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Effects of Antipsychotic Medication on Psychiatric Service Utilization and Cost

Aileen Rothbard,[1] Mary Rose Murrin,[2] Neil Jordan,[3] Eri Kuno,[4] Bentson H. McFarland,[5] T. Scott Stroup,[6] Joseph P. Morrissey,[7] Paul G. Stiles,[8] Roger A. Boothroyd,[8] Elizabeth Merwin,[9] David L. Shern[8]

[1] *Sc.D., University of Pennsylvania, School of Social Practice and Policy, Center for MH Policy and Services Research, Philadelphia, PA, USA*
[2] *University of South Florida, Tampa, FL, USA*
[3] *Ph.D., Northwestern University, Chicago, IL, USA*
[4] *Ph.D., University of Pennsylvania, Philadelphia, PA, USA*
[5] *M.D., Ph.D., Oregon Health Sciences University, Portland, OR, USA*
[6] *M.D., M.P.H., University of North Carolina, Chapel Hill, NC, USA*
[7] *Ph.D., University of North Carolina, Chapel Hill, NC, USA*
[8] *Ph.D., University of South Florida, Tampa, FL, USA*
[9] *Ph.D., University of Virginia, Charlottesville, VA, USA*

Abstract

Background: Based on randomized clinical trials, consensus has been emerging that the first line of treatment for individuals with psychotic disorders should be the newer atypical or second generation antipsychotic medications rather than the older neuroleptics. Given that acquisition costs of atypical antipsychotics are generally higher than typical antipsychotics, uncertainty exists whether the newer atypicals are cost effective alternatives when used in ordinary practice settings.

Aims of the Study: The introduction of newer atypical antipsychotic agents has prompted evaluation of their overall effectiveness in reducing health care costs given their higher acquisition costs. This paper focuses on the effects of differing classes of atypical versus typical antipsychotic medications on psychiatric service utilization and cost for persons with serious mental illness treated in usual practice settings.

Methods: Descriptive statistics are used to compare patient characteristics, service rates and costs across psychotropic medication groups. Prediction equations employing ordinary least squares regression models are used to explain variation in cost due to pharmacy group membership controlling for demographics, clinical diagnoses and symptoms. Subjects were 338 Medicaid clients with serious mental illness from Florida, Pennsylvania and Oregon treated in ordinary clinical settings. Resource utilization and costs were operationalized using administrative databases to measure consumption of treatment services and pharmaceuticals for a six month period.

Results: Inpatient service use was significantly higher for individuals on atypical only and combination atypical/typical medications compared to those on typical medications only, whereas outpatient use was highest for those on typicals. Furthermore, six-month costs for both pharmacy and psychiatric services were significantly greater for persons in the atypical only ($6528) and combination typical/atypical groups ($6589) compared to those on typicals only ($3463). There were still significantly higher costs associated with atypical only and the combination typical/atypical users after multivariate controls were used.

Discussion: This study showed that Medicaid clients in community settings using atypical only and typical/atypical combination medications had the highest costs both in pharmacy and service use when compared to those on typical only medications. However, this study design does not allow us to ascribe a causal relationship between medication group and service costs. Given that olanzapine was the most recent medication in the compendium of available drugs at the time of this study, it is possible that those in the olanzapine only group were failing on other drugs. Caution must be used in drawing policy implications regarding cost effectiveness of newer medications since individuals who are getting the newer atypical or combination medications in community mental health center settings may be unstable on the older medications.

Implications for Future Research: A longer follow-up period is needed to determine if the cohort remaining on current atypical medications stabilize over time while those taking the newest drug on the market become the most costly population.

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Introduction

There is considerable variation in psychotropic prescribing patterns for persons with serious mental illness.[1] Numerous factors contribute to this variation including case mix differences, prescriber preferences, and formulary policies. Nonetheless, consensus has been emerging, based on randomized clinical trials, that the first line of treatment for individuals with psychotic disorders should be the newer atypical or second generation antipsychotic medications rather than the older neuroleptics.[2-4] Given that acquisition costs of atypical antipsychotics (AAPs) are generally higher

* **Correspondence to:** Aileen Rothbard, Center for MH Policy and Services Research, Department of Psychiatry, University of Pennsylvania, Philadelphia, PA. 19104, USA.
Tel.: +1-215-349 8707
Fax: +1-215-349 8715
E-mail: rothbard@mail.med.upenn.edu
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than typical antipsychotics (TAPs),[5] uncertainty exists whether the newer atypicals (AAPs) are cost effective alternatives when used in ordinary practice settings.

