UNINTENDED CONSEQUENCES OF CURRENT ANTIDEPRESSANT USE IN A GERIATRIC POPULATION: DRUG-DRUG INTERACTIONS AND THEIR IMPLICATIONS FOR ADHERENCE

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OBJECTIVES: Antidepressants can cause undesirable drug-drug interactions when taken concomitantly with certain medications. Elderly patients may be particularly vulnerable to antidepressant interactions due to slower metabolism and utilization of multiple pharmacotherapies. The objective of this study was to determine rates of potential drug-drug interactions involving antidepressants in a geriatric population and their impact on prescription adherence. METHODS: Data were from the MarketScan® Medicare Database, a claims database from retirees with employer-sponsored Medicare supplemental insurance. Subjects were age >65 years, new antidepressant users, and had a depression diagnosis between 7/1/2001-12/31/2006. Potential drug-drug interactions involving at least one antidepressant and another drug with overlapping days supplied were identified over the one year following antidepressant initiation using MicroMedex DRUG-REAX® software. Multinomial logistic regression and bivariate statistics were used to evaluate the association between potential interactions and whether patients discontinued, reffilled or switched their first antidepressant prescription. RESULTS: Among the 39,513 patients who met inclusion criteria, 25.4% had potential contraindicated or major interactions, 36.1% had moderate interactions, and 38.5% had minor or no interactions. Compared to the moderate/minor/no interactions groups, the contraindicated/major group had a greater prevalence of medical comorbidities and higher comorbidity indices (p < 0.001). Amitriptyline hydrochloride was involved in 19.1% of the potential contraindicated major interactions. Tramadol hydrochloride and oxycodone, opioid analgesics, were the most common medications with contraindicated/major interactions. Presence of contraindicated/major and moderate interactions was associated with an increase in probability of switching to a different antidepressant and 11 percentage points, respectively (p < 0.001) and decreased probability of discontinuing of 3.5 and 2.5 percentage points (p < 0.001), after controlling for age, gender, pre-period mental disorders, antidepressant use at baseline, antidepressant treatment type, and use of psychotropic medications. CONCLUSIONS: Elderly antidepressant users frequently use medications with the potential for interactions with their antidepressant medication. There is a need for antidepressants with improved interaction profiles.

ADHERENCE AND PERSISTENCE IN SECOND-GENERATION ATYPICAL ANTIPSYCHOTIC MEDICATIONS IN PATIENTS ENROLLED IN EMPLOYER-SUPPORTED HEALTH PLANS

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OBJECTIVES: Patients prescribed a regimen of atypical antipsychotic medications face many challenges. Adherence and persistence rates are typically low. We investigated determinants of adherence and persistence to second-generation antipsychotic medications (SGAs) for patients with schizophrenia and bipolar disorder, including financial factors (patient cost-sharing and out-of-pocket burden) and formulary status. METHODS: A retrospective study of patients aged 18-64 years with at least one SGA claim, 24 months of continuous enrollment and employer-based coverage via large US firms in 2003–2006 (n = 9714). The study initiation index date was defined as the first SGA fill following a 12-month period without use of SGAs. Multivariate Cox proportional hazards models were estimated for persistence to SGAs (using a 30-, 60- and 90-day gap in therapy) and multivariate cross-section/time-series models were estimated for SGA adherence (PDC >= 80%). Explanatory variables included patient, plan, and provider characteristics, health status, cost-sharing (prescription drug and medical) and time. An empirical measure of SGA formulary status was developed. RESULTS: Over three quarters of patients (78%) discontinued SGA treatment and average persistence until a 90-day gap was 184 days. Higher prescription drug and office visit patient cost-sharing amounts were associated with shorter time on SGAs, especially when cost-sharing exceeded $40 per fill or visit (95% confidence interval hazard ratio for 90-day gap (1.01,1.13) prescription drug (1.00,1.24) office visit) relative to cost-sharing of <$5. Higher prescription drug cost-sharing and patient total (drug and medical) out-of-pocket burden (measured in the previous 12 months) were associated with lower levels of adherence (both p < 0.01). CONCLUSIONS: Even in a well-insured patient population, benefit plan design factors can affect adherence and persistence to SGAs for patients with schizophrenia and bipolar disorder. Insurers and plan managers should take note of the prescription drug and medical plan design attributes that influence adherence to medications among this vulnerable patient group.

