MEDICARE DRUG PLAN FORMULARY RESPONSE TO THE PATENT EXPIRATION OF ATYPICAL ANTIPSYCHOTICS IN THE STATE OF WASHINGTON FOR FISCAL YEAR 2010

By

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To the Faculty of Washington State University:

The members of the Committee appointed to examine the thesis of CHAITANYA CHANDRATRE find it satisfactory and recommend that it be accepted.

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MEDICARE DRUG PLAN FORMULARY RESPONSE TO THE PATENT EXPIRATION OF RISPERIDONE IN THE STATE OFWASHINGTON FOR FISCAL YEAR 2010

Abstract

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OBJECTIVE:

To assess the impact of new generic atypical antipsychotics on Medicare drug plan formularies in the State of Washington.

BACKGROUND:

Schizophrenia is a serious mental illness that places a tremendous burden on patients, family members, and society. The introduction of atypical antipsychotics gave a new hope to those being treated for schizophrenia. Risperidone (Risperdal), an effective atypical antipsychotic, lost its patent protection and market exclusivity in June 2008. In October 2008, a number of generic drug manufacturing companies brought new generic versions of risperidone in the market. The generic version of clozapine is also available in the market but it is rarely used due to its risk profile.

Medicare is the largest third-party payer for antipsychotic drugs. Medicare Prescription Drug plans are required to cover all antipsychotics. However, they are allowed to design their own policies regarding cost sharing.

METHODS:

The study assesses Medicare Advantage Plan (MAPs) and Prescription Drug Plan (PDPs) plans in Washington using representative zip codes and the online Prescription Drug Plan Finder tool on the Medicare Website.

HYPOTHESIS:

It is hypothesized that in 2010, MAPs and PDPs will have lower rates of cost-sharing and lesser use of pharmacy management tools for generic risperidone and clozapine compared to patent protected atypical antipsychotics; Risperidone (Risperdal®), Clozapine (Clozaril®), Olanzapine (Zyprexa®), Paliperidone (Invega®).

RESULTS:

The branded antipsychotics have consistently higher cost sharing. A significant number of plans have dropped the branded preparations from their formularies. Pharmacy management tools are often employed to encourage use of the generic versions.

CONCLUSION:

Medicare Plans have lower costs and fewer restrictions on newly designated generic medications, relative to patent protected medications.

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CHAPTER ONE

INTRODUCTION

This study focuses on the response of Medicare Advantage Drug Plans (MAP) and Prescription Drug Plans (PDP) to the advent of the generic versions of risperidone and clozapine in the State of Washington in 2010. This chapter consists of five parts: introduction, purpose of the proposed research, research problem, research question/hypothesis, and the significance of study.

Introduction

Medicare is the most popular federally funded program in the United States, providing health insurance for people above 65 years of age and for others who qualify under a disability criteria. (Henry J. Kaiser Family Foundation, 2008). In January, 2006 Medicare began offering private prescription drug coverage through Part D. Private Prescription Drug Plans (PDPs) offer a standalone alternative to private HMOs or Medicare Advantage Plans (MAPs) (Henry J. Kaiser Family Foundation, 2008).

Medicare is the largest payer for mental health services in the nation, with 53% of disabled younger beneficiaries and 12% of older non-disabled beneficiaries reporting a mental or psychiatric disorder (*Building Partnerships to Better Serve Beneficiaries with Mental Illness,* 2009). In addition, Medicare is the largest third-party payer for antipsychotic drugs, paying for 40% of all antipsychotic prescriptions (Chen, Nwangwu, Aparasu, Essien, Sun, & Lee, 2008). All Medicare drug plans are required to cover "all or substantially all" antipsychotic drugs (Center for Medicare and Medicaid Services, 2005). However, Medicare private plans are

allowed to design their own policies regarding the cost sharing. To contain the cost, private plans generally use 5 tier formulary systems. Some plans also use step therapies, quantity limits and prior authorization requirements.

Purpose of Proposed Research

The purpose of this study is to assess whether MAPs and PDPs formularies favor utilization of generic antipsychotics. The study compares cost sharing requirements and the use of pharmacy management tools for following drugs; Risperidone (generic), Risperidone (Risperdal®), Clozapine (Clozaril®), Clozapine (generic), Olanzapine (Zyprexa®), Paliperidone (Invega®).

Research Problem

In the early 1990s, the introduction of atypical antipsychotics gave a new hope to those being treated for schizophrenia, whose treatment options had previously been limited to a decades-old class of drugs associated with severe side effects including extra pyramidal symptoms such as tardive dyskinesia. Compared to typical antipsychotics, atypical antipsychotics appear to have fewer side effects. (Correll, Leucht, & Kane, 2004; Lieberman, Stroup, McEvoy, Swartz, Rosenheck, Perkins et al., 2005). Many atypical antipsychotics entered the market in the 1990s and became blockbuster drugs. By 2007, five leading antipsychotics appeared on the list of top-selling drugs by dollar amounts: Seroquel was #7 with $2.5 billion in sales; Risperdal, #14, ($1.8 billion); Abilify, #15, ($1.8 billion); Zyprexa, #18, ($1.6 billion); and Geodon Oral, #58, ($665 million) (*Top 200 Brand Drugs By Retail Dollars In 2007*).