Most pharmacoeconomic researchers agree that the total cost of healthcare should be taken into consideration when evaluating cost issues.[6-9] Many studies show that the newer atypicals are associated with decreased psychiatric hospitalization rates,[10-14] shortened length of stay per episode[15] and fewer hospital days per year.[13,16,17] These findings, based primarily on cohort studies of hospitalized patients, those discharged from inpatient facilities and community samples, provide evidence of cost savings given that inpatient care is the most expensive service type. Additionally, a study comparing individuals on typicals versus atypicals in ordinary settings in Italy, which was closest in design to the current study, found total healthcare cost reductions for those on atypicals although the impact was small.[18] In contrast, a VA study on a large number of patients discharged from psychiatric inpatient facilities found that patients receiving clozapine for less than a year had more inpatient days in a three year follow-up period.[19] Additionally, a study of Medicaid recipients receiving atypical antipsychotic medications in California found that the shift to atypicals significantly increased government spending on antipsychotics 30% with no reduction in utilization of hospitalization and no observable improvements in measures of health. [20]

There are, however, few randomized clinical trials comparing the cost effectiveness of atypical versus typical medications in ordinary community practice settings.[21] One such study of public sector clients with schizophrenia being treated under usual practice conditions with olanzapine, risperidone, or typical antipsychotic medication, found annual psychiatric medication costs were greater in the atypical group with no differential symptom or service use outcomes found, but compliance was better in the olanzapine group.[22] Rosenheck *et al*.[23] found substantial cost savings with clozapine in a small number of high-cost patients, but those savings were much harder to achieve in typical inpatient populations. The Clinical Antipsychotic Trials of Intervention Effectiveness (CATIE) program, a randomized multi-site national study funded by NIMH to evaluate the effectiveness of antipsychotic drugs in typical settings and populations in routine clinical situations, is expected to provide extensive information about antipsychotic drug effectiveness and costs over an eighteen month period.[24]

In the present study, we took advantage of data collected for a group of 338 individuals with serious mental illness recruited for a multi-site prospective study on outcomes under managed care versus fee-for-service financing.[25] These data provided a unique opportunity to examine psychiatric service use, including medication, of individuals with serious mental illness in community practice settings for a six month period before and after an initial interview assessment. Total psychiatric care costs were constructed for a six month period following assessment based on pharmacy use patterns of individuals on atypical versus typical antipsychotic medications. Although this was an observational cohort study, detailed information was collected at baseline on sociodemographic characteristics, prior treatment history, including medications, and clinical status. This allowed us to investigate the marginal impact of medication group affiliation on service use and cost while controlling statistically for any differences between groups. Our objective was to determine to what extent overall psychiatric costs are less for persons on newer atypical antipsychotic medications. The hypothesis is that there is a potential substitution of cost between atypical medication and psychiatric service use that results in lower or equal costs for persons receiving AAPs when compared to persons receiving typical medications. Resource utilization is operationalized using administrative databases to measure consumption of treatment services and pharmaceuticals and costs are constructed directly using reimbursement data from paid claims records. The effect of being in a particular medication group is assessed using prediction equations in which cost is predicted from the pharmacy use group at initial interview.

Methods

Data from the Medicaid Managed Behavioral Health Care and Vulnerable Populations Project (supported by the Substance Abuse and Mental Health Services Administration) were used to examine utilization and cost for 338 individuals with severe mental illness enrolled in Medicaid programs in Florida, Oregon and Pennsylvania during 1997. Subjects from Oregon and Pennsylvania were a convenience-based sample primarily identified by staff who were involved in their treatment. The Florida sample was a community-based population, some of whom were not in treatment at the time of recruitment. Subjects were interviewed with a comprehensive assessment battery at recruitment into the study during 1997/1998 and again approximately six months later. In addition, administrative data were obtained from state computer systems that included information on Medicaid enrollment as well as outpatient, inpatient and pharmacy claims for mental health. A description of the study and population is presented elsewhere.[25,26]