IMPACT OF ALTERNATIVE DEFINITIONS OF MEDICATION COMPLIANCE ON FIRST YEAR TREATMENT COST FOR PATIENTS WITH SCHIZOPHRENIA

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OBJECTIVES: To investigate the relationship between compliance and first-year post-treatment cost for patients with schizophrenia. METHODS: Commercial health plan data from July 1, 2003 to June 30, 2006 were used to identify patients with schizophrenia who initiated treatment using a typical or atypical antipsychotic, a mood stabilizer or an antidepressant. Episodes were divided into three categories: restarting a new drug at any time; switching after 31-90 days with the drug used in the previous episode; switching therapy with or without a break in treatment; and augmentation therapy. First observed episodes were excluded due to uncertainty concerning the patient’s prior treatment history. A total of 21,872 episodes were included in ordinary least squares (OLS) regression models of post-treatment cost as a function of alternative definitions of compliance adjusting for age, gender, geographic region, drug use history, prior medical care use, schizophrenia diagnosis and co-morbid medical conditions. RESULTS: Adding a second medication within one year is the key factor in the relationship between compliance and one-year costs. One year of uninterrupted therapy on the initial drug without adding a second medication increased drug costs by $3314, while reducing medical costs by $3919 (p < 0.0001 for both estimates) and total cost by $655 (p < 0.05). One year of therapy on the initial drug augmented with a second medication increased drug costs (+$5062) and medical costs (+$4777) compared to non-compliance (p < 0.0001 for both estimates). One year of uninterrupted therapy on a second drug after terminating the initial therapy was associated with the highest costs: +$5,955 for drugs and +$8,902 for medical services (p < 0.0001 for all estimates). Analyses conducted separately by type of episode confirmed these patterns of cost estimates. CONCLUSIONS: Compliance and switching may not pay off in reduced medical costs only if the patient is maintained on their initial drug regimen. Changes in therapy are associated with higher medical costs.

IMPACT OF REJECTED CLAIMS ON PERSISTENCE TO SECOND GENERATION ANTI-PSYCHOTIC MEDICATIONS

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OBJECTIVES: To examine the impact of having a newly prescribed second generation antipsychotic (SGA) claim rejected due to formulary restrictions on subsequent medication persistence to the SGAs. METHODS: A retrospective cohort study was conducted using data from a national pharmacy benefit management company. Newly initiated antipsychotic users, aged 18-64 years who had a rejected SGA (aripiprazole, olanzapine, quetiapine, risperidone, ziprasidone) claim due to benefit reasons (step
therapy, prior authorization, not in formulary) between January 1, 2005 to December 31, 2006 but who subsequently filled an SGA or conventional antipsychotic within six months of the rejected claim, formed the case group (n = 328). Newly initiated antipsychotic users who were in health plans with an open formulary and thus did not experience rejection of SGA claim formed the control group (n = 1097). All claims were followed up for 13 months. Cox regression models were used to estimate the effect of having rejected claims on all-cause discontinuation of the index drug, defined as discontinuation, add-on or switch. The model controlled for age, sex, co-morbidities, geographic location, index drug, prescription co-payment. RESULTS: Reasons for rejected claims were distributed as follows: 1) drug not on formulary (72.9%); 2) required prior authorization (19.5%); and 3) required step therapy (7.6%). Median time to discontinuation was 120 days for the case group and 127 days for the control group. The adjusted hazard for discontinuation of the index drug (HR = 1.29, 95% CI: 1.08–1.53) was significantly higher for patients with rejected initial SGA claims compared to controls. Co-payments ranging from $20 to $39 were associated with lower discontinuation compared with copayment ranging from $0 to $4 (HR = 0.75, 95% CI: 0.60–0.93). CONCLUSIONS: New antipsychotic users with rejected initial SGA claims due to formulary restrictions were more likely to discontinue their antipsychotic drugs compared to users who did not face such restrictions.

