
Use of Conventional Antipsychotics and the Cost of Treating Schizophrenia

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This study documents the drug therapy patterns and 1-year treatment costs for 18,833 Medicaid patients with schizophrenia treated with conventional antipsychotic medications in Michigan, Kentucky, Alabama, and Georgia. One in four patients used no antipsychotic, but had total costs that were less than for treated patients (-\$2,576, $p < .0001$); 18 percent of treated patients delayed therapy for at least 1 month and had significantly higher total costs of \$3,994 ($p < .0001$); 41 percent of treated patients changed therapy with similar results (+\$4,067, $p < .0001$). Only 20 percent of patients were compliant with drug therapy but this had no significant impact on total treatment costs.

INTRODUCTION

Schizophrenia is a profoundly debilitating illness that is correlated with other medical illness and patient mortality, often from suicide (Keith, Regier, and Rae, 1991; Fenton, 1996; Jeste et al., 1996; McGlashan, 1988). Long-term therapy is required, including repeated efforts by caregivers and family members to reduce the frequency and severity of acute episodes and to reduce the devastating psychological, behavioral, and health effects of schizophrenia, including mortality (American

Psychiatric Association, 1997). The long-term treatment of schizophrenia usually involves continuous specialty mental health care, including maintenance therapy with antipsychotic agents. Acute medical care services, including emergency room and hospital services, are often required to manage acute psychotic episodes. Intensive family management and social, vocational, and cognitive rehabilitation are also required (Souetre, 1997).

The onset of schizophrenia is most prevalent between the ages of 18 to 24 in males and 25 to 34 in females (Rice and Miller, 1996). Although schizophrenia afflicts only 1.1 percent of the U.S. population, or 2.5 million people (Keith, Regier and Rae, 1991), patients with schizophrenia constitute approximately 10 percent of the disabled population in the United States and 14 percent of the homeless (Rupp and Keith, 1993). Moreover, this illness claims a disproportionate share of U.S. health care resources, especially resources available for treating psychological disorders (Rice and Miller, 1996; Buckley, 1998). For example, patients with schizophrenia occupy 25 percent of psychiatric hospital beds and account for 40 percent of all long-term-care days (Talbot, Golman, and Ross, 1987). Rice and Miller (1996) estimated the total economic burden of schizophrenia in the United States to be \$32.5 billion in 1990, of which \$17 billion was attributable to direct medical costs. Croghan et al. (1999) document that the majority of direct medical care costs are paid through State Medicaid programs. Dickey et al. (1996) estimated

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the direct cost of caring for patients with schizophrenia in the Massachusetts Medicaid program range between \$15,000 and \$19,600 per patient, per year which translates into approximately \$250 million per year for schizophrenia related expenses (Hanson, 1999).

The direct health care costs of treating schizophrenia to the California Medicaid (Medi-Cal) program were estimated at \$23,000 over 1 year and more than \$44,000 per patient over a 2-year period (McCombs et al., 1999b; McCombs et al., 2000). The cost of treating schizophrenia in the Georgia Medicaid program estimated at \$16,000 per patient per year over a 3-year period from 1991 to 1993 (Martin and Miller, 1998).

Antipsychotic drug therapy has been the cornerstone for the treatment of schizophrenia since chlorpromazine was introduced in the 1950s. These first-generation medications were effective in treating the positive symptoms of schizophrenia (e.g., auditory hallucinations, delusions) resulting in the deinstitutionalization of patients during the 1970s (Stroup and Manderscheid, 1988). However, these medications often result in significant side effects that inhibit compliance. Some side effects, such as extrapyramidal effects and tardive dyskinesia, can be irreversible and untreatable. Not surprisingly, many patients may limit the use of these medications to periods of acute symptoms punctuated by extended periods when patients discontinue their medication against medical advice (McGlashan, 1988; Croghan et al., 1999).

McCombs et al. (1999a,b; 2000) found significant evidence of intermittent use of antipsychotic medications in Medi-Cal. Approximately 24 percent of Medi-Cal patient with schizophrenia did not receive any antipsychotic drug treatment for more than 1 year. Delays in drug therapy for at least a month were found in 24 percent of

the patients, while nearly one-half of treated patients changed their initial antipsychotic medications within 1 year. Finally, only 11 percent of patients received uninterrupted antipsychotic drug therapy for a period of 1 year (McCombs et al., 1999b). More importantly, these suboptimal drug use patterns were correlated with increased direct health care costs (McCombs et al., 1999a; 2000).

Fortunately, several second-generation antipsychotic medications have been developed that may improve drug therapy for patients with schizophrenia. Most Medicaid programs now provide unrestricted access to second-generation antipsychotic medications but have experienced a very rapid increase in their drug budgets. For example, olanzapine and risperidone are the two most costly drugs covered by Medi-Cal after their addition to the formulary in fall 1997. In the first 6 months of 1999, expenditures for these two medications amounted to more than \$83 million for nearly 10 million days of therapy (California's Medical Assistance Program, 1999). Much of this difference is due to the higher cost per day of therapy in the Medi-Cal program for olanzapine (\$10.41) and risperidone (\$6.32) relative to conventional antipsychotics (e.g., thioridazine at \$1.02 per day).

The rapid growth in expenditures for second-generation antipsychotic medications has raised concerns on the part of payers, primarily State Medicaid programs, about the value received in return for these expenditures. The answer to this question comes in two parts. First, more data are needed to confirm the earlier Medi-Cal results indicating that sub-optimal drug treatment patterns achieved through the use of conventional antipsychotic medications are frequent and costly. This study investigates these issues using data for patients with schizophrenia covered by the Medicaid programs in

Alabama, Georgia, Kentucky, and Michigan. Second, data are needed which document the extent to which the second-generation antipsychotic medications improve drug therapy. Data for these latter studies are not yet available due to the limited time these medications have been available to Medicaid patients without prior authorization restrictions.

