONARY ARTERY BYPASS GRAFTING AMONG ELDERLY PATIENTS – A RETROSPECTIVE ANALYSIS OF MEDICARE CLAIMS DATA

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OBJECTIVES: Conventional (on-pump) coronary artery bypass grafting (CABG) is a surgical procedure used to restore blood flow to the cardiac muscle in patients with coronary artery disease. Recently, some have suggested that an off-pump CABG procedure has lesser post-operative morbidity and mortality. Few studies to corroborate this finding have been conducted in the elderly population. The purpose of this study was to compare outcomes associated with on-pump and off-pump CABG among Medicare beneficiaries. **METHODS:** A retrospective cohort study design was used to analyze the 5% national sample of Medicare claims data. Elderly patients (≥65 years) who underwent CABG from July 1, 2006 to June 30, 2008 were identified using ICD-9-CM codes. Outcomes were assessed (using ICD-9-CM codes) following CABG surgery to December 31, 2008. Outcomes included acute myocardial infarction (AMI), revascularization such as percutaneous coronary intervention (PCI), stroke, in-hospital and all-cause mortality. Propensity scores were calculated to predict the likelihood of each individual receiving on-pump versus off-pump CABG surgery based on patient demographics and comorbidities (identified from January 1to June 30, 2006) which were then used to match (1:1) patients in the two groups. Conditional logistic regression was used to compare the outcomes associated with the two procedures. **RESULTS:** 2,760 patients (1,380 in each group) met the inclusion criteria. Patients who underwent on-pump CABG had lower odds of in-hospital mortality (OR: 0.57; 95% CI: 0.39 – 0.83) and all-cause mortality (OR: 0.69; 95% CI: 0.56 – 0.85) as compared to off-pump CABG patients. The procedures were found to be comparable in terms of clinical outcomes including AMI, PCI and stroke. **CONCLUSIONS:** This study found that in-hospital and all-cause mortality associated with on-pump CABG was lower than off-pump CABG. Further clinical trials need to be conducted to compare the safety of on-pump versus off-pump CABG among elderly patients.

SB3

INCREMENTAL CLINICAL AND ECONOMIC BURDEN OF UNCONTROLLED PARTIAL-ONSET SEIZURES IN A PRIVATELY-INSURED POPULATION

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OBJECTIVES: To assess clinical and economic consequences attributable to loss of seizure control in privately-insured patients with partial-onset seizures (POS). **METHODS:** Health insurance claims from 58 self-insured US companies between 1999 and 2009 were analyzed. Adult patients with POS (ICD-9: 345.4x, 345.5x, or 345.7x) receiving antiepileptic drugs (AED) were selected. A retrospective matched-cohort design was used to classify patients into cohorts of "uncontrolled POS" (≥2 AED therapy changes, followed by ≥1 epilepsy-related inpatient/ER visit within 1 year; and ≥ 1 diagnosis of POS) and "well-controlled POS" (no AED change and no epilepsy-related inpatient/ER visit). Patients in the well-controlled POS group were matched 1:1 with uncontrolled POS patients via propensity score matching. Matched cohorts were compared for healthcare resource use, morbidity, and costs. Statistical differences between cohorts were assessed using multivariate regressions, adjusted for demographics, baseline AED use, comorbidities and costs. **RESULTS:** From 14,377 eligible patients, 279 with uncontrolled POS (mean age=53.4, 55.6% female) were identified and matched 1:1 with well-controlled POS patients. Compared to the well-controlled POS group, the uncontrolled POS cohort had significantly more hospitalizations (adjusted rate ratio [ARR] (95% confidence interval [CI])=7.01 [5.97-8.82]), longer hospital stays (ARR (95% CI)=10.43 [9.69-11.23]), more ER visits (ARR (95% CI)=4.99 [4.25-5.87]), and more frequent outpatient visits (ARR (95% CI)=1.58 [1.55-1.62]). Fractures occurred three times more often in the uncontrolled POS group (ARR (95% CI)=3.43 [2.77-4.23]), while head injuries were twice as frequent (ARR (95%CI)=2.28 [2.02-2.56]). The uncontrolled POS group incurred nearly $15,000 increase in direct healthcare costs (adjusted cost difference (95% CI)=$14,966 [$11,695-$18,944]) versus the well-controlled group. Higher direct costs for the uncontrolled POS group were observed consistently across prescription drug and medical service categories. **CONCLUSIONS:** Uncontrolled POS was associated with significantly higher rates of healthcare resource utilization, more frequent occurrence of fractures and head injuries, and increased direct health care costs.

