Open Access to Innovative Drugs: Treatment Substitutions or Treatment Expansion?

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Granting open access to new antipsychotic medications by the California Medicaid Program fostered the desired substitution of second-generation medications for conventional antipsychotics. However, open access also generated an immediate but temporary influx of previously treated patients, many with a recent institutionalization, who restarted drug therapy using the new antipsychotics.Persistence with initial therapy declined, but cost outcomes improved due primarily to reduced nursing home use. Racial disparities were also reversed. Program administrators must use caution when evaluating the impact of unrestricted access on drug therapy outcomes and treatment costs given the changes in the characteristics of patients seeking treatment.

INTRODUCTION

Many health plans and State Medicaid Programs use preferred drug lists and prior authorization to restrict the use of newer, more expensive medications within a given therapeutic class. Formulary restrictions are particularly common for new subclasses of medications immediately after their approval by the FDA as it is not yet clear how well these newer medications will work as substitutes for older drugs in real-world clinical practice. It is also common for health plans and Medicaid Programs to modify or drop prior authorization restrictions over time if evidence mounts documenting the advantages of substituting newer products for older drugs.

Removing formulary restrictions on new medications (open access) may produce two very distinct changes in treatment patterns for chronic disorders. Open access is intended to facilitate the substitution of innovative drugs for conventional medications among the population of patients who would normally use drug therapy under prior authorization restrictions, either as their initial drug therapy or as replacement therapy for an active drug regimen using older medications (substitution effects). However, open access may also alter physician/patient decisions about if and when to initiate treatment if these medications are considered to be safer and/or better tolerated than older products. These access effects may be most pronounced for three distinct patient groups. For novice patients, access to new medications with better safety profiles may induce physicians to initiate therapy for less severely ill patients. For example, a long-term change in the clinical threshold for drug therapy was observed in the California Medicaid (Medi-Cal) Program when it dropped restrictions on the use of Selective Serotonin Reuptake Inhibitor (SSRI) antidepressants in May 1996 (McCombs et al., 2003).

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Open access may also induce treatment refractory patients and patients who were sensitive to the older medications' side effects to restart drug therapy using the innovative medications. Similarly, patients currently using conventional medications may add a new drug to their current drug regimens (augmenting) once open access is granted. If these access effects do exist, then patients restarting or augmenting therapy under open access may do so without experiencing the usual acute exacerbations of symptoms that typically preceded restarting or changing therapy under closed access. Moreover, the surge in use from these forms of the access effect may be a relatively short lived once the pent-up demand for new treatment options is satisfied.

In October 1997, Medi-Cal granted open access to three second-generation antipsychotic medications: risperidone, olanzapine, and quetiapine. Prior to this date, the use of a second-generation antipsychotic medication required prior authorization verifying that the patient had failed therapy using two conventional medications, such as haloperidol, perphenazine, thioridazine, or chlorpromazine. Both substitution and access effects could significantly influence how this open access policy affected patient outcomes and the cost of treating severe mental disorders. Substitution of newer antipsychotic medications for older medications is expected to improve average patient outcomes. However, the impacts of access effects on patient characteristics, and therefore on average outcomes, are difficult to predict. For example, if less severely ill patients were treated with antipsychotics under open access or the use of antipsychotics was expanded to other disease states (e.g., bipolar disorders), then average duration of therapy may be reduced. If treatment refractory patients returned to restart therapy, then both average duration of therapy and treatment costs could fall if a few high-cost, refractory patients benefit from the newer medications. All three access effects could significantly alter the characteristics of the patients receiving drug therapy in the open access period relative to patients treated previously. Such changes in the characteristics of the patient population will significantly compromise attempts to measure the impact of open access on patient outcomes using simple before versus after comparisons.

OBJECTIVE

The primary objective of this article was to document whether or not granting open access to a new therapeutic class of medications improved persistency of antipsychotic use or reduced future health care costs. Special attention was paid to documenting if an access effect was created by this formulary expansion, whether such an effect was permanent or temporary, the extent to which the characteristics of the patient population changed with open access and the impact of these changes on patient compliance and treatment costs.

BACKGROUND

The addition of the second-generation antipsychotics to the Medi-Cal formulary may generate a significant substitution effect, especially in the treatment of schizophrenia. The superior side effect and clinical profiles of the various second-generation antipsychotics are clearly documented (Citrome and Volavka, 2002; Worrel et al., 2000). Published treatment guidelines also list atypical antipsychotics as a first-line treatment for schizophrenia, rather than limiting their use to patients who have failed therapy using typical antipsychotics (Lehman et al., 1998).

Moreover, substitution effects may not be uniform across all patient groups. Prior to the formulary change, Medi-Cal officials expressed concern about the under-use of newer antipsychotics in minority populations. Differences in rates of psychotropic drug metabolism across racial groups suggested that many minorities were at increased risk for serious side effects with the conventional antipsychotics (Lawson, 2000). This may create a greater potential value of the second-generation antipsychotics among certain minorities.

