Antipsychotic Medication Use Patterns and Associated Costs of Care for Individuals with Schizophrenia

Danielle L. Loosbrock,^{1*} Zhongyun Zhao,² Bryan M. Johnstone,³ Lisa Stockwell Morris⁴

¹M.H.A, Outcomes Research, United States Medical Division, Eli Lilly and Company, Indianapolis, IN, USA

²Ph.D., Outcomes Research, United States Medical Division, Eli Lilly and Company, Indianapolis, IN, USA

³Ph.D., Neurosciences Department, US Medical Division, Eli Lilly and Company, Indianapolis, IN, USA and School of Public and Environmental Affairs,

Indiana University, Bloomington, IN, USA

⁴Ph.D., Disease, Treatment and Outcomes Information Services, IMS Health, Plymouth Meeting, PA, USA

Abstract

Background: Schizophrenia is a costly and complicated disorder to treat. A variety of schizophrenia treatment guidelines have been developed to provide valuable expert advice to practicing psychiatrists on various treatment options that are presumed to result in the best outcomes. However, examination of antipsychotic medication use patterns has suggested that current prescribing practices do not mirror recommended treatment guidelines and may have adverse economic consequences.

Aim of the Study: This study seeks to describe antipsychotic medication treatment patterns and estimate the total costs of care associated with treatment patterns for individuals diagnosed with schizophrenia in usual care settings.

Methods: Use of outpatient antipsychotic medications and other health services during 1997 was obtained for 2,082 individuals with a diagnosis of schizophrenia in the IMS Health LifeLinkTM employer claims database. We describe outpatient antipsychotic treatment patterns, estimated the costs of schizophrenia care by treatment pattern, and compared costs by treatment pattern using regression models.

Results: During 1997, 26% (n = 536) of individuals diagnosed with schizophrenia received no antipsychotic medication in the outpatient setting, while 52% (n = 1,088) were treated with only one antipsychotic (*Monotherapy*). For individuals who received more than one antipsychotic medication during 1997 (n = 458), 13% (n = 262) switched antipsychotic medications (*Switch*), 7% (n = 154) augmented their original antipsychotic therapy with an additional antipsychotic (*Augment*), and 2% (n = 42) of individuals were on more than one antipsychotic therapy at the start of the year. After adjusting for covariates, *Switch* and *Augment* patterns were associated with significant increases in total costs (an increase of \$4,706 (p<0.0001) and \$4,244 (p = 0.0002), respectively) relative to *Monotherapy*.

Discussion: These results indicate that a substantial proportion of individuals with a diagnosis of schizophrenia were not treated with

Tel.: +1-773-728 3855 Fax: +1-773-728 4078 E-mail: Loosbrock_Danielle_L@Lilly.com Source of Funding: Eli Lilly and Company. or had low exposure to antipsychotic therapy. Individuals treated with antipsychotic monotherapy experienced nearly half the annual costs as individuals who were treated with antipsychotic polytherapy or who switched antipsychotic medications. These observations should be interpreted in the context of the study limitations.

Implications for Health Care Provision and Use: This analysis indicates that there may be considerable room for improvement in the treatment for individuals diagnosed with schizophrenia.

Implications for Health Policies: Though schizophrenia affects a very small portion of the population, the individual and societal burden associated with the disorder is quite high. This paper suggests that antipsychotic monotherapy and continuous therapy, commonly recommended by published treatment guidelines, may be associated with economic savings.

Implications for Further Research: Future research should evaluate the impact of newer antipsychotic medications on patterns of care and economic outcomes. More information is also needed on which individual patient characteristics are likely to predict success or failure on specific treatments. Finally, more detailed information on the reasons or rationale for switching or augmenting original pharmacotherapy would be valuable in improving medication management in these complex and often difficult to treat patients.

Received 16 November 2001; accepted 20 August 2003

Introduction

The one-year prevalence of schizophrenia has been estimated to be 0.5 to one percent of the United States population.^{1,2} Individuals with schizophrenia suffer from a variety of impairments in psychological, social and occupational functioning. Given the debilitating and chronic nature of schizophrenia, it is not surprising that the annual costs of caring for individuals with schizophrenia have been estimated in certain populations to be as high as \$65,253 per patient per year.³

Guidelines recommend that schizophrenia patients receive antipsychotic therapy as first line treatment.^{4,5} While most guidelines recommend using either a conventional or atypical antipsychotic agent,^{4,5} the expert consensus guidelines⁶ recommend the use of atypical antipsychotic medications as

^{*} **Correspondence to:** Danielle L. Loosbrock, M.H.A., Outcomes Research, Eli Lilly and Company, Lilly Corporate Center, Indianapolis, IN 46285, USA

primary medication therapy. This recommendation may be the result of recent findings that newer antipsychotic agents have demonstrated superior efficacy in the treatment of negative symptoms associated with schizophrenia⁷⁻¹² and are less likely to produce side events¹³⁻¹⁵ that often lead to the discontinuation of medication.^{12, 16-19}

