# Use Patterns for Antipsychotic Medications in Medicaid Patients With Schizophrenia

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Objective: We investigated the use patterns for antipsychotic medications generated by Medicaid patients with schizophrenia. Method: Paid claims data from the California Medicaid program (Medi-Cal) were used to identify 2655 patients with schizophrenia. Data from 1987–1996 were used, during which time Medi-Cal maintained prior authorization restrictions on second generation antipsychotic drugs. Prescription records were used to identify 3 patterns of antipsychotic drug use: no drug therapy for over 1 year; delayed onset of antipsychotic drug therapy; and switches in antipsychotic drugs within 1 year. Multiple logistic regression models were used to identify factors affecting these antipsychotic drug use patterns. Results: Conventional antipsychotic medications account for over 98% of all patient treatment episodes. Over 24% of patients with schizophrenia do not use any antipsychotic medication for periods lasting up to 1 year. Over 24% of treated patients delayed the use of antipsychotic medications at least 30 days. For those patients who did not delay their use of antipsychotic medications, over 47% switched or augmented their initial antipsychotic medication during the first treatment year. Only 11.6% of treated patients achieved 1 year of uninterrupted antipsychotic drug therapy. The mean duration of uninterrupted therapy was 142 days. *Discussion:* Antipsychotic drug use patterns suggest that conventional antipsychotic medications do not meet the therapeutic needs of patients with schizophrenia. (J Clin Psychiatry 1999;60/suppl 191:5–11)

Chizophrenia is a chronic psychotic disorder that adversely affects a broad range of psychological processes, including perception, ideation, affect, attention, concentration, motivation, and judgment. No single symptom is pathognomonic of schizophrenia, and the psychological and behavioral characteristics of the disorder are associated with a variety of impairments in occupational and social functioning. The majority of patients alternate

between acute psychotic episodes and stable periods characterized by full or partial remission of symptoms. The disorder affects men and women equally, although the peak onset for women is later than for men (late 20s/early 30s for women vs. early 20s for men). Overall, the lifetime prevalence of schizophrenia has been estimated at approximately 1% of the population.

The effective treatment of schizophrenia depends critically on antipsychotic medications to treat acute psychotic episodes, prevent future episodes, and improve symptoms between episodes. However, conventional antipsychotics can cause a broad spectrum of side effects that often lead to the discontinuation of therapy. For example, Van Putten<sup>3</sup> found that 46% of schizophrenic patients treated in a 30-bed teaching service in a university-affiliated Veterans Affairs hospital took less medication than prescribed owing to side effects, especially drug-induced extrapyramidal symptoms. Lehman and Steinwachs<sup>4</sup> found that fewer than two thirds of inpatients received appropriate medication dosages during acute treatment episodes, and less than one third of outpatients successfully received appropriate maintenance dosages. The side effect profiles of the older antipsychotics, coupled with the episodic nature of the acute phase of the disorder, may result in a significant proportion of schizophrenic outpatients discontinuing the use of antipsychotic medications until an acute episode of psychotic symptoms reemerges.<sup>5,6</sup>

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Several new antipsychotic medications with atypical symptom response and safety profiles have been approved by the U.S. Food and Drug Administration (FDA) in the past decade: clozapine,<sup>7</sup> risperidone,<sup>8</sup> olanzapine,<sup>9</sup> and quetiapine.<sup>10</sup> These agents show promise for enhanced tolerability, improved efficacy profile for negative symptoms that affect the patient's quality of life and community adjustment, and reduced utilization of health services.<sup>11–13</sup>

As with any new medication, the atypical second generation antipsychotic medications must overcome significant hurdles to gain acceptance by public and private health insurance programs, health maintenance organizations (HMOs), and managed care organizations. Specifically, HMOs and state Medicaid programs require data that document the extent to which existing medications do not meet the therapeutic needs of schizophrenic patients. The present research used data from the California Medicaid program (Medi-Cal) to investigate these issues. These data were abstracted from a time period (1987-1996) during which the second generation antipsychotic medications were either not available or subject to prior authorization. The drug use patterns investigated here include abstinence from treatment, delays in initiating treatment, and changes over time in the antipsychotic drug taken. Analyses of the factors associated with these patterns of antipsychotic drug use were undertaken.

