FACTORS ASSOCIATED WITH THE PRESCRIPTION OF ANTIPSYCHOTICS:

MEDICARE UTILIZATION AND COSTS IN 2004

By

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To the Faculty of Washington State University:

The members of the Committee appointed to examine the thesis of Yu-Yu Tien find it satisfactory and recommend that it be accepted.

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ABSTRACT

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Objective: To determine whether the use of typical, atypical, or combination antipsychotics vary by patient attributes, and whether the type of antipsychotic medication affects the utilization and costs of healthcare services.

Methods: The cross-sectional study is conducted by using the data from the 2004 Medicare Current Beneficiary Survey (MCBS). The antipsychotic users are divided into two groups: 1) typical antipsychotics only, and 2) atypical antipsychotics (with or without concurrent use of typical antipsychotics). Bivariate and multivariate analyses examine how predisposing, enabling, and need factors influence Medicare beneficiaries' receipt of typical and atypical prescriptions,

and examine the effects that typical and atypical antipsychotic medications have on total prescribed medication events, inpatient admission rates, outpatient visits, and costs.

Results: An estimated 1.26 million Medicare beneficiaries filled one or more antipsychotic prescriptions in 2004. Hispanics, those eligible for Medicaid and Medicare, Medicare HMO enrollees, and those with fair or poor health are at highest risk of receiving typical antipsychotics. The costs of prescribed medicine, inpatient costs, and total health costs are substantially higher for atypical users in the Medicare population.

Discussion: Prescriptions for atypical antipsychotics outpace prescriptions for typical antipsychotics. This study found ethnic disparities for antipsychotic users among Medicare beneficiaries. Insofar as atypical agents are the treatment of choice, it is crucial that providers are aware of these disparities and provide the appropriate medications to all patients. In addition, atypical antipsychotics are associated with higher hospitalization rates which could have important implications for clinical practice. It is possible that atypical agents are simply not as efficacious as initially thought. Some metabolic side effects induced by atypical agents might aggravate health conditions other than mental illness, leading to hospitalization for cardiac conditions, diabetes related problems, or other chronic conditions. Additional research that attempts to control for these factors is urgently need.

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CHAPTER ONE

INTRODUCTION/SIGNIFICANCE OF STUDY

This chapter introduces the current trends in use and costs of antipsychotics, and the characteristics of typical and atypical antipsychotics. This chapter contains the following parts: introduction and purpose of the study, statement of the research problem, importance/significance of the proposed study, key research questions, and study hypothesis.

Introduction and purpose of the study

This study analyzes the cost and use of conventional and atypical antipsychotics in 2004, the year before Medicare Part D was implemented. Atypical antipsychotic medications, also known as second-generation antipsychotics, were introduced in the late 1990s, and are now widely prescribed. Compared to conventional antipsychotics, atypical antipsychotics are more expensive, but are thought to be more effective and have fewer side effects (Brody, Larner, & Minneman, 1998). Prescription of antipsychotic medications is a function of patient and physician characteristics, as well as the perceived efficacy and side-effect profile of the prescribed drug. This research examines patient factors associated with class of antipsychotic medications prescribed and associated health costs, using the data from 2004 Medicare Current Beneficiary Survey (MCBS).

Patient age, gender, race, ethnicity, chronic condition, health status, income and supplemental insurance coverage are identified as factors that may influence the prescription of conventional or atypical antipsychotics (Sankaranarayanan & Puumala, 2007). Cost measures include prescription drug expenditures, inpatient (hospital costs), outpatient costs, and total annual health costs.

Statement of research problem

Since 1997, spending on psychotropic medications has increased much more than overall prescription drug spending (Frank, Conti, & Goldman, 2005). In 2003, antidepressant and antipsychotics costs exceeded $18 billion (Frank et al.). The amount spent on antipsychotics increased 22% from the previous year (Frank et al.). The introduction of new drugs with higher prices, as well as greater use of existing drugs, accounts for the increased cost of antipsychotics (Huskamp, 2005). In particular, demand for atypical antipsychotics increased 43% per year from 1997 to 2001 (Frank et al.).

Clinical studies have reported that atypical antipsychotics have been more effective in treating negative symptoms of schizophrenia, have relatively fewer extrapyramidal side effects, and are easier for patients to tolerate (Brody et al., 1998; Mauri, Regispani, Beraldo, Volonteri, Ferrari, Fiorentini, et al., 2005). However, these patent-protected medications cost substantially more than conventional antipsychotics, with significant

cost implications for large insurers. Given the clinical importance of these drugs, as well as their relatively high costs, it is important to indentify the rates of use in the Medicare population, and patient level factors associated with use. By comparing prescription drug patterns among different types of antipsychotics, this research identifies patients at risk of receiving the older, and arguably less effective conventional antipsychotics, and identifies the relationship between medications prescribed and health care costs.

Importance/significance of the proposed study

One fifth of Americans have a mental health disorder (Sankaranarayanan & Puumala, 2007). The prevalence rate of schizophrenia, a population with high antipsychotics use, is approximately 0.5 to 1% of American population. The costs of antipsychotics are a significant burden to the US health care system, especially to large public programs. In 2001, 67% of the antipsychotic prescriptions in the U.S. were paid by Medicaid (Sankaranarayanan & Puumala). With the implementation of Medicare Part D in 2006, a portion of these costs (for dual eligible beneficiaries) were assumed by the Medicare program (Huskamp & Shinogle, 2005). By 2007, the top three most costly drugs in the Medicare Part D program were atypical antipsychotics (O'Donnell, 2009). In order to manage the increased costs of atypical antipsychotics, it is important to understand utilization patterns.

This study provides the information on antipsychotic use and costs among Medicare beneficiaries in 2004, the year before Medicare Part D implementation. These analyses will provide baseline data to assess changing prescription patterns and associated costs within the Medicare program.

Key research question(s) and hypotheses

The key research questions are whether the use of typical, atypical, or combination antipsychotics vary by patient attributes, and whether the type of antipsychotic medication affects the utilization and costs of healthcare services. The identification of patient attributes is derived from the Andersen's Behavioral Model of health care utilization (Andersen, 1995).

It is hypothesized that specific groups of Medicare beneficiaries will be at higher risk of receiving prescriptions for conventional rather than atypical antipsychotics, including racial and ethnic minorities, older beneficiaries, low income beneficiaries, and beneficiaries without supplemental insurance. Moreover, it is assumed that atypical users will have higher medication costs than typical users, but that the rates of hospitalization, outpatient visits and total health care costs will be less for atypical users than typical users.

CHAPTER TWO

LITERATURE REVIEW

This literature review describes the features of antipsychotics, and the factors associated with antipsychotic use, inclusive of race, ethnics, age, and insurance types.

PUBMED was used as the key search database in this study. The primary search terms used were “typical/atypical”, “antipsychotic”, “utilization”, “trends”, ”pattern”, “costs”, “pharmacoepidemiology”, “MCBS”, “Medicare”, “factors influencing prescription of antipsychotic”, ”racial”, in varying combinations. The reference sections of key articles and their related articles provided by PUBMED were reviewed to select some other relevant articles. Articles discussing antipsychotic use, costs and prescribing patterns are included. Clinical studies focusing solely on efficacy or side-effects were excluded. The number of total searched articles is 280. After using inclusive and exclusive criteria to check titles and abstracts, there were 56 articles included in this study.