METHODS AND ANALYTICAL PLAN

Data

The data for this analysis were derived from the State Medicaid Research Files (SMRF) provided by CMS for Alabama, Georgia, Kentucky, and Michigan. Data from 1992 to 1995 were used in this analysis. SMRF provides patient-level demographic data combined with a summary of each claim for covered services paid on behalf of the recipient. Data include type of service, date of service, amount billed, and length of service. Prescription drug claims identify the specific product dispensed, quantity, strength, and the date the prescription was filled.

Study Population

Schizophrenia patients in these four States were identified from the SMRF, based on having at least one paid Medicaid claim with a recorded diagnosis of schizophrenia (*International Classification of Diseases, 9th Revision, Clinical Modification* [ICD-9-CM] codes: 295.0 - 295.9 [Public Health Service and Health Care Financing Administration, 1980]). Patients were included in the study cohort if they were between the ages of 14 and 100 on the first date of treatment (index date) as indicated either by a recorded diagnosis of schizophrenia or a paid claim for a first-generation (typical) antipsychotic medication, whichever was first. Study patients were

also required to have a minimum of 30 days of paid claims data prior to the index date and a minimum of 1 year of paid claims data following the index date.

Patients with paid claims exceeding \$50,000 per year during the first post-diagnosis year for services of which the type of provider was either unknown or was not considered to be relevant to a study of schizophrenia (such as dental services) were excluded ($n=61$; 0.3 percent). Patients with a recorded diagnosis of schizophrenia who were under age 14 or over age 100 were excluded due to possible errors in their reported age.

General population survey data suggest that substantial proportions of non-institutionalized patients with schizophrenia may disengage from the health care system for extended periods of time (McGlashan, 1988; Johnstone, Croghan, and Kessler, 1997). Patients with gaps in Medicaid eligibility or in their stream of paid claims present a dilemma for a cost-of-illness analysis. Patients who voluntarily withdraw from the health care system should be included since their Medicaid paid claims data are an accurate measure of their cost-of-illness and drug use patterns. Excluding this low cost population from the study will overestimate the cost of treating schizophrenia. Conversely, patients who enter correctional facilities or who seek care from an alternative health care system (e.g., Department of Veterans Affairs, Veterans Health Administration) continue to consume health care and other societal resources that are not included in the Medicaid data base. Including these patients in the cost-of-illness study would bias downward the estimated cost of treating schizophrenia.

In this study, patients who were not eligible for Medicaid coverage in any 1 month within the first treatment year were excluded from the study population if this reported

loss of eligibility was confirmed by gaps in their paid claims data in excess of 3 months within that year. Patients with gaps in paid claims but continuous reported eligibility were included in the study. The final study cohort numbered 18,833 for all four States.

Patients were categorized into institutionalized and ambulatory subpopulations. Institutionalized patients were defined as those patients who were in long-term care facilities in the month prior to and after the date of treatment initiation. Institutionalized patients are likely to be more severely disabled and consume significantly more health care services compared with ambulatory patients, particularly nursing home services. Therefore, separate analyses were performed for institutionalized and ambulatory patients. This division of the study cohort resulted in 743 institutionalized patients (4 percent) and 18,090 ambulatory patients with schizophrenia (96 percent) for all 4 States combined.

Cost Definitions

Medicaid paid claims were partitioned by type of service for the purpose of estimating costs. The types of service identified include hospital services, long-term care, community mental health services, outpatient services, prescription drugs, and miscellaneous services.

For non-institutional services, the amount paid by State Medicaid programs understate total expenses incurred by elderly and disabled Medicaid beneficiaries who are dually eligible for Medicare, the primary payer for these patients. Therefore, costs of non-institutional services for patients who are age 65 or over, or who are eligible for Medicare coverage during the first treatment year, were estimated using a methodology based on the amount paid by Medicaid and the Medicare Part B deductible and coinsurance rate.

First, the total amount paid by Medicaid for Part B covered services were totaled and the Part B deductible amount subtracted to approximate the amount of the Medicaid payments that corresponded to the Medicare coinsurance liability. If the estimated coinsurance liability was greater than zero, it was then multiplied by a factor of 5 to re-inflate the estimated coinsurance liability to an estimate of the total payments allowed by Medicare and the deductible was re-added. If the estimated coinsurance liability was zero or negative, the actual amount paid by Medicaid was used as the estimate of total Part B payments. Actual Medicaid expenditures for non-institutional services were used for non-elderly patients without dual eligibility status.

For institutional services, the cost for hospital, skilled nursing facilities (SNF), and intermediate care facilities (ICF) care were estimated for all patients based on the days of services. To facilitate comparisons with the previous Medi-Cal schizophrenia studies, days of care were multiplied by the average per diem cost reported for these services by Medi-Cal and Medicare. Hospital days were assigned a cost of \$979 per day (California's Medical Assistance Program, 1995), while SNF and ICF costs were valued at \$270 per day (Health Care Financing Administration, 1996). While this approach will mask the impact of per diem cost differences across States, the results reported here can be easily converted into State specific estimates by dividing reported institutional costs by the Medi-Cal per diem rates, then revaluing using a State-specific per diem cost estimate.

Drug Use Pattern Definitions

This study investigates the health care use and cost patterns for patients with schizophrenia in the four States based on their conventional antipsychotic medica-

tion use. Four drug use patterns were analyzed in both the institutionalized and ambulatory populations. These drug use pattern definitions are consistent with the previous Medi-Cal schizophrenia study (McCombs et al., 1999a,b; 2000).

Untreated Patients

Since conventional antipsychotics can cause severe and sometimes irreversible side effects, it is likely that a proportion of patients with schizophrenia will not use any antipsychotics for extended periods of time (Kane, 1987; Kane and Marder, 1993). This may be particularly true if the positive symptoms of the disease are in full or partial remission and the patient is able to reside in the community. Therefore, active antipsychotic drug therapy may not be associated with lower health care costs, especially for non-institutionalized patients. To test this hypothesis, this analysis identified patients with schizophrenia who did not receive antipsychotic drug therapy at any time during the first year.