In recent studies, however, the clinical advantages of atypical antipsychotics have been questioned. The landmark Clinical Antipsychotic Trials of Intervention Effectiveness (CATIE)

study revealed very high rates of discontinuation of atypical antipsychotics: between 64% and 82%, depending on the medication (Lieberman et al., 2005). A growing body of literature suggests that the difference in the extra pyramidal symptoms is less than initially reported. The metabolic syndrome side-effect of the atypicals is also a growing concern (Fischer-Barnicol Lanquillon, Haen, Zofel, Coch, Dose et al., 2008; Newcomer, 2005).

Research Question and Hypothesis

This study focuses on MAP and PDP responses to the risperidone patent expiration in 2008 and entry of the generic version. High levels of profitability and therapeutic necessity make risperidone an excellent test case for observing how Medicare prescription drug programs revise coverage. Also, this study examines the formulary coverage of generic and branded formulations containing clozapine. Medicare plans have high incentives to favor generic formulations of risperidone and clozapine primarily because of high cost of their branded versions. The key research question to be addressed here is: how have MAPs and PDPs in Washington restructured their formularies to respond to the introduction of generics?

The hypothesis is that in 2010, MAPs and PDPs will have lower rates of cost-sharing and lesser use of pharmacy management tools for generic risperidone and clozapine compared to patent protected atypical antipsychotics; Risperidone (Risperdal®), Clozapine (Clozaril®), Olanzapine (Zyprexa®), Paliperidone (Invega®).

Significance of the Study

Considering schizophrenia's dramatic social and economic impact (Pomerantz, 2006; E. Q. Wu, Kennedy, Cohen, Wang, 2005; E. Q. Wu, Shi, Birnbaum, Hudson, & Kessler, 2006), the long-term treatment typically required (Turner & Stewart, 2006), and the established effectiveness of oral atypical antipsychotics (Correll, Leucht, & Kane, 2004; Lieberman et al., 2005; Masand, 2007), the market success of these drugs is not surprising. However, in the next six years all the major atypical antipsychotic drugs will lose their patent protection ending the golden era for the atypical antipsychotic brand owners but reducing cost for public and private insurers.

The patent for risperidone expired in mid 2008. Ortho-McNeil-Janssen has already secured multiple patents for other uses of Risperdal, such as treatment of bipolar disorder in children and treatment of irritability associated with autistic disorder (*Electronic Orange Book*, 2009). They also have successfully introduced a long-acting injectable formulation of risperidone, Risperdal Consta (*About Risperdal Consta*, 2009). Furthermore, Janssen has introduced paliperidone (Invega), the active metabolite of risperidone, as the most recent atypical antipsychotic approved by the U.S. Food and Drug Administration for the treatment of schizophrenia in adults (Citrome, 2007; Dolder, Nelson, & Deyo, 2008; Nussbaum & Stroup, 2008). So far, paliperidone has been proved promising in preventing schizophrenia symptoms and reducing relapses relative to placebo (Dolder et al., 2008; Kramer Simpson Maciulis, Kushner, Vijapurkar, & Lim, 2007; Marder, Kramer, Ford, Eerdekens, Lim, Eerdekens, 2007; Nussbaum & Stroup, 2008; Tzimos, Samokhvalov, Kramer, Ford, Gassmann-Mayer,& Lim, 2008). The side effects of paliperidone are similar to those of risperidone, although it also increases the risk for hyperprolactinemia

(Dolder et al., 2008). It is not proved yet that paliperidone has advantages over risperidone in treating schizophrenia (Marino & Caballero, 2008).

Since generic medications are often less expensive than their brand counter parts, generic substitution is common method to bring down the costs (Roman, 2009). However, this financial driven substitution may influence adherence. The patients on branded antipsychotic medication may perceive the generic substation as not equally effective or different from branded drugs. (Treur, Heeg, Moller, Schmeding & Hout, 2009, Roman, 2009). Patients who do not follow the course of antipsychotic treatment have higher rates of relapses, require involuntary hospital admissions, and have longer length of stays (Treur et al., 2009).

CHAPTER TWO

THEORETICAL BASIS/LITERATURE REVIEW

This chapter describes the literature review methodology, including: the reference database, keywords, and inclusion/exclusion criteria. A summary of significant research findings and any prevalent gaps in the literature are also included.

Review Methodology

A systemic literature review was conducted by using peer reviewed articles from electronic datasets. The articles were collected through PubMed search using combinations of keywords "Medicare D", "formulary", "generic" and "antipsychotics". The search was limited to articles published after 2006. Articles published in languages other than English were not considered. Initial searches identified 47 articles which were then narrowed down to 11 articles, specifically dealing with Medicare plans' management of antipsychotics drugs.

Literature Review

A study conducted by Chen et. al. assessed effect of Medicare Part D implementation on out of pocket cost for the enrollees. The research used claim data from a retail pharmacy chain. The reserach found that the enrollees in 2006 paid 21% less out of pocket than to in 2005 for antipsychotics (Chen et al., 2008). However, the study aggregated all antipsychotics rather than assessing intra class costs.