Medication Groups

For the purposes of this study, subjects were categorized based on pharmacy claims data showing use of antipsychotic medication(s) during the six months prior to the first interview. There were two classifications: (i) for all subjects and (ii) for users of atypical antipsychotic drugs. The ''all subjects'' categories were: (i) atypical antipsychotic medication only, (ii) typical antipsychotic medication only, and (iii) both atypical and typical agents. Individuals in the ''atypical only'' group had claims data showing receipt of at least one dispensing of clozapine, olanzapine, or risperidone during the six months prior to the initial interview; these individuals did not have claims for any other antipsychotic medication during that time period. Individuals in the ''typical only'' group had claims data showing receipt of at

least one dispensing of a first generation, conventional, neuroleptic, or typical antipsychotic medication during the six months prior to the initial interview and had no claims for clozapine, olanzapine, or risperidone during that time period. These were the only atypical agents widely available at the time of the study. Individuals in the ''both'' category had claims showing receipt of both an atypical and a typical antipsychotic medication during the six-month period prior to the initial interview (but these medications were not necessarily taken concurrently).

Subjects in the ''atypical only'' and the ''both'' group were further categorized based on their pharmacy claims during the six months prior to the initial interview. These subjects were labeled as ''clozapine only'', ''olanzapine only'', ''risperidone only'', or ''combination'' based on their pharmacy claims for atypical antipsychotic medications during those six months. Diagnostic information was obtained from Medicaid outpatient or inpatient claims, and a substance abuse indicator was obtained from the interview data when no substance abuse treatment was found in the service files. Information about subjects' use of psychotropic medications other than antipsychotic drugs was obtained from Medicaid pharmacy claims data. These psychotropic medications included anti-depressants, anxiolytics, mood stabilizers, hypnotics, and extra-pyramidal side effect medications. Pharmacy use during inpatient stays was not included in the data set.

Service Utilization and Cost

Service use information was obtained from Medicaid claims for the six-month period prior to and following the subject's initial assessment. Data included inpatient hospital stays, partial hospitalization, outpatient therapy, medication management and case management. Reimbursement data from the claims records were used to construct cost or expenditure measures for both pharmacy and service utilization. For purposes of the service analysis, only fee-for-service (FFS) enrollees were used because encounter data for managed care enrollees was believed to be less comprehensive than FFS claims and, in most cases, had no cost information attached to the record. In cases where service use information was present but no reimbursement information was provided, the unit cost was derived by service type from other populated cost elements (that were site specific). In cases where no cost was provided (Oregon inpatient services), the average cost per day was derived from the other sites and imputed for the Oregon data.

Data Analytic Procedures

Descriptive analysis of the utilization rates, cost of services and medications was done by medication group. Chi-square and F tests of significance were employed on the 338 subjects. Because all subjects had some cost associated with their use patterns, an ordinary least square (OLS) regression model was employed (versus a two stage probability and cost model) to explain the variation in total cost of services (treatment and pharmaceutical use) as a function of group membership at initial interview. Covariates were included to control for differences in sociodemographic characteristics (age, race, gender), clinical characteristics (initial level of severity using the global severity index score [GSI], diagnosis), service use history (psychiatric inpatient admission, outpatient visits, psychotropic medication use during prior 6 months) as well as drug pattern (whether or not the subjects changed or switched their medication sometime in the 6 months prior to and following their interviews). Switchers in the atypical or typical only groups switched only with their respective drug classes. A site indicator was also included to reduce variation associated with particular practice patterns. The dependent variable was constructed using the log of the total cost of services and pharmaceuticals (both antipsychotic and other psychotropic medications) during the 6 months following the initial assessment.

Results

Demographic and Clinical Characteristics of Subjects

Table 1, **Table 2** and **Table 3** show sociodemographic characteristics, clinical characteristics, and treatment patterns of subjects who used a psychotropic medication during the study period. There were more typical only (46%) than atypical only users (36%). However, 18% of the sample used both a typical and an atypical drug. Within the atypical only category, olanzapine (34%) and risperidone (29%) users made up the majority of the group. Clozapine users were also well represented at 25%. In the atypical/typical combination group, olanzapine users made up the largest subgroup (47%).