Delayed Therapy

The previous Medi-Cal study observed that a substantial proportion of patients with schizophrenia who used antipsychotics within the first treatment year did not use antipsychotic drug therapy within 30 days of the index date (McCombs et al., 1999b). These patients may have taken an extended drug holiday to avoid the substantial side effects of conventional antipsychotics, yet a subsequent exacerbation of symptoms during the year caused them to restart the drug treatment. Therefore, delaying drug therapy may also be widespread and costly among patients with schizophrenia across other States.

Delayed therapy patients were defined as patients who received antipsychotics within the year, but delayed the onset of drug therapy for more than 30 days.

Continuous Therapy

If antipsychotic drug therapy is safe and effective, patients are expected to continue drug treatment for an extended period of time. Duration of drug therapy may be correlated with lower total direct health care costs if antipsychotic drugs are clinically effective. However, many clinicians may typically withdraw their patients from antipsychotic drug therapy during periods of symptom remission in order to avoid the significant and sometimes irreversible side effects associated with conventional antipsychotics.

Patients were classified as having continuous drug therapy if no interruption of antipsychotic therapy was found during the first treatment year. Interruption of drug treatment is defined as a gap of 45 days or more between consecutive antipsychotic medication purchases as reported in pharmacy paid claims records. This definition of compliance assumes that most prescriptions for antipsychotic medications were limited to no more than a 30-day supply and allows for a 15-day grace period between refills. Therefore, patients with schizophrenia provided with prescriptions for more than 45 days will likely be classified as having interrupted their drug therapy. Previous research using Medi-Cal data, which allows up to a 3-month supply to be dispensed, did not find that this practice was common for patients with schizophrenia. As a result, the calculated compliance rates based on a 100-day gap were very similar to those based on the 30-day supply assumption.

Changes in Drug Therapy

Medication changes are expected for many patients with schizophrenia because of the toxicity and limited efficacy of conventional antipsychotic medications (Kane, 1987). In order to focus on issues associated with medication changes, patients were identified who changed or augmented their antipsychotic medications with a second antipsychotic medication within 1 year.

Limitations

Several significant limitations arise from this study's research design and from the data set used to conduct the analysis. Medicaid programs are managed by each State individually under broad Federal guidelines. Therefore, important coverage differences and data reporting anomalies may exist across States and these policies change over time. This makes cross-State comparisons difficult, especially if paid claims data are retrieved across multiple years, as in this study. Differences across States could have a significant impact on this analysis:

- Coverage for newly approved medications vary. For example, Alabama provided free access to the newer atypical antipsychotic medications during the data period while their use in Kentucky and Michigan required prior authorization.
- Although State mental health systems have a financial incentive to bill their Medicaid programs for services rendered to Medicaid-eligible patients, States such as Georgia do not pay for these services through its Medicaid system. If this is the case, the analysis here will underestimate the total cost of psychiatric hospital services in these States. However, hospitalization data are available for patients hospitalized in a psychiatric unit in a community hospital.
- States may bundle the cost of pharmaceuticals consumed in nursing homes into the nursing home payments, thus eliminating access to the prescription drug data needed to document drug use patterns of nursing home patients. Specifically, patients admitted to a nursing home under these conditions will appear to experience a break in their antipsychotic drug therapy. Moreover, patients confined to a nursing home for over 1 year will be classified as untreated, while patients institutionalized for less than a year may appear to delay the start of antipsychotic drug therapy. Therefore, the drug use patterns found in the institutionalized patient population must be interrupted with caution.
- The definition of what facilities constitute Medicaid-eligible nursing homes can vary across States and across time within States. Therefore, it is possible that this analysis may underestimate the nursing home costs associated with the treatment of patients with schizophrenia. Patients institutionalized in non-Medicaid qualified facilities may be excluded from the analysis if the stay extended beyond 90 days, as would Medicaid-eligible beneficiaries incarcerated in a local, State, or Federal penal institution.
- States vary on the rapidity with which Medicaid recipients can lose and regain Medicaid eligibility, making it possible that recipients who lose eligibility for less than 90 days to be considered as continuously eligible in this study. While this may be a significant problem for studies concerned with most disease States, such short-term losses of eligibility are unlikely for patients with schizophrenia who typically qualify for Medicaid due to their disability status.
- Diagnostic data are typically not required by Medicaid for a claim to be paid. Therefore, there is no binding

incentive for providers to record a diagnosis. Moreover, the recorded diagnosis may not necessarily reflect the medical condition for which the patient received the service being billed. Finally, the diagnosis of severe mental disorders typically evolves over time based on the provider's interactions with the patient and the patient's response to therapy. Therefore, selecting patients based on a single service with a schizophrenia diagnosis may not be accurate. However, the presence of a schizophrenia diagnosis is very likely to indicate that the patient suffers from a severe mental illness, many of which are treated using antipsychotic medications.

Statistical Models

Multivariate ordinary least squares (OLS) regression models were used to estimate the impact each drug use pattern had on total direct health care costs and the components of cost (SAS®, 1993). The dichotomous variable for having received drug treatment during the first year was entered directly into the cost models. The effects of delayed therapy, completed therapy, and changes in therapy were all measured using interaction terms between these dichotomous variables and the dichotomous treatment variable. In this way, each effect is measured relative to other treated patients. For example the estimated regression coefficient for the interaction term (treated*switched) measures the incremental costs associated with switching medication relative to treated patients who did not change drugs.

Up to 63 independent variables were included in the OLS cost models. These independent variables included the prior use of health care services, demographic characteristics, mental and medical diagnostic information, and prescription drug

profile. While possible multi-collinearity may exist between some of these explanatory variables, their inclusion in the model improves the regression estimates for the drug use pattern variables that are the focus of the analysis. In addition, the cost effects of being treated in Alabama, Georgia, or Kentucky were estimated relative to patients treated in Michigan.