These guidelines provide valuable expert advice to practicing psychiatrists on various treatment options that are presumed to result in the best outcomes. Despite recent advances in treatment guidelines, individuals with schizophrenia remain very complicated and difficult to treat. Often, schizophrenia patients have comorbid disorders,²⁰⁻²² are not adherent with treatment,^{24,27} and/or require combination therapies in which the patient is treated with a number of different therapies to address their needs.²⁸ Consequently, treatment patterns seen in usual care often do not mirror recommended guidelines.²⁹ Further, physician or prescriber characteristics may confound the link between actual care and guildelines, as physician preferences, practice experience, and knowledge about current guideline recommendations may also contribute to differences seen between treatment patterns in usual care and guideline recommendations.

Previous work^{30,31} has examined medication use patterns for schizophrenia patients initiating therapy primarily on conventional antipsychotics in the California Medicaid system from January 1987 through July 1996. In this population, one quarter of the individuals did not receive antipsychotic medication therapy for at least a year subsequent to their initial diagnosis of schizophrenia. An additional 25 percent of individuals experienced a delay of 30 days or more between schizophrenia diagnosis and receipt of an antipsychotic medication during the year. Further, nearly half of the individuals treated with an antipsychotic medication without a delay in receipt of therapy switched medications or augmented their original medication with an additional antipsychotic. Individuals who delayed treatment or changed therapy experienced significantly higher costs associated with treatment.³¹ If the primary therapeutic goal for some patients is to maintain functioning and reduce the risk of relapse⁵ through the long-term use of antipsychotic medications during the maintenance phase of treatment,^{4,6} the results from McCombs et al. indicate that treatment for individuals with schizophrenia may be suboptimal. The work of Lehman et al.²⁹ support the findings of McCombs, et al.^{30,31} The authors examined individuals treated at acute inpatient settings and continuing outpatient programs and found that less than 50% of schizophrenia patients received treatment that conformed to guidelines.

The purpose of this study is to supplement existing literature on antipsychotic medication use patterns by examining outpatient antipsychotic use patterns for privately insured schizophrenia patients and by examining the association between different medication use patterns and costs of care. Information on the usual or routine practice patterns and their associated costs can be especially valuable in helping psychiatrists and health care decision-makers make more informed treatment decisions that may ultimately result in better therapeutic and economic outcomes.

Methods

Data

The data for this study were extracted from the IMS Health LifeLinkTM employer claims database. The LifeLinkTM database contains drug and medical claims drawn from indemnity and Preferred Provider Organizations for a population of approximately 1.6 million employees, dependents, and retirees.

A previously validated algorithm^{32,33} (at least one ICD-9 295.0 – 295.9 diagnosis from inpatient care or at least two diagnoses from outpatient care settings in 1996) was used to identify individuals with schizophrenia in the LifeLinkTM database. To ensure that complete information was available for all individuals in the analytic dataset, individuals must have been continuously enrolled for a 2-year period (January 1996 through December 1997). In addition, the sample was restricted to individuals 10 years of age or older at the time of their first diagnosis. 2,082 individuals met these criteria and were included in this analysis.

Medication use patterns and resource utilization were examined for the 1997 calendar year. Given that the average days supply for prescriptions in this dataset was 30 days, a 30day grace period was allowed at the start of the year to account for individuals who might have filled an antipsychotic prescription that carried over into1997. A 15-day grace period was allowed at the end of the 1997 calendar to account for individuals who might not promptly obtain refills for their medications. Therefore, medication use patterns and compliance was based on the 320 days following the first 30 days of 1997. Actual charge claims submitted by provider organizations to private insurance agencies for reimbursement were used to approximate incurred costs.

Medication Use Patterns

Individuals were segmented into five main use pattern categories based on their antipsychotic medication use during the observation period. Individuals receiving no antipsychotic treatment during the observation period were categorized as Not Treated. Individuals who received only one antipsychotic medication during the observation period were grouped into the Monotherapy category. The Switch medication use category consisted of individuals who discontinued their initial antipsychotic treatment and had a subsequent prescription for another antipsychotic medication. If a patient was on an antipsychotic at the beginning of the observation period, and then during the year filled subsequent prescriptions for that same medication and at least one additional antipsychotic medication, they were placed into the Augment use group. Lastly, individuals who were on more than one antipsychotic medication concomitantly at the start of the observation period were placed into the Concomitant Use group. Only a small proportion of individuals (n = 42, 2%) were in this group. We report descriptive information on the Concomitant Use individuals; however, given the small sample size, we did not include them in the cost analysis.