Among the major drug groups in **Table 1**, typical only users were significantly older than members of the other groups (F=11.08, p=. 001). Severity of symptoms (GSI score) was significantly higher for those on atypical/typical combinations (F=5.12, p=. 01). Also, the location or site of the study was highly significant (chi-square=17.33, p=. 01). Oregon and Pennsylvania had more individuals using atypicals only and both types of drugs, whereas Florida had more people using typicals only. Not surprisingly, changes in medication in the six-month period before the initial interview and between the initial interview and follow-up period were greatest for individuals in the combination typical/atypical group (62% before, chi-square=49.87, p=. 001; 45% after the interview, chi-square=10.09, p=. 01). Since this category was comprised of those taking both types of drugs sequentially as well as concurrently, it was likely that study subjects were switching medications during this period. Inpatient use prior to the interview was significantly higher among the atypical only and typical/atypical combination groups (chi-square=19.73, p=. 001) than the typical only group.

Among the atypical only groups in **Table 2**, those on clozapine had significantly fewer individuals with an affective disorder diagnosis (chi-square=14.34, p=. 01). Comparison of drug pattern changes prior to the initial

Table 1. Sample Characteristics by Major Medication Groups at Initial Assessment Period

Major Groups	Typical Only n=156 (46%)			Atypical Only n=122 (36%)			Both Typical/Atypical n=60 (18%)			Chi-square	F statistic	P value
	%	Mean	SD	%	Mean	SD	%	Mean	SD			
Sociodemographic Characteristics												
Age	–	44.95	8.78	–	39.55	10.53	–	41.03	10.57	–	11.08	≤ .001
Race												
White	55%	–	–	68%	–	–	60%	–	–			
African American	37%	–	–	27%	–	–	28%	–	–	6.63	–	NS
Other or Unknown	8%	–	–	5%	–	–	12%	–	–			
Gender												
Male	41%	–	–	51%	–	–	55%	–	–	4.91	–	NS
Female	59%	–	–	49%	–	–	45%	–	–			
Site												
PA	28%	–	–	42%	–	–	35%	–	–			
OR	32%	–	–	38%	–	–	43%	–	–	17.33	–	≤ .01
FL	40%	–	–	20%	–	–	22%	–	–			
Clinical Characteristics												
Diagnosis												
Any psychosis diagnosis	74%	–	–	71%	–	–	73%	–	–	–	–	–
Any affective diagnosis	28%	–	–	20%	–	–	22%	–	–	–	–	–
Any substance abuse indicator	50%	–	–	–	52%	–	–	–	60%	–	–	–
Global Severity Score (GSI)	–	0.95	0.69	–	0.97	0.71	–	1.28	0.77	–	5.12	≤ .01
Treatment Patterns Prior to Interview												
Inpatient	7%	–	–	16%	–	–	24%	–	–			
Outpatient only	63%	–	–	48%	–	–	35%	–	–	19.73	–	≤ .01
None	29%	–	–	36%	–	–	42%	–	–			
Medication switch	16%	–	–	46%	–	–	62%	–	–	49.87	–	≤ .001
Treatment Patterns Following Interview												
Medication switch	24%	–	–	26%	–	–	45%	–	–	10.09	–	≤ .01

Table 2. Sample Characteristics by Atypical Subgroups at Initial Assessment Period

Atypical Sub Groups	Clozapine Only n=30			Olanzapine Only n=42			Risperidone Only n=36			Atypical Combination n=14			Chi-square	F statistic	P value
	%	Mean	SD	%	Mean	SD	%	Mean	SD	%	Mean	SD			
Sociodemographic Characteristics															
Age	–	41.03	8.62	–	38.48	12.25	–	40.83	10.16	–	36.29	9.45	–	0.97	NS
Race															
White	77%	–	–	69%	–	–	64%	–	–	57%	–	–	6.81	–	NS
African American	20%	–	–	29%	–	–	25%	–	–	43%	–	–			
Other or Unknown	3%	–	–	2%	–	–	11%	–	–	0%	–	–			
Gender															
Male	53%	–	–	50%	–	–	47%	–	–	57%	–	–	0.50	–	NS
Female	47%	–	–	50%	–	–	53%	–	–	43%	–	–			
Site															
PA	43%	–	–	52%	–	–	25%	–	–	50%	–	–			
OR	37%	–	–	36%	–	–	44%	–	–	36%	–	–	7.93	–	FS
FL	20%	–	–	12%	–	–	31%	–	–	14%	–	–			
Clinical Characteristics															
Diagnosis															
Any psychosis diagnosis	80%	–	–	69%	–	–	72%	–	–	57%	–	–	2.61	–	NS
Any affective diagnosis	3%	–	–	29%	–	–	33%	–	–	0%	–	–	14.34	–	$\leq$ .01
Any substance abuse indicator	53%	–	–	53%	–	–	56%	–	–	43%	–	–	0.67	–	NS
Global Severity Score (GSI)	–	0.88	0.59	–	1.08	0.80	–	0.93	0.75	–	0.91	0.61	–	0.57	NS
Treatment Patterns Prior to Interview															
Inpatient	3%	–	–	31%	–	–	17%	–	–	–	–	–			
Outpatient only	63%	–	–	43%	–	–	39%	–	–	50%	–	–	15.85	–	$\leq$ .01
None	33%	–	–	26%	–	–	44%	–	–	50%	–	–			
Medication switch	30%	–	–	67%	–	–	25%	–	–	71%	–	–	20.36	–	$\leq$ .001
Treatment Patterns Following Interview															
Medication switch	7%	–	–	31%	–	–	31%	–	–	43%	–	–	8.77	–	$\leq$ .05