Evidence of dysfunctional use patterns such as delay, early cessation, or switching of therapy with conventional antipsychotics provides a compelling argument that open access will also result in significant access effects. McCombs and colleagues (1999) found that over 24 percent of Medi-Cal patients with schizophrenia did not use any antipsychotic medication for over 1 year after the patient's initial recorded diagnosis, and 24 percent of treated patients delayed initiating therapy for over 30 days. For those patients with no delay in therapy, 47 percent changed or augmented their initial antipsychotic therapy within 1 year. Only 11.6 percent of patients maintained continuous use for 1 year. At 2 years, over 16 percent of patients continued in an untreated status, 56 percent of treated patients changed therapies, and the 2-year continuous therapy rate was 3.2 percent (McCombs et al., 2000a). These results suggest that a large pool of previously treated patients exists who may restart drug therapy under open access.

Data from these earlier studies also suggest that an earlier return to therapy could significantly reduce the amount of health care use that often precedes patients' restarting or switching therapies. McCombs et al. (2000b) estimated that patients who delayed antipsychotic therapy were associated with increased health care costs of $9,418 over the first treatment year, primarily due to $5,210 in incremental expenditures for acute hospital care. Switching or augmentation of the patient's initial antipsychotic therapy was also associated with significantly higher health care costs over 1 year (+$9,719) due primarily to higher costs for acute hospital care (+$3,050) and nursing home care (+$4,022). McCombs et al., (2000a) documented that the costs associated with these dysfunctional drug use patterns continued to increase into the second treatment year. Delays in drug therapy were associated with an increase in post-treatment costs of $12,285 over the 2 years after the initial diagnosis, while switches in therapy were associated with an increase in total cost of $17,644 over 2 years. In this latter study, the total costs for patients receiving medication immediately after diagnosis were $10,833 lower than the total costs for patients who received no medication after diagnosis.

The frequency and cost of dysfunctional patterns of drug use associated with conventional antipsychotic medications have been confirmed in other studies that also found frequent gaps in conventional antipsychotic medication therapy among patients with schizophrenia (McGlashan, 1998; Mojtabai et al., 2003). Using data from four other State Medicaid Programs, Lyu and colleagues (2001) found 24 percent of ambulatory patients with schizophrenia did not use any drug therapy for the first treatment year, 18 percent of treated patients delayed therapy, and 41 percent switched therapies. Continuous therapy over 1 year was achieved by only 18 percent of patients. Treated patients were found to be significantly less costly than patients not on antipsychotic therapy (-$3,200), while delays in therapy and changes in therapy were estimated to increase cost in the first treatment year by $3,936 and $4,019, respectively. As in

Medi-Cal, most of the increased costs associated with dysfunctional treatment patterns were for hospital and nursing home care. Recent studies indicate that some of the newer antipsychotics are associated with improved medication persistence and other use patterns (Mojtabai et al., 2003; Opolka et al., 2003).

ANALYTIC METHODS

Data

Paid claims data from Medi-Cal's FFS system were retrieved for the period January 1994 to August 2000 for use in this analysis. Although patients with severe mental illnesses were not eligible for enrollment in Medi-Cal's managed care plans, a few newly diagnosed patients may have been treated initially within the managed care setting. The paid claims data include type of service, provider type, physician specialty, date of service, amount paid, and units of service. For institutional services provided by hospitals and nursing homes, the unit of service is 1 patient day. Paid claims data also include data on patient age, sex, type of Medi-Cal eligibility, race, and county of residence. Census data from 1990 were used to assign counties to rural, mixed, and urban categories based on population density (<25 percent urban; 25-90 percent urban and >90 percent urban, respectively). Diagnostic data (ICD-9-CM) may be recorded on the paid claim (Centers for Disease Control and Prevention, 2003) but is not required for payment, resulting in significant underreporting.

Many Medi-Cal patients with severe mental disorders are dually eligible for both Medicare and Medicaid coverage, with Medicare assuming fiscal responsibility as first payer. A method of adjustment for missing Medicare ambulatory service (Part B) payment data has been employed by the authors in previous Medicaid-based analyses and are reported elsewhere (Lyu et al., 2001; McCombs et al., 2003; 1999; 2000a; 2000b). In brief, this methodology calculates the total amount paid by Medi-Cal for Medicare covered services consumed by dually eligible patients over an extended period of time (6 months and 1 year) and subtracts off the Medicare deductible. If the resulting cost is positive, then this amount is multiplied by a factor of 5 to reflect the 20 percent Medicare coinsurance rate and the deductible payment is re-added. Actual payment amounts are used for Medi-Cal only patients and for dually eligible patients for whom total payments did not exceed the deductible.

The total cost for institutional care was estimated using per diem cost estimates and reported days of service. Hospital days were assigned a cost of $1,032 (California Medical Assistance Program, 1998) while nursing home costs per day were valued at $270 (Health Care Financing Administration, 1996). To avoid potential problems of differential costing methods being applied to dually eligible and Medi-Cal only populations, the per diem pricing method was applied to all patients.