SB4

PROPENSITY-SCORE MATCHING (PSM) TO CONTROL FOR SELECTION BIAS IN "REAL-WORLD" TREATMENT COMPARISONS: A CAUTIONARY TALE CONCERNING ANTIBIOTIC THERAPY FOR INFECTIOUS DISEASE

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OBJECTIVES: In infectious disease, treatment decisions are often influenced by concerns about antibiotic resistance, which often leads to restriction of newer agents to sicker patients (i.e., selection bias). PSM is often used to control for this problem in "real-world" comparisons. We examined the adequacy of PSM in a "real-world" comparison of vancomycin versus daptomycin as treatment for complicated skin and skin structure infections (cSSSI). **METHODS:** Using a database

comprising >100 US hospitals, we identified admissions (1/1/2007 - 6/30/2010) with cSSSI who received initial antibiotic therapy with vancomycin or daptomycin. A propensity score model was estimated, using demographics, comorbidities, laboratory values, and receipt of vancomycin ≤30 days prior to hospitalization. Vancomycin patients were matched 1:1 to daptomycin patients in stepwise fashion to minimize the difference in propensity scores for each matched pair (i.e., "greedy" matching). **RESULTS:** We identified 347 patients who received daptomycin and 8963 patients who received vancomycin as initial antibiotic therapy for cSSSI. Four hospitals contributed 54% of daptomycin patients, but only 17% of vancomycin patients. Daptomycin and vancomycin patients differed significantly in a number of respects. Only 47.6% of daptomycin patients could be matched to vancomycin patients (i.e., most patients had nonoverlapping propensity scores). Unmatched daptomycin patients were older than those in the matched subset (mean age: 57.3yrs vs. 52.3yrs); they also were more likely to have chronic/ulcerative infections (23% vs. 10%), comorbidities (e.g., diabetes [19% vs. 0%], malnutrition [4% vs. 0%], alcohol/drug abuse [11% vs. 1%]), and to have been hospitalized previously (63% vs. 39%) (all $p<0.01$). **CONCLUSIONS:** While PSM is often used to control for selection bias, the problem of nonoverlapping propensity score distributions is often overlooked and can adversely impact generalizability. Use of PSM to control for selection bias in "real-world" comparisons of initial antibiotic therapy for infectious diseases may be limited; alternate study designs may be needed.

PODIUM SESSION II: COMPARATIVE EFFECTIVENESS RESEARCH & HEALTH CARE

CE1

COST EFFECTIVENESS TRENDS OF HIGH BUDGET IMPACT DRUGS (2006-2012)

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OBJECTIVES: The recently made coverage decisions by UK's NICE, Scotland's SMC and the allocation of $1.1 billion for comparative effectiveness research by the United States, are strong indicators of trends in pricing and reimbursement that are likely to be observed in the future. To gain an additional insight into these trends, we analyzed the cost effectiveness studies for the top twenty highest selling drugs (~$90-100B worldwide sales) **METHODS:** The Top 20 drugs were selected based on their worldwide sales. For this analysis, we segmented these drugs into categories as primary care, specialty, small molecules, biologics, therapy areas and availability of generic alternatives. We analyzed the cost effectiveness studies that were published in peer-reviewed journals. Search was conducted using generic names of the drugs and the phrase "cost effectiveness" in abstract of the published study. **RESULTS:** During 2005-2010, the number of published studies on "cost effectiveness" have increased by more than 30%. There is a large variability in CERs for same drugs for different indications, in some cases also varying by biomarkers. Primary care drugs had lower and less variable CERs than specialty drugs. Variations also exist in methodology used by different groups in modeling cost effectiveness, especially for time horizon and comparator. Majority of primary care drugs were modeled for a time horizon of 35-40 years or lifetime to demonstrate cost effectiveness. **CONCLUSIONS:** This analysis shows the range, variability and methods used for calculation of ICER values for these high budget impact drugs and provides lessons for executives and policy makers.

CE2

COMPARATIVE EFFECTIVENESS OF MONOTHERAPY WITH MOOD STABILIZERS VERSUS ATYPICAL ANTIPSYCHOTICS FOR THE TREATMENT OF BIPOLAR DISORDER IN CHILDREN AND ADOLESCENTS: A RETROSPECTIVE CLAIMS-DATA STUDY

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OBJECTIVES: Monotherapy with a mood stabilizer (MS) or second generation antipsychotic (SGA) is recommended as the first-line treatment for pediatric bipolar disorder (PBD). The existing evidence regarding the relative effectiveness of MSs and SGAs for PBD is predominantly based on short-term studies and does not adequately address long-term effectiveness. This study compared adherence, persistence, and bipolar-related hospitalization of these treatments during a one-year observation period. **METHODS:** The 2003-2007 Medicaid Analytic eXtract data for four states were used. Bipolar children and adolescents (aged 6-18 years) initiating treatment with SGA or MS monotherapy were identified. Adherence was measured using medication possession ratio (MPR) and persistence was measured as time to medication discontinuation and time to augmentation. Survival Analyses was conducted to compare time to first bipolar-related hospitalization, time to discontinuation and time to augmentation between MS and SGA recipients during a one-year period after treatment initiation. Heckman's Two-Step Selection Correction was used in all survival models to control for treatment selection bias. **RESULTS:** A total of 8424 PBD patients were identified. Prescription of SGAs (64.08%) was predominantly higher than that of MSs (35.92%). The most frequently prescribed SGA was risperidone, followed by quetiapine and aripiprazole. Divalproex sodium and oxcarbazepine were most frequently prescribed among MSs. 55% of the patients initiated on either of the therapeutic category were fully adherent. After correcting for selection bias, there was no statistically significant difference in the MPR, time to discontinuation and time to hospitalization between the two study groups. Patients initiating on SGAs took a longer time to augment (Hazard Ratio: 0.71; 95%CI: 0.57-0.88) with MSs as compared to those who initiated with MSs. **CONCLUSIONS:** Although SGAs were prescribed predominantly more than MSs, the two therapeutic classes were comparable in adherence and preventing bipolar related hospitalization. SGAs appeared to be slightly better than MSs in terms of time to augmentation.