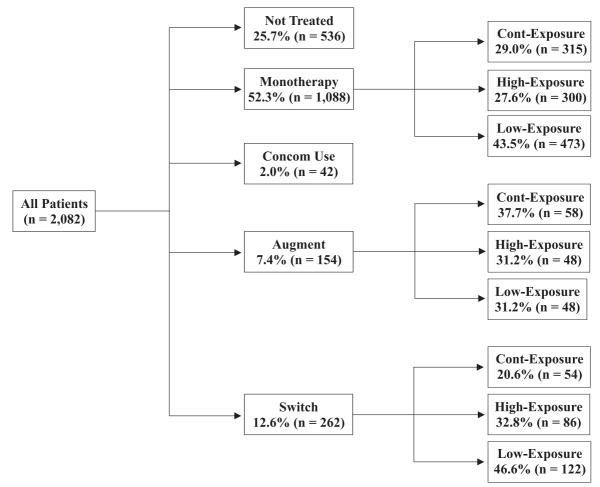


Figure 1. The patterns of medication use during 1997.

Medication Persistence

The use pattern groups were further segmented by medication persistence based on total days on therapy during the observation period. Individuals who had a gap of two weeks or less (≤ 14 days) in between their filled antipsychotic prescriptions consistently for the duration of the year were considered as having Continuous-Exposure to antipsychotic medication therapy.³¹ Individuals who experienced at least one interruption in therapy that lasted 15 days or more and also had approximately 80% exposure^{34,35} (<250-days) to antipsychotic medication were also considered persistent with their medication therapy and grouped into the High-Exposure medication persistence category. Individuals who had gaps in therapy in combination with less than 250-days exposure to antipsychotic medication during the observation period were considered not persistent with medication therapy and grouped into the Low-Exposure medication persistence category.

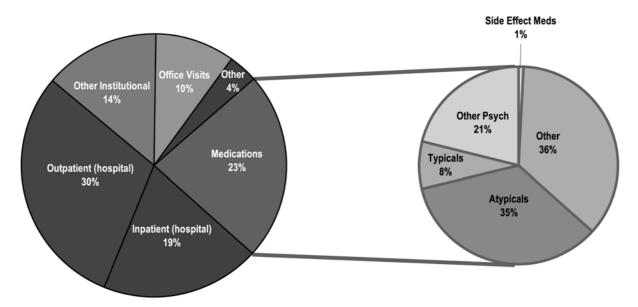
Data Analytic Procedures

Multiple regression procedures were used to test for differences in total costs between treatment pattern groups using the SAS System for Windows, Version 8.1. All regression models adjusted for differences in patient characteristics and indicators of disease complexity.

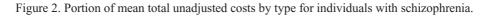
ANTIPSYCHOTIC MEDICATION USE PATTERNS AND ASSOCIATED COSTS

Specifically, the following types of patient-level variables were used as independent variables in multivariate analyses: demographics (age, gender, region); insurance (coverage, plan type); member (relationship to employee, active employee); type of schizophrenia (paranoid, catatonic, residual, disorganized, schizoaffective, disorganized, unspecified, other); comorbid psychiatric diagnoses (substance-related, bipolar disorder, nonorganic psychoses, organic psychoses); comorbid medical diagnoses (infectious disease, neoplasms, endocrine, blood, other mental, nervous system, circulatory system, respiratory system, digestive system, system, genitourinary pregnancy, skin, musculoskeletal system, congenital, perinatal, other illdefinied conditions, injury); treatment pattern (Not Treated, Switched, Augmented, Monotherapy); drug use (prior clozapine* use, post clozapine use); and total costs in the prior year. Costs were grouped into 4 main categories: institutional costs (hospital inpatient, hospital outpatient, psychiatric day/night facility, nursing facility, and emergency room costs), outpatient medications (outpatient medication

^{*} The commercial name for clozapine is Clozaril[®], a trademark of Novartis AG.



Mean Total Charges: \$11,042 (±164.5)



costs), office visits (physician office and psychotherapy costs), and other miscellaneous costs (substance abuse treatment, laboratory, and other costs).

Results

Figure 1 displays the antipsychotic medication use patterns for the study population. Over one quarter of individuals (n = 536) in this population did not receive any antipsychotic medication to treat their schizophrenia diagnosis during the entire calendar year. An additional 20% of individuals (n = 416) who initiated antipsychotic therapy either switched antipsychotic medications or augmented their original antipsychotic with an additional antipsychotic medication. Of the 52% of individuals (n = 1,088) who received only one antipsychotic during the year, over 40% of the individuals (n = 473) fell into the *Low-Exposure* category, or experienced gaps in therapy and less than 80% exposure to antipsychotic medication.

The descriptive statistics for the study population segmented by treatment pattern are provided in Table 1. The gender, age, and schizophrenia diagnosis distributions were similar across all use pattern groups. The average number of prescribed days on therapy for individuals receiving antipsychotic treatment was similar across use pattern, ranging from 70 to 80% adherent (230-267 out of 320 days). The individuals with schizophrenia in this population had an overall average of 4.2 recorded comorbid diagnoses during the observation period, when examining the number of comorbidities across use pattern results were similar. Mental illness comorbidity was particularly apparent in the Switch and Augment patient groups, who had higher proportions of individuals with comorbid nonorganic psychosis or comorbid bipolar disorder than the other use pattern groups. In addition, the proportion of individuals who had been 70

prescribed clozapine, a medication indicated to treat refractory schizophrenia patients, in the year prior to the observation period was higher in *Augment* individuals than in other use pattern groups (12% for *Augment* compared with 1-8% across the other patterns).