## **METHOD**

#### **Data Source**

The data for this analysis were derived from Medi-Cal, which finances a wide range of health care services, including outpatient prescription drugs, for the poor and persons with disability. The Medi-Cal program generates a longitudinal research database for a random 5% sample of all recipients for as long as the sample recipient is eligible. This database 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, amount paid, and units (days) of service. Prescription drug claims identify the specific product dispensed, quantity, strength, and the date the prescription was filled. Prescription drugs are provided under Medi-Cal and are subject to a \$1 copayment by the recipient, although anecdotal information suggests that copayments are not routinely collected by area pharmacies. Data for this analysis were drawn from the period January 1987 to July 1996.

## **Episodes of Care**

The "gold standard" for studies comparing alternative drug therapies is the randomized clinical trial, which evaluates new episodes of drug therapy. Therefore, drug studies that use paid claims data often attempt to identify "new" episodes of drug therapy for analysis. This is commonly done by screening patients for 6 or more months of pretreatment paid claims, during which time the patient does not use medications within selected therapeutic classes. Under this approach, the episode of care begins with the initial purchase of one of the drugs under study. Multiple episodes of new drug therapy can also be defined for patients with longitudinal data that include recurrent episodes of illness.

The present analysis did not use new drug treatment episodes as its unit of analysis, but focused instead on a single treatment episode per patient independent of drug therapy. This approach was selected for several reasons. First, it allowed for an analysis of patients who do not use antipsychotic drugs to treat their condition. Episodes of treatment were defined based on the initial service provided for which a schizophrenia diagnosis was recorded. Second, the analysis was not limited to new episodes of treatment. It was believed that most Medi-Cal patients with schizophrenia were likely to have qualified for Medi-Cal coverage while undergoing treatment due to the disabling effects of this disorder.14 A focus on new episodes of treatment would have limited the sample available for study. However, in order to gain some insight into possible differences in health care use rates prior to treatment, a minimum of 30 days of prior use data were required in this study. Third, this research was designed to determine if patients with schizophrenia used antipsychotic medications in an episodic manner. Therefore, a single episode of care is defined for each patient with schizophrenia and may contain multiple, disjointed "episodes" of drug therapy.

## **Inclusion and Exclusion Criteria**

Patients were selected for study based on their Medi-Cal paid claims history using the following inclusion criteria:

- 1. A diagnosis of schizophrenia recorded on at least 1 paid claim or the use of clozapine or risperidone. During the study period (1987–1996), prior authorization was required by Medi-Cal for clozapine and risperidone that limited their use to patients with schizophrenia who had failed at least 2 treatment attempts using older antipsychotics. To further ensure that the study population was limited to patients with schizophrenia, patients selected based solely on risperidone use were also required to be under the age of 50 years, reducing the probability of including patients who may have taken this medication to treat Alzheimer's disease or dementia.
- 2. A minimum of 30 days of paid claims data prior to the treatment episode start date, which was determined as the date of the first prescription for an antipsychotic drug or the date of the first diagnosis of schizophrenia, whichever was earliest.

3. A minimum of 1 year of paid claims data following the initiation of the treatment episode to ensure adequate posttreatment data for analysis.

Patients were excluded from the analysis if any of the following criteria were met:

- 1. Patient expenditures for "other" services were over \$50,000 per year in either of the first 2 posttreatment years. Other services consisted of all paid claims for which the type of provider was either unknown or was not considered to be relevant to a study of schizophrenia (e.g., dental services).
- 2. Patients were under the age of 14 years or over 100 years at the beginning of the treatment episode.
- 3. Patients exhibited gaps in excess of 90 days in their paid claims data during the first year of treatment.