**PMH45**

THE ASSOCIATION OF COPAY BURDEN AND MEDICATION ADHERENCE AMONG PATIENTS WITH SCHIZOPHRENIA

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OBJECTIVES: To assess the association between self-perceived copay burden and medication adherence among patients with schizophrenia. METHODS: Data were collected from December 2007 to February 2008 from a web-based consumer panel. Adults (age 18+) self-reporting a diagnosis of schizophrenia were invited to participate in the study through e-mail and phone. Responses were collected over 45 interviews across the facilities. Inclusion criteria for analysis were; current use of an SGA, and no exposure to clozapine or a depot formulation antipsychotic. Adherence was assessed using the MMAS, with general adherence defined as MMAS < 2, and complete adherence defined as MMAS < 1. Logistic regression models were developed to assess the effects of self-perceived copay burden on adherence while adjusting for demographics, substance use, concomitant psychotropic medications, comorbidities, and health insurance. RESULTS: Of the 351 study respondents who met criteria for analysis, 39% (n = 137) perceived experiencing burden from copay medication copays. Adjusting for covariates, the effects of copay burden on general adherence approached but did not reach significance (p = 0.060). However, patients who experienced a copay burden were less than half as likely to have complete adherence [OR = 0.427; 95% CI: (0.257, 0.711); p = 0.001]. Effects of copay burden on the individual components of the MMAS varied. Patients with copay burden were more likely to forget to take medication [OR = 2.058; 95% CI: (1.270, 3.335); p = 0.001] and to discontinue medication when feeling worse [OR = 2.000; 95% CI: (1.140, 3.507); p = 0.016]. Being careless about taking medication and discontinuing medication when feeling better were not significantly affected by copay burden. CONCLUSIONS: Among patients with schizophrenia using SGAs, copay burden is associated with forgetting to take medication, discontinuing medication when feeling worse, and a lack of likelihood of complete adherence. Less restrictive formulations that reduce copay burden for SGAs may have a positive effect on medication adherence among patients with schizophrenia.

**PMH46**

PREDICTORS OF DULOXETINE TREATMENT PERSISTENCE FOR PATIENTS WITH MAJOR DEPRESSIVE DISORDER

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OBJECTIVES: Treatment of depression is often accompanied by discontinuation and switching of antidepressant medications. Information on factors predicting persistence (and avoidance of switching) would thus be of value to medical decision makers. We assess the impact of demographics, initial dose, prior medications, and comorbidities on duloxetine treatment persistence for patients with major depressive disorder (MDD) using retrospecitive claims data. MEthODS: Using the PharMetrics Database, we studied individuals aged 18–64 who initiated duloxetine treatment between April 2005 and March 2006, had ≥1 prior MDD diagnosis, and had continuous insurance coverage 6 months before and 12 months after initiation. Persistence was defined as ≥3 months’ continuous duloxetine treatment. Stepwise logistic regression and tree analyses of demographics, initial dose, prior medications, and comorbidities assessed predictors of persistence. Sensitivity analysis was done by analyzing factors associated with switching to venlafaxine XR or a selective serotonin reuptake inhibitor (SSRI) within 60 days of initiating duloxetine. RESULTS: Among 9,104 patients (74.1% female; mean age = 45.6, SD = 11.1) who initiated duloxetine treatment, 61.5% had persistence of duloxetine treatment for ≥3 months. Regression results showed the most significant factors for persistence to be initial dose of ≥260 mg QD (OR = 1.38), age group and injection of H1 prior to age 18–25 yrs vs. 18–34 yrs (OR = 1.63), and venlafaxine XR initiation in the prior 3 months (OR = 1.64) (all p-values < .001). Sensitivity analysis showed initial dose of <600 mg QD was associated with switching from duloxetine (OR = 1.22), although other factors showed differences from the persistence analysis. CONCLUSIONS: The results suggest that for MDD patients, initial dose, age group, and recent venlafaxine XR/SSRI use predict persistence on duloxetine treatment. Sensitivity analysis on switching showed a consistent effect of initial dose.