Law and colleagues in 2008 examined the effect of prior authorization policy on the access of second generation antipsychotic drugs. The authors used Medicaid drug utilization data to assess market share and total pharmacy cost in Texas and West Virginia. The study found that the

atypical drugs lost their market share in both the states, but pharmacy reimbursements did not decrease significantly in either of the states (Law, Ross-Degnan, & Soumerai, 2008). The study concluded that the prior authorization program may not save costs. A similar study performed on Maine Medicaid found that the beneficiaries who started antipsychotic treatment after the implementation of policy were 29% more likely to face discontinuities in the treatment (Soumerai, Zhang, Ross-Degnan, Ball, LeCates, Law, 2008).

The Medicare Prescription Drug Improvement and Modernization Act of 2003 required 6 million dually eligible beneficiaries to shift from Medicaid prescription drug coverage and be enrolled in Medicare Part D drug plans. A study by Donohue and Frank (2007) estimated the rates of medication switching among dually eligible beneficiaries for antipsychotics attributable to their enrollment in Medicare. The Medicare Beneficiary Survey and drug plan formulary were analyzed to demonstrate likelihood of switching medication. The study found that 6 to 10% of beneficiary switched antipsychotic medication after changing to Medicare Part D. The study concluded that although a low percentage of people are likely to switch medications, beneficiaries in some plans may experience significant barriers to medication access.

As mentioned earlier antipsychotics are a "protected" class of drugs. A study examined coverage and prior authorization requirements for different types of drugs including antipsychotics, in Medicare Part D plans (Huskamp, Stevenson, Donohue, Newhouse, & Keating, 2007). This study found that most plans used prior authorization requirements to limit use of antipsychotics. Atypical antipsychotics were restricted in 8 to 48% of plans with the level of restriction varied depending on molecules and types of formulation. The most restricted drugs were Zyprexa IM ® (olanzapine) (prior authorization required by 48% of plans) and Geodon IM®

(ziprasidone) (prior authorization required in 47% of plans). The study concluded that even though antipsychotics are protected, prior authorization requirements can make it challenging for beneficiaries with mental illness to have access to the therapy.

Similarly, Wang and associates examined coverage levels, coverage restrictions, and the cost for each of the atypical antipsychotics in Medicare drug plans available in Washington. The study found that the coverage and restrictions varied between MAP and PDP plans (Wang, Kennedy, Cohen, & Sclar, 2008).

Following two articles described lack of bioequivalence between generic and branded atypical antipsychotics. A group of researchers assessed bioequivalence between generic risperidone oral solution and branded risperidone tablets (Risperdal). The study assessed drug concentration in blood plasma as a parameter to determine whether both the formulations are bioequivalent. A two periods, laboratory blind, and randomized study was conducted in 30 healthy volunteers. The subjects were divided into two groups. One group was administered 1 mg/ml dose of Risperdal and the other group was administered equivalent dose of the generic version. The results showed with 90% confidence interval that the drug concentration levels found in the subjects on the generic version were not within the accepted limits of 80-125% (Os, Relleke, Synthon, & Nijmegen, 2006).

Another prospective crossover study was conducted by a group of physicians and pharmacists to determine bioavailability of generic clozapine as compared to Clozaril. The subjects recruited for the study were schizophrenic patients taking a stable dose of Clozaril. After a baseline two week run-in period on their respective dosage of Clozaril, the patients were randomly assigned to receive equivalent dose of either generic clozaine or Clozaril. Based on their findings, it was

concluded that a significant difference existed between bioavailability of generic and branded formulations among 40% of the patients. The research suggested that the decision of switching patients from Clozaril to generic must be made with extreme caution (Lam, Ereshefsky, Toney, & Gonzales, 2006).

Several studies assessed the effect of generic substitution on patient compliance or adherence to the atypical antipsychotic drugs. A study conducted a questionnaire based survey in a hypothetical pharmacy setting. A group of 106 schizophrenic patients who were on branded atypicals was selected. The group was receiving Risperdal®, Zyprexa®, Abilify®, and Seroquel® branded drugs. The participants were given a set of stimulus generic medical packages. These packages stated the drug name on it but were significantly different in appearance from their branded counterparts. The survey questionnaire was administered without disclosing the objective of the study to the participants and 73% of participant they are less likely to take the substitute generic medications. The study concluded that the most of the antipsychotic patients regarded generic medications as significantly different from branded ones (Roman, 2009).

Another study used pharmaco economic DES model to predict probability of non compliance to generic risperidone among schizophrenic patients. The DES model considers patients' history and heterogeneity and simulates individual patients suffering from schizophrenia over the period of five years. The researchers found that schizophrenic patients are more likely to lose adherence after switching to generic risperidone. Moreover, the study concluded that loss of adherence is likely to reduce symptom control which may result in patients being treated intensively and in a more expensive way. Ultimately, it is inferred that it may be cost effective to keep a patient with

schizophrenia on branded risperidone instead of switching him/her to generic versions (Treur et al., 2009).