CE3

GRACE CHECKLIST: RATING THE STRENGTH OF EVIDENCE FOR OBSERVATIONAL STUDIES OF COMPARATIVE EFFECTIVENESS

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OBJECTIVES: Observational studies are often necessary for assessing the comparative effectiveness of therapeutics in "real-world" settings. The strength of evidence generated by individual studies, however, varies. We describe the development of the GRACE Checklist, a tool for rating the quality of observational CER and assessing whether studies merit consideration for decision making. **METHODS:** A checklist was developed based on existing guidelines for the conduct and reporting of observational studies, including the GRACE Principles, and existing scales for the inclusion of observational studies in systematic reviews. An external advisory board reviewed the checklist content and scoring options; majority opinion of the advisors was used to refine the question items and scoring. The construct validity of the checklist was measured using two rounds of testing where over 100 volunteer testers rated articles, to determine if the checklist can distinguish studies of known quality. Articles of "known quality" were first extracted from systematic reviews and then, in the second round, were based on reviews of observational CER studies by recognized experts. **RESULTS:** Two domains, internal validity and applicability, were identified for inclusion with a total of 15 questions. Results and proposed scoring algorithms will be presented for a categorical assessment of study quality to determine if studies are 1) of sufficient quality for decision support; 2) sufficiently flawed to make interpretation unreliable; or 3) require additional consideration. First round testing results showed that subsets of item responses could yield positive predictive values for identifying high quality studies as high as 0.86, and negative predictive values as high as 0.91. **CONCLUSIONS:** A validated checklist to assess the quality of observational CER can help decision makers recognize strong evidence without substantial advanced training.

CE4

A FRAMEWORK FOR STAKEHOLDER ENGAGEMENT IN COMPARATIVE EFFECTIVENESS RESEARCH

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OBJECTIVES: Soliciting stakeholder input is becoming commonplace in comparative effectiveness research (CER), yet methods for stakeholder engagement in CER are evolving. Drawing from CMTP and University of Maryland's experiences across a variety of NIH, PCORI, and industry-funded activities as well as previously published case analyses, we describe a framework for stakeholder engagement in CER that standardizes approaches for generating meaningful evidence. **METHODS:** We conducted a literature search to explore engagement practices in biomedical sciences, social sciences, and business which included the gray literature. The results were combined with investigator experience to develop a process framework and corresponding activities for successful stakeholder engagement. **RESULTS:** We defined five steps- recruitment, preparation, engagement, dissemination, and evaluation- broadly applicable to stakeholder engagement. Recruitment should begin with clearly defined expectations for involvement and end with balanced representation of stakeholders that meet the needs of the project and disclose conflicts of interest. Preparing stakeholders for participation in CER requires customized and relevant background materials. Stakeholder engagement by an experienced facilitator should guide iterative engagement procedures by using deliberative methods that ensure a fair, competent and trustworthy process. Dissemination must document the stakeholders' input and how this information was incorporated into decision-making or pathways for implementation. Publications should also acknowledge stakeholder involvement and contributions. Following dissemination, evaluation provides both researchers and stakeholders an opportunity to assess the engagement experience and outcomes, which is necessary for refining practices for future work. **CONCLUSIONS:** CER is transitioning toward an interactive framework of stakeholder engagement that enhances the traditional research paradigm. This process model provides a standard methodology to guide this transition to stakeholder-based research. This process is adaptable across multiple CER activities including priority-setting, study design, and methods guidance as well as various therapeutic areas. Further research is needed to refine, evaluate, and apply this model to ongoing CER activities.

PODIUM SESSION II: CARDIOVASCULAR DISORDERS OUTCOMES RESEARCH

CV1

DIFFERENCES IN PROCESSES AND OUTCOMES OF CARE IN ELDERLY HYPERTENSIVE DIABETIC PATIENTS WITH AND WITHOUT DEMENTIA

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OBJECTIVES: To determine differences in processes and outcomes of care in elderly hypertensive diabetic patients with and without dementia. **METHODS:** This cross-sectional study was conducted using the household and medical provider component files of Medical Expenditure Panel Survey (MEPS) data from 2003, 2005, 2007 and 2009. Hypertensive diabetic patients >50 years of age were identified using