Mean total costs incurred during 1997 by this population was \$11,042 per patient (see **Figure 2**). Total institutional costs, including inpatient (hospital), outpatient (hospital) and other institutional costs, accounted for 63% of total costs. Outpatient medications, including antipsychotic, psychiatric, side effects and other medications, represented an additional 23% of total costs. Atypical antipsychotics, specifically, represented 8% of total costs, or approximately one third of outpatient medication costs.

After controlling for potential confounding factors, the Switch and Augment patterns were associated with significant increases in medication, institutional, and total costs relative to Monotherapy (see Table 2; full regression results are available upon request). Specifically, the Switch pattern relative to the Monotherapy pattern was associated with an increase of \$581 in medication costs (p<0.0001) and \$4,706 in total costs (p<0.0001). The Augment pattern relative to Monotherapy was associated with an increase of \$888 in medication costs (p<0.0001), and \$4,244 in total costs (p = 0.0002). Across use patterns, institutional costs were lowest for individuals in the Monotherapy treatment pattern group. The Switch and Augment patterns (relative to Monotherapy) were associated with increases of \$4,157 in institutional costs (p<0.0001) and \$2,547 in institutional costs (p = 0.0205), respectively. The Not Treated pattern was also associated with an insignificant increase in institutional costs (\$352, p = 0.6111).

Costs also varied by medication adherence within use pattern (see **Table 3**; full regression results are available upon request). After controlling for differences, *Monotherapy Continuous-Exposure* was associated with significant cost sav-

	All Patients	Not Treated	Monotherapy	Concom. Use	Augmented	Switched
Number of Patients (%)	2082 (100%)	536 (26%)	1088 (52%)	42 (2%)	154 (7%)	262 (13%)
Average Age in years (s.d.)	51 (土14)	51 (土14)	52 (±11)	$49 (\pm 14)$	47 (土14)	$49~(\pm 14)$
% Female	49.0%	49.0%	49.5%	45.0%	44.8%	48.1%
% with Full Coverage	22.6%	19.0%	25.6%	14.3%	18.8%	21.0%
Type of Schizophrenia						
% Paranoid	37.8%	31.2%	39.8%	45.2%	42.2%	39.3%
% Schizoaffective	34.5%	37.5%	33.9%	21.4%	28.6%	36.3%
% Catatonic	1.2%	1.9%	1.3%	0.0%	1.3%	0.0%
% Residual	6.3%	6.5%	6.0%	11.9%	5.2%	6.9%
% Simple	7.3%	9.7%	6.3%	9.5%	9.1%	5.3%
% Disorganized	1.1%	0.4%	1.4%	2.4%	2.0%	0.8%
% Unspecified	7.1%	6.7%	8.0%	2.4%	5.2%	6.1%
% Other	4.7%	6.2%	3.4%	7.1%	6.5%	5.3%
Number of Comorbidities $(\pm s.d.)$	4.18 (±2.8)	4.1 (±2.8)	4.03 (±2.7)	3.83 (±3.3)	4.4 (土2.9)	4.89 (±2.8)
% with Bipolar	10.4%	8.2%	9.7%	7.0%	13.6%	16.4%
% with Alcohol/Drug Dependence	7.9%	9.3%	6.7%	2.4%	7.8%	10.7%
% with Non-Organic Psychosis	26.7%	22.2%	23.4%	11.9%	43.5%	42.0%
% with Organic Psychosis	1.8%	1.1%	1.2%	2.4%	3.9%	4.6%
% Prior Clozapine Use (1996)	5.5%	0.9%	6.1%	4.8%	12.3%	8.4%
Number Days on Antipsychotic Therapy $(\pm {\rm s.d.})$	ı	0	$230~(\pm 109)$	241 (±104)	267 (主88)	232 (±96)
% Continuous-Exposure	I	I	28.9%	28.6%	37.7%	20.6%
% High-Exposure	ı	ı	27.6%	28.6%	31.2%	32.8%
% Low-Exposure	ı	ı	43.5%	24.9%	31.2%	46.6%