Potential Contribution of the Proposed Research

The current literature has focused on the effect of prior authorization on access to protected classes of drugs. A small number of articles focus on Medicare coverage of antipsychotics. A few articles have examined discrepancy by the MMA in the medical treatment for the dually eligible beneficiaries. With the exception of Wang et al., (2007) and Wu et al., (2009) no research has focused on state wide coverage of atypical antipsychotics in terms of cost sharing, and use of pharmacy management tools.

Atypical antipsychotics have high cost, high utilization, and an imminent shift to generic availability. The future will benefit from a more comprehensive look at the formulary management in atypical antipsychotics after introduction of a generic version of risperidone.

The recent expiration of risperidone's patent will shed light on the cost and access implications of pharmaceutical patent expiration for Medicare plans. This information will be useful for those involved in designing the Medicare Standard Benefit and private formulary experts who are involved in designing individual plan formularies.

CHAPTER THREE

METHODOLOGY

The following chapter explains the study design, the evaluative components, the data source, and the method of data collection used for this study. Furthermore, the study population, research constructs, operational definitions, variables and its type, measures, and the analytical approach are presented in this chapter.

Study Design

This study examines the change in formulary restrictions and the patient cost for seven atypical antipsychotics: Risperidone (generic), risperidone (Risperdal®), clozapine (Clozaril®), Clozapine (generic), olanzapine (Zyprexa®), paliperidone (Invega®) under PDPs and MAPs, in Washington for 2010.

Data Source

This is a secondary data analysis. The Center of Medicare and Medicaid Services (CMS) has released Prescription Drug Plan Data for fiscal year 2010 in October 2009. A Medicare website provides an interactive online tool called 'Prescription Drug Plan Finder'. The site provides detail information about the drug plans in terms of formulary restrictions and cost structure. Formulary restrictions include four categories: coverage level, quantity limits, step therapy, and prior authorization. The coverage level is first tier (generic), second tier (preferred branded), third tier (Non-preferred), forth tier (Specialty I), and fifth tier (Specialty II). A step therapy requirement mandates a prior treatment before utilizing the drug. There are four components of the cost; 1) full cost of drug; 2) the cost in the initial coverage period; 3) the full cost of the drug

in the "coverage gap" (unless the plan offers coverage in the "doughnut hole"), and 4) the cost in the catastrophic coverage.

Study Population and Plan Identification

The study population is defined by the available drug plans and the appropriate dosage for each antipsychotic drug. This section describes the study population through an examination of plan identification and dosage definition.

Plan identification

As PDPs are statewide plans, each county in Washington has identical number of plans. In 2010, a total of 44 PDPs were identified which were used in the study for analysis. MAPs are not state wide. In order to collect the state wide data, ZIP codes were entered in the CMS website. On entering a ZIP code, the website brings up all the MAP plans that are offered the drug coverage in that particular area. A total of five ZIP codes were randomly selected; 99151(Marcus), 99350 (Benton), 99363 (Wallula), 98557 (McCleary), and 98498 (Lakewood). The information gathered from these ZIP codes represented MAP offerings of the whole state.

A total of 82 MAPs were identified in Washington State with this method, but only unique plans were selected. Ultimately, 49 MAPs were analyzed. Medicare Special Need plans were excluded from the study.

Dosage Definition

MAPs and PDPs may charge different prices for different dosages of the same drug. In this study, the most common daily dosage information was established by soliciting opinions of key psychiatrists at mental health facilities in the Spokane area and by using Physician Desk Reference (PDR 63rd Ed., 2009). The official proved dosage and the actual therapeutic treatment

dosage may differ among individuals. Unfortunately, there is no established resource to provide the most common dosage information (Wang, 2007). The dosage information for each drug is summarized in table 1.

Table. 1 Dosage Information of all the Atypical Antipsychotics used in the Study

Drug Name	**Dosage**
Clozapine (generic) 200mg	three times a day
Clozapine (Clozaril®) 200mg	three times a day
Olanzapine (Zyprexa®) 15 mg	once a day
Paliperidone (Invega®) 6mg	once a day
Risperidone (generic) 4 mg	once a day
Risperidone (Risperdal®) 4mg	once a day
Risperidone (Risperdal® Consta®) 25mg	once in two weeks (IM)

Research Constructs and Operation Definitions

The objective of this research is to assess the difference between the generic and patent protected drug formulations of atypical antipsychotics in terms of their cost sharing and formulary restrictions in MAPs and PDPs for the year 2010. The difference between the cost sharing is defined as difference in the mean, median, and standard deviation of monthly premiums, annual deductibles, the costs in the initial coverage level, the full drug cost in the gap, and catastrophic costs of generic risperidone and the brand name drugs. The difference in the formulary restrictions is assessed by percent of MAP and PDP plans that used pharmacy management tools. Table 2 & 3 summarize the dependant and independent variables.

Table. 2 Variables (Independent)

Variable Name	**Measure**
Drug Type Clozapine (generic) Clozaril®, Invega®, Risperdal®, Risperidone (generic) Zyprexa®	mean, standard deviation, median.
Plan Type (PDPs/MAPs)	mean, standard deviation, median.