The methods used to impute missing Medicare payments for dually eligible Medi-Cal patients do introduce important limitations for this study. Specifically, the average cost of treating Medi-Cal patients with severe mental disorders reported in this article do not reflect actual Medi-Cal and Medicare payments. Moreover, it is difficult to predict whether the amounts reported over- or understate actual payment. However, the focus of this study is to estimate the extent to which open access changed treatment costs over time. While the magnitude of estimated impact of open access must be viewed with some caution, the direction and statistical significance of

the estimated effects should be largely independent of the specific imputation methods used.

Data for prescription drug claims include quantity dispensed, days supply, payment amount, and the FDA-issued National Drug Code (NDC) for each medication used by the patient. The NDCs for antipsychotic medications were used to create a variable for medication strength, in milligrams per unit (www.fda.gov/cder/ndc/database).

Prescription drug payment claims were not filed for medications used by Medicare and/or Medi-Cal only patients while hospitalized, or for dually eligible patients covered under Medicare Part A for institutionalization in a SNF subsequent to a hospitalization. Therefore, this analysis cannot document the extent to which open access in the ambulatory Medi-Cal program affected the use of second-generation antipsychotics in hospitals or Medicare SNFs. However, this analysis does capture the extent to which institutionalized patients use these medications on discharge. Anecdotal information suggests that closed access discouraged community-based physicians from prescribing second-generation antipsychotics for newly discharged patients, regardless of the drug regimens used in the inpatient setting. Moreover, previously treated patients may elect not to use older medications once discharged based on previous treatment experiences. If this is true, then open access may increase the overall proportion of patients restarting antipsychotic drug therapy who have a recent history of institutionalization. Specifically, under open access, second-generation antipsychotics may be substituted for conventional antipsychotics prescribed by the community-based physician, but left unfilled by the patient.

A primary mental health diagnosis was assigned to each episode of care based on a hierarchical ranking of the patient's mental health diagnoses reported during the 6 months immediately prior to starting an episode of antipsychotic drug therapy (pre-index period). The hierarchical order of the diagnoses was determined based on the extent to which antipsychotic medications played a primary role in treating each disease state. A patient was coded as having primary mental health diagnosis of schizophrenia if an ICD-9-CM diagnostic code of 295.00-295.99 appeared at any time during the 6-month pre-index period, regardless of the presence of other mental health diagnoses. Other diagnoses were assigned based on the importance of antipsychotic medications in treating each disorder. In order, these diagnoses are non-schizophrenic psychosis (291.00-294.99), bipolar disorder (296.00-296.19, 296.40-296.89), depression (296.20-296.39, 300.40-300.49), other affective disorders (296.90-296.00), anxiety (297.00-297.99, 300.00-300.99), substance abuse (303.00-305.99), personality disorder (301.00-301.99), dementia (290.00-290.99), other mental health diagnoses (299.00-299.99, 302.00-302.99, 306.00-314.99, 316.00-316.99). A patient was recorded as not having a mental health diagnosis if none of the previous ICD-9-CM codes were recorded in the pre-index period.

EPISODES OF CARE

An access effect may both increase the number and change the characteristics of patients initiating treatment after October 1997. In order to evaluate these changes, episodes of drug therapy were specified as the unit of observation for this analysis. The start of an episode of care was defined

as a patient's beginning treatment with a different medication or restarting a medication used previously after a break in drug therapy in excess of 15 days. This definition of a break in therapy is consistent with previous research (Lyu et al., 2001; McCombs et al., 2003; 1999; 2000a; 2000b) and reflects the fact that the majority of Medi-Cal prescriptions report days supply of approximately 30 days.

Three different types of episodes of care were identified. Episodes initiated following a break in excess of 15 days from a previous episode were classified as restarts. Episodes were classified as switching or augmentation if the patient changed or added a second medication without a 15-day break in therapy. Switchers' and augmenters, constitute only 11 percent of all episodes which limits the usefulness of conducting separate analyses for these episode types. Finally, each patient's first episode in the data set was classified as first use, although many patients almost certainly had used antipsychotic medications before entering this study's data period or prior to qualifying for Medi-Cal coverage. As a result, first use should be interpreted as a mix of treatment naïve patients and treatment restarters.

Three time periods were defined for each episode: the month in which the episode was initiated (index month), 6 months prior to the index month (pre-index period), and 12 months after the index month (post-index period). Episodes of drug therapy were excluded from the analysis if less than 6 months of prior use data or 12 months of post-index data were available. No other exclusion criteria were applied. In particular, the analysis did not trim outlier episodes based on cost as these more severely ill and costly patients may constitute the highest risk patients for whom the new medications may be most cost effective. The final data set consisted of 216,017 episodes of antipsychotic drug therapy of which 105,685 were first use, 86,178 were restarts, and 24,154 were switching/augmentation.

Open and Closed Access Time Periods

Open access to second-generation antipsychotic medications was granted as of October 1, 1997. Episodes were grouped into three access-related time periods according to the month in which the episode was initiated. The closed-access period covers episodes of drug therapy initiated between January 1994 and September 30, 1997. A 6-month transition period is defined from October 1, 1997-March 30, 1998, to account for temporary access effects that follow. Specifically, it appears that the total number of episodes of care initiated per month increased dramatically starting in October 1997, but returned to normal levels after 6 months. The open-access period is specified as May 1, 1998-April 30, 1999, and is thought to represent a steady-state in which the transition to second-generation antipsychotics from typical antipsychotics has been completed.