RESULTS

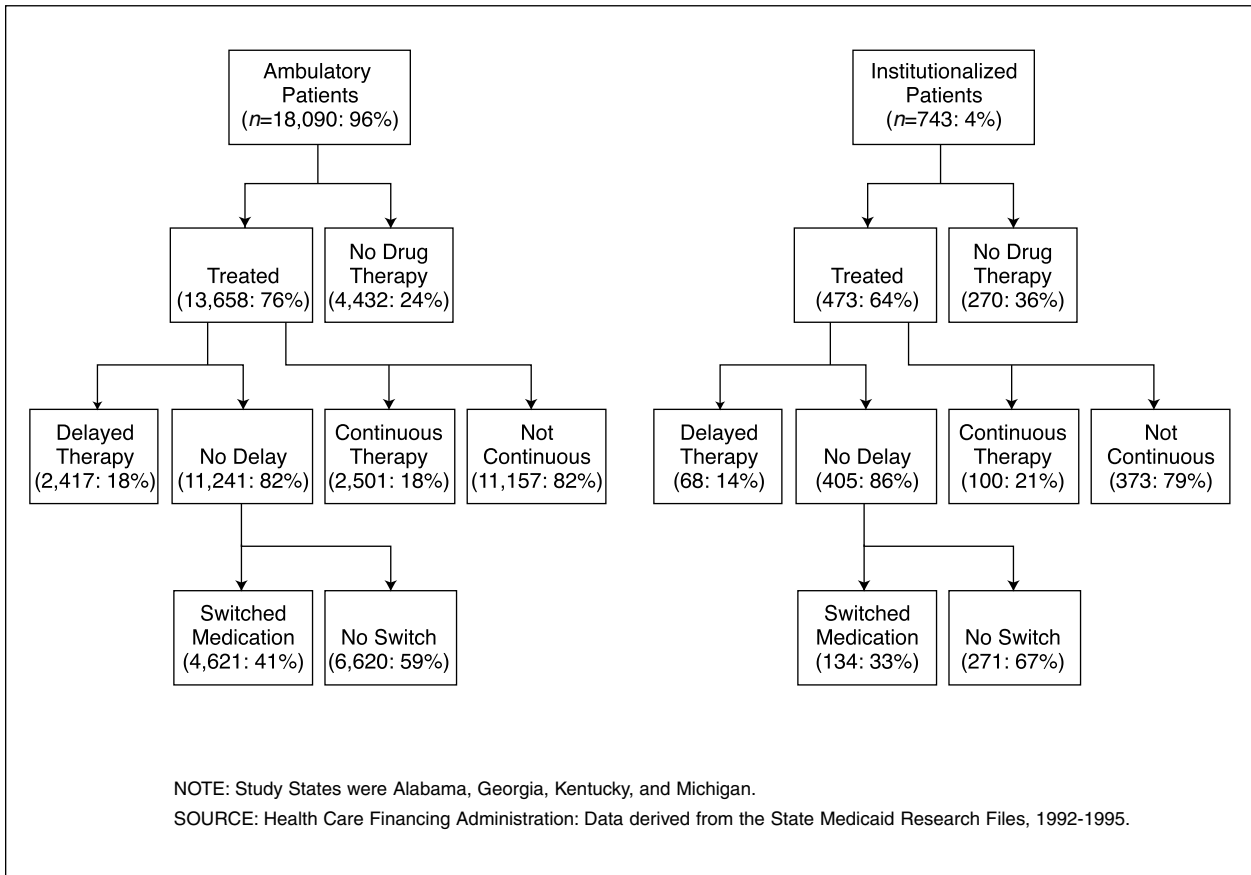
Antipsychotic Drug Use Patterns

Figure 1 displays the antipsychotic drug use patterns of both ambulatory and institutionalized cohorts for all four States. Nearly one-quarter of the ambulatory schizophrenic patients and 36 percent of the institutionalized cohort received no antipsychotic drug treatment for 1 year after their initial recorded diagnosis of schizophrenia. Delaying drug therapy for at least 1 month was found in 18 percent of ambulatory patients treated with an antipsychotic medication and 14 percent of treated institutionalized patients. In addition, 41 percent of ambulatory patients treated-without-delay and 33 percent of institutionalized patients treated without delay changed or augmented their initial drug therapy with a second antipsychotic medication during the first year. Finally, only 18 percent of the treated ambulatory patients and 21 percent of the treated institutionalized patients achieved uninterrupted continuous antipsychotic drug therapy in their first year of drug treatment.

Descriptive Statistics

Table 1 presents demographic, concomitant medication use, and comorbidity information broken down by treatment status for both ambulatory and institutionalized patients. The overall prevalence of report-

Figure 1
Drug Use Patterns for Study States: 1992-1995



ed comorbid mental disorders typically exceeds that of the general population. For example, in the ambulatory population with schizophrenia, these disorders include alcohol and substance abuse (12.7 percent), anxiety (15.3 percent), bipolar disorder (16.7 percent), major depression (25.4 percent), neurotic depression (8.9 percent), other neurotic disorders (11.2 percent), drug psychoses (13.5 percent), and non-organic psychoses (21.1 percent). The use of antidepressants (16.9 percent) and anti-anxiety drugs (2.3 percent) reflect these prevalence rates.

Table 2 presents information on the type of initial antipsychotic medication used for all treated patients. Overall, antipsychotics selection patterns were similar across both the ambulatory and institutionalized cohorts. Haloperidol was the most fre-

quently prescribed initial medication, followed by thioridazine. Institutionalized patients appeared to have a more limited range of antipsychotic medications used as initial therapy. Haloperidol and thioridazine accounted for more than 60 percent of all institutionalized patients as compared with 40 percent in ambulatory patients.