Features of antipsychotics

Typical antipsychotic medications

Typical antipsychotics, also named conventional antipsychotics or first generation antipsychotics, were developed in the 1950s (Reilly & Kirk, 2007). Typical

antipsychotics, such as chlorpromazine and haloperidol, are used to treat schizophrenia. From a pharmacology standpoint, typical antipsychotics act as antagonists on acetylcholine, dopamine, serotonin, and norepinephrine receptors (Brody et al., 1998). The efficacy of antipsychotics is believed to be dependent on the ability to block dopamine receptors.

Typical antipsychotics have demonstrated an improvement of positive symptoms for schizophrenia, but they do not have an impact on the negative symptoms. Because typical antipsychotics do not selectively target the dopamine receptors in the pre-frontal cortex, several side effects are reported, such as extrapyramidal symptoms (EPS) (e.g., parkinsonian syndrome, akathisia dystonia, tardive dyskinesia). Other side effects not caused by dopamine include dry mouth and urinary retention (Brody et al., 1998). Therefore, patients taking typical antipsychotics may experience more difficulty in comparison to than atypical antipsychotics for patients to tolerate, which may result in poor treatment adherence.

Atypical antipsychotics

Atypical antipsychotics, known as second generation antipsychotics, were introduced in late 1990s (Reilly & Kirk, 2007). Compared to typical antipsychotics, this type of drug has more selective antagonism of the D2-dopaminergic receptor. Atypical

antipsychotics increase the ability to treat negative as well as positive symptoms of schizophrenia, and reduce the unwanted side effects, extrapyramidal symptoms and tardive dyskinesia (Reilly & Kirk). The reduced side effects of atypical antipsychotics resulted in an increased tolerance of their use with patients and result in higher rates of compliance.

However atypical antipsychotics are associated with metabolic side effects which could induce weight gain, and are dangerous for patients with hyperglycemia and diabetes (Brody et al., 1998; Nasrallah, 2008). Atypical antipsychotics, such as risperidone, olanzapine, quetiapine, ziprasidone, and aripiprazole, are now in widespread use.

Factors associated the prescription of antipsychotic use

Race/ethnicity

It is estimated that the non-white population will compose nearly half of the American population in 2050 (Opolka, Rascati, Brown, & Gibson, 2004). A number of studies have found that racial and ethnic minorities are less likely to receive a prescription for atypical antipsychotics than their white counterparts (Baillargeon & Contreras, 2001; Copeland, Zeber, Valenstein, & Blow , 2003; Herbeck, West, Ruditis, Duffy, Fitek, Bell, et al., 2004; Kuno & Rothbard, 2002; Kuno & Rothbard, 2005;

Lehman & Steinwachs, 1998; Mallinger, Fisher, Brown, & Lamberti, 2006; Mark, Palmer, Russo, & Vasey, 2003; Opolka, Rascati, Brown, Barner, Johnsrud, & Gibson, 2003; Opolka et al., 2004; Rothbard, Kuno, & Foley, 2003; Van Dorn, Swanson, Swartz, & Elbogen, 2005; Wang, West, Tanielian, & Pincus, 2000). Other studies suggest that African Americans are more likely to take combination or typical antipsychotics (Daumit, Crum, Guallar, Pwe, Primm, Steinwachs, et al., 2003; Sankaranarayanan & Puumala, 2007; Van Brunt, Gibson, Ramsey, & Obenchain, 2003).

Current research asserts that cultural and socioeconomic factors affect antipsychotic prescription use patterns (Daumit et al., 2003; Kuno & Rothbard, 2002; Opolka et al., 2004; Ren, Kazis, Lee, Hamed, Huang, Cunningham, et al., 2002). Racial and ethnic minorities may have less access to more effective, newer, higher-cost health technologies and pharmacotherapies for mental disorders. During the past decade, the difference in prevalence of atypical antipsychotic prescription by race disparity has decreased, but still persisted for African Americans with psychotic disorders (Daumit et al.).

The variation of the symptoms presented by the patients may account for some of the observed race/ethnic disparities. African Americans with schizophrenia have more positive symptoms, such as hallucinations and delusions than other ethnic groups (Opolka et al., 2003).

Another key factor associated with limited access to atypical antipsychotics is low socioeconomic status, which is more common among racial and ethnic minorities (Daumit et al., 2003). The cost of atypical antipsychotics is 10 times more expensive than typical antipsychotics, which may result in access limitations for consumers with limited income (Daumit et al.).

Patients' preference may also play a role in the gap of atypical prescription between African American and white patients (Copeland et al., 2003; Daumit et al., 2003). Racial minorities appear to switch to atypical antipsychotics only when necessary due to deterioration of their clinical condition (Daumit et al.). African American and Hispanic patients refusing to take newer drugs (Opolka et al., 2003) and the lack of a good physician-patient relationship are also suggested as potential reasons which could result in the racial/ethnic disparities (Copeland et al.).

Age

Several studies indicate that older patients are more likely to use typical antipsychotics than atypical and combination antipsychotics (Mirandola, Andretta, Corbari, Sorio, Nosè, & Barbui, 2006; Rothbard, Murrin, Jordan, Kuno, McFarland, Stroup, et al., 2005; Sankaranarayanan & Puumala, 2007; Van Brunt et al., 2003). However, the Medical Expenditure Panel Survey in 1996-2004 shows that second

generation antipsychotics are consistently increasing among elderly patients, despite the costs of first-generation drugs remaining stable (Jano, Chen, Johnson, & Aparasu, 2007; Wang et al., 2000). The elderly are at significantly greater risk of tardive dyskinesia and other EPS, making atypical medications a more attractive option for prescribing physicians (Jeste, Lacro, Bailey, Rockwell, Harris, & Caligiuri, 1999; Huskamp, 2005; Sankaranarayanan & Puumala; Schneider, Tariot, Lyketsos, Dagerman, Davis, Davis, et al., 2001; Zuvekas, 2005).

Insurance type

Insurance status plays a role involving antipsychotic utilization patterns. The overall expenditures of antipsychotics in 2001 were financed 36% by private insurance, 36% by out-of pocket, and 28% by public programs (Zuvekas, 2005). Private insurance plans were more likely to cover atypical antipsychotic prescriptions during the introduction period for these medications from 1996-2003 (Sankaranarayanan & Puumala, 2007), and still provide relatively generous coverage. Public plans now cover most atypical antipsychotics, but prescribing rates appear to lag behind private plans (Daumit et al., 2003). Drug costs and antipsychotic utilization patterns will be affected by the new Medicare Part D prescription drug benefit.