The last exclusion criterion requires explanation. For most Medi-Cal patients, gaps in their paid claims history often indicate that the patients may have lost Medi-Cal eligibility during the episode of treatment. However, for schizophrenic patients, such gaps are more likely to indicate that the patient withdrew from the Medi-Cal health care system for an extended period of time despite being eligible for continuous Medi-Cal coverage. Several types of withdrawal are possible, including incarceration within the criminal justice system, seeking treatment from an alternative health care system such as Veterans Affairs hospitals and clinics, or true withdrawal from all sources of health care. General population survey data indicate that substantial proportions of community residents with schizophrenia and other psychotic disorders may disengage from the health care system for lengthy periods of time.<sup>2,15</sup> However, given the uncertainty concerning the cause for these gaps in paid claims history, a total of 615 patients were excluded from this study, leaving a final study population of 2655 patients.

# Study Cohorts Based on Antipsychotic Drug Use Patterns

This research investigates the factors that affect the drug use patterns achieved by schizophrenic patients treated primarily with conventional antipsychotic medications. Three sequential subgroups of schizophrenic patients were identified for study.

*Treated population.* Most older antipsychotic medications can cause significant and sometimes irreversible side effects, suggesting that the effectiveness of these medications may be limited in actual practice owing to dose restrictions and noncompliance. Patients with schizophrenia may interrupt or delay the onset of antipsychotic drug therapy until they experience an exacerbation of symptoms that requires drug therapy. <sup>16–18</sup> If such episodic drug therapy patterns are common, a significant proportion of

patients with schizophrenia will not use any pharmacologic therapy for extended periods of time. This may be especially 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, the first analysis of risk factors that affect antipsychotic drug use patterns compared the population receiving antipsychotic drug therapy at any time within the first year with patients with a recorded diagnosis of schizophrenia who received no antipsychotic drug therapy within 1 year of the first service for schizophrenia.

Delays in antipsychotic drug therapy. Patients with schizophrenia who have interrupted their antipsychotic drug therapy are likely to relapse. Relapse after drug discontinuation is common even if patients are in long-term remission of symptoms, although the time to relapse can be expected to vary. <sup>5,19</sup> Given the likelihood that patients gain Medi-Cal eligibility after the patient's initial drug treatment for schizophrenia, a second manifestation of interrupted drug utilization patterns will appear in the Medi-Cal paid claims as a delay in drug therapy. Specifically, such "delayed therapy" patients may have experienced an exacerbation of their symptoms that required a restart of antipsychotic drug therapy.

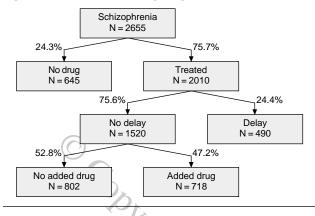
To assess the risk factors associated with delays in therapy, analyses were conducted using the treated patient population, and compared patients treated within 30 days after the first recorded service that assigned a diagnosis of schizophrenia with patients who delayed therapy for up to 1 year. Patients with delays in therapy of longer than 1 year may not have experienced an exacerbation of symptoms within the first year and were classified as untreated patients.

Medication changes. Changes in therapy may be common among schizophrenic patients treated with conventional antipsychotic medications because of the drugs' adverse safety profile, limited efficacy for negative symptoms, and limited response profile.<sup>16</sup> To focus on the risk factors related to medication changes only, these analyses used data from the population of patients who filled a prescription for an antipsychotic medication within 30 days of the first service with a schizophrenia diagnosis. Patients were classified as having changed therapy if a second antipsychotic medication was used within 1 year, either concomitantly with their initial medication or as replacement therapy. An intent-to-treat analysis was performed that estimated the impact of alternative medications as initial therapy on the likelihood that a patient would switch medications.20

#### **Statistical Methods**

Multiple logistic regression models were used to investigate the factors that affect antipsychotic drug use patterns using the 3 study cohorts (SAS Proc LOGISTIC<sup>21</sup>). Specifically, the analysis of the initiation of drug therapy within the first year used all patients, the analysis of delays in drug

Figure 1. The Patterns of Drug Usage Over 1 Year



therapy beyond 30 days used all treated patients, and the analysis of switches in antipsychotic therapies was conducted using data for all patients treated without delays.