Table 3. Sample Characteristics by Atypical/Typical Sub Group at Initial Assessment Period

Atypical/Typical Sub Groups	Olanzapine + Typical n=28			Other Atypical + Typical n=32			Chi-square	F statistic	P value
	%	Mean	SD	%	Mean	SD			
Sociodemographic Characteristics									
Age	–	38.96	11.67	–	42.84	9.30	–	2.05	NS
Race									
White	61%	–	–	59%	–	–			
African American	29%	–	–	28%	–	–	0.05	–	NS
Other or Unknown	11%	–	–	12%	–	–			
Gender									
Male	57%	–	–	53%	–	–	0.10	–	NS
Female	43%	–	–	47%	–	–			
Site									
PA	39%	–	–	31%	–	–			
OR	39%	–	–	47%	–	–	0.47	–	NS
FL	22%	–	–	22%	–	–			
Clinical Characteristics									
Diagnosis									
Any psychosis diagnosis	61%	–	–	84%	–	–	2.28	–	$\leq .05$
Any affective diagnosis	25%	–	–	19%	–	–	0.35	–	NS
Any substance abuse indicator	61%	–	–	59%	–	–	0.01	–	NS
Global Severity Score (GSI)		1.33	0.82	–	1.25	0.73	–	0.15	NS
Treatment Patterns Prior to Interview									
Inpatient	21%	–	–	25%	–	–			
Outpatient only	53%	–	–	60%	–	–	.49	–	NS
None	46%	–	–	38%	–	–			
Medication switch	79%	–	–	37%	–	–	6.35	–	$\leq .05$
Treatment Patterns Following Interview									
Medication switch	50%	–	–	41%	–	–	0.53	–	NS

interview showed 67% of those in the olanzapine only group and 71% in the atypical combination group had changed drugs compared to those in the risperidone only (25%) and clozapine only subgroups (30%, chi-square= 20.36, p=. 001). During the six-month follow-up period, changes between groups were significant but generally smaller, with those on atypical combinations having the largest change (43%) and clozapine only the smallest (7%, chi-square=8.77, p=. 05). **Table 3** shows differences between olanzapine/typical users and other atypical/typical users, most of whom were on risperidone. Significance differences were found with 79% of the olanzapine/typical users showing changes in their drug pattern in the period prior to their initial interview versus 37% from the other combination groups (chi-square=6.35, p=. 05). Inpatient use was highest for those on olanzapine only (31%), with the highest outpatient use for olanzapine only and clozapine only (chi-square=15.85; p=. 01).

Service Use Patterns by Medication Group following the Interview Period

Table 4 shows inpatient and outpatient service utilization rates during the six-month following the initial interview by medication groups. The services are any inpatient utilization, outpatient only and neither. The categories are mutually exclusive.

Costs for Pharmacy and Services by Medication Group

Table 5 shows the cost of all psychotropic medications and services for the six-month period following the initial assessment by medication groups. Six-month costs for both pharmacy and treatment were significantly greater for persons in the atypical only ($6528) and combination typical/atypical groups ($6589) compared to those on typicals only ($3463)(F=3.53, p=. 05). The high costs for atypical only and atypical/typical users was due to both higher pharmacy and inpatient costs.

Among the atypical only users, those receiving olanzapine only had total costs of $10,231 compared to those on clozapine only ($4656), risperidone only ($4862) and combination atypicals ($3712). Within the atypical/typical group, expenditures were similar with the olanzapine/typical costing $6643 per person over six months and the other atypical/typical users costing $6542. In both comparisons, the differences were not statistically significant.

