terms in the treatment selection equation and the TED equation proved to be independent, we re-estimated by univariate probit. Sensitivity analyses estimating the effect of olanzapine, risperidone, and quetiapine independently versus TAP were also conducted. RESULTS: A Wald test of the correlation coefficient of the disturbances suggests that treatment selection is exogenous in our model \((\rho = -0.049\text{ (p = 0.57)})\) using a Huber-White sandwich estimator of the variance. The univariate probit parameter estimates of AAP is statistically significantly positive \((p = 0.044)\) suggesting that AAP are associated with an increased risk of TED relative to TAP. The marginal effect of AAP is 0.0827; that is the TED propensity of AAP is 8.27% higher than that of TAP. A univariate probit model demonstrated that olanzapine \((p = 0.10)\), quetiapine \((p = 0.10)\) and risperidone \((p = 0.31)\) were independently associated with an increased risk of TED, though not significantly. A bivariate probit model omitting prior comorbidity, drug use and quarterly dummy variables demonstrates selection bias \((\rho = -0.630\text{ (p = 0.0029)})\). CONCLUSION: The results of this study show that AAP are associated with an increased risk of TED relative to TAP. Evidence of unobserved selection bias was not present. Explanatory variables that may explain treatment selection that were included in our model were sufficient to control for choice of therapy.

**SUICIDALITY AND ANTIDEPRESSANTS USE IN CHILDREN AND ADOLESCENTS**

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**OBJECTIVES:** The association between suicidality and antidepressant use has been reported in literature using clinical trial data. This study 1) investigates the relationship between suicidality and antidepressants use in children and adolescents using managed care claims data; 2) examines the effect of an FDA black box warning on antidepressant use in children and adolescents. **METHODS:** Subjects 5–19 years old, continuously enrolled in a large Midwestern IPA model health plan, diagnosed with depression (using ICD-9-CM codes) or issued at least one antidepressant prescription between January 1, 2004 and June 30, 2005 were included in the study. Descriptive statistics, paired samples t-test, Chi-Square test, and stepwise logistic regression were used to analyze the data. RESULTS: A total of 5104 subjects \((7.2\% \text{ continuously enrolled in 5–19 year olds})\) met the study criteria; 53% female; mean age was 15 years; 67% had depression diagnosis. Antidepressant use was modestly associated with suicidality using Chi-square test \((x^2 = 3.03, p = 0.08)\); contingency odds ratio = 1.67). Logistic regression showed that antidepressant use is not a significant predictor to suicidality, while gender, depression diagnosis, other comorbid mental health, drug and alcohol abuse, and specialty provider were significant predictors to suicidality. While average days on antidepressant drug therapy decreased significantly \((p = 0.009)\) after the black box warning, the number of inpatient stays for depression after the black box warning increased significantly \((p = 0.007)\). CONCLUSION: From this claims database, the association between suicidality and antidepressant use in children and adolescents is not clear. Caution is needed in the use of antidepressants in this population. Increased inpatient stays following the black box warning may be an indication that providers are more aware of the suicidality risk or due to decreased use of antidepressants. It is important to balance appropriate usage and concerns for the safety of medications with the risk of adverse events and subsequent health service use.