Up to 54 independent variables were included in the logistic regression models of the patient's antipsychotic drug use patterns. These independent variables included the prior use of health care by type of service, demographic characteristics, mental and medical diagnostic mix, and prescription drug profile. For brevity, only those variables found to have a significant impact on the dependent variable studied are reported.

## **RESULTS**

## Patterns of Antipsychotic Drug Use

Figure 1 displays the antipsychotic drug use patterns of the study population. Over 24% (N = 645) of study patients received no drug therapy for 1 year following their first recorded Medi-Cal service with a schizophrenia diagnosis. Furthermore, an additional 24% of patients (N = 490) treated with an antipsychotic medication within the first year did so after a delay in therapy of at least 30 days. Finally, nearly half (47.2%) of all patients treated with an antipsychotic medication without a delay in therapy switched therapies or augmented their initial therapy with a second antipsychotic medication during the year after the initiation of antipsychotic drug therapy. If the goal of drug therapy is to achieve stable, long-term use of 1 or more antipsychotic medications, these results provide strong evidence that these therapeutic goals were not being met in the Medi-Cal population during the time period under evaluation (1987–1996).

#### **Descriptive Statistics**

The descriptive statistics for the study population are provided in Table 1. Schizophrenic patients covered by the Medi-Cal program were very likely to have other mental disorders recorded on their paid claims, especially major depressive disorder (22.7%), bipolar disorder (15.5%), anx-

Table 1. Demographic, Diagnostic, and Concomitant Drug Use Data

Characteristic	All Patients (N = 2655)	Treated Patients (N = 2010)	No Drug Therapy (N = 645)
Demographic characteristics			
Age, y, mean	43.2	42.6	45.2
Urban, %	82.3	81.6	84.3
Gender, % female	54.5	54.4	54.6
Concomitant drug use, %			
Prescription narcotics	8.1	7.7	9.3
Hypnotics	6.2	6.7	4.7
Seizure medications	12.4	12.5	11.9
Antiparkinsonian drugs	0.8	0.8	0.6
Antianxiety drugs	1.2	1.1	1.4
Antidepressants	17.4	18.9	12.7
Disulfiram	0.3	0.3	0.0
Drugs to treat extrapyramid	al		
side effects	22.3	28.9	1.7
Used one pharmacy, %	14.0	11.2	22.8
Other mental disorders, %			
Dementia	4.7	5.0	3.6
Alcohol or drug abuse	4.2	4.5	3.4
Mania	2.0	2.2	1.1
Major depressive disorder	22.7	23.7	19.7
Bipolar disorder	15.5	17.9	8.2
Anxiety disorders	14.3	14.3	14.3
Nonorganic psychoses	21.7	24.6	12.7
Neurotic depression	12.0	11.6	13.0
Other neurotic disorders	7.3	8.2	4.8
Drug psychoses	8.1	8.0	8.7
Transient organic psychoses	3.9	4.3	2.6
Chronic organic psychoses	3.0	3.6	1.2
Other affective disorders	1.2	1.4	0.8
Other mental disorders	33.4	33.5	33.3

iety (14.3%), nonorganic psychoses (21.7%), and neurotic depression (12.0%). Their common use of concomitant psychotropic medications, especially antidepressants (17.4%), reflected this pattern of comorbid mental disorders. Moreover, patients with schizophrenia who were not using antipsychotic medications appeared to have fewer reported comorbid mental disorders and lower psychotropic drug use than did patients treated with an antipsychotic medication.