Table 3 presents data on average direct health care costs for ambulatory and institutionalized patients with schizophrenia in the month prior to and the first year after the initiation of the treatment episode. Several health care use patterns are of interest. First, ambulatory patients with schizophrenia utilize more than \$2,600 in services in the month immediately prior to their treatment episode, primarily due to hospital costs (\$2,075 or 79.2 percent). These data may indicate that many patients

Table 1
Treatment Status for Ambulatory and Institutional Patients in Study States, by Descriptive Statistics: 1992-1995

Descriptive Statistic	Patients	
	Ambulatory ¹	Institutionalized ²
Demographics		
Age	³ 40.0	³ 70.0
	Percent	
Urban	³ 72.6	³ 63.8
Female	³ 58.3	³ 65.3
White	³ 49.8	³ 66.9
Concomitant Drug Use		
Antabuse	0.4	0
Anticonvulsants/Seizure Medications	³ 9.0	³ 12.7
Antidepressants	³ 16.9	³ 12.9
Antidyskinetics/Antiextrapyramidal Effects Medications	³ 18.0	³ 11.0
Anti-Parkinsonian Medications	41.0	³ 2.4
Anxiolytics/Anti-Anxiety Medications	2.3	3.2
Narcotic Analgesics	6.6	6.5
Sedative Hypnotics	³ 3.1	³ 7.0
Use of 1 Pharmacy	³ 16.4	³ 49.7
Comorbid Mental Disorders		
Alcohol/Drug Abuse	³ 12.7	³ 3.2
Anxiety	³ 15.3	³ 2.6
Bipolar Disorder	³ 16.7	³ 4.3
Dementia	³ 2.4	³ 22.5
Mania	³ 2.6	(4)
Major Depressive Disorder	³ 25.4	³ 7.0
Neurotic Depression	³ 8.9	³ 2.7
Other Neurotic Disorders	³ 11.2	³ 3.8
Drug Psychoses	³ 13.5	(4)
Chronic Organic Psychoses	³ 2.6	³ 7.0
Transient Organic Psychoses	4.7	4.2
Non-Organic Psychoses	³ 21.1	³ 16.2
Other Affective Disorders	³ 3.1	(4)
Other Mental Disorders	³ 40.6	³ 32.4

¹ n=18,090.

² n=743.

³ p<0.01 for comparisons between the ambulatory and institutionalized populations.

⁴ Meets current Centers for Medicare & Medicaid Services privacy guidelines.

NOTE: Study States were Alabama, Georgia, Kentucky, and Michigan.

SOURCE: Health Care Financing Administration: Data derived from the State Medicaid Research Files, 1992-1995.

with schizophrenia begin their episode of treatment after an acute psychotic episode requiring hospitalization. Average total direct cost of treatment in the first year is \$13,650 due primarily to ambulatory (33.3 percent) and hospital services (41.3 percent). Drug costs are 5.5 percent of the total cost of treating ambulatory patients with schizophrenia. Conversely, the pre- and post-treatment health care utilization patterns for institutionalized patients with schizophrenia are much more stable and

are dominated by the cost of nursing home care. Total direct cost for institutionalized patients with schizophrenia exceeds \$95,000 based on the average daily cost of a nursing home day in California of \$270.

Table 4 presents information on State-specific post-diagnosis direct health care cost for all ambulatory and institutionalized patients. As in other disease States, significant differences in use and costs do appear across States (Chassin et al., 1986). Michigan has the highest total health care

Table 2
Initial Antipsychotic Medications Used, by Treated Ambulatory and Institutionalized Patients in Study States: 1992-1995

Initial Medication	Patients			
	Ambulatory ¹		Institutionalized ²	
	Number	Percent	Number	Percent
Haloperidol	³ 3,243	23.7	³ 201	42.5
Haloperidol Decanoate	⁴ 379	2.8	(5)	(5)
Thioridazine	³ 2,343	17.2	³ 103	21.8
Fluphenazine	³ 1,010	7.4	³ 19	4.0
Fluphenazine Decanoate/Enanthate	645	4.7	14	3.0
Thiothixene	1,472	10.8	42	8.9
Lithium Carbonate/Citrate	³ 1,422	10.4	³ 18	3.8
Perphenazine	³ 906	6.6	(5)	(5)
Trifluoperazine	817	6.0	19	4.0
Chlorpromazine	³ 680	5.0	³ 37	7.8
Loxapine	³ 431	3.2	(5)	(5)
Mesoridazine	212	1.6	(5)	(5)
Other Antipsychotics ⁶	98	0.7	(5)	(5)

¹ n=13,658.

² n=473.

³ p<0.01.

⁴ p<0.05 for comparisons between the ambulatory and institutionalized populations.

⁵ Meets current Centers for Medicare & Medicaid Services privacy guidelines.

⁶ Includes Chlorprothixene, Molindone, and Promazine.

NOTE: Study States were Alabama, Georgia, Kentucky, and Michigan.

SOURCE: Health Care Financing Administration: Data derived from the State Medicaid Research Files, 1992-1995.

cost for ambulatory patients (\$16,560), while Alabama has the lowest average annual cost (\$7,818). Ambulatory patients in Michigan spent significantly more on outpatient/Part-B services compared with patients in the other three States, although Georgia spends proportionally more on these services (41.4 percent versus 33.2 percent). These observed differences in cost of outpatient services are due to either real differences in utilization or differences in unit prices, or both.

Differences across States for hospital costs for ambulatory patient with schizophrenia also exist with Michigan exhibiting the highest costs in absolute and relative terms. Unlike ambulatory services, differences in hospital costs reflect true differences in use of hospital days per patient-year since days of institutional care were valued using the California Medicaid per diem price of \$979. Only minor statistically significant differences in total direct

cost were found across the four States among institutionalized patients who comprise only 3.9 percent of all patients with schizophrenia.