**MENTAL HEALTH—Cost Studies**

**FORECASTING U.S. MEDICAID PROGRAM EXPENDITURE ON ANTIDEPRESSANT DRUGS**

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**OBJECTIVES:** Depression is the most prevalent major mental health disorder, affecting between eight and ten percent of the U.S. population. The U.S. Medicaid programs spent approximately $2 billion on antidepressant drugs in 2005, across three categories of antidepressants including selective serotonin reuptake inhibitors, tricyclic antidepressants, and other antidepressants. Predicting future prices and utilization of antidepressants would facilitate Medicaid’s planning process. Our objective is to build forecasting models that can be used to improve Medicaid’s budgeting efforts. **METHODS:** We gather quarterly data (1991–2004, Centers for Medicare & Medicaid Services) on Medicaid national antidepressant expenditure. We use Box-Jenkins forecasting techniques on expenditure and utilization time series for specific antidepressants including Paxil, Prozac, Wellbutrin and Zoloft. Intervention analysis is used to determine the effects of patent expiration, new branded-drug entry, and new indication approval. Forecasts are computed and compared to a holdout sample, comprised of the 2005 data, to assess the performance of the models. RESULTS: The Box-Jenkins ARIMA algorithms for fitting and diagnosing the expenditure and utilization data resulted in four distinct non-stationary forecasting models. Final models were selected using standard information-based criteria. The Paxil and Prozac models incorporated an intervention term corresponding to patent expiration: a step function for Paxil and an exponential decay for Prozac. The best fitting model for Wellbutrin is a third order moving average in the first differences; the Zoloft model is a Random Walk. Maximum likelihood was used for estimations. Usual checks on the residuals proved to be satisfactory. CONCLUSION: ARIMA modeling can be used to capture the time series of individual antidepressant drugs purchased by Medicaid. Moreover, intervention analysis can be used to demonstrate the effect that generic entry has on the utilization of or expenditure on a branded medication. We find that the drugs studied are affected differently by this type of event.

**NET BENEFIT ANALYSIS OF DIVALPROEX SODIUM EXTENDED-RELEASE COMPARED TO VALPROIC ACID IN THE TREATMENT OF BIPOLAR DISORDER**

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**OBJECTIVES:** To analyze, from a payer perspective, the net benefit of prescribing divalproex sodium extended-release (DVPX-ER) versus valproic acid (VPA) in patients who suffer from bipolar disorder. **METHODS:** The study used a decision analytic framework to compare the net benefit of DVPX-ER relative to VPA in the treatment of bipolar disease. The decision model incorporated on two primary outcomes: GI side effects, and treatment success. Levels of health service utilization and probability values were obtained from an expert panel comprised of 15 psychiatrists. Costs were obtained from an academic medical center. Two-way sensitivity analysis on the probability of GI events and the probability of disease control for VPA was used to provide further insight regarding the set of combinations of values in the model consistent with the decision to use VPA and DVPX-ER. **RESULTS:** The average probability of GI side...
COST-EFFECTIVENESS ANALYSIS OF LONG ACTING MICROSPHERES OF RISPERIDONE (RISPERDAL CONSTA) IN THE TREATMENT OF SCHIZOPHRENIA IN MEXICO