Table. 3 Variables (Dependent)

Variable Name	**Measures**
Formulary restriction	
Degree of drug coverage	Tier level 1,2,3,4,5
Prior authorization requirements	Yes/No
Quantity limits	Yes/No
Step therapy requirements	Yes/No
Cost-sharing structure	
Full Drug costs The costs for the initial coverage The costs in the "Donut Hole" The costs of catastrophic coverage	Cost
Premium charges	Drug plan premiums (monthly)
Annual deductible charges	Annual deductibles

Statistical Analysis

All data were exported to MS Excel spreadsheets. Formulary restriction rates were calculated in terms of percent of plans. Furthermore mean and median costs were calculated for each drug and plan type.

CHAPTER FOUR

RESULTS

This chapter discusses formulary analysis of 49 MAPs and 44 PDPs offered in Washington in 2010. Table compares premiums and annual deductibles. The average monthly premium of PDPs is almost half of that of MAPs. MAPs have relatively wide range of monthly premiums as compared to PDPs. Almost 62% MAPs do not have annual deductibles, while 14% have annual deductable below the standard mark of $310. PDPs were found to be equally distributed across above mentioned categories as far annual deductible is concerned.

Table 4. Premiums and Deductibles for MAP and PDP plans in Washington in 2010

	MAP (49)	PDP (44)
Monthly Premiums		
mean	$101	$ 58
median	$90	$ 46
range	$0-262	$9- 109
Annual Deductible		
No Annual Deductible	62%	36%
less than Standard Annual Deductible	14%	31%
Standard Annual Deductible	18%	33%

Source: CMS website data for Washington State collected in February 2010.

In table 5, three drugs containing risperidone are compared in terms of their coverage in Medicare plans. Risperidone (generic) which came out in the market in late 2008 is covered by 89% of MAPs as “Tier 1” drug, whereas 68% PDPs cover it under this category. Respectively, 11% and 27% of MAPs and PDPs cover generic risperidone as a Tier 2 drug.

Table 5. Coverage of the Drugs Containing Risperidone among MAPs (n=49) and PDPs (n=44) in WA in 2010.

	Risperidone (Generic)		Risperdal® (Branded)		Risperdal Consta® (Branded)	
	MAP	PDP	MAP	PDP	MAP	PDP
Not Covered (Not on Formulary)	0%	0%	48%	63%	0%	0%
Covered	100%	100%	52%	37%	100%	100%
Coverage Level if Covered						
Tier 1 - generic	89%	68%	0%	0%	0%	0%
Tier 2 - preferred brand	11%	27%	4%	5%	37%	29%
Tier 3 - non-preferred brand	0%	5%	48%	22%	48%	34%
Tier 4 - Specialty I	0%	0%	0%	10%	15%	34%
Tier 5 - Specialty II	0%	0%	0%	0%	0%	2%

Source: CMS website data for Washington State collected in February 2010.

The coverage policies for branded Risperdal® are dramatically different from the generic version. 48% of MAPs and almost 2/3 of PDPs do not have this drug in their formularies. Of those which do, 48% of MAPs and 22% of PDPs cover it as a Tier 3 drug. None of the plans cover it as a Tier 1 drug and a very few plans cover it under Tier 2 category. A modified (long acting injectible) formulation of risperidone is marketed as "Risperdal Consta". This sustain release formulation has no generic equivalents available for the same type of formulation. Although all plans cover this drug, they typically place it in higher tiers. MAPs and PDPs with more or less variations cover it under Tier 2, 3, 4, and a few PDPs also categorize this as Tier 5 drug.

Table 6. Cost of the Drugs Containing Risperidone among MAPs (n=49) and PDPs (n=44) in WA in 2010.

	Risperidone (Generic)		Risperdal (Branded)		Risperdal Consta (Branded)	
	MAP	PDP	MAP	PDP	MAP	PDP
Full Drug Cost						
mean	$64	$109	$468	$465	$521	$518
Standard Deviation	$43	$79	$22	$21	$6	$6
median	$42	$63	$480	$480	$520	$517
range	$32-217	$24-272	$442-495	$441-487	$511-527	$507-527
Initial Coverage Level						
mean	$11	$14	$115	$83	$69	$125
Standard Deviation	$11	$14	$79	$26	$45	$89
median	$6	$7	$80	$80	$65	$91
range	$4-50	$0-68	$44-274	$43-150	$14-170	$22-386
Catastrophic Coverage						
mean	$51	$99	$468	$465	$521	$518
Standard Deviation	$49	$85	$22	$21	$6	$5
median	$41	$63	$480	$480	$520	$517
range	$3-201	$4-273	$442-495	$441-487	$511-528	$504-527

Source: CMS website data for Washington State collected in February 2010.

Table 6 compares the same three drugs in terms of cost. The generic version is the cheapest, with mean cost being $63.7 for MAPs and $109 for PDPs. Risperdal Consta is the costliest drug, average cost being $520. Comparing initial coverage offered by the plans, MAPs are cheaper than PDPs for generic risperidone. For the branded drug with no generic substitute, MAPs are generally cheaper than PDPs. The mean initial cost for Risperdal Consta with MAPs is $69, compared to $124 for PDPs. For the generic drugs, MAPs offer better gap coverage and catastrophic coverage than PDPs. There is no Gap Coverage for branded drugs on either type of plans.