ANTIPSYCHOTIC MEDICATION USE PATTERNS AND ASSOCIATED COSTS

Variables	Total costs	sts	Medication costs	costs	Institutional costs	l costs
	Estimated Coefficient	P value	Estimated Coefficient	P value	Estimated Coefficient	P value
Switched	4705.9	<0.0001	581.2	<0.0001	4156.8	<0.0001
Augmented	4243.6	0.0002	887.9	<0.0001	2547.2	0.021
No Antipsychotic	-980.4	0.169	-618.1	<0.0001	351.6	0.611
Initiated on Multiple Antipsychotics	7108.6	0.0005	-5.1	0.983	6360.7	0.001
Intercept	-2727.0	0.291	609.4	0.042	-4072.5	0.104
Age	-35.9	0.200	-4.8	0.138	-21.8	0.422
Gender (Male versus Female)	-309.0	0.652	-42.3	0.593	-191.0	0.773
Region (Central Northeast versus other)	-1567.3	0.031	-109.4	0.192	-1515.5	0.032
Status (Enrollee versus Dependent)	-652.4	0.356	2.2	0.978	-802.8	0.242
Coverage (Full versus Partial)	-534.2	0.591	-111.0	0.334	-489.8	0.611
Plan (Indemnity versus PPO)	2377.5	0.063	60.7	0.681	2565.0	0.039
Employment (Active versus Retired)	-1002.6	0.154	-49.9	0.540	-1054.1	0.122
Clozapine Use in 1996	3599.1	0.070	-283.8	0.224	1671.7	0.384
Clozapine Use in 1997	-436.2	0.837	826.3	0.0008	-1635.2	0.426
Total Costs in 1996	0.2	<0.0001	0.9	<0.0001	0.2	<0.0001
Adj R-Sq	0.3835		0.6768		0.3115	10

Copyright © 2003 ICMPE

Table 3. Regression Results for the Effect of Persistence and Treatment Pattern on Total Costs Relative to *Monotherapy Continuous-Exposure*.

Variables	Total costs		
	Estimated Coefficient	P value	
Monotherapy High-Exposure	447.6	0.673	
Monotherapy Low-Exposure	472.9	0.625	
Switch Continuous-Exposure	2158.9	0.262	
Switch High-Exposure	4433.0	0.0058	
Switch Low-Exposure	6778.0	< 0.0001	
Augmented Continuous-Exposure	2643.5	0.1565	
Augmented High-Exposure	4056.4	0.0450	
Augmented Low-Exposure	7418.4	0.0003	
No Antipsychotic	-617.1	0.521	
Initiated on Multiple Antipsychotics	7416.5	0.0005	
Intercept	-2886.1	0.278	
Age	-35.3	0.209	
Gender (Male versus Female)	-351.5	0.608	
Region (Central Northeast versus other)	-1558.7	0.032	
Status (Enrollee versus Dependent)	-677.6	0.339	
Coverage (Full versus Partial)	-616.6	0.536	
Plan (Indemnity versus PPO)	2253.9	0.079	
Employment (Active versus Retired)	-960.9	0.172	
Clozapine Use in 1996	3803.3	0.0561	
Clozapine Use in 1997	-79.6	0.970	
Total Costs in 1996	0.2	< 0.0001	
Adj R-Sq	0.3843	0.3843	

Note: Regressions also controlled for: type of schizophrenia (acute, paranoid, schizo-affective, catatonic, residual, disorganized, unspecified, or other schizophrenia), comorbid psychiatric diagnoses (substance-related, bipolar disorder, nonorganic psychoses, organic psychoses); and 17 comorbid medical categories of the international classification of diseases. Full regression results are available upon request.

ings compared to *Switch High-Exposure* and *Low-Exposure* (\$4,433 p = 0.0058 and \$6,778 p<0.0001, respectively) patterns. *Monotherapy Continuous-Exposure* was also associated with significant cost savings compared to *Augment High-Exposure* and *Low-Exposure* (\$4,056 p = 0.0450 and \$7,418 p = 0.0003, respectively) patterns. Within use pattern, *Continuous-Exposure* to medication was consistently associated with lower costs over both *High-Exposure* and *Low-Exposure* and *Low-Exposure* and *Low-Exposure* and *Low-Exposure* both *High-Exposure* and *Low-Exposure* both *High-Exposure* and *Low-Exposure* and *Low-*

Discussion

This study describes the antipsychotic medication use patterns for individuals with a schizophrenia diagnosis in an employer claims database. The results suggest that routine medication treatment of schizophrenia, as documented in this primarily private care setting, may not be meeting the therapeutic needs of this population as defined by current treatment guidelines.^{4,6} A substantial proportion of individuals with a diagnosis of schizophrenia did not receive

ANTIPSYCHOTIC MEDICATION USE PATTERNS AND ASSOCIATED COSTS

any antipsychotic medication, or switched medications or augmented their original medication therapy during the year. These findings are consistent with recent literature documenting that switching and/or augmenting antipsychotic medication therapy is commonplace in routine care for Medicaid and indigent schizophrenia populations.^{30,31,36}

The costs associated with the different treatment patterns observed in routine care were also examined. Not surprisingly, even after controlling for differences across treatment group, costs (total, medication and institutional) were significantly greater for individuals who switched or augmented their original antipsychotic therapy than for individuals who received antipsychotic monotherapy. It should be noted that although some individual characteristics are controlled for in the regression models, unobservables, such as the effects of severity of illness and the patient's characteristic treatment responsiveness, could be driving the use of medications and these unobservables could also be driving total treatment costs. Therefore, these results do not imply that encouraging individuals to stay on monotherapy, for example, would reduce overall costs. Existing literature on antipsychotic medication switching and augmentation have also found that individuals who switch or augment medication therapy are more costly than individuals who do not switch/ augment.³¹ Generally, guidelines recommend that switching antipsychotic therapy should occur when individuals have failed to respond to current medications or if they incur persistent side effects that cannot be managed with adjunctive medications.⁴⁻⁶ For these complex patients, it may be especially difficult at initiation of therapy to find the appropriate medication to manage and control the patient's symptoms. If patients do not adequately respond to therapy or experience intolerable adverse events, switching or augmenting medication therapy may be necessary and may actually represent better matching of patients with medication.