Other associated factors

It appears that atypical antipsychotic users are less likely to be diagnosed with schizophrenia or psychotic disorders than typical and combination antipsychotics users. These medications are prescribed for depression, bipolar disorder, and anxiety, as well as schizophrenia (Opolka et al., 2004; Sankaranarayanan & Puumala, 2007; Van Brunt et al., 2003; Wang et al., 2000). Patients with more severe symptoms, multiple psychiatric comorbidities, or treatment resistance are more likely to receive atypical antipsychotics (Opolka et al.; Wang et al.).

Health care providers also influence which type of antipsychotics are prescribed. Psychiatrists are more likely to prescribe atypical antipsychotics than primary care physicians (Sankaranarayanan & Puumala, 2007; Opolka et al., 2004).

Some studies have also evaluated the regional differences in antipsychotic use. However, due to different sample sizes and region, there was no clear conclusion regarding whether people living in different areas have different preferences towards different types of antipsychotic utilization (Opolka et al., 2004).

Medical costs associated with antipsychotics

The 2003 sales of antipsychotics in the U.S. were $ 8.1 billion, up 22.1 % from 2002 (Frank et al., 2005). People receiving atypical antipsychotics increased from 0.3 million

in 1996 to 1.6 million in 2001, while typical users decreased from 1.1 million to 0.5 million (Zuvekas, 2005). The expanded use of atypical antipsychotics has had a major impact on Medicaid and drug spending for other public programs (Frank et al.; Sankaranarayanan & Puumala, 2007).

Atypical antipsychotics accounted for 71% of the antipsychotic medication in U.S. in 2005 (Farley, Cline, Schommer, Hadsall, & Nyman, 2008). The increased costs for atypical agents are expected to be offset by minimized side effects, increased patient complacence, improved treatment outcomes, and reduced the need for other psychiatric services (Gasquet, Gury, Tcherny-Lessenot, Quesnot, & Gaudebout, 2005; Rosenheck, Leslie, Sindelar, Miller, Lin, Stroup, et al., 2006).

Medication persistence has implications for both cost and quality of care (Gibson, Damler, Jackson, Wilder, & Ramsey, 2004). People who receive monotherapy experience nearly half of the annual costs in comparison to polytherapy users or those who switched antipsychotic medications (Loosbrock, Zhao, Johnstone, & Morris, 2003). Some of the atypical antipsychotics, such as risperidone or olanzapine, are associated with better persistence (Gibson et al.; Lieberman, Stroup, McEvoy, Swartz, Rosenheck, Perkins, et al., 2005) while the continuous use of antipsychotic treatment is particularly important to reduce the rate of relapse associated with schizophrenia (dosReis, Johnson, Steinwachs,

Rohde, Skinner, Fahey, et al., 2008).

Some studies have demonstrated that the total costs associated with atypical antipsychotics are no different and sometimes even less than the conventional agents (Gibson et al., 2004; Hudson, Sullivan, Feng, Owen, & Thrush, 2003; Mauri et al., 2005; McCombs, Nichol, Johnstone, Stimmel, Shi, & Smith, 2000). Moreover, several studies affirmed that most atypical antipsychotics significantly reduce hospitalized admission rates and shorten the length of hospital stay (Coley, Carter, DaPos, Maxwell, Wilson, & Branch, 1999; Gau, Chung, & Gau, 2008; Gianfrancesco, Durkin, Mahmoud, & Wang, 2002; Tunis, Ascher-Svanum, Stensland, & Kinon, 2004).

However, the difference in continuity and efficacy measured in terms of rates of hospitalization between typical and atypical agents has been mixed. The Clinical Antipsychotic Trials of Intervention Effectiveness (CATIE) suggested that among 74% of treatments that are discontinued before 18 months, only the olanzapine group is still effective, and there is no significant different between other atypical and conventional antipsychotic agents (Lieberman et al., 2005). Some studies proposed atypical antipsychotics are more effective for severe schizophrenia but do not reduce the costs of associated psychiatric services (Rothbard et al., 2003; Rothbard et al., 2005; Stargardt, Weinbrenner, Busse, Juckel, & Gericke, 2008).

Summary

The findings from this review reveal typical and atypical antipsychotics have different features, such as improvement in symptoms and side effects. This review also finds age, race/ethnicity, and insurance types are factors that influence the prescription of antipsychotics. Disease co-morbidity and heath care providers also affects antipsychotic prescription choice in some articles. Among these potential factors associated with the type of prescribed antipsychotic, ethnicity is a significant predictor. The review findings correspond with the hypothesis that non-white patients are more likely than white patients to use typical antipsychotics.

Contribution

This study of the associated factors that affect the different types of antipsychotics utilization is important in that it provides information for clinical practices and health policy administration. There is little in the way of large, population based survey data on antipsychotic use and associated costs within the Medicare program. This research proposal will analyze antipsychotic use populations and the associated factors that influence the utilization of antipsychotics to provide an overall concept of antipsychotic use patterns.

From a clinical perspective, due to difference of the efficacy, side effects, and costs

among typical and atypical antipsychotics, as well as patients' preferences, it is important to understand variation in use and cost of antipsychotics by patient attributes.

From a policy standpoint, since psychotropic medication expenditures grew at a higher rate than overall drug expenditures, it is important to assess the associated costs and benefits of prescribing patterns. This study provides baseline information on Medicare patterns of antipsychotic utilization before the introduction of Part D.

CHAPTER THREE

STUDY DESIGN/EVALUATIVE COMPONENT

This chapter describes the methodology applied in this study. It consists of six parts: data sources, population and sample, study design, methods of data collection, study variables, and analytic methods.

Data Sources

Secondary data from the 2004 Medicare Current Beneficiary Survey (MCBS) Cost and Use files are used. The MCBS is sponsored by the Centers for Medicare & Medicaid services (CMS). It is a nationally representative survey of Medicare enrollees and is widely used to estimate the determinants of medical utilization and expenditures for Medicare beneficiaries (Centers for Medicare and Medicaid Services, 2008). The MCBS is an annual survey that uses a stratified random sample of Medicare beneficiaries. Sample beneficiaries are interviewed in person three times a year for three years (Adler, 1994). The main purposes of MCBS are to determine expenditures, and sources of payment for all services used by Medicare beneficiaries.

The fiscal year 2004 is used as the most current year prior to Medicare part D implementation. The data act as baseline information for the use and cost of medical services among Medicare beneficiaries in order to compare and analyze the impact of

Medicare Part D.

Population and sample (sample selection criteria)

The sample frame of MCBS is Medicare beneficiaries in United States, and uses 107 geographic primary sampling units (PSUs) to represent the nation (Adler, 1994). Beneficiaries residing in these areas were selected by systematic random sampling within age strata (Adler, 1994).

The study population is typical or atypical antipsychotic users in Medicare in fiscal year 2004. The sample consists of noninstitutionalized Medicare beneficiaries aged 18 years old or older who are receive at least 1 typical or atypical antipsychotic prescription. This information is contained in "2004 Cost and Use: Prescribed Medicine Events" file, inclusive of therapeutic class under psychotherapeutic drugs and off-label users. Drugs are examined by the MicroMedex database. The typical antipsychotics were Chlorpromazine (Thorazine®), Fluphenazine (Prolixin®), Fluphenazine Dec. (Prolixin Decanoate®), Haloperidol (Haldol®), Haloperidol Dec, Perphenazine, Thiothixene (Navane®), Thioridazine (Mellaril®), Trifluoperazine (Stelazine®), Trifluoperazine HCl. The atypical antipsychotics were Aripiprazol (Abilify®), Clozapine (Clozaril®), Olanzapine (Zyprexa®), Quetiapine (Seroquel®), Risperidone (Risperdal®), Ziprasidone (Geodon®).