Table 4. Rates of Service Use by Medication Groups Six Months Following the Interview

Major Groups (N = 338)	Typical Only (n=156)	Atypical Only (n=122)	Both Typical/Atypical (n=60)	Chi-Square	P value
Inpatient (Any)	11%	19%	17%		
Outpatient (Only)	56%	41%	38%	9.93	.04
Neither	33%	40%	45%		
Total	100%	100%	100%		

Atypical Subgroups (N = 122)	Clozapine Only (n=30)	Olanzapine Only (n=42)	Risperidone Only (n=36)	Atypical Combination * (n=14)	Chi-Square	P value
Inpatient (Any)	3%	36%	19%	–		
Outpatient (Only)	53%	33%	42%	36%	17.63	.007
Neither	44%	31%	39%	64%		
Total	100%	100%	100%	100%		

Typical Combinations (N = 60)	Olanzapine + Typical (n=28)	Other Atypical + Typical (n=32)	Chi-Square	P value
Inpatient (Any)	18%	16%		
Outpatient (Only)	36%	41%	.16	.92
Neither	46%	43%		
Total	100%	100%		

* Atypical Combination Group not used in this analysis

Multivariate Analysis of Cost

Variation in psychiatric service costs during the six month period following initial assessment was examined using an OLS regression model where the logs of service and pharmacy costs were regressed on sociodemographic, clinical, service and site variables using the pharmacologic group level at initial interview as the intervention variable of interest, as shown in **Table 6**. Model 1 shows the variation in cost as a function of medication group with the typical only serving as the reference group.

Medication group continued to be a strong predictor of expenditures, even when controlling for other characteristics. Individuals who received atypical antipsychotic medication only or both an atypical and typical agent had significantly higher health services expenditures than individuals who received typical agents only. A diagnosis of psychosis and residence in Pennsylvania were significantly related to higher total costs, whereas African Americans had significantly lower costs than Caucasians. Demographics, diagnosis, severity and site explained 13% of the variance. Also influencing cost during the follow-up was a prior history of inpatient and outpatient care. Prior utilization variables explained 9% of the variance in costs. Medication change following the initial interview added another 1%, though it was not significant. Membership in the atypical/typical or atypical only medication group of interest explained 12% of the total costs. Thus after controlling for other factors, subjects in the atypical and typical/atypical groups had significantly higher total costs than subjects in the typical only group in both regression analyses. The total variation explained was 35% for Model 1.

In Model 2, the atypical only and atypical/typical combination groups were examined separately, with the typical only group as the reference category. The same control variables were specified. Each atypical only subgroup as well as the combination atypical group had significantly higher total costs than the typical only group (p=.001). As in the other model, race, diagnosis and inpatient use were all significant predictors of higher costs. The combination atypical sub-group had the highest standardized beta coefficient estimate. The R-square was 36%. To determine the extent to which a few outliers were contributing to these effects, a logistic regression was run on a dichotomous variable (0 for increased costs, 1 for decreased costs), with essentially the same results.

To examine the extent to which variation in cost was a function of state Medicaid policy, the regressions were run independently by state with essentially the same results. The atypical only and atypical/typical combination groups had the highest overall costs and, in two of the three states, psychosis, race and a history of inpatient use were also significantly related to cost.

Table 5. Mean Expenditures for Psychiatric Services and Psychotropic Drugs Six–Months Following Interview

Major Groups	Typical Only (n=156)	Atypical Only (n=122)	Both Typical/Atypical (n=60)	t	P value
Antipsychotic Medication	$ 291	$ 1798	$ 1434	85.45	< .001
Other Psychotr/pic Medication	$ 287	$ 376	$ 333	.32	NS
All Psychotropic Medication	$ 578	$ 2174	$ 1767	76.78	< .001
Inpatient Services	$ 2140	$ 3746	$ 4200	1.20	NS
Outpatient Services	$ 745	$ 608	$ 623	.48	NS
All Psychiatric Services	$ 2885	$ 4354	$ 4823	1.01	NS
Both Medications and Services	$ 3463	$ 6528	$ 6590	3.53	< .05 (NS)