Table 7. Coverage of the Drugs Containing Clozapine among MAPs (n=49) and PDPs (n=44) in WA in 2010.

	Clozapine (Generic)		Clozaril (Branded)	
	MAP	PDP	MAP	PDP
Not Covered (Not on Formulary)	0%	0%	74%	93%
Covered	100%	100%	26%	7%
Coverage Level				
Tier 1 – generic	80%	41%	0%	0%
Tier 2 - preferred brand	20%	51%	0%	0%
Tier 3 - non-preferred brand	0%	7%	26%	7%
Tier 4 - Specialty I	0%	0%	0%	0%
Tier 5 - Specialty II	0%	0%	0%	0%

Source: CMS website data for Washington State collected in February 2010.

Table 7 compares coverage of branded and generic formulations containing clozapine. 80% of MADP plans cover the generic clozapine in Tier 1, and 20% cover it as a Tier 2 drug. 41% PDPs cover it as a Tier 1 drug, and 51% as a Tier 2 drug. 7% of PDPs cover this generic version in Tier 3. The branded version of the same active ingredient is not covered by 74% of MAPs and 93% PDPs in Washington. Others cover it as a Tier 3 drug.

Table 8. Cost of the Drugs Containing Clozipine among MAPs (n=49) and PDPs (n=44) in WA in 2010.

	Clozapine (Generic)		Clozaril (Branded)	
	MAP	PDP	MAP	PDP
Full Drug Cost				
mean	$401	$427	$1,119	$612
Standard Deviation	$206	$109	$245	$479
Median	$417	$467	$1,205	$335
Range	$214-546	$214-545	$335-1206	$335-1165
Initial Coverage Level				
mean	$28	$39	$970	$71
Standard Deviation	$66	$39	$409	$21
Median	$6	$31	$1,205	$61
Range	$4-407	$0-124	$56-1207	$56-95
Catastrophic Coverage				
mean	$28	$22	$896	$612
Standard Deviation	$57	$4	$512	$479
Median	$406	$23	$1,207	$335
Range	$11-407	$10-27	$17-1207	$335-1165

Source: CMS website data for Washington State collected in February 2010.

Table 8 depicts the cost structure for clozapine and Clozaril, and the pattern is similar to risperidone. The full cost of the generic drug is lower for MAPs that for PDPs ($401 vs. $ 427). However, for the branded counterpart, MAPs have a high drug cost compared to PDPs ($1119 vs. $612). In the initial coverage, MAPs have slightly lower cost for the generic drug as compared to PDPs. A beneficiary is more likely to pay higher amount in the catastrophic coverage for the branded drug in case enrolled in MAPs as compared to PDPs ($896 vs. $611).

Table 9. Coverage of the Drugs Containing Paliperidone and Olanzapine among MAPs (n=49) and PDPs (n=44) in WA in 2010.

	Invega (Paliperidone, Branded)		Zyprexa (Branded, Olanzapine)	
	MAP	PDP	MAP	PDP
Not Covered (Not on Formulary)	0%	0%	0%	0%
Covered	100%	100%	100%	100%
Coverage Level				
Tier 1 - generic	0%	0%	0%	0%
Tier 2 - preferred brand	22%	29%	91%	54%
Tier 3 - non-preferred brand	65%	44%	7%	32%
Tier 4 - Specialty I	13%	20%	2%	12%
Tier 5 - Specialty II	0%	7%	0%	2%

Source: CMS website data for Washington State collected in February 2010.

Table 9 represents the pair of branded drugs Invega and Zyprexa. These are atypical drugs with no generic substitutes currently available in the market. Most of the MAPs cover Invega as a Tier 3 and Zyprexa as a Tier 2 drug. PDPs are more likely to cover these drugs but under a specialty tier.

Table 10. Cost of the Drugs Containing Paliperidone and Olanzapine among MAPs (n=49) and PDPs (n=44) in WA in 2010.

	Invega (Branded, Paliperidone)		Zyprexa (Branded, Olanzapine)	
Full Drug Cost	MAP	PDP	MAP	PDP
mean	$374.0	$373.9	$616.5	$612.7
standard deviation	$10.7	$7.7	$6.7	$6.7
Median	$376.6	$374.8	$614.7	$612.1
Range	$350-382	$382-350	$605-624	$597-623
Initial Coverage Level				
mean	$80.1	$97.0	$69.2	$112.1
standard deviation	$47.1	$57.7	$123.6	$112.8
Median	$72.0	$85.0	$35.0	$43.0
Range	$25-191	$30-280	$14-70	$22-457
Catastrophic Coverage				
mean	$18.7	$18.7	$30.8	$30.6
standard deviation	$0.5	$0.4	$0.3	$0.3
Median	$18.8	$18.7	$30.7	$30.6
Range	$18-19	$17-19	$30-32	$29-31

Source: CMS website data for Washington State collected in February 2010.