Typical antipsychotic users are defined as using at least 1 typical antipsychotic medication without any atypical antipsychotic in the 2004 fiscal year. Atypical/ combination antipsychotic users are defined as receiving at least 1 atypical antipsychotic medication, with or without typical antipsychotic medication(s), in FY2004.

Methods of data collection

The MCBS is a stratified random sample of Medicare beneficiaries. 107 geographic primary sampling units (PSUs), consisting of counties or groups of counties, are chosen to represent the nation. The survey captures information on sociodemographic characteristics, health status, health insurance, health care encounters, and services used.

The main drug data is extracted from the Cost and Use file of MCBS in 2004. The records on Prescribed Medicine Events (PME) include interviewees' types of prescribed medicine and their therapeutic class. Also, the costs of each prescription event are recorded by different types of payment, inclusive of total payment and out-of-pocket payment. The data of types of prescribed medicine are used to extract the antipsychotic users. The Person Summary file summarizes utilization data which contains the number of prescribed medicine events of each person in the sample. Combined with the information on types of prescription from the PME record, the data are constructed as per-person-based profiles. The information on age, gender, race, ethnicity, income,

additional insurance coverage, health status, and types of antipsychotic use are aggregated and coded on each individual person.

Study designs

This study is a cross-sectional analysis of nation survey data on the use and costs of antipsychotic medications in the Medicare program in fiscal year 2004. The antipsychotic users are divided into two groups: 1) typical antipsychotics only, and 2) atypical antipsychotics (with or without concurrent use of typical antipsychotics).

According to the literature, the associated factors which influence the prescribing of different types of antipsychotic are examined including age, gender, race, ethnicity, income, insurance types and health status. This study assumes that race affects the use and costs of drug types (typical versus atypical/combination antipsychotic). To test the hypothesis, this study uses logistic regression models to test whether the non-white groups compared to white groups are more likely to choose typical antipsychotic, while controlling for patient age, gender, ethnicity, income, and additional insurance coverage.

To examine whether types of antipsychotics affects the utilization and costs of healthcare services, this study examines four aspects of health services: 1) Average cost of prescriptions and number of prescriptions, 2) Average cost of outpatient services and number of outpatient events, 3) Average cost of inpatient services and number of

inpatient events. 4) Average total health costs.

Study variables

The dependent variable is the use of antipsychotic medications by Medicare beneficiaries. The independent variables include age (18 to less than 64 years of age versus 65 years old and older), gender (male and female), ethnicity (Hispanics, non-Hispanics), income level ($20,000 or less, or more than $ 20,000), and supplemental insurance coverage including Medicaid, Medicare HMO, or private insurance plans. General health status (better than others, and fair/poor) is included as a need factor.

Regarding the second hypothesis, the dependent variables are four aspects of health services as mentioned above. The independent variable is whether beneficiaries use typical or atypical antipsychotics.

Analytic methods

The individual patients are the unit of analysis. By compiling individual prescription records by beneficiary from the PME record, the data present in per-patient-based profiles. Data are weighted to represent the total Medicare population, based on the MCBS Cross-Sectional Weights record.

To evaluate the characteristics of atypical and typical antipsychotic users, chi-squared (X^2) statistics is used for each categorical variable. Logistic regression

analysis is also conducted to discern the influence of patient's age, gender, race, ethnicity, income, supplemental insurance coverage, and general health status on receiving types of antipsychotics (typical versus atypical/combination antipsychotic) among Medicare beneficiaries. Odds ratios and 95 percent confidence interval generated by logistic regression determine the significant level of the association between independent variables and dependent variables.

To evaluate the difference between atypical and typical antipsychotic use on medical events and costs, the T-test analysis is used for each continuous variable to identify the T-test and P values. Chi-squared (x^2) statistics is also used for categorical variables.

The statistical analyses will be performed using SAS® software (Release 9.0, SAS Institute Inc., Cary, North Carolina). Statistical significance is set at $P< 0.05$.

CHAPTER FOUR

RESULTS

This chapter compares rates of antipsychotic utilization and associated health care costs among specific groups of Medicare beneficiaries in 2004.

The distribution of antipsychotic drug use in the MCBS sample

In the 2004 MCBS sample, 445 respondents reported one or more prescriptions for antipsychotics (table 1). About 74.8% (333) had a prescription for one or more atypical antipsychotics only, 7.0% (31) had prescriptions for both conventional and atypical antipsychotics, and 18.2% (81) had prescriptions only for conventional antipsychotics.

The most commonly prescribed antipsychotics were Olanzapine (27.9%), Risperidone (26.5%), Quetiapine (26.3%), and Haloperidol (9.2%). Most of the users (80.4%) were taking one antipsychotic, 16% used two prescriptions, 2.7% used three and 0.9% used four different antipsychotics.

Table 1. Prevalence of antipsychotic medications used by Medicare beneficiaries in 2004

	Users	% of total antipsychotic users
Total Antipsychotic users (N = 445)		
Atypical user *only*	333	74.8%
Typical user *only*	81	18.2%
Combination user	31	7.0%
Typical users (N = 112)*		
Haloperidol (Haldol®), Haloperidol Dec.	41	36.6%
Thioridazine (Mellaril®)	19	17.0%
Perphenazine	17	15.2%
Chlorpromazine (Thorazine®)	14	12.5%
Fluphenazine (Prolixin®)	12	10.7%
Trifluoperazine (Stelazine®), Trifluoperazine HCl.	6	5.4%
Thiothixene (Navane®)	5	4.5%
Atypical users (N = 364)*		
Olanzapine (Zyprexa®)	124	34.1%
Risperidone (Risperdal®)	118	32.4%
Quetiapine (Seroquel®)	117	32.1%
Aripiprazol (Abilify®)	40	11.0%
Ziprasidone (Geodon®)	23	6.3%
Clozapine (Clozaril®)	16	4.4%
Number of prescriptions per user (N = 445)		
1	358	80.4%
2	71	16.0%
3	12	2.7%
4	4	0.9%

Source: 2004 Medicare Current Beneficiary Survey, Cost and Use File, Prescribed Medication Events

Atypical and typical antipsychotic are identified by brand name and generic names according to MicroMedex database

*Typical or atypical users are identified as with at least one of typical or atypical antipsychotics prescription

Characteristics of antipsychotic users

An estimated 1.26 million Medicare beneficiaries filled one or more antipsychotic prescriptions in 2004. Table 2 shows the weighted counts and proportion of users by subpopulation. Younger beneficiaries (83.7%) are more likely to use atypical antipsychotics than the older beneficiaries (81.4%). Female beneficiaries are slightly more likely than the male beneficiaries to use atypical antipsychotics. White beneficiaries (83.4%) are more likely to use atypical agents than Non-white beneficiaries (78.9%). Non-Hispanics (83.8%) are statistically significant more likely to use atypical agents than Hispanics (73.4%) as well ($X^2 = 9.83$, $P = 0.0017$).