Data for the type of antipsychotic drug used are presented in Table 2 for all treated patients, patients with delayed therapy, and patients who had a second antipsychotic added. Overall, all 3 patient populations exhibit similar drug selection patterns: haloperidol is the most frequently prescribed initial medication, followed by thioridazine. The use of the second generation antipsychotics (only clozapine and risperidone were available during the study period) was under 3% for all 3 populations. This low use rate was primarily due to the formulary restrictions placed on these drugs by the Medi-Cal program and the approval of risperidone late in the data period (1994). Probably the most significant finding in Table 2 is the relatively small number of schizophrenia patients who continued to purchase at least 1 prescription for any antipsychotic medication consecutively for 1 year (11.6% overall). The mean length of a drug therapy episode was only  $142 \pm 179$  days, even after accounting for changes in initial therapy.

Table 2. Antipsychotic	Drug	Use				
	Pati Initial	reated ents, Therapy 2010)	in Pa With I The	Therapy tients Delayed rapy 490)	Secon Thera Patient Added (N =	py in s With Drug
Characteristic	N	%	N	%	N	%
Antipsychotic medications	540	27.2	105	25.5	165	10.1
Haloperidol	549	27.3	125	25.5	165	19.1
Chlorpromazine	149	7.4	44	9.0	88	10.2
Fluphenazine Fluphenazine (decanoate/	210	10.4	50	10.2	75	8.7
enanthate)	59	2.9	19	3.9	57	6.6
Lithium	222	11.0	48	9.8	117	13.5
Perphenazine	134	6.7	36	7.3	38	4.4
Thioridazine	354	17.6	87	17.8	134	15.5
Thiothixene	194	9.7	30	6.1	83	9.6
Trifluoperazine	158	7.9	35	7.1	60	6.9
Atypicals (clozapine,		9%	X			
risperidone)	36	1.8	-8	1.6	24	2.8
Other						
antipsychotics	38	1.9	8	1.6	25	2.9
2 antipsychotics						
as initial therapy	93	4.6	0	0	0	0
Achieved 360 days						
of uninterrupted			~	0 4		
antipsychotic drug				100		
therapy, %	1	1.6	1	6.1	1	1.1
Total days of				` ` (	30	45
uninterrupted drug					100	Y
therapy, mean	1	42	1	.62	.81	41

#### **Multivariate Statistical Results**

Factors affecting the use of antipsychotic medications within 1 year. Several clinically relevant patient characteristics were found to be correlated with use of an antipsychotic medication (Table 3). The likelihood of antipsychotic drug treatment decreased approximately 1.3% per year of age. Patients who used prescribed hypnotic medications or antidepressants within 30 days of the episode start date were significantly more likely to use an antipsychotic medication (odds ratios [ORs] of 1.69 and 1.83, respectively), as were patients with concomitant mental disorders such as chronic organic psychoses (2.90), bipolar disorder (1.98), and nonorganic psychoses (1.91). These results suggest that more severely ill patients were more likely to have used an antipsychotic during the first year.

Factors affecting delays in antipsychotic drug therapy. Over 24% of the 2010 patients who used an antipsychotic medication during the first posttreatment year (N = 490) delayed the use of these medications for at least 30 days from the start of the treatment episode. As with the decision to not use antipsychotic medications within the first year, patients who delayed therapy appeared to be less severely ill. Specifically, patients using hypnotic medications (OR = 0.50), seizure medications (OR = 0.49), and antidepressants (OR = 0.37) were less likely to delay drug therapy (Table 4). Patients with a concomitant diagnosis

Table 3. Factors Significantly Affecting the Likelihood of Using an Antipsychotic Medication in First Treatment Year<sup>a</sup>

	Estimated	
Independent Variable	Odds Ratio	p Value
Prior use of health services (\$100s/mo)		
Prescribed drugs	0.710	.0001
Age (in years)	0.987	.0002
Used 1 pharmacy	0.350	.0001
Drug profile		
Hypnotics	1.687	.0222
Antidepressants	1.827	.0001
Diagnostic profile (mental health)		
Chronic organic psychoses	2.898	.0067
Bipolar disorder	1.978	.0001
Nonorganic psychoses	1.905	.0001
Diagnostic profile (medical conditions)		
Respiratory illnesses	0.674	.0004
Pregnancy	0.517	.0019
Muscle disorders	0.686	.0007

\*2010 (75.7%) of 2655 patients used an antipsychotic in the first treatment year. Association of predicted probabilities and observed responses: Concordant = 71.2%; Discordant = 28.5%; Tied = 0.4%; (1,177,804 pairs); Somers' D = 0.427; Gamma = 0.429; Tau-a = 0.157; c = 0.714.