Table 10 provides a comparative analysis of Invega® and Zyprexa® in terms of costs. There is no significant difference between the full costs of drugs in either type of plans. MAPs have consistent lower costs in the initial coverage. Gap coverage is unavailable for these drugs. Furthermore, no significant difference has observed in the cost in the catastrophic coverage phase. MAPs and PDPs formulary structures appear to be consistent with the federal coverage requirements of atypical antipsychotics.

Table 11 provides a comparison between generic and branded drugs in terms of number of plans providing coverage in the donut hole. Plan formularies clearly prefer gap coverage for the generics drugs. Among MAPs 26% plans cover each generic drug in the gap. PDPs have

relatively lower gap coverage. 15% and 12% of PDPs cover the generic versions of risperidone and clozapine respectively.

Among branded drugs, gap coverage is rarely observed. Only 2% of MAPs offer it for Clozaril® and 4% of the same offer it for Zyprexa®. Other branded drugs are not covered by any of the plans.

Table 11. Percentage of Medicare Plans providing Gap Coverage in 2010

	Gap Coverage	
	MAP	PDP
Generic		
Risperidone	26%	15%
Clozapine	26%	12%
Branded		
Risperdal®	0%	0%
Risperidone Consta®	0%	0%
Clozaril®	2%	0%
Invega®	0%	0%
Zyprexa®	4%	0%

Source: CMS website data for Washington State collected in February 2010.

Table 12 explains the trend of using pharmacy management tools among MAP and PDP plans. The use of generic drugs is mostly regulated by prior authorization techniques. Risperidone has highest number of plans (61% MAPs & 78% PDPs) requiring prior approval. For Clozaril®, only 17% MAPs and 24% PDPs require prior authorization before. About 4% of MAPs use step therapy.

Table 12. Percentage of Medicare Plans using Pharmacy Management Tools in 2010

	Prior Authorization		Step Therapy	
	MAP	PDP	MAP	PDP
Generic				
Risperidone	61%	78%	0%	0%
Clozapine	17%	24%	4%	0%
Branded				
Risperdal®	0%	32%	30%	7%
Risperidone Consta®	20%	63%	46%	0%
Clozaril®	4%	0%	0%	0%
Invega®	57%	66%	0%	39%
Zyprexa®	57%	76%	0%	5%

Source: CMS website data for Washington State collected in February 2010

About 32% and 63% PDPs require Prior Authorization for Risperdal® and Risperidone Consta® respectively. A significant number of MAPs require step therapy especially for branded drugs; around 30% MAPs and 7% PDPs require step therapy for Risperdal®. No PDPs require a step therapy before authorizing the use of Risperidone Consta. Clozaril® is not highly regulated in either type of Medicare plan. This may be attributed to the side effects associated with it. More than half of MAPs and 60% and 77% of PDPs required prior authorization before using Invega® and Zyprexa®. MAPs do not require a step therapy but 36% and 5% of PDPs require it. PDPs may require patients to first try risperidone, as Invega® is an active metabolite of risperidone.

CHAPTER FIVE

CONCLUSIONS/ LIMITATIONS

This chapter includes the conclusion with interpretation of key findings and policy as well as clinical implications. Additionally, limitations of the study and future research recommendations are offered.

Conclusion

The findings of this study support the hypothesis that MAP and PDP formularies have lower rates of cost sharing, and lower use of pharmacy management tools for generic versions of atypical antipsychotics than for branded medications.

The generic drugs have significantly lower costs, and are covered under Tier 1 category where as branded drugs are observed in the higher categories. MAPs and PDPs may drop the generic substitutable branded drugs from their formulary lists. In terms of cost, there is a significant difference between the branded and generic formulations. For example, the initial mean co-pay of Risperdal® is almost $105 higher than the generic equivalent. Risperidone Consta is covered by all formularies, but the full drug cost is high.

To effect of patent expiration appears distinctly after contrasting the finding of previous studies. Wang et al. (2008) performed a cross-sectional descriptive analysis to assess the coverage levels of some of the key atypical antipsychotics in 2007. As per this research the branded version of risperidone was covered by all MAPs and PDPs. Majority of the plans placed this drug in Tier 2. Furthermore, in 2007, the average monthly co-pays in the initial coverage for MAPs and PDPs were $33 and $44 respectively. Similarly, Wu at el. (2009) conducted a longitudinal study assessing the changes in the coverage of atypical antipsychotics among

Medicare drug plans in Washington for 2007 to 2008. A similar trend was observed in the coverage levels of the branded risperidone. In 2008, all MAPs and most of PDPs covered this drug in their formulary and majority of the plans placed it in Tier 2 and Tier 3. There was no plan that did not have this drug listed on their formularies. The mean monthly co-pays in the initial coverage for branded Risperdal® were $36 and $47 for MAPs and PDPs respectively (Wu at el., 2009).

The generic version came to the market in late 2008. As per current results the initial coverage co-pay for the branded risperidone went up to $115 and $83 for MAPs and PDPs respectively. In terms of coverage levels, within two years of the arrival of the generic version of risperidone, 45% of MAPs and 59% of PDPs dropped it from their formularies. Other plans increased the cost sharing for the branded drug.