STATISTICAL METHODS

Initiation of Episodes

A simple time-series of the number of episodes of care initiated per month by type of episode (first use, restart, switch/augment) was created to document whether or not open access increased the incidence of episodes of drug therapy immediately after October 1997. A second time-series was generated comparing conventional antipsychotics to the second-generation drugs, as the access effect should be limited

to second-generation antipsychotic medications. Conversely, substitution effects should reduce the use of conventional antipsychotics in the open-access period. These time series are presented graphically.

Changes in Patient Characteristics

A wide range of data describing the characteristics of patients initiating drug therapy were compared across the closed, transition, and open access periods. These characteristics include age, sex, urban or rural county of residence, primary diagnosis, aid category, race, type of episode initiated, type of antipsychotic used as initial therapy, and the prior use of health services by type of service. Simple univariate statistical tests were used to compare patient characteristics across three access time periods: chi-square tests for categorical data (i.e., race) and ANOVA for continuous data, such as prior use of services in dollars.

Health Care Costs and Drug Therapy Outcomes

Medi-Cal administrators require information on whether or not the investment in second-generation antipsychotic medications generated better use patterns, and reductions in the cost of other services. Health care costs by type of service were calculated over the 6 months prior to the index month, during the index month, and over the 1-year post-treatment period. Duration of use was calculated for each antipsychotic medication used during the treatment episode. The count of days of therapy was based on the sum of the days between prescription fill dates so long as each period between prescriptions did not exceed the reported days supply by more than 15 days. Total days of therapy across all antipsychotics used by the patient were also calculated so long as any subsequent antipsychotic was filled before 15 days had lapsed from the termination of the previous prescription. Dichotomous variables were also defined if the patient used a second antipsychotic medication (switching or augmentation) during the 1 year post-index period. These health care cost and drug use outcome variables were compared across the three access periods using ANOVA and chi-square statistical tests. All database manipulations and statistical tests were conducted using SAS®, version 8.2.

RESULTS

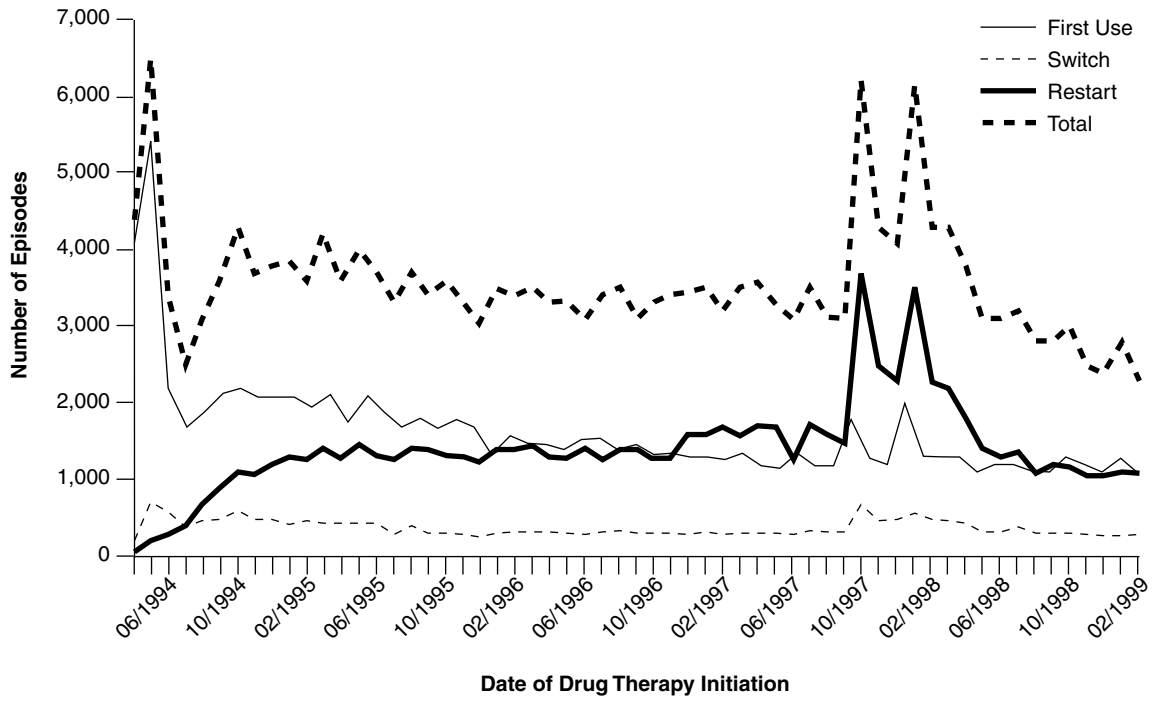
Initiation of Episodes

Figure 1 displays the time trend of episode initiation by type of episode. A clear increase in the number of episodes initiated per month appears in October 1997, the first month of the transition period under open access. This increase is consistent with the access effect hypothesis, as the total number of episodes would not have increased simply due to substitutions across alternative medications. Moreover, for patients restarting therapy, the access effect appears to be only temporary as the rate of restart episodes actually drops below levels experienced in the closed access period. The access effects for new patients and patients who switched or augmented their antipsychotic drug therapy returned to closed-access levels within 6 months.