These differences across States are difficult to interpret given differences in the cost per unit of service for ambulatory care that may exist across States. Moreover, the classification of services by type of service may also differ across State Medicaid programs thus affecting which services are allocated to the residual category of other services in this analysis. However, with this in mind, it appears that southern States may devote considerably fewer resources to the treatment of schizophrenia than Michigan, especially Alabama. One hypothesis concerning these differences suggests that the more intensive treatment patterns in Michigan may contribute to the higher rate of drug therapy compliance achieved in Michigan (27 percent) relative to Alabama (2 percent).

Table 3
Pre-Diagnosis Direct Health Care Cost for Ambulatory and Institutionalized Patients in Study States, by Service and Episode: 1992-1995

Service and Episode	Patients			
	Ambulatory ¹		Institutionalized ²	
	Cost	Percent	Cost	Percent
1 Month Prior to Initial Episode³				
Outpatient (Part B)	\$337	12.9	\$182	2.2
Prescription Drugs	453	2.0	4101	1.2
Community Mental Health Center	42	(3)	0	(3)
Dental Service	42	(3)	0	(3)
Other Services	4139	5.3	448	(3)
Hospital Service	42,075	79.2	4821	9.7
Nursing Home	412	(3)	47,269	86.3
Total Cost	42,620	—	48,421	—
1 Year After Initial Episode³				
Outpatient (Part B)	44,539	33.3	42,324	2.4
Prescription Drugs	4746	5.5	41,235	1.3
Community Mental Health Center	415	(3)	0	(3)
Dental Service	418	(3)	42	(3)
Other Services	41,839	13.5	4763	(3)
Hospital Service	45,644	41.3	42,691	2.8
Nursing Home	4851	6.2	488,653	92.7
Total Cost	413,650	—	495,668	—

¹ n=18,090.

² n=743.

³ Percentage of total cost is below 1 percent.

⁴ p<0.01 for comparisons between the ambulatory and institutionalized populations.

NOTE: Study States were Alabama, Georgia, Kentucky, and Michigan.

SOURCE: Health Care Financing Administration: Data derived from the State Medicaid Research Files, 1992-1995.

Effects of Antipsychotic Drug Use Patterns

Direct Health Care Costs

Ambulatory Patients—Tables 5 and 6 present the results of the OLS models on total direct health care cost for patients with schizophrenia in which the cost effects of all antipsychotic medication use patterns were estimated jointly. For ambulatory patients, all antipsychotic drug use patterns, except for uninterrupted drug therapy, were found to be associated with significantly higher total health care cost: being treated with antipsychotics, +\$3,200; delayed drug therapy, +\$3,936; and changed medication, +\$4,019. The majority of the additional costs associated with delays in therapy and changes in therapy

were due to increased cost for hospital care and ambulatory services (Table 6). The use of antipsychotic drug therapy was associated primarily with higher ambulatory service costs with smaller increases in hospital care and other services.

Completing a year of uninterrupted antipsychotic drug therapy was not found to be associated with total direct cost in ambulatory patients. However, completed therapy was associated with significantly lower hospital costs (-\$1,337) and nursing home costs (-\$652) that were offset by increased use of ambulatory care (+\$1,237) and other services (+\$939). The cost results estimated here for the entire population are presented to facilitate comparisons with similar results reported for the California Medicaid population (McCombs et al., 1999b, 2000).

Table 4
Post-Diagnosis Direct Health Care Cost for Ambulatory and Institutionalized Patients in Study States, by Service and Episode: 1992-1995

Type of Service	Alabama		Georgia		Kentucky		Michigan	
	Cost	Percent	Cost	Percent	Cost	Percent	Cost	Percent
Ambulatory ¹								
1 Year After Initial Episode								
Outpatient (Part B)	⁵ \$1,428	18.3	⁴ \$4,636	41.4	44,582	34.1	³ 5,492	33.2
Prescription Drugs	³ 876	11.2	4591	5.3	³ 877	6.5	³ 727	4.4
Community Mental Health Center	40	(2)	³ 23	(2)	³ 23	(2)	³ 14	(2)
Dental Service	54	(2)	418	(2)	³ 93	(2)	50	(2)
Other Services	41,289	16.5	5996	8.9	41,396	10.4	³ 2,478	15.1
Hospital Service	⁶ 3,122	39.9	⁵ 4,204	37.5	45,464	40.6	³ 7,078	42.7
Nursing Home	³ 1,099	14.1	³ 732	6.5	³ 1,011	7.5	³ 771	4.7
Total Cost	⁶ 7,818	—	⁵ 11,199	—	413,447	—	³ 16,560	—
Institutionalized ⁷								
1 Year After Initial Episode								
Outpatient (Part B)	⁵ 358	(2)	³ 3,206	3.4	42,156	2.2	^{3,4,5} 42,825	3.0
Prescription Drugs	41,116	1.2	41,190	1.2	³ 2,044	2.1	4965	1.0
Community Mental Health Center	40	(2)	40	(2)	40	(2)	40	(2)
Dental Service	40	(2)	45	(2)	³ 4	(2)	40	(2)
Other Services	⁵ 245	(2)	4784	(2)	31,288	1.3	^{3,4,5} 4822	(2)
Hospital Service	^{4,2} 293	2.4	41,154	1.2	^{3,5} 916	6.0	42,860	3.0
Nursing Home	^{3,9} 1,894	95.8	^{3,4,8,9} 204	93.4	^{4,8,7} 161	88.4	486,769	92.1
Total Cost	^{3,4,9,5} 9,906	—	^{3,4,9,5} 5,43	—	^{3,9,8} 569	—	^{4,9,4} 243	—

¹ n=18,090.

² Percentage of total cost is below 1 percent.

^{3,4,5,6} Duncan groupings: State means with the same footnote numbers are not statistically different.

⁷ n=743.