Table 4. Factors Significantly Affecting the Likelihood of Delaying Antipsychotic Medication Use in First Treatment Year<sup>a</sup>

	Estimated	
Independent Variable	Odds Ratio	p Value
Prior use of health services (\$100s/mo)		
Psychologists	0.893	.0127
Urban residence	1.524	.0063
Used 1 pharmacy	1.391	.0446
Drug profile		
Hypnotics	0.502	.0158
Antidepressants	0.371	.0001
Seizure medications	0.492	.0006
Diagnostic profile (mental health)		
Anxiety	1.588	.0055
Diagnostic profile (medical conditions)		
Respiratory illnesses	0.700	.0047

 $^{3}$ 490 (24.4%) of 2010 patients delayed therapy in the first treatment year. Association of predicted probabilities and observed responses: Concordant = 68.5%; Discordant = 31.0%; Tied = 0.5%; (897,645 pairs); Somers' D = 0.375; Gamma = 0.376; Tau-a = 0.138; c = 0.687.

of anxiety were more likely to delay therapy (OR = 1.59), while patients with respiratory illnesses were less likely to do so (OR = 0.70).

Factors affecting switching or augmentation. Over 47% of the 1520 patients who started antipsychotic drug therapy at the beginning of the treatment episode switched medications or augmented their initial therapy within 1 year (Table 5). Increasing age was found to decrease the likelihood of a change in antipsychotic medications. Conversely, the presence of several concomitant mental disorders was found to increase the likelihood of a change in medication, including manic disorder (OR = 2.73, p = .0256), major depressive disorder (OR = 1.40, p = .0157), bipolar disorder (OR = 1.88, p = .0001), and nonorganic psychoses (OR = 1.34, p = .0308).

Table 5. Factors Significantly Affecting the Likelihood of Switching Medications or Augmenting Initial Therapy: Patients With No Delay in Therapy (N = 1520)<sup>a</sup>

	Estimated	
Independent Variable	Odds Ratio	p Value
Age	0.989	.0057
Used 1 pharmacy	0.549	.0024
Diagnostic profile (mental health)		
Manic disorder	2.727	.0256
Major depressive disorder	1.403	.0157
Bipolar disorder	1.879	.0001
Nonorganic psychoses	1.338	.0308
Antipsychotic drugs (vs haloperidol)		
Chlorpromazine	1.109	.6474
Fluphenazine	1.682	.0072
Fluphenazine (decanoate injectable)	2.724	.0053
Lithium	1.367	.1093
Perphenazine	1.037	.8770
Thioridazine	1.167	.3435
Thiothixene	1.031	.8739
Trifluoperazine	1.179	.4424
Second generation antipsychotics	0.799	.6011
Other antipsychotic medications	2.413	.0301

<sup>a</sup>Association of predicted probabilities and observed responses: Concordant = 67.5%; Discordant = 32.1%; Tied = 0.4%; (595,350 pairs); Somers' D = 0.354; Gamma = 0.355; Tau-a = 0.176; c = 0.677.

The intent-to-treat results from the model of switching behavior also indicate that several drugs were associated with an increased risk of medication changes relative to haloperidol when used as initial therapy, including fluphenazine (OR = 1.68, p = .0072), long-acting fluphenazine (OR = 2.72, p = .0053), and the residual category of other conventional antipsychotics (OR = 2.41, p = .0301). Initial therapy with a second generation antipsychotic was estimated to reduce the likelihood of switching or augmentation, but the estimated effect was not statistically significant. The number of patients who used a second generation antipsychotic medication as their initial Medi-Cal-covered medication was very limited, due to the small number of second generation antipsychotics (clozapine and risperidone) available during the study period and the restrictions placed on these medications that limited their use to refractory patients.