Atypical Sub Groups	Clozapine Only (n=30)	Olanzapine Only (n=42)	Risperidone Only (n=36)	Atypical Combination (n=14)	t	P value
Antipsychotic Medication	$ 2709	$ 1296	$ 1249	$ 2768	16.57	< .001
Other Psychotropic Medication	$ 261	$ 523	$ 309	$ 353	1.46	NS
All Psychotropic Medication	$ 2970	$ 1819	$ 1558	$ 3121	10.80	< .001
Inpatient Services	$ 1042	$ 7873	$ 2640	$ 0	3.36	=.05
Outpatient Services	$ 644	$ 539	$ 664	$ 591	.07	NS
All Psychiatric Services	$ 1686	$ 8412	$ 3304	$ 591	3.18	=.05
Both Medications and Services	$ 4656	$ 10231	$ 4862	$ 3712	2.53	NS

Atypical/Typical Sub Groups	Olanzapine + Typical (n=28)	Other Atypical + Typical (n=32)	t	P value
Antipsychotic Medication	$ 1412	$ 1454	.02	NS
Other Psychotropic Medication	$ 282	$ 377	.81	NS
All Psychotropic Medication	$ 1694	$ 1831	.13	NS
Inpatient Services	$ 4421	$ 4006	.01	NS
Outpatient Services	$ 528	$ 705	.49	NS
All Psychiatric Services	$ 4949	$ 4711	.00	NS
Both Medications and Services	$ 6643	$ 6542	.00	NS

Discussion

The use of second generation antipsychotic medications was associated with higher cost of treatment for people with serious mental illness, particularly those with schizophrenia. Based on this study sample, there were more people using an atypical medication alone or in combination with a typical (54%) than using typical medications alone (46%). For those using atypicals only, the largest category of users were those on olanzapine, which was the newest medication at the time these data were collected.

Since patients with schizophrenia use a large number of hospital bed days annually, to be cost-effective the newer atypical medications must improve outcomes or reduce other psychiatric care costs enough to offset their higher acquisition costs. In this naturalistic study of seriously mentally ill persons treated in public sector clinical settings, patients on typical only medications were found to have much lower hospitalization rates and overall costs during a six-month period following their initial community assessment. The costliest patients, with respect to pharmacy and service use, were those on atypicals alone, or on a combination of an atypical and a typical. The study by Duggan[20] using California Medicaid recipients diagnosed with schizophrenia between 1993 and 2001 supports these findings in that patients in the early 1990s using traditional antipsychotics had lower costs and similar utilization patterns with no difference in health status as a later cohort using atypicals. However, the analysis also shows that shifts to antipsychotic medication is related to the probability of hospitalization.

There are several caveats to the study findings that should be noted. First, the subjects were not randomized into medication groups and may have been selected into these groups due to their specific clinical needs or responses to other medications. In contrast, prior studies on outcomes between drug types have generally looked at subjects discharged from hospitals or in crisis at the time the various medications are prescribed, making the contrast groups more equivalent with respect to severity than may be true in the current research. In this study, given the relatively recent availability of the atypical agents, particularly olanzopine, and the tendency for individuals who are not responding well

Table 6. Factors Predicting Cost of Psychiatric Services & Medications During Six–Month Study Period By Medication Groups

	MODEL 1 Typical vs. Atypical N=337			MODEL 2 Type of Atypical N=337		
Dependent Variable	Cost			Cost		
	Predictor	SE	P	Predictor	SE	P
Sociodemographic						
Age	0.002	0.008	NS	0.003	0.008	NS
Gender (Male)	0.035	0.149	NS	0.040	0.148	NS
Race						
African-American	–0.412	0.183	P<.03	–0.438	0.186	P<.02
Other or Unknown	–0.300	0.278	NS	–0.256	0.281	NS
Site						
PA	0.486	0.209	P<.02	0.465	0.210	P<.03
FL	0.341	0.247	NS	0.370	0.249	NS
Clinical Characteristics						
Diagnosis						
Substance Abuse	0.040	0.152	NS	0.066	0.153	NS
Psychosis Diagnosis	0.383	0.194	P<.05	0.425	0.196	P<.03
Affective Diagnosis	–0.087	0.187	NS	–0.042	0.190	NS
Global Severity Index Score	0.170	0.102	NS	0.162	0.102	NS
Treatment Patterns						
Medication switch prior to interview	–0.238	0.164	NS	–0.315	0.171	NS
Medication switch following interview	–0.154	0.164	NS	–0.154	0.166	NS
Any inpatient use prior to interview	1.665	0.292	P<.0001	1.655	0.297	P<.0001
Outpatient use prior to interview	0.525	0.216	P<.02	0.495	0.218	P<.02
Medication Category						
Both Atypical/Typical	1.051	0.216	P<.0001	–	–	–
Olanzapine and a typical	–	–	–	1.203	0.289	P<.0001
Other combination	–	–	–	0.994	0.263	P<.0002
Atypical only	1.277	0.169	P<.0001	–	–	–
Clozapine only	–	–	–	1.325	0.263	P<.0001
Olanzapine only	–	–	–	1.422	0.250	P<.0001
Risperidone only	–	–	–	1.025	0.239	P<.0001
Combination of any 2 or 3	–	–	–	1.734	0.379	P<.0001
R^2 Step 1: Demographics Only	0.11			0.11		
Step 2: Add Severity	0.13			0.13		
Step 3: Add Types of Utilization	0.22			0.22		
Step 4: Add Medication Change Prior	0.22			0.22		
Step 5: Add Medication Change post	0.23			0.23		
Step 6: Add Medication Type	0.35			0.36		