NOTES: Study States were Alabama, Georgia, Kentucky, and Michigan. The following are the number and percent of ambulatory patients: Alabama—n= 2,910; 16.1 percent; Georgia—n=3,555; 19.7 percent; Kentucky—n=2,614; 14.4 percent; and Michigan—n=9,011; 49.8 percent. The following are the number and percent of institutionalized patients: Alabama—n=155; 20.9 percent; Georgia—n=230; 31.0 percent; Kentucky—n=116; 15.6 percent; Michigan—n=242; 32.6 percent.

SOURCE: Health Care Financing Administration: Data derived from the State Medicaid Research Files, 1992-1995.

Institutionalized Patients—The estimated associations between antipsychotic drug use patterns and total direct costs in institutionalized patients with schizophrenia are mixed. Active drug therapy and delays in drug therapy were associated with higher ambulatory care costs while completed therapy was associated with a significant reduction in these costs. Changes in drug therapy were associated with higher hospital costs.

Differences Across States

Tables 5 and 6 also document the differences in health care costs for patients with schizophrenia across the four States studied. In the ambulatory population,

Michigan displayed higher total health care costs relative to the other three States though differences vary by type of service. Michigan has significantly higher hospital costs for ambulatory patients relative to Alabama and Kentucky; higher nursing home costs than Alabama or Georgia; and higher costs for ambulatory and other services for ambulatory patients relative to all three other States. The differences in institutional costs represent differences in use rates per patient as days of institutional care were evaluated using California Medicaid prices. Differences in ambulatory care costs and the cost for other services may reflect differences in price or use or both.

Table 5
Total Health Care Costs for Patients in the First Treatment Year in Study States, by Independent Variables: 1992-1995

Independent Variable	Ambulatory ¹	Estimated Effect Institutionalized ²	All ³
Prior (1 Month) Use of Health Services			
Hospital Services	0.14	—	0.16
Long-Term Care Services	7	—	10
Outpatient/Part B (Per \$1 Spent)	5	—	5
Other Services (Per \$1 Spent)	2	—	2
Demographics			
Age	105	—	129
Male	1,402	—	1,446
White	1,138	—	1,208
Used 1 Pharmacy	—	7,464	—
Concomitant Medication Profile			
Anticonvulsants/Seizure Medications	1,171	—	1,237
Antidepressants	—	4,794	—
Antidyskinetics/Anti-Extrapyramidal Effects Medications	—	—	829
Narcotic Analgesics	—	—	-1,137
Antipsychotics Utilization Patterns			
		(In Dollars)	
Received Drug Therapy During First Year	43,200	30	42,576
Treated and Delayed in Therapy	43,936	1,423	43,994
Treated and Switched	44,019	435	44,067
Treated and Completed Continuous Therapy	414	-1,731	386
Being Treated in Alabama, Georgia, or Kentucky Versus Michigan			
Alabama	4-4,315	-1,545	4-3,864
Georgia	4-1,924	-881	4-1,192
Kentucky	4-3,617	2,654	4-3,163

¹ n=18,090. Adjusted R²=0.2726.

² n=743. Adjusted R²=0.1164.

³ n=18,333. Adjusted R²=0.5340.

⁴ Statistically significant ($p < 0.05$) for estimated regression coefficients. Only statistically significant ($p < 0.05$) factors are listed except for State and antipsychotic drug use pattern factors.

NOTE: Study States were Alabama, Georgia, Kentucky, and Michigan.

SOURCE: Health Care Financing Administration: Data derived from the State Medicaid Research Files, 1992-1995.

DISCUSSION

This analysis documents the antipsychotic drug use patterns achieved by patients with schizophrenia treated with first-generation antipsychotics in Alabama, Georgia, Kentucky, and Michigan and estimates the impact of these patterns on treatment costs. This study confirms results from an earlier study that used data for ambulatory patients with schizophrenia from the California Medicaid program (McCombs et al., 1999a,b; 2000). Schizophrenia is a costly disease to treat: \$17,000 to \$26,000 per ambulatory patient, per year.

In general, ambulatory patients with schizophrenia treated with traditional antipsychotic medications did not display drug utilization patterns that are consistent with successful drug therapy or the effective management of the disease and its treatment costs. Specifically:

- Approximately one-quarter of ambulatory patients in these four States did not use any antipsychotics for at least 1 year, which is almost identical to the California study results. Treated ambulatory patients in these four States were found to experience significantly higher total direct health care costs relative to untreated

Table 6
Summary of Health Care Cost Impacts in Study States, by Drug Use Pattern: 1997

Use Pattern	Ambulatory Patients <i>n</i> =18,090					
	Total Costs <i>R</i> ² =0.2726	Hospital <i>R</i> ² =0.2779	Nursing Home <i>R</i> ² =0.1442	Outpatient <i>R</i> ² =0.2262	Drugs <i>R</i> ² =0.3463	Other <i>R</i> ² =0.1990
(In Dollars)						
Antipsychotic						
Received Drug Therapy During First Year	13,200	1615	256	11,722	- 7	1627
Treated After Delayed in Therapy	13,936	12,245	209	11,181	1239	61
Treated and Switched	14,019	12,185	199	11,184	1248	1203
Treated and Completed Continuous Therapy	414	1-1,337	1-652	11,237	223	1939
State Effects Versus Michigan						
Alabama	1-4,315	1-1,259	1423	1-3,119	191	1-456
Georgia	1-1,924	-162	1478	1-1,133	1-81	1-1,045
Kentucky	1-3,617	1-1,382	162	1-1,638	-9	1-847
Institutionalized Patients <i>n</i> =743						
	<i>R</i> ² =0.1150	<i>R</i> ² =0.3763	<i>R</i> ² =0.2144	<i>R</i> ² =0.1257	<i>R</i> ² =0.3401	<i>R</i> ² =0.1315
Antipsychotic						
Received Drug Therapy During First Year	30	-425	-574	11,458	-162	-264
Treated After Delayed in Therapy	1,423	628	-1,523	11,206	1335	1776
Treated and Switched	435	11,697	-1,713	176	96	179
Treated and Completed Continuous Therapy	-1,731	-1,073	558	1-1,375	1334	-177
State Effects Versus Michigan						
Alabama	-1,545	1,374	-100	1-2,830	179	-169
Georgia	-881	1,332	-2,467	-60	228	77
Kentucky	2,654	12,595	433	-1,018	1374	265
All Patients <i>n</i> =18,833						
	<i>R</i> ² =0.5340	<i>R</i> ² =0.2783	<i>R</i> ² =0.7963	<i>R</i> ² =0.2255	<i>R</i> ² =0.3501	<i>R</i> ² =0.1975
Antipsychotic						
Received Drug Therapy During First Year	12,576	1549	-278	11,723	-16	1611
Treated After Delayed in Therapy	13,994	12,205	307	11,163	1243	75
Treated and Switched	14,067	12,169	309	11,146	1243	1200
Treated and Completed Continuous Therapy	386	1-1,322	1-572	11,144	1231	1902
State Effects (Versus Michigan)						
Alabama	1-3,864	-1,127	765	13,128	194	1-474
Georgia	1-1,192	-66	11,085	11,134	1-64	1-1,031
Kentucky	1-3,163	-1,193	402	11,637	8	1-837