For the enabling factors, beneficiaries whose annual income were greater than $20,000 (83.6%) are slightly more likely to receive atypical antipsychotics than those whose annual incomes were $20,000 or less (82.2%). Dually eligible beneficiaries (79.8%) who are qualified for Medicare and Medicaid are statistically significant less likely to receive atypical agents than Medicare only beneficiaries (85.4%) ($X^2 = 6.66$, $P = 0.01$). People did not enroll in Medicare HMO are statistically significant more likely to receive atypical agents ($X^2 = 5.03$, $P = 0.02$).

Regarding need factors, beneficiaries with good self-reported health status are statistically significant more likely to receive atypical antipsychotics (85.8%) than for

those with fair or poor health (80.8%) ($X^2 = 5.53$, P = 0.0187).

Table 2. Characteristics of antipsychotic users in the Medicare program in 2004

Characteristic	Typical		Atypical		X^2	P-value
	est. N (1000s)	%	est. N (1000s)	%		
Age					1.14	0.286
18-64	105.3	16.3%	539.6	83.7%		
65+	114.5	18.6%	500.7	81.4%		
Gender					0.09	0.7636
Male	106.7	17.8%	493.4	82.2%		
Female	113.1	17.1%	546.9	82.9%		
Race					2.73	0.0985
White	168.2	16.6%	844.2	83.4%		
Non-white	51.5	21.1%	192.8	78.9%		
Ethnicity					9.83	0.0017††
Hispanic	39.5	26.6%	108.9	73.4%		
Non-Hispanic	180.2	16.2%	931.5	83.8%		
Income					0.32	0.5696
≤ $20,000	163.8	17.8%	756.2	82.2%		
> $20,001	55.9	16.4%	284.1	83.6%		
Medicaid					6.66	0.0099††
Medicaid (dual eligible)	128.7	20.2%	509.6	79.8%		
Non-Medicaid	91.0	14.6%	530.8	85.4%		
Private					1.04	0.3085
Private	74.7	19.0%	318.2	81.0%		
Non-private	142.4	16.6%	713.1	83.4%		
HMO					5.03	0.0249†
HMO	49.8	22.7%	170.1	77.3%		
Non-HMO	169.9	16.3%	870.2	83.7%		
Self-reported health status*					5.53	0.0187†
Better than others	85.4	14.2%	516.3	85.8%		
Fair/ Poor	120.2	19.2%	505.6	80.8%		

Source: 2004 Medicare Current Beneficiary Survey, *Cost and Use File,*
Survey Identification, Health Status & Functioning and Prescribed Medication Events

* Self-reported conditions were identified by asking respondents, "What is your general health compare to others same age? " and then naming the condition

† P < 0.05

†† P < 0.01

Patient factors associated prescription of atypical antipsychotics

Table 3 shows the odds ratios and 95% confidence intervals (CI) for patient level factors associated with the use of atypical antipsychotics among Medicare antipsychotics users. Age, gender, race, income, and Medicaid as additional insurance are not related to receipt of atypical antipsychotics. Non-Hispanics are nearly 1.7 times more likely to have atypical prescription than are Hispanics (AOR = 1.66; 95% CI = 1.09 – 2.54). Beneficiaries who did not enroll in Medicare HMO are around 1.6 times more likely to receive atypical agents compared to Medicare HMO enrollees (AOR = 1.60; 95% CI = 1.07 – 2.40). Beneficiaries in fair or poor health are less likely than healthier beneficiaries to receive atypical antipsychotics (AOR = 0.70; 95% CI = 0.51 – 0.95).

Table 3. Logistic regression model predicting atypical antipsychotic use among all Medicare antipsychotic users, 2004

	Multivariate	
Characteristic	AOR	95% CI
Age		
18-64	referent	
65+	0.74	(0.53 - 1.04)
Gender		
Male	referent	
Female	1.04	(0.76 - 1.43)
Race		
White	referent	
Non-white	0.75	(0.52 - 1.09)
Ethnicity		
Hispanic	referent	
Non-Hispanic	**1.66**	**(1.09 - 2.54)**
Income		
≤ $20,000	referent	
> $20,001	1.13	(0.72 - 1.76)
Medicaid		
Medicaid (dual eligible)	referent	
Non-Medicaid	1.44	(0.95 - 2.16)
HMO		
HMO	referent	
Non-HMO	**1.60**	**(1.07 - 2.40)**
Self-reported health status*		
Better than others	referent	
Fair/ Poor	**0.70**	**(0.51 - 0.95)**

AOR = Adjusted Odds Ratio

CI = Confidence Interval

Numbers in boldface are statistically significant at $P < 0.05$

Source: 2004 Medicare Current Beneficiary Survey, *Cost and Use F*
Person Summary and Prescribed Medication Events

* Self-reported conditions were identified by asking respondents, "What is your general health compare to others

Medical events and costs

Prescription events and costs

Table 4 shows that atypical antipsychotic users have significantly higher numbers of prescription drug events ($t = -2.62$, $p = 0.01$), and total prescription drug costs ($t = -6.41$, $p < 0.0001$) than typical users. The difference in drug costs is expected, given the relatively high cost of atypical as compared with typical medications, but the difference in usage was unexpected.

Table 4. Average cost of prescriptions and number of prescriptions for typical and atypical antipsychotic Medicare users in 2004

	Typical	Atypical	T-test	P-value
	Mean	Mean		
Costs	$1,609	$4,245	-6.41	<.0001‡
Events	37.4	51.8	-2.62	0.0092††

Source: 2004 Medicare Current Beneficiary Survey, *Cost and Use File*, Person Summary and Prescribed Medication Events

†† P < 0.01

‡ P < 0.001

Outpatient events and costs

The average number of outpatient events and outpatient costs are shown in Table 5.

No statistical differences were found between the two groups.

Table 5. Average cost of outpatient services and number of outpatient events for typical and atypical antipsychotic Medicare users in 2004

	Typical	Atypical	T-test	P-value
	Mean	Mean		
Total antipsychotic users				
Annual outpatient visits	$1,400	$1,420	-0.05	0.9583
Number of outpatient visits	7.5	6.5	0.72	0.4697
Excluded antipsychotic users without any outpatient visits				
Annual outpatient visits	$1,751	$1,827	-0.16	0.8712
Number of outpatient visits	8.7	8.1	0.37	0.7119

Source: 2004 Medicare Current Beneficiary Survey, *Cost and Use File*, Person Summary and Prescribed Medication Events

Inpatient events and costs

Table 6 shows that atypical antipsychotic users have significantly higher rates of hospitalization and associated costs – a surprising finding in light of prior research. Atypical users were more likely than typical to be hospitalized at least once (72 % vs. 58%; $X^2 = 16.72$, p = < 0.0001). Associated total inpatient costs were also significantly higher for atypical users vs. typical users (t = -2.19, p = 0.03). Once beneficiaries without any hospital admissions were omitted from the comparison, the inpatient costs were not significantly different (t = -1.04, p = 0.30).