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OBJECTIVES: The aim of the study was to estimate the cost-effectiveness relation of the long-acting injection formulation of Risperidone (LARI) IM every 2 weeks vs oral antipsychotics Olanzapine and Risperidone and the traditional prolonged-action antipsychotic injection formulation of haloperidol depot in the pharmacological management of schizophrenia in Mexico. Consequently, a pharmacoeconomic study was proposed using a cost-effectiveness model in adult patients treated in the Mexican Social Security Institute (IMSS). METHODS: A decision analysis was developed using a retrospective and comparative cost-effectiveness model over a 24 month period. A sample of Schizophrenic patients was obtained using IMSS databases and a decision tree based on relapses, hospitalization, pharmacological treatment, hospital discharges and re-hospitalizations. To determine the criteria for the effectiveness of each alternative, a meta-analysis was carried out based on national and international literature taking the clinical outcomes: total PANSS, changes in body weight, AE, adherence, hospitalization, re-hospitalization and relapses. The factors for costs were: specific pharmacological therapy, outpatient consultations for treatment, basal hospitalization, re-hospitalization, length of hospital stay and absence from work. The decision tree was validated by a panel of experts. RESULTS: Risperidone LA was the alternative with the lowest cost for annual treatment ($84,877 pesos). Differences versus the other treatment therapies were found in regards to hospitalization, subsequent hospitalizations and, to a lesser degree, absenteeism from work. Treatment with LARI produced savings of $8324 pesos compared to Haloperidol Depot (the most widely used injected antipsychotic in Mexico); compared to the second generation antipsychotics (atypical), savings were $27,733 pesos versus Olanzapine and $18735 pesos versus oral Risperidone. LARI produced the lowest number of re-hospitalized patients and events requiring re-hospitalization as well as superior clinical improvements compared to the other therapies. CONCLUSION: The study demonstrated that LARI is a cost-efficient and dominant alternative for the treatment of schizophrenia patients in Mexico.
Valproic Acid: Overused in Bipolar Disorder? Reappraising a Preference for Valproate. We read with interest the article by David N. Osser, MD, “Valproic Acid: Overused in Bipolar Disorder?” A randomized, placebo-controlled, multicenter study of divalproex sodium extended release in the treatment of acute mania. J Clin Psychiatry. 2006;67(10):1501-10. 8. Wagner KD, Redden L, Kowatch RA, Wilens TE, Segal S, Chang K, et al. Divalproex sodium versus placebo in the treatment of acute bipolar depression: a systematic review and meta-analysis. J Affect Disord. 2010;124(3):228-34. 12. Wang PW, Nowakowska C, Chandler RA, Hill SJ, Nam JY, Culver JL, et al. Divalproex extended-release in acute bipolar II depression. J Affect Disord. 2010;124(1-2):170-3. To analyze, from a payer perspective, the net pharmaceutical and medical costs of prescribing divalproex sodium extended-release (DVPX-ER) versus valproic acid (VPA) in patients with bipolar disorder. The study used a decision analytic framework to compare the total costs associated with DVPX-ER relative to VPA in the treatment of bipolar disease. Divalproex sodium-treated patients compared with valproic acid-treated patients were less likely to have discontinued their medication because of side effects (4.0% vs. 12.7%, p = .0066). Twelve (63.2%) of 19 patients who discontinued valproic acid because of gastrointestinal side effects were subsequently treated with divalproex sodium, of whom only 2 continued to have gastrointestinal side effects. Divalproex sodium extended-release tablets USP, 250 mg and 500 mg are for oral administration. Divalproex sodium extended-release tablets, USP contain divalproex sodium, USP in a once-a-day extended-release formulation equivalent to 250 and 500 mg of valproic acid. Inactive Ingredients. Divalproex sodium dissociates to the valproate ion in the gastrointestinal tract. The mechanisms by which valproate exerts its therapeutic effects have not been established. It has been suggested that its activity in epilepsy is related to increased brain concentrations of gamma-aminobutyric acid (GABA). pharmacodynamics. The relationship between plasma concentration and clinical response is not well documented. OBJECTIVES: To compare divalproex sodium and valproic acid for therapeutic patterns, persistence rates, and predictors of hospitalization among bipolar patients on monotherapy in the Veterans Affairs Health care system. METHODS: Using VA administrative data bases, we conducted a retrospective inception cohort study of VA patients 18 years of age who had at least one outpatient diagnosis of bipolar disorder and two continuous prescription records for the study drugs in the VA PBM pharmacy database during the study period of April 1, 2001 to September 30, 2003. One such use is the treatment of bipolar disorder with sodium valproate. This paper reviews the evidence for using the licensed alternative, valproate semisodium, under the headings of licence, efficacy, pharmacokinetics and tolerability. Type. In the UK, sodium valproate and valproic acid are available in enteric coated formulations, but this is not the case in the USA. A modified release formulation of a combination of sodium valproate and valproic acid in a 2:3:1 ratio is also available in the UK. Valproate semisodium (divalproex semisodium in the USA) is a more recent product, marketed in the UK by Sanofi-Synthelabo under the trade name of Depakote. It consists of a compound of sodium valproate and valproic acid in a 1:1 molar relationship in an enteric coated form.