The results also revealed that, regardless of medication use pattern, treated individuals with continuous exposure to antipsychotic medication consistently experienced lower total costs than individuals who were had interruptions in medication therapy and had low exposure to antipsychotic medications. For example, *Continuous-Exposure* to antipsychotic medication *Monotherapy* was associated with significant cost savings of \$6,778 and \$7,418 over *Switch* and *Augment Low-Exposure* individuals, respectively. McCombs *et al.*³¹ found similar results in California Medicaid patients. Patients who completed one year of uninterrupted medication therapy incurred on average \$7,824 less in total costs than patients who switched or augmented therapy during the first year.³¹

These findings suggest that individuals receiving treatment consistent with the published treatment guidelines may also incur lower costs than individuals receiving treatment that is inconsistent with the guidelines. Individuals treated with antipsychotic *Monotherapy* experienced significantly lower costs than *Switch* or *Augment* individuals. In addition, individuals who were *Continuously-Exposed* to antipsychotic medication generally experienced lower total costs than *Low-Exposure* individuals. Total costs for *Continuous-Exposure* individuals among *Monotherapy*, *Switch*, and *Augment* groups were not statistically significantly different. This indicated the importance of continuous therapy, and might also reflect that unobservable personal characteristics might drive both the choice of type of therapy and healthcare costs.

It is, nevertheless, perplexing that over a quarter of these careseeking individuals did not receive any antipsychotic medication therapy for a full year, despite a diagnosis of schizophrenia. Previous research examining use patterns for California Medicaid patients with schizophrenia similarly found that over 24% of patients did not use any antipsychotic medication for periods lasting up to 1 year.³⁰ Results reported by McCombs *et al.*³⁰ suggest that patients who are more severely ill (for example, had recently used other psychiatric medications or had concomitant mental disorders) were more likely to receive antipsychotic medication therapy. Therefore, it is possible that the individuals in our analyses who did not receive treatment with antipsychotics may have been less severely ill and, therefore, may have been less likely to have received or filled a prescription for an antipsychotic medication.

Additionally, these results may have direct implications for medical and financial decision-makers involved in the 74 treatment of individuals with schizophrenia, as medication formularies and guidelines sometimes require individuals to fail on one medication before being able to use another medication. The results of this study suggest that having switched antipsychotic medications is associated with increased costs.

These findings should be interpreted in the context of the limitations of the study design. This study used medical service and prescription claims data from a large employer database. Individuals in this system may not reflect persons utilizing services in other systems of care and, therefore, these results might not be generalizable to other care settings. This analysis only examines antipsychotic treatment patterns and, consequently, does not account for use of other psychotropic medications sometimes prescribed to treat patients with schizophrenia. In addition, the data does not include information on clinical and functional outcomes and, consequently, we were unable to link differences in treatment patterns and costs to changes in clinical and functional outcomes. Similarly, the reasons for switching or augmenting antipsychotic therapy were not available. The reasons at the time of changing medication therapy need to be explored further, as such information could be used to identify and improve potentially inappropriate prescribing and reduce health care costs. Also, the medication persistence estimates were derived using methodology used in the literature^{30,31},

³⁴⁻³⁶ to approximate compliance. However, these definitions may be somewhat arbitrary, though they do provide valuable information about the medication use patterns for these patients. Finally, provider charges instead of actual payments were included in the database, which will limit our ability to conduct any cost analysis from specific payers' perspective. However, charges data have their advantages because charges are relatively stable across years and are independent of specifications on patients and their insurance. Additionally, it is worth to note that "charges" used in this analysis may not heavily overestimate "costs" as evidenced by that the mean annual charges in this analysis (\$11,042) were similar to annual costs reported in the literature.^{30,31,37}

It should also be noted that it is likely that the individuals diagnosed with schizophrenia in this analysis may be at different, fluctuating stages and courses of their illness. When symptoms are uncontrolled or the side effects are unmanageable, the guidelines recommend switching or augmenting the original medication therapy.⁴⁻⁶ At these times, it may be that patients also consume more extensive mental health services and incur higher costs compared to times when symptoms are under control. This dataset contained limited information on the severity or complexity of illness at the time of service. Despite our attempts to control for proxy measures of patient disease complexity and severity (prior and post use of medications reserved from refractory patients (clozapine), specific schizophrenia subtype, comorbid psychiatric and medical diagnoses), other unobserved patient differences in disease acuity may also have contributed to the differences in costs across the Monotherapy, Switch and Augment use patterns.