Table 6. Average cost of inpatient services and number of inpatient events for typical and atypical antipsychotic Medicare users in 2004

	Typical		Atypical			
	est. N (1000s)	%	est. N (1000s)	%	X^2	P-value
Any hospitalization					16.72	<.0001‡
None	159.1	72.4%	598.7	57.5%		
≥ 1	60.6	27.6%	441.6	42.5%		
	Mean		Mean		T-test	P-value
Total antipsychotic users						
Annual hospitalization	$3,407		$6,987		-2.19	0.029†
Number of hospital stay	0.5		0.9		-2.16	0.0316†
Excluded antipsychotic users without any hospitalization						
Annual hospitalization	$12,353		$16,458		-1.04	0.2989
Number of hospital stay	1.8		2.1		-0.68	0.4966

Source: 2004 Medicare Current Beneficiary Survey, *Cost and Use File*, Person Summary and Prescribed Medication Events

† P < 0.05

‡ P < 0.001

Total health costs

Table 7 shows that total Medicare payments were significantly higher for atypical antipsychotic users (mean = $20,273) than for typical users (mean = $13,855; t = -2.26, p = 0.02).

Table 7. Average total health costs for typical and atypical antipsychotic Medicare users in 2004

	Typical	Atypical	T-test	P-value
	Mean	Mean		
Costs	$13,855	$20,273	-2.26	0.0243†

Source: 2004 Medicare Current Beneficiary Survey, *Cost and Use File*, Person Summary and Prescribed Medication Events

† P < 0.05

CHAPTER FIVE

IMPLICATION/LIMITATIONS/RECOMMENDATION

This chapter discusses key study findings, study limitations, and policy and clinical implications.

The prevalence of atypical antipsychotic prescriptions in the Medicare program

Consistent with previous studies of other populations (Aparasu, Bhatara, & Gupta, 2005), prescriptions for atypical antipsychotics outpace prescriptions for typical antipsychotics Medicare population. The three most frequently used antipsychotics in this analysis, representing 80% of antipsychotic users, were atypical agents.

Compared to conventional antipsychotics, atypical agents seem able to reduce negative symptoms and to produce fewer extrapyramidal side effects, which can also enhance patient compliance (Coley et al., 1999; dosReis et al., 2008; Gau et al., 2008; Gianfrancesco et al., 2002; Gibson et al., 2004; Lieberman et al., 2005; Tunis et al., 2004). However, atypical antipsychotics are also associated with several metabolic side effects, particularly weight gain, glucose abnormalities, cerebrovascular effects, and mortality risk (Madhusoodanan, Sinha, Sajatovic, Gupta, & Brenner, 2006). Given the widespread use of these medications in the Medicare program, surveillance of these side-effects is warranted.

Factors associated with the prescription of antipsychotics

The intention of this study is to understand and identify the factors associated with receipt of atypical antipsychotics in the Medicare program. It is hypothesized that specific groups of Medicare beneficiaries are at higher risk of receiving prescriptions for conventional rather than atypical antipsychotics, including racial and ethnic minorities,

older beneficiaries, low income beneficiaries, and beneficiaries without supplemental insurance. This hypothesis was only partly confirmed in this study. Hispanics, dual eligibles, Medicare HMO enrollees, and those with fair or poor health were more likely to receive typical antipsychotics.

The observed ethnic disparity may be accounted for by the lower socioeconomic status and patient preference of Hispanics (Copeland et al., 2003; Gaskin, Briesacher, Limcangco, & Brigantti, 2006). Some ethnic minorities may be less willing to take or switch to newer drugs (Opolka et al., 2003). Moreover, concern about weight gain and diabetes, may inhibit the prescription of atypical agents to groups that have a higher risk for diabetes (Copeland et al.; Meyer, Rosenblatt, Kim, Baker, & Whitehead, 2009; Ramaswamy, Kozma, & Nasrallah, 2007). Whether differences in atypical antipsychotic use are due to ethnicity or other unobserved factors related to ethnicity require further study (Gaskin et al.; Kuno & Rothbard, 2002).

Medicaid or Medicare HMO enrollees were less likely to receive atypical antipsychotics. Both programs have incentives to contain drug costs, and may therefore have more stringent tiering or physician approval requirements that limit access to the more expensive atypical medications (Eppig & Poisal, 1996; Surles, 2005). It will be important to track the impact of insurance status in subsequent Medicare studies that include Part D plans.

Beneficiaries receiving atypical agents reported better health status than those receiving typical agents. This could be related to the clinical efficacy of the drug, and the minimization of EPS side effects. Atypical users are also more compliant, and therefore have lower relapse rates.

Medical events and costs

Previous studies have argued that the high acquisition costs of atypical medications are offset in part by reductions in other health service costs. This study compared utilization and costs of healthcare services among atypical and typical users, and hypothesized that the users of the newer atypical antipsychotics would have higher acquisition costs, but lower total health costs, hospitalization rates, and outpatient visits than typical users. The results were rather surprising in light of prior research: the costs of prescribed medicine, inpatient costs and total health costs are substantially higher for atypical users. This study failed to reject the null hypothesis. Moreover, to reiterate, atypical users in this study reported better health status. It is surprising that these healthier beneficiaries using 'better' drugs reported higher and more costly usage of health care services.

We can speculate about possible reasons for these findings, but clearly additional research is needed to verify this pattern of use and cost within the Medicare population. Perhaps prescription of typical antipsychotics is a general marker for unmet need, e.g., Hispanics (who are more likely to receive typical antipsychotics) may also lack access to specialists and other health services. Atypical users might also have more co-morbid conditions or a longer history of mental illness, which causes them to use more health services. Finally, it is possible that atypical agents are simply not as efficacious as initially thought, particularly as prescribing has moved beyond patients with acute schizophrenia. Moreover, some metabolic side effects induced by atypical agents might aggravate health conditions other than mental illness, leading to hospitalization for cardiac conditions, diabetes related problems, or other chronic conditions. Additional

research that attempts to control for these factors is urgently need.

Limitations

This study has several limitations. First, the sample size of antipsychotic users is relatively small, limiting statistical power. Second, the data used in this analysis lacks diagnostic and clinical information to adjust for the severity of illness of schizophrenia, and other conditions. Third, the cross-sectional nature of the dataset precludes an examination of channeling bias, or prior use of a different medication of class of antipsychotic. Finally, a number of variables in this study are based on self-reported information, and are vulnerable to recall bias.

Clinical Implications

This study found some ethnic disparity among antipsychotic users in the Medicare population. Insofar as atypical agents are the treatment of choice according to clinical guidelines, it is crucial that providers are aware of these disparities, and provide the appropriate medications to all patients.

More generally, the finding that atypical antipsychotics are associated with higher hospitalization rates could have important implications for clinical practice. If these findings are confirmed in subsequent studies, they could and should be used to deter overprescribing of these clinically important, but hardly risk free, medicines.