## **DISCUSSION**

This study documents the antipsychotic drug use patterns associated with patients treated with conventional antipsychotic medications. These drugs were used as initial therapy by over 97% of all patients studied. The results of this study suggest that the conventional antipsychotic medications used to treat schizophrenic patients in the outpatient setting are not meeting the therapeutic needs of this population. First, over 24% of patients in this sample of schizophrenic patients did not use any antipsychotic medication for at least 1 year. In addition, 24% of treated patients started or restarted antipsychotic drug therapy at some point during the first year. Both results suggest that

schizophrenic patients commonly take extended "drug holidays" when treated in the outpatient setting. Second, nearly half of the patients treated without apparent delays in therapy switch antipsychotic medications or augment their initial therapy within 1 year. Finally, under 12% of treated patients achieved 1 year of uninterrupted drug therapy, and the mean duration of therapy for all treated patients was 142 days.

Each of these patterns of suboptimal antipsychotic drug use are consistent with clinical studies that have documented the difficulties patients with schizophrenia have experienced when treated with conventional antipsychotic medications. These difficulties include suboptimal dosing, significant side effect profiles, and limited efficacy. Therefore, taken as a whole, there appears to be a significant therapeutic need for new antipsychotic therapies to treat patients with schizophrenia.

Data from the randomized clinical trials of the second generation antipsychotic medications suggest that this new class of antipsychotic medications may improve patient outcomes and reduce costs across a broad population of schizophrenic patients. Second generation antipsychotic agents have been associated with superior treatment response rates<sup>7,9,22</sup>; superior control of the positive symptoms of schizophrenia<sup>9,22</sup>; superior efficacy for disabling negative symptoms such as restricted affect, avolition, and alogia<sup>23,24</sup>; reduced incidence of serious adverse events such as prominent extrapyramidal symptoms, acute dystonia, pseudoparkinsonism, akathisia, and tardive dyskinesia<sup>9,23,25</sup>; and improved maintenance therapy.<sup>26</sup> These symptomatic relief and safety advantages may also improve the patient's quality of life and community functioning while reducing the need for hospitalization or other costly treatments.<sup>11</sup> Evidence from early cost-effectiveness studies of these second generation antipsychotic agents shows promise. 13,27

More research is needed before a clear picture of the effectiveness of second generation antipsychotic medications in improving drug treatment patterns can be determined. An important component of this research will be the study of outcomes achieved using alternative conventional and second generation antipsychotic medications in real-world clinical practice settings. The results presented here provide a baseline for the performance of the older antipsychotics that can be used in future research comparing the performance of conventional and second generation antipsychotic medications. Specifically, nearly all state Medicaid programs have elected to make the second generation antipsychotics available to their covered populations without restrictions. The Medi-Cal program removed its formulary restrictions on the second generation antipsychotics in October 1997. These agencies have made a significant financial commitment in covering these medications. Therefore, it is likely that these agencies will require data that assess the extent to which improved rates of long-term antipsychotic drug use are achieved. Furthermore, this assessment should also determine if any offsetting reductions in total direct costs have been achieved in patients treated with the second generation antipsychotics. Paid claims data for these patients will be available in the future to investigate the effects of these medications relative to conventional antipsychotic drugs.

*Drug names:* chlorpromazine (Thorazine and others), clozapine (Clozaril), disulfiram (Antabuse), fluphenazine (Prolixin and others), haloperidol (Haldol and others), olanzapine (Zyprexa), perphenazine (Trilafon), quetiapine (Seroquel), risperidone (Risperdal), thioridazine (Mellaril and others), thiothixene (Navane), trifluoperazine (Stelazine).

Disclosure of off-label usage: The authors of this article have determined that, to the best of their clinical estimation, no investigational information about pharmaceutical agents has been presented herein that is outside Food and Drug Administration—approved labeling.

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