to their current regimen to switch medications, the atypical group may overrepresent unstable patients. As an illustration, 50% of the patients in the combination typical/atypical group changed their medication pattern during the study period, while most other groups had a high degree of continuity in the same class.

Further evidence is suggested in a paper analyzing outcome measures using the same population.[27] In that analysis, the atypical only and typical/atypical combination groups had higher symptom levels during the pre-assessment period as well as higher severity scores on other clinical outcome measures. Also, reduction in symptom levels between baseline and six months was significantly higher for those in the olanzapine/typical and risperidone/typical groups than the other drug groups, suggesting that these patients were in a more acute state. Additional support is provided in a study of switching behavior between antipsychotic medications of veterans with schizophrenia in outpatient settings. The study showed that switching was related to high service utilization and that persons who were older and had

higher functioning levels were less likely to switch their medications to atypicals or between atypicals.[28]

Another limitation to the study involves the sample characteristics. Since service and cost data were only available on the Fee For Service subset of the study subjects and since the FFS sample had a larger proportion of Blacks, males, psychosis diagnoses, and substance abuse diagnoses than the managed care conditions, our sample may represent a more severe population than those in the overall population of antipsychotic users. In addition, though we used a log transformation to normalize the cost measures, they are still highly skewed, as is the case in many cost analyses that involve inpatient hospital expenditures. Furthermore, in the regression model examining the atypical only subgroups, the combination group with multiple atypicals had a small number of observations leading us to be cautious in interpreting the results.

Despite these design limitations, the study does suggest that, as a group, individuals in community settings using typical only medications are likely to have the lowest costs both in pharmacy and service use, whereas those using the newer atypical medications only or combinations of atypical/typical medications are the most costly – even after controlling for demographic and clinical characteristics as well as prior service utilization. Additionally, these costs do not include the potential complications related to the various metabolic and endocrine disorders that are associated with the atypical agents which might further increase group differences in cost.

In order to have more confidence in the policy implications from these findings, a longer follow-up period is needed to determine if, over time, the population that remains in a particular drug group will be comprised of those who have responded well to and stabilized on that medication, and those in the newest drug group will overepresent individuals who are doing poorly on older agents. Two currently funded National Institute of Mental Health studies should help provide insight into some of these questions. The first is a randomized trial of public sector community mental health outpatients with schizophrenia currently on typical antipsychotic medications. Subjects are being randomized to treatment as usual on typicals versus olanzapine or risperidone and followed for up to a year to determine clinical and service use outcomes[29] (NIMH study on Effectiveness of Switching from Conventionals to Atypicals). The second study, the CATIE schizophrenia trial, blends features of efficacy studies and large, simple trials to create a pragmatic trial that will provide extensive information about antipsychotic drug effectiveness over 18 months.[24] Approximately 1500 persons with schizophrenia are being randomized to double-blinded treatment with an atypical (olanzapine, quetiapine, risperidone or ziprasidone) or to the mid-potency typical, perphenazine. If the first medication does not work well or is poorly tolerated, a second randomized drug treatment is available. Both of these prospective randomized studies will look at cost of treatment during the course of the study period, thus adding to the knowledge base regarding cost-effectiveness of newer atypical medications in naturalistic settings.

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