Policy implications

Use of high cost atypical antipsychotics is common in the Medicare program, and has driven up the overall prescription costs. If the findings presented here are confirmed, they may also be driving up total health costs through higher rates of hospitalization. This should give pause to policymakers as well as providers. In some cases, cost containment

measures like formulary tiering, fail first, or preapproval by insurers may be warranted. These medications have the potential to help people with severe mental illness, but they should be prescribed only when warranted, and health care providers must carefully monitor side effects other than EPS during the course of treatment. Post-market surveillance is critical for these and any other new drugs.

REFERENCES

Adler, G. S. (1994). A profile of the Medicare Current Beneficiary Survey. *Health Care Financ Rev, 15*(4), 153-63.

Andersen, R. M. (1995). Revisiting the behavioral model and access to medical care. Does it matter? *J Health Soc Behav, 36*, 1–10.

Aparasu, R. R., Bhatara, V., & Gupta, S. (2005). U. S. national trends in the use of antipsychotics during office visits, 1998-2002. *Ann Clin Psychiatry, 17*(3), 147-52.

Baillargeon, J., & Contreras, S. A. (2001). Antipsychotic prescribing patterns in the Texas prison system. *J Am Acad Psychiatry Law, 29*(1), 48-53.

Brody, T. M., Larner, J., & Minneman, K. P. (1998). Human Pharmacology: Molecular to Clinical (3rd ed.). Missouri: Mosby-Year Book, Inc.

Centers for Medicare and Medicaid Services (2008). Medicare Current Beneficiary Survey. Retrieved April 5, 2008, from http://www. cms. hhs. gov/MCBS/01_Overview. asp#TopOfPage

Coley, K. C., Carter, C. S., DaPos, S. V., Maxwell, R., Wilson, J. W., & Branch, R. A. (1999). Effectiveness of antipsychotic therapy in a naturalistic setting: A comparison between risperidone, perphenazine, and haloperidol. *J Clin*

Psychiatry, 60(12), 850-6.

Copeland, L. A., Zeber, J. E., Valenstein, M., & Blow, F. C. (2003). Racial disparity in the use of atypical antipsychotic medications among veterans. *Am J Psychiatry, 160*(10), 1817-22.

Daumit, G. L., Crum, R. M., Guallar, E., Powe, N. R., Primm, A. B., Steinwachs, D. M., et al. (2003). Outpatient prescriptions for atypical antipsychotics for African Americans, Hispanics, and whites in the United States. *Arch Gen Psychiatry, 60*(2), 121-8.

dosReis, S., Johnson, E., Steinwachs, D., Rohde, C., Skinner, E. A., Fahey, M., et al. (2008). Antipsychotic treatment patterns and hospitalizations among adults with schizophrenia. *Schizophr Res, 101*(1-3), 304-11.

Eppig, F. J., & Poisal, J. A. (1996). Prescribed medicines: A comparison of FFS with HMO enrollees. *Health Care Financ Rev, 17*(4), 213-5.

Farley, J. F., Cline, R. R., Schommer, J. C., Hadsall, R. S., & Nyman, J. A. (2008). Retrospective assessment of Medicaid step-therapy prior authorization policy for atypical antipsychotic medications. *Clin Ther, 30*(8), 1524-39.

Frank, R. G., Conti, R. M., & Goldman, H. H. (2005). Mental Health Policy and Psychotropic Drugs. *Milbank Q, 83*(2), 271-98.

Gaskin, D. J., Briesacher, B. A., Limcangco, R., & Brigantti, B. L. (2006). Exploring racial and ethnic disparities in prescription drug spending and use among Medicare beneficiaries. *Am J of Geriatr Pharmacother, 4*(2), 96-111.

Gasquet, I., Gury, C., Tcherny-Lessenot, S., Quesnot, A., & Gaudebout, P. (2005). Patterns of prescription of four major antipsychotics: A retrospective study based on medical records of psychiatric inpatients. *Pharmacoepidemiol Dru Saf, 14*, 805–11.

Gau, S. S., Chung, C. H., & Gau, C. S. (2008). A pharmacoeconomic analysis of atypical antipsychotics and haloperidol in first-episode schizophrenic patients in Taiwan. *J Clin Psychopharmacol, 28*(3), 271-8.

Gianfrancesco, F., Durkin, M. B., Mahmoud, R., & Wang, R. H. (2002). Use of healthcare services by patients treated with risperidone versus conventional antipsychotic agents. *Pharmacoeconomics, 20*(6), 413-27.

Gibson, P. J., Damler, R., Jackson, E. A., Wilder, T., & Ramsey, J. L. (2004). The impact of olanzapine, risperidone, or haloperidol on the cost of schizophrenia care in a Medicaid population. *Value Health, 7*(1), 22-35.

Herbeck, D. M., West, J. C., Ruditis, I., Duffy, F. F., Fitek, D. J., Bell, C. C., et al. (2004). Variations in use of second-generation antipsychotic medication by race among

adult psychiatric patients. *Psychiatr Serv, 55*(6), 677-84.

Hudson, T. J., Sullivan, G., Feng, W., Owen, R. R., & Thrush, C. R. (2003). Economic evaluations of novel antipsychotic medications: A literature review. *Schizophr Res, 60*(2-3), 199-218.

Huskamp, H. A. (2005). Pharmaceutical cost management and access to psychotropic drugs: The U.S. context. *Int J Law and Psychiatry, 28*, 484–95.

Huskamp, H. A., & Shinogle, J. A. (2005). Economic grand rounds: Potential effects of the new Medicare drug benefit on pricing for psychotropic medications. *Psychiatr Serv, 56*(9), 1056-8.

Jano, E., Chen, H., Johnson, M. L., & Aparasu, R. R. (2007). Antipsychotic utilization and expenditure trends among elderly persons. *Psychiatr Serv, 58*(11), 1400.

Jeste, D. V., Lacro, J. P., Bailey, A., Rockwell, E., Harris, M. J., & Caligiuri, M. P. (1999). Lower incidence of tardive dyskinesia with risperidone compared with haloperidol in older patients. *J Am Geriatr Soc, 47*, 716–9.

Kuno, E., & Rothbard, A. B. (2002). Racial disparities in antipsychotic prescription patterns for patients with schizophrenia. *Am J Psychiatry, 159*(4), 567-72.

Kuno, E., & Rothbard, A. B. (2005). The effect of income and race on quality of psychiatric care in community mental health centers. *Community Ment Health J,*

41(5), 613-22.

Lehman, A. F., & Steinwachs, D. M. (1998). Patterns of usual care for schizophrenia: Initial results from the Schizophrenia Patient Outcomes Research Team (PORT) Client Survey. *Schizophr Bull, 24*(1), 11-20.

Lieberman, J. A., Stroup, T. S., McEvoy, J. P., Swartz, M. S., Rosenheck, R. A., Perkins D. O., et al.(2005). Effectiveness of antipsychotic drug in patients with chronic schizophrenia. *N Engl J Med, 353*(12), 1209-23.