This analysis examined the medication use patterns and the associated costs for individuals diagnosed with

schizophrenia. Results indicate that a substantial proportion of individuals with a diagnosis of schizophrenia either were not treated with or did not receive adequate exposure to antipsychotic medication treatment. Specifically, individuals who received antipsychotic monotherapy, the most commonly recommended treatment guideline, experienced lower total costs than individuals who switched or augmented their original antipsychotic medication therapy.

Acknowledgements

This paper is based on an early, preliminary version of a similar analysis, using the same data but different methodology, reported in the poster, "Antipsychotic Medication Treatment Patterns and Associated Costs of Care of Patients with Schizophrenia," which was presented at the 5th Annual International Center of Mental Health Policy and Economics (ICMPE) Value of Psychiatry Meeting in Chicago, IL, May 10th-12th, 2000 and the 5th Annual International Society for Pharmacoeconomic and Outcomes Research Meeting in Arlington, VA, May 22nd-24th, 2000.

References

- Regier DA, Narrow WE, Rae DS, Manderscheid RW, Locke BZ, Goodwin FK. The de facto US mental and addictive disorders service system. Epidemiologic catchment area prospective 1-year prevalence rates of disorders and services. *Arch Gen Psychiatry* 1993; **50** (2): 85-94.
- Kessler RC, McGonagle KA, Zhao S, Nelson CB, Hughes M, Eshleman S, Wittchen HU, Kendler KS. Lifetime and 12-month prevalence of DSM-III-R psychiatric disorders in the United States. Results from the National Comorbidity Survey. *Arch Gen Psychiatry* 1994; **51** (1): 8-19.
- Rosenheck R, Cramer J, Allan E, Erdos J, Frisman LK, Xu W, Thomas J, Henderson W, Charney D. Cost-effectiveness of clozapine in patients with high and low levels of hospital use. Department of Veterans Affairs Cooperative Study Group on Clozapine in Refractory Schizophrenia. *Arch Gen Psychiatry* 1999; 56 (6): 565-572.
- Lehman AF, Steinwachs DM. Translating research into practice: the Schizophrenia Patient Outcomes Research Team (PORT) treatment recommendations. *Schizophr Bull* 1998; 24 (1): 1-10.
- American Psychiatric Association. Practice guideline for the treatment of patients with schizophrenia. *Am J Psychiatry* 1997; 154 (4 Suppl): 1-63.
- McEvoy JP, Scheifler PL, Frances A. Treatment of schizophrenia 1999. The expert consensus guideline series. *J Clin Psychiatry* 1999; 60 (11 Suppl): 3-80.
- Tollefson GD, Sanger TM. Negative symptoms: a path analytic approach to a double-blind, placebo- and haloperidol-controlled clinical trial with olanzapine. *Am J Psychiatry* 1997; **154** (4): 466-474.
- Tollefson GD, Beasley CM, Jr., Tran PV, Street JS, Krueger JA, Tamura RN, Graffeo KA, Thieme ME. Olanzapine versus haloperidol in the treatment of schizophrenia and schizoaffective and schizophreniform disorders: results of an international collaborative trial. *Am J Psychiatry* 1997; **154** (4): 457-465.
- Beasley CM, Jr., Sanger T, Satterlee W, Tollefson G, Tran P, Hamilton S. Olanzapine versus placebo: results of a double-blind, fixed-dose olanzapine trial. *Psychopharmacology* 1996; **124** (1-2): 159-167.
- Beasley CM, Jr., Tollefson G, Tran P, Satterlee W, Sanger T, Hamilton S. Olanzapine versus placebo and haloperidol: acute phase results of the North American double-blind olanzapine trial. *Neuropsychopharmacology* 1996; 14 (2): 111-123.
- 11. Moller HJ, Muller H, Borison RL, Schooler NR, Chouinard G. A pathanalytical approach to differentiate between direct and indirect drug effects on negative symptoms in schizophrenic patients. A re-evaluation of the North American risperidone study. *Eur Arch Psychiatry Clin Neurosci* 1995; 245 (1): 45-49.
- 12. Bhana N, Foster RH, Olney R, Plosker GL. Olanzapine: An updated

ANTIPSYCHOTIC MEDICATION USE PATTERNS AND ASSOCIATED COSTS

review of its use in the management of schizophrenia. *Drugs* 2001; **61** (1): 111-161.