Figure 2 presents time trend data for olanzapine, risperidone, quetiapine, and typical antipsychotic medications. Open access resulted in an immediate increase in the use of olanzapine and risperidone, while quetiapine's availability coincided with the Medi-Cal formulary expansion and its use grew steadily thereafter. Use of

Figure 1

Episodes of Antipsychotic Drug Therapy Initiated per Month by Episode Type: First Use, Switch, Restart



SOURCES: McCombs, J.S., University of Southern California, Mulani, P., Abbott Laboratories, and Gibson, P.J., Eli Lily and Company, 2003.

typical antipsychotics dropped significantly, but not enough to offset the increased use of second-generation antipsychotics. Specifically, episode starts per month for typical antipsychotics dropped by 639 (-26 percent) in the transition period, and by 1,388 (-57 percent) under open access. Episode starts per month for the second-generation antipsychotics increased by 2,214 (+237 percent) in the 6-month transition period, but fell back to an increase of 876 (+94 percent) under open access. Thus in the long term, the monthly incidence of treatment initiation decreased by 512 (-15 percent) under open access relative to closed access. This result may simply reflect the selection criteria for the study that required a minimum of 12 months of post-treatment data, a criteria that is less likely to be confirmed as the end of the data period approaches.

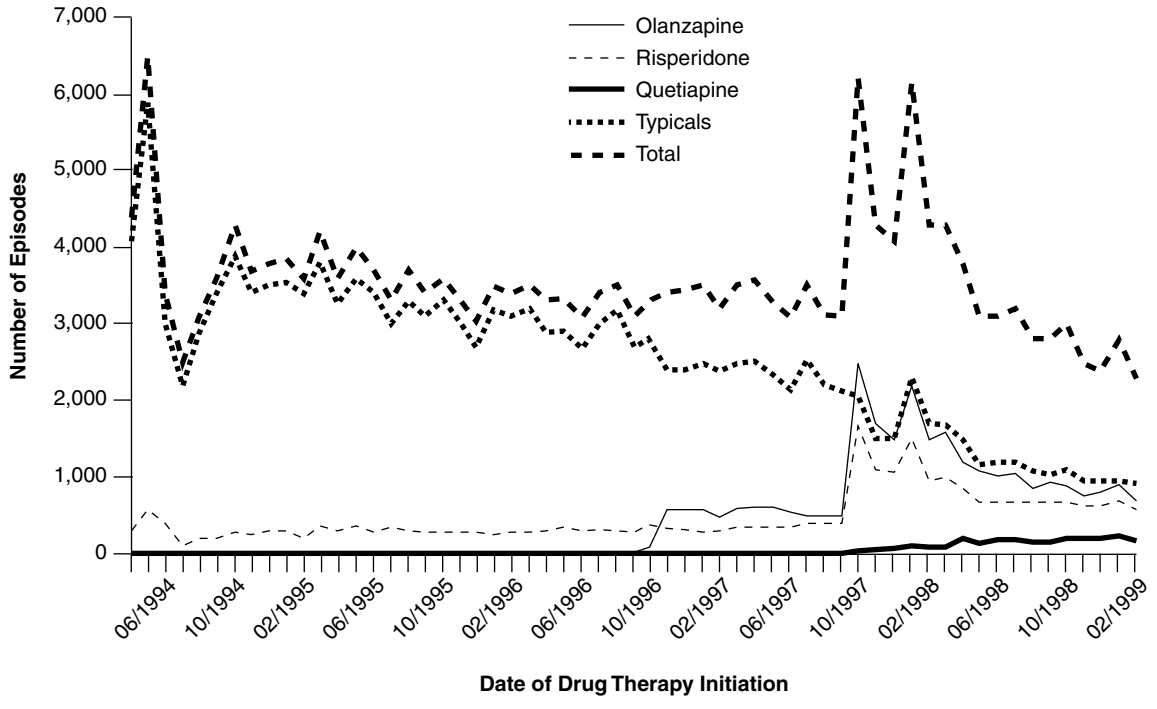
Changes in Patient Characteristics

Tables 1-3 present data documenting the changes over time in the baseline characteristics of patients as the started or restarted episodes of antipsychotic treatment or made a change to an active antipsychotic drug regimen. Open access resulted in a very rapid uptake of second-generation antipsychotics after October 1997 as typical antipsychotic use dropped from 85.9 percent of all closed-access episodes to only 36.6 percent in the open-access period. Olanzapine became the most frequently used second-generation antipsychotic used under open access, though quetiapine appears to be growing in use at the expense of olanzapine.