Loosbrock, D. L., Zhao, Z., Johnstone, B. M., & Morris, L. S. (2003). Antipsychotic medication use patterns and associated costs of care for individuals with schizophrenia. *J Ment Health Policy Econ, 6*(2), 67-75.

Madhusoodanan, S., Sinha, A., Sajatovic, M., Gupta, S., & Brenner, R. (2006). The role of atypical antipsychotic agents in the treatment of schizophrenia and schizoaffective disorders in the elderly. *Curr Drug Saf, 1*(3), 227-41.

Mallinger, J. B., Fisher, S. G., Brown, T., & Lamberti, J. S. (2006). Racial disparities in the use of second-generation antipsychotics for the treatment of schizophrenia. *Psychiatr Serv, 57*(1), 133-6.

Mark, T. L., Palmer, L. A., Russo, P. A., & Vasey, J. (2003). Examination of treatment pattern differences by race. *Ment Health Serv Res, 5*(4), 241-50.

Mauri, M. C., Regispani, F., Beraldo, S., Volonteri, L. S., Ferrari, V. M., Fiorentini, A., et al. (2005). Patterns of clinical use of antipsychotics in hospitalized psychiatric patients. *Prog Neuropsychopharmacol Biol Psychiatry, 29*(6), 957-63.

McCombs, J. S., Nichol, M. B., Johnstone, B. M., Stimmel, G. L., Shi, J., & Smith, R. (2000). Antipsychotic drug use patterns and the cost of treating schizophrenia. *Psychiatr Serv, 51*(4), 525-7.

Meyer, J. M., Rosenblatt, L. C., Kim, E., Baker, R. A., & Whitehead, R. (2009). The moderating impact of ethnicity on metabolic outcomes during treatment with olanzapine and aripiprazole in patients with schizophrenia. *J Clin Psychiatry, 70*(3), 318-25.

Mirandola, M., Andretta, M., Corbari, L., Sorio, A., Nosè, M., & Barbui, C. (2006). Prevalence, incidence and persistence of antipsychotic drug prescribing in the Italian general population: Retrospective database analysis, 1999-2002. *Pharmacoepidemiol Drug Saf, 15*(6), 412-20.

Nasrallah, H. A. (2008). Atypical antipsychotic-induced metabolic side effects: Insights from receptor-binding profiles. *Mol Psychiatry, 13*(1), 27-35.

O'Donnell, B. (2/04/09). *Part D Statistics*. CMS Adjunct Meeting, "How to Use Medicare Part D Data," 2009 Academy Health National Health Policy Conference,

Washington DC.

Opolka, J. L., Rascati, K. L., Brown, C. M., & Gibson, P. J. (2004). Ethnicity and prescription patterns for haloperidol, risperidone, and olanzapine. *Psychiatr Serv, 55*, 151–6.

Opolka, J. L., Rascati, K. L., Brown, C. M., Barner, J. C., Johnsrud, M. T., & Gibson P. J. (2003). Ethnic differences in use of antipsychotic medication among Texas Medicaid clients with schizophrenia. *J Clin Psychiatry, 64*, 635-9.

Ramaswamy, K., Kozma, C. M., & Nasrallah, H. (2007). Risk of diabetic ketoacidosis after exposure to risperidone or olanzapine. *Drug Saf, 30*(7), 589-99.

Reilly, T. H., & Kirk, M. A. (2007). Atypical antipsychotics and newer antidepressants. *Emerg Med Clin North Am, 25*(2), 477-97.

Ren, X. S., Kazis, L. E., Lee, A. F., Hamed, A., Huang, Y. H., Cunningham, F., et al. (2002). Patient characteristics and prescription patterns of atypical antipsychotics among patients with schizophrenia. *J. Clin. Pharm. Ther, 27*(6), 441-51.

Rosenheck, R. A., Leslie, D. L., Sindelar, J., Miller, E. A., Lin, H., Stroup, T. S., et al. (2006). Cost-effectiveness of second-generation antipsychotics and perphenazine in a randomized trial of treatment for chronic schizophrenia. *Am J Psychiatry, 163*(12), 2080-9.

Rothbard, A., Murrin, M. R., Jordan, N., Kuno, E., McFarland, B. H., Stroup, T. S., et al. (2005). Effects of antipsychotic medication on psychiatric service utilization and cost. *J. Ment. Health Policy and Econ, 8*(2), 83-93.

Rothbard, A. B., Kuno, E., & Foley, K. (2003). Trends in the rate and type of antipsychotic medications prescribed to persons with schizophrenia. *Schizophr Bull, 29*(3), 531-40.

Sankaranarayanan, J., & Puumala, S. E. (2007). Antipsychotic use at adult ambulatory care visits by patients with mental health disorders in the United States, 1996-2003: National estimates and associated factors. *Clin Ther, 29*(4), 723-41.

Sankaranarayanan, J., & Puumala, S. E. (2007). Epidemiology and characteristics of emergency departments visits by US adults with psychiatric disorder and antipsychotic mention from 2000 to 2004. *Curr Med Res Opin, 23*(6), 1375-85.

Schneider, L. S., Tariot, P. N., Lyketsos, C. G., Dagerman, K. S., Davis, K. L., Davis, S., et al.(2001). National Institute of Mental Health Clinical Antipsychotic Trials of Intervention Effectiveness (CATIE): Alzheimer disease trial methodology. *Am J Geriatr Psychiatry, 9*(4), 346-60.

Stargardt, T., Weinbrenner, S., Busse, R., Juckel, G., & Gericke, C. A. (2008). Effectiveness and cost of atypical versus typical antipsychotic treatment for

schizophrenia in routine care. *J Ment Health Policy Econ, 11*(2), 89-97.

Surles, R. C. (2005). Atypical antipsychotics: Considerations for Medicaid coverage. *Am J Manag Care, 11*(8 Suppl), S248-53.

Tunis, S. L., Ascher-Svanum, H., Stensland, M., & Kinon, B. J. (2004). Assessing the value of antipsychotics for treating schizophrenia: The importance of evaluating and interpreting the clinical significance of individual service costs. *Pharmacoeconomics, 22*(1), 1-8.

Van Brunt, D. L., Gibson, P. J., Ramsey, J. L., & Obenchain, R. (2003). Outpatient use of major antipsychotic drugs in ambulatory care settings in the United States, 1997-2000. *Medscape general medicine, 5*(3), 16.

Van Dorn, R. A., Swanson, J. W., Swartz, M. S., & Elbogen, E. B. (2005). The effects of race and criminal justice involvement on access to atypical antipsychotic medications among persons with schizophrenia. *Ment Health Serv Res, 7*(2), 123-34.

Wang, P. S., West, J. C., Tanielian, T., & Pincus, H. A. (2000). Recent patterns and predictors of antipsychotic medication regimens used to treat schizophrenia and other psychotic disorders. *Schizophr Bull, 26*(2), 451-7.

Zuvekas, S. H. (2005). Prescription drugs and the changing patterns of treatment for

mental disorders, 1996-2001. *Health Aff (Millwood), 24*(1), 195-205.