- Casey DE. The relationship of pharmacology to side effects. J Clin Psychiatry 1997; 58 (10 Suppl): 55-62.
- Tran PV, Dellva MA, Tollefson GD, Beasley CM, Jr., Potvin JH, Kiesler GM. Extrapyramidal symptoms and tolerability of olanzapine versus haloperidol in the acute treatment of schizophrenia. *J Clin Psychiatry* 1997; 58 (5): 205-211.
- Simpson GM, Lindenmayer JP. Extrapyramidal symptoms in patients treated with risperidone. J Clin Psychopharmacol 1997; 17 (3): 194-201.
- Kampman O, Lehtinen K. Compliance in psychoses. Acta Psychiatr Scand 1999; 100 (3): 167-175.
- Rosenheck R, Chang S, Choe Y, Cramer J, Xu W, Thomas J, Henderson W, Charney D. Medication continuation and compliance: A comparison of patients treated with clozapine and haloperidol. *J Clin Psychiatry* 2000; 61 (5): 382-386.
- Van Putten T. Why do schizophrenic patients refuse to take their drugs? Arch Gen Psychiatry 1974; 31 (1): 67-72.
- Kopala LC. Spontaneous and drug-induced movement disorders in schizophrenia. Acta Psychiatr Scand (Suppl) 1996; 389: 12-17.
- 20. Dixon L, Postrado L, Delahanty J, Fischer PJ, Lehman A. The association of medical comorbidity in schizophrenia with poor physical and mental health. *J Nerv Ment Dis* 1999; **187** (8): 496-502.
- Cassano GB, Pini S, Saettoni M, Rucci P, Dell'Osso L. Occurrence and clinical correlates of psychiatric comorbidity in patients with psychotic disorders. *J Clin Psychiatry* 1998; **59** (2): 60-68.
- 22. Miller NS, Fine J. Current epidemiology of comorbidity of psychiatric and addictive disorders. *Psychiatr Clin North Am* 1993; **16** (1): 1-10.
- Brown MC, Akpaffiong MJ, Oji VU, Bethea C. Re-admissions to psychiatric hospital associated with non-compliance to neuroleptics. *ASHP Midyear Clinical Meeting* 1994; 29 (Dec): 368.
- Weiden P, Glazer W. Assessment and treatment selection for "revolving door" inpatients with schizophrenia. *Psychiatr Q* 1997; 68 (4): 377-392.
- Weiden PJ, Olfson M. Cost of relapse in schizophrenia. Schizophr Bull 1995; 21 (3): 419-429.
- 26. Haywood TW, Kravitz HM, Grossman LS, Cavanaugh JL, Jr., Davis JM, Lewis DA. Predicting the "revolving door" phenomenon among patients with schizophrenic, schizoaffective, and affective disorders. *Am J Psychiatry* 1995; **152** (6): 856-861.
- 27. Meltzer HY. Treatment-resistant schizophrenia-the role of clozapine. *Curr Med Res Opin* 1997; **14** (1): 1-20.
- Canales PL, Olsen J, Miller AL, Crismon ML. Role of antipsychotic polypharmacotherapy in the treatment of schizophrenia. *CNS Drugs* 1999; **12** (3): 179-188.
- 29. Lehman AF, Steinwachs DM. Patterns of usual care for schizophrenia: initial results from the Schizophrenia Patient Outcomes Research Team (PORT) Client Survey. *Schizophr Bull* 1998; **24** (1): 11-20.
- McCombs JS, Nichol MB, Johnstone BM, Stimmel GL, Shi J, Smith RR. Use patterns conventional antipsychotic medications in medicaid patients with schizophrenia. *J Clin Psychiatry* 1999; 60 (0 Suppl): 5-11.
- McCombs JS, Nichol MB, Johnstone BM, Stimmel GL, Shi J, Smith R. Antipsychotic drug use patterns and the cost of treating schizophrenia. *Psychiatr Serv* 2000; 51 (4): 525-527.
- Lurie N, Popkin M, Dysken M, Moscovice I, Finch M. Accuracy of diagnoses of schizophrenia in Medicaid claims. *Hosp Community Psychiatry* 1992; 43 (1): 69-71.
- 33. Soumerai SB, McLaughlin TJ, Ross-Degnan D, Casteris CS, Bollini P. Effects of limiting Medicaid drug-reimbursement benefits on the use of psychotropic agents and acute mental health services by patients with schizophrenia. N Engl J Med 1994; 331 (10): 650-655.
- Revicki D, Brown R, Keller M, Gonzales J, Culpepper L, Hales R. Costeffectiveness of newer antidepressants compared with tricyclic antidepressants in managed care settings. *J Clin Psychiatry* 1997; 58: 47-58.
- Clark W, Churchill D, Forwell L, MacDonald G, Foster S. To pay or not to pay? *Can Med Assoc J* 2000; 162: 195-198.
- 36. Williams CL, Johnstone BM, Kesterson JG, Javor KA, Schmetzer AD. Evaluation of antipsychotic and concomitant medication use patterns in patients with schizophrenia. *Med Care* 1999; **37** (4 Suppl): AS81-86.
- Wyatt RJ, Henter I, Leary MC, Taylor E. An economic evaluation of schizophrenia – 1991. Soc Psychiatry Psychiatr Epidemiol 1995; 30 (5): 196-205.