Changes over time in the mix of episode types are consistent with both temporary and permanent access effects. Under

Figure 2

Episodes of Antipsychotic Drug Therapy Initiated per Month by Type of Drug Used as Initial Therapy



SOURCES: McCombs, J.S., University of Southern California, Mulani, P., Abbott Laboratories, and Gibson, P.J., Eli Lily and Company, 2003.

closed access, first use episodes represented just over one-half of all episodes of treatment (52.6 percent), followed by restart episodes (36.3 percent) and switching/ augmentation episodes (11.1 percent). During the transition period, restart episodes grew to nearly 55 percent of all episodes, but then subsided to a level approaching that documented in the closed access period (41.7 versus 36.3 percent). This is consistent with the hypothesized temporary access effect that suggested that persons dissatisfied with previously available treatment would re-enter the system to try the innovative therapy. The average time off therapy for patients restarting therapy increased significantly in the transition period (from 270 days under closed access to 644 days), then dropped back again under open access to an average of 388 days. Conversely, first-use episodes declined as a proportion of all episodes in the transition period, then rebounded to a level in the open access period (47 percent) that approached the proportion of first-use episodes under closed access (52.7 percent).

In the closed access period, schizophrenia was the most common diagnosis among patients with a mental health related diagnosis (46.4 percent), followed by depression (14.3 percent), non-schizophrenic psychoses (11.5 percent), anxiety (8.7 percent) and bipolar disorders (6.2 percent). In the open-access period, a schizophrenia diagnosis was recorded for only 31.6 percent of all episodes with a mental disorder diagnosis. Diagnoses for non-schizophrenic psychoses (16.2 percent), anxiety (10.1 percent), bipolar disorder (9.6 percent), substance abuse (3.8 percent), dementia (2.4 percent) and other mental disorders (14.2

Table 1

Patient Treatment Episode Characteristics, by Formulary Access Period: All Patients

Variable	Closed Access January 1994-September 1997 (*N*=152,013)	Transition October 1997-March 1998 (*N*=33,314)	Open Access April 1998-April 1999 (*N*=30,690)
Initial Medication Used			
Typical Antipsychotic	130,596 (85.9)	12,238 (36.7)	11,241 (36.6)
Olanzapine	6,793 (4.5)	12,296 (36.9)	9,674 (31.5)
Risperidone	14,614 (9.6)	8,134 (24.4)	7,652 (24.9)
Quetipine	0 (0)	646 (1.9)	2,123 (6.9)
Episode Type			
First Use	80,043 (52.7)	11,254 (33.8)	14,388 (46.9)
Restart	55,131 (36.2)	18,237 (54.7)	12,810 (41.7)
Switch or Augmentation	16,839 (11.1)	3,823 (11.5)	3,492 (11.4)
Number of Days Between Episodes[1]	270	644	388
		Percent	
No Mental Health Diagnosis	34.8	39.8	51.7
Mental Health Diagnoses Among Those With Any Mental Health Diagnosis			
Schizophrenia	46.4	44.5	31.6
Non-Schizophrenic Psychosis	11.5	12.9	16.2
Bipolar	6.2	8.0	9.6
Depression	14.3	14.0	11.9
Other Affective	0.2	0.2	0.3
Anxiety	8.7	6.4	10.1
Substance Abuse	1.9	1.9	3.8
Personality Disorder	0.4	0.4	0.4
Dementia	1.2	1.8	2.4
Other Mental Health Diagnosis	9.2	9.8	14.2

[1] All comparisons of patient characteristics across formulary access periods are statistically significant at $p<0.001$.

NOTE: Numbers shown in parentheses are percentages.

SOURCES: McCombs, J.S., University of Southern California, Mulani, P., Abbott Laboratories, and Gibson, P.J., Eli Lily and Company, 2003.

percent) also increased in the open access period. The likelihood that a patient would start antipsychotic drug therapy without any mental health diagnosis recorded in the prior 6 months increased from 34.8 percent under closed access to 51.7 percent under open access.

Patient demographic characteristics are presented in Table 2. Average age increased from 44.8 to 45.1 in the open-access period among patients with an episode of therapy. However, this modest increase in average age does not reflect the near doubling of patients under age 25 (7.7 to 12.4 percent) or the growth in the proportion of patients age 65 or over (15.7 to 18.4 percent) under open access. The proportion of the patient population classified as disabled decreased significantly from 68.3 to 55.7 percent, offset mostly by an increase in TANF-eligible patients from 22.4 to 32.2 percent. Hispanic patients increased from 6.4 to 7.2 percent of users of antipsychotic drugs, which was offset primarily by a reduction in the proportion of white patients from 48.4 to 46.6 percent. The proportion of black patients also dropped from 15.7 to 14.8 percent.