As far as the rate of use of pharmacy management tools is concerned, in 2008, none of them required a prior authorization or a step therapy (Wu at el., 2009). After two years from the introduction of the generic version in 2008, 29% of MAPs and 7% PDPs require a step therapy before using the branded drug.

Usually drug plans require patients to first try cheaper generics before authorizing branded drugs. Step Therapy is a widely utilized pharmacy management tool among MAPs and PDPs to restrict use of branded drugs. Around 46% of MAPs require step therapy before using Rispedral Consta. Rispedral Consta is a long acting injectable and has extended its patent. Therefore, currently there are no equivalent generics available to replace this drug. Although, it is not possible to find exact nature of step therapies through “Prescription Drug Plan Finder”, it may force clinicians to prescribe from available generics. Similarly, 39% of PDPs require a step

therapy before using Invega. Paliperidone, the active ingredient in Invega, is an active metabolite of risperidone. Therefore it is possible that plans may require patients to first fail on risperidone before receiving an authorization for utilization of Invega.

Medicare Part D has a gap in coverage also popularly known as “donut hole”. Medicare does not cover drugs if the total expenditure falls in the range of $2830 – 4550. MAPs and PDPs may choose to not offer drug coverage in the gap. Less than one third of the Medicare drug plans provide gap coverage for generics drug and almost none cover branded drugs in the coverage gap. This may have a significant impact on health outcomes of schizophrenic patients as high out of pocket expenditure may lead to cost related non adherence. Non adherence with antipsychotic drugs often results in relapses further worsening quality of life.

Limitations

The study was limited by insufficient plan information on the CMS website. The CMS was not able to provide complete information about five plans; two PDPs and three MAPs. This led to disqualification of five plans from the consideration.

For MAPs, the five randomly selected zip codes were may have missed some plans which are offered only in other Washington counties.

The current research is limited only to Washington. A nationwide analysis might give a comprehensive view of the formulary analysis in terms of cost and coverage characteristics. Furthermore, the study only relied upon the plan information provided by CMS. In order to understand the implications of formulary structures for the Medicare beneficiaries claim data should be assessed. A limitation of the study design is that the enrollments were not considered. This may restrict the validity of the study in terms of applying it to the real majority of

beneficiaries among Medicare drug plans in Washington State. Moreover, because this study only indicates the general formulary structure, coverage information for special beneficiary populations, such as disabled or low-income beneficiaries, may not be represented.

The study focused on only one year to perform a cross-sectional analysis. To see change in formulary structures over a period of time, a longitudinal study would be more beneficial.

Recommendations for Further Research

This study provided a comprehensive view of structural differences among Medicare drug formularies in terms of generic and branded atypical antipsychotic drugs. It is important to improve external validity by considering nationwide drug plans in the analysis and evaluate access to at the national level.

Replication of this study is important over time as within the next ten years all atypical antipsychotics are set to lose their patent protection and exclusive marketing rights opening the market for generic competitors. Ultimately, to find out real effects of the generic competition in the market on beneficiaries, the drug claims or plan enrollment data must be assessed in the future.

Policy Implications

Invega and Zyprexa are the two atypicals with patent protections. They do not have any generic substitution and are covered in higher tiers by all formularies. Their patent protections are set to expire in the next couple of years. Zyprexa is losing its patent in 2011 and Invega's patent is expiring in 2012. There is a high probability for generic versions of these drugs to hit the market in next two to three years. It is predicted from the study results that the formularies will change their structure quickly on the advent of their generic versions which may lead to

higher out of pocket cost and may cause barriers in the access to patented drugs for the Medicare beneficiaries.

Clinical Implications

As mentioned in the literature review, schizophrenia is usually associated with paranoia. Paranoia predisposes patients to reluctance to any kind of change. It has been observed that patients with schizophrenia are less likely to adhere with the dosage regimen if the medication appearance changes e.g. due to generic substitutions. Non adherence with antipsychotic medication increases risk of relapses (Treur et al., 2009).

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APPENDIX

Table. 13 List of drugs and patent status

Drug Name	Type	Patent Status
Risperidone (Risperdal®)	Brand Name	Expired (June, 2008)
Risperidone (Risperdal Consta®)	Brand Name	On Patent (2012)
Risperidone	Generic	NA
Clozapine (Clozaril®)	Brand Name	Expired (1998)
Clozapine	Generic	NA
Olanzapine (Zyprexa®)	Brand Name	On Patent (2011)
Paliperidone (Invega®)	Brand Name	On Patent (2012)

Table. 14 Change in cost and coverage of Risperdal from 2007 to 2010

Year	Number of Plans Covering Risperdal®		Cost of Risperdal®		Reference
	MAP	PDP	MAP	PDP	
2007	100% *Tier 2: 96%* *Tier 3: 4%*	100% *Tier 2:100%*	$ 33	$ 44	Wang et al. , 2008
2008	100% *Tier 2 :100%*	98% *Tier 2: 87%* *Tier 4: 11%*	$ 36	$47	
Late 2008	Advent of generic risperidone				
2010	52% *Tier 2: 4%* *Tier 3: 48%*	37% *Tier 2: 5%* *Tier 3: 22%*	$115	$83	Chandratre et al., 2010