**PMH47**

REASONS FOR DISCONTINUATION AND CONTINUATION OF ANTIPSYCHOTIC THERAPY FROM PATIENT AND CLINICIAN PERSPECTIVES


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OBJECTIVES: To assess the reasons for discontinuation and for continuation of antipsychotic medication in the treatment of schizophrenia from patient and clinician perspectives. METHODS: Two measures were developed to assess the Reasons for Antipsychotic Discontinuation/Continuation (RAD), one from patient’s perspective (RAD-I), and the other from clinician’s perspective (RAD-Q). These measures were administered to patients enrolled in a 12-week study of antipsychotic medication in the treatment of schizophrenia (N = 630). Reasons for discontinuation and reasons for continuation with the assigned antipsychotic during the study were assessed. Reported reasons were rated as being a primary reason, very important, somewhat important, or of minor importance. The top three primary reasons for medication discontinuation and continuation were identified from patient and clinician perspectives, and level of concordance between patients’ and clinicians’ reasons was assessed. RESULTS: The top primary reasons for medication discontinuation differed from the top primary reasons for continuation on the medication, with a high level of concordance between patients’ and clinicians’ perspectives. The top three primary reasons for medication discontinuation were insufficient improvement or worsening of positive symptoms, medication-related adverse events, and insufficient improvement or worsening of mood symptoms. The top three primary reasons for medication continuation were improvement in positive symptoms, subjective perception of improvement, and improvement in level of functioning. CONCLUSIONS: Medication efficacy appears to be the core driver of medication continuation and discontinuation, especially with regard to positive symptoms. Reasons for medication discontinuation differ somewhat from reasons for continuation, with a high level of concordance between patients’ and clinicians’ perspectives.

**PMH48**

BURDEN OF ILLNESS OF DEPRESSION SYMPTOMS AMONG PATIENTS WITH TYPE 2 DIABETES MELLITUS

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OBJECTIVES: The purpose of this analysis is to quantify the additive burden associated with experiencing depression symptoms in patients with type-2 diabetes mellitus (T2DM). METHODS: Data were from the 2008 US National Health and Wellness Survey (NHWS), an annual cross-sectional survey of self-reported health care attitudes, behaviors, disease states, and outcomes of adults aged 18+. Analyses were limited to respondents self-reporting a diagnosis of T2DM. Depression symptoms were defined as an affirmative response in the past month to: bothered by feeling down, depressed or hopeless; or bothered by having little interest or pleasure in doing things. Outcomes included health care utilization in the past six months, work productivity as measured by the Work Productivity and Activity Impairment (WPAI) questionnaire, and SF-12v2 summary scores. Logistic and linear regression models were developed to assess independent effects of depression on outcomes, while adjusting for demographics and co-morbidities. RESULTS: Among patients with T2DM, 38% self-reported depression symptoms. Adjusting for demographic and co-morbid factors, depression symptoms were 1.7 (p < 0.001) times as likely to visit the emergency room, 1.6 (p < 0.001) times as likely to be hospitalized, and 2.2 (p < 0.001) additional provider visits compared to T2DM patients without depression symptoms. Depression symptoms were also associated with 21.4% (p < 0.001) greater impairment in daily activities and a decrease in SF-12v2 physical and mental summary scores of 4.0 (p < 0.001) and 12.7 (p < 0.001) points, respectively. Among patients who were employed full-time, depression symptoms were associated with 4.3% (p < 0.001) greater missed work time, 15.2% (p < 0.001) greater lost productivity while working, and 13.4% (p < 0.001) greater overall work impairment. CONCLUSIONS: In patients with T2DM, depression symptoms were associated with significant burden on health care utilization, work productivity, and health-related quality of life. Proper treatment of both T2DM and co-morbid depression in this population may reduce humanitarian and economic burden of disease.

**PMH49**

ASSESSMENT OF TYPE 2 DIABETES MELLITUS PATIENTS WITH AND WITHOUT SYMPTOMS OF ADDH: PATIENT CHARACTERISTICS AND RESOURCE UTILIZATION DATA FROM AN INTERNET-BASED SURVEY

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OBJECTIVES: Type 2 Diabetes Mellitus (T2DM) is an adult-onset, chronic, metabolic disorder that affects approximately 23.5 million adults in the United States and requires management with daily medications, blood glucose monitoring, regular HbA1c assessments, diet, and exercise. If T2DM patients also have difficulties with planning, working memory, and organization, their health problems may be compounded due to inappropriate management of their chronic health condition. The current study sought to estimate the prevalence of T2DM patients with the