Table 3 presents data on the use and cost of health care services by type of service in the 6-month pre-index period and index month. For each access period, the prior use of health care services increased significantly in the transition period, primarily because of a significant increase in nursing home costs from $1,100 under closed-access period to $2,354 in the transition period. The proportion of patients with prior use of nursing home services increased from 2.97 to 5.88 percent in the transition period, then dropped to 4.84 percent under open access. Similar increases in nursing

Table 2

Patient Treatment Episode Characteristics, by Formulary Access Period: All Patients

Variable	Closed Access January 1994-September 1997 (*N*=152,013)	Transition October 1997-March 1998 (*N*=33,314)	Open Access April 1998-April 1999 (*N*=30,690)
Demographics		Percent	
Age[1]	44.8	44.6	45.1
< 25 Years	7.7	10.0	12.4
25-36 Years	20.9	19.0	18.5
36-55 Years	37.0	35.4	31.3
55-65 Years	18.7	20.3	19.4
>= 65 Years	15.7	15.3	18.4
Male	44.0	46.3	44.7
Aid			
Blind	0.8	0.7	0.6
Old Age Assistance	8.5	8.6	11.5
Disabled	68.3	66.3	55.7
TANF	22.4	24.4	32.2
Urban Residence	73.5	75.0	73.6
Rural Residence	1.8	1.9	2.2
Race			
White	48.4	49.0	46.6
Black	15.7	14.3	14.8
Hispanic	6.4	5.9	7.2
Other	29.5	30.8	31.4

[1] In years at episode start.

NOTE: All comparisons of patient characteristics across formulary access periods are statistically significant at $p<0.001$.

SOURCES: McCombs, J.S., University of Southern California, Mulani, P., Abbott Laboratories, and Gibson, P.J., Eli Lily and Company, 2003.

home costs and the likelihood of nursing home use are also evident in the month in which the episode of care was initiated.

Drug Therapy Outcomes

Average duration of uninterrupted therapy on the initial medication used by the patient was 69.1 days during the closed-access period (Table 4). Duration across all antipsychotics was 100.9 days. Only 6.51 percent of patients used their initial drug for more than 360 consecutive days. This result is consistent with previous results (Lehman and Steinwachs, 1998) that found an 11.3 percent 1-year compliance rate across all medications for Medi-Cal patients with schizophrenia. Days of continuous therapy and 1-year compliance increased significantly in the transition period, possibly due to the influx of patients restarting therapy, often from the nursing home environment. However, during the open-access period, duration of therapy falls below the average from the closed-access period, especially when measured across all medications (70.4 days open access versus 100.9 in the closed-access period).

The absolute cost statistics over time in Table 4 clearly suggests that open access increased post-treatment costs. Average total cost of the first post-index year increased from $10,114 per patient under closed access to $13,777 per patient in the transition period, then decreased to $12,886 in the open-access period. However, health care costs prior to treatment also increased over time, as indicated in Table 3. It is unclear whether or not the increase in absolute costs over time can be attributed to open access. Specifically, the majority of the observed increase in post-treatment costs under open access is due to a significant increase in average nursing home costs in the 12-month post-treatment period over time ($2,577; $5,034; and $4,152 for closed-, transition-, and open- access periods, respectively). Such increases are to be

Table 3

Health Care Use and Cost in the 6 Months Prior to Treatment Episode Initiation, by Formulary Access Period: All Patients

Variable	Closed Access January 1994-September 1997 (*N*=152,013)	Transition October 1997-March 1998 (*N*=33,314)	Open Access April 1998-April 1999 (*N*=30,690)
6-Month Pre-Index Cost			
Ambulatory Care	2,166	2,543	2,426
Drug	562	848	982
Acute Hospitalization (1=Yes)	(10.5)	(9.9)	(9.4)
Acute Hospital Services	273	154	138
Psychiatric Hospitalization (1=Yes)	(1.1)	(3.0)	(3.3)
Psychiatric Hospital Services	5	29	26
LTC (1=Yes)	(3.0)	(6.0)	(4.9)
Nursing Home	1,100	2,354	1,843
Psychologist	14	15	6
Home Health	27	50	59
Hospice	4	17	1
Other	81	77	114
Net[1]	3,670	5,240	4,613
Total	4,232	6,088	5,595
Index Month Cost			
Ambulatory Care[2]	569	535	559
Drug	180	348	371
Acute Hospitalization (1=Yes)	(2.7)	(2.0)	(2.1)
Acute Hospital Services	78	37	44
Psychiatric Hospitalization (1=Yes)	(0.40)	(1.1)	(1.1)
Psychiatric Hospital Services	3	9	8
LTC (1=Yes)	(2.7)	(5.2)	(4.3)
Nursing Home Costs	206	415	340
Psychologist	3	3	1
Home Health	6	7	11
Hospice	1	5	1
Other	19	16	25
Net[1]	855	1,026	987
Total	1,066	1,374	1,358

[1] All comparisons of health care use and cost across formulary access periods are statistically significant at $p<0.05$ unless otherwise indicated.

[2] Not statistically significant difference across formulary access periods.

NOTE: Numbers in parentheses are percentages.

SOURCES: McCombs, J.S., University of Southern California, Mulani, P., Abbott Laboratories, and Gibson, P.J., Eli Lily and Company, 2003.

expected given the influx of nursing home patients under open access and the likelihood that these patients would continue to use nursing home services in the future.