1 *p* < 0.05 for estimated regression coefficients.

NOTE: Study States were Alabama, Georgia, Kentucky, and Michigan.

SOURCE: Health Care Financing Administration: Data derived from the State Medicaid Research Files, 1992-1995.

patients (\$2,576: *p*=0.0001), while no significant difference on health care cost was found between treated and untreated ambulatory patients in California within the first year.

- Delayed drug therapy was found in nearly 18 percent of all treated ambulatory patients in this study while a 24-percent delayed therapy rate was found in Medi-Cal. Delaying antipsychotic drug therapy was associated with an increase in

total cost in both studies (\$3,994: *p*=0.0001 for the four-State sample and \$9,418: *p*=0.0001 in California).

- Approximately 18 percent of all treated ambulatory patients across the four States completed 1 year of uninterrupted drug therapy. Only 11 percent of treated patients in California completed 1 year of therapy. This difference in completion rates is not surprising given the variation observed across the four States studied

here (2 percent in Alabama to 27 percent in Michigan). In general, uninterrupted antipsychotic drug therapy was not correlated with reduced overall health care costs in both studies although reductions in hospital costs were observed.

- More than 41 percent of all treated ambulatory patients switched antipsychotic medications or augmented their initial therapy within 1 year. In California, 45 percent of treated patients changed their antipsychotic medications during the first post-diagnosis year. Patients who switched or augmented their initial antipsychotic drug regimen in this study were found to experience significantly higher total health care cost (\$4,067; $p=0.0001$). Similar effect of medication change on health care costs was found in California with a greater impact (\$9,719; $p=0.0001$).

Persistent abstinence and delays in the initiation of antipsychotic drug therapy in the ambulatory setting are consistent with a hypothesis that patients with schizophrenia take frequent drug holidays from therapy with conventional antipsychotic medications (Keith, Regier, and Rae, 1991; McGlashan, 1988). While many clinicians may withdraw their patients from active drug therapy due to side effects during periods of symptom remission, these periods of drug abstinence often end when the patient experiences an acute psychotic episode. This leads to the correlation between delayed drug therapy and total health care costs, especially hospital costs. Moreover, persistence with drug therapy for 1 year was correlated with significantly reduced costs for institutional services. The frequency of augmentation and switching within 1 year and the low rate of persistence with drug therapy provide additional evidence that conventional antipsychotics are not meeting the therapeutic needs of patients with schizophrenia.

The increased cost associated with medication persistence is due to increased costs for ambulatory care, prescription drugs, and other services which were offset by lower hospital costs. One interpretation of these results is that compliance with antipsychotic drug treatment benefits from consistent contact with outpatient providers. However, while several factors may be contributing to the frequency of the observed dysfunctional drug use patterns, such as access to specialty mental health providers, the clinical profile of conventional antipsychotics must be considered as an important factor.

The limitations inherent in the research design employed here and the SMRF data system are unlikely to have had a significant effect the results of the analysis of ambulatory patients. The use of nursing home services was minimal for ambulatory patients in the first post-treatment year. Therefore, it is unlikely that having used nursing home services would have significantly limited access to accurate prescription drug data or the calculation of drug use patterns. However, the significant level of hospital use by ambulatory patients with schizophrenia could have been the cause of patients interrupting therapy rather than the other way around. Therefore, the estimated correlation between the continuous use of an antipsychotic medication and significantly lower use of hospital and nursing home cost must be viewed with caution. The possibility that some nursing home use was not covered by individual State Medicaid programs would tend to reduce the level of nursing home use reported here.

The possible bundling of prescription drug costs into the nursing home fee calls into question the results reported here for patients institutionalized at the time of treatment initiation. Equally important, compliance with drug therapy is monitored

in most nursing home environments, setting up an artificial correlation between drug therapy compliance and nursing home use. Finally, the sample size for the analysis of institutionalized patients was quite limited. Therefore, these results should be viewed with caution.

Interventions that improve antipsychotic drug use by patients with schizophrenia may garner significant offsetting savings. One such option now being considered by State Medicaid programs is providing unrestricted access to second-generation antipsychotic medications. In clinical trials, these medications have exhibited favorable safety and side effect profiles, and improved efficacy against positive and negative symptoms. However, second-generation antipsychotics (such as Clozapine, Risperidone, and Olanzapine) are significantly more expensive than conventional antipsychotic medications. For example, since their recent addition to the California Medicaid program formulary, Olanzapine has become the most expensive to the Medi-Cal program while Risperidone ranks second in terms of prescription costs (California's Medical Assistance Program, 1999). This rapid uptake of these medications and the resulting increase in costs makes it increasingly important that any potential cost saving associated with their use be documented.

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