Simple methods were used to adjust post-treatment costs for changes in prior use, over time. The data in Table 4 are based on the ratio of average monthly costs in the 12-month post-treatment period (post cost/12) to the cost per month in the 6-month pre-treatment period (pre-cost/6). A ratio of 1.50 would indicate a 50-percent increase in monthly costs in the post-treatment period relative to the average monthly level of prior use. Similarly, a ratio of 0.50 represents a 50-percent decrease in costs in the post-treatment period.

On average, patients initiating treatment in the closed-access period experienced an increased total cost per month of 19.5 percent in the post-treatment period relative to the average monthly costs in the pre-treatment period. Costs net of drug costs increased 13.3 percent, while nursing home costs increased by 17.1 percent. Patients initiating treatment in the open access period experienced a smaller increase in net cost per month of 5 percent due primarily to a smaller increase in nursing home cost of 12.6 percent. These smaller increases in relative costs were offset by increases in drug costs, resulting in a 15.2-percent increase in total cost per month under open access, down from 19.5 percent under

Table 4

Health Care Use and Cost in the First Year Following Treatment Episode Initiation, by Formulary Access Period: All Patients

Variable	Closed Access January 1994-September 1997 (*N*=152,013)	Transition October 1997-March 1998 (*N*=33,314)	Open Access April 1998-April 1999 (*N*=30,690)
Drug Therapy Outcomes			
Total Days of Therapy on Initial Drug	69	99	62
Total Days of Therapy: All Drugs	101	122	70
1 Year of Uninterrupted Therapy	(6.5)	(9.2)	(2.4)
Health Care Costs			
Ambulatory Care	4,244	4,303	3,958
Drug	1,831	3,420	3,197
Acute Hospitalization (1=Yes)	(13.1)	(12.3)	(9.1)
Acute Hospital Services	1,153	568	694
Psychiatric Hospitalization (1=Yes)	(1.8)	(3.7)	(4.6)
Psychiatric Hospital Services	42	124	459
LTC (1=Yes)	(4.2)	(6.8)	(6.0)
Nursing Home Costs	2,577	5,034	4,152
Psychologist	28	10	3
Home Health	68	85	162
Hospice[1]	19	19	14
Other	182	203	248
Net Costs[2]	8,314	10,352	9,689
Total Costs (1 Year-Post)	10,114	13,777	12,886
Relative Change in Costs Per Month			
Nursing Home (LTC) Costs	(+17.1)	(+6.9)	(+12.6)
Net Costs[2]	(+13.3)	(-1.3)	(+5.0)
Total Costs	(+19.5)	(+13.1)	(+15.2)

[1] Not statistically significant difference across formulary access periods.

[2] Net cost = total cost – drug cost.

NOTE: Numbers in parentheses are percentages.

SOURCES: McCombs, J.S., University of Southern California, Mulani, P., Abbott Laboratories, and Gibson, P.J., Eli Lily and Company, 2003.

closed access. Therefore, the conclusions derived from the relative monthly cost data over time lead to the opposite conclusion from the comparison of unadjusted absolute cost over time. Specifically, open access appears to attenuate the observed increases post-treatment costs per month.

Further clarification of the association between open access and patient outcomes can be gained by focusing the analysis on more homogeneous subgroups of patients. To avoid the potentially confounding effects of differences in nursing home use, diagnoses, and episode type, we analyzed ambulatory patients who restart therapy and have a diagnosis of schizophrenia in the prior 6 months. The patient outcome data for this sub-group are provided in Table 5. It is not possible to calculate the relative reduction in nursing home costs as ambulatory patients were defined as those patients with no history of nursing home or hospice use prior to initiating therapy.

In general, the results from this more homogeneous subpopulation did not vary substantially from the general results. Duration of therapy and the likelihood that a patient would achieve 360 days of uninterrupted therapy on their initial medication increased from 79 days and 7.5 percent under closed access to 110 days and 12 percent during the transition period, but fell to 65.7 days and 2.2 percent in the open-access period. Absolute costs in the 12-month post-index period increased under open access, primarily due to higher drug costs.

The pattern of pre- to post-index month cost changes also parallels the full population results. Ambulatory patients with schizophrenia who restarted antipsychotic

Table 5

Health Care Use and Cost in First Year Following Treatment Episode Initiation, by Formulary Access Period: Ambulatory Restart Patients with Schizophrenia

Variable	Closed Access January 1994-September 1997 (*N*=24,614)	Transition October 1997-March 1998 (*N*=5,677)	Open Access April 1998-April 1999 (*N*=2,501)
Drug Therapy Outcomes			
Total Days of Therapy on Initial Drug	79	110	66
Total Days of Therapy: All Drugs	116	141	77
1 Year of Uninterrupted Therapy	(7.5)	(12.0)	(2.2)
Added Second Antipsychotic within 1 Year	(41.2)	(38.1)	(41.1)
Health Care Costs			
Ambulatory Care	9,815	10,478	11,865
Drug	2,908	4,672	4,361
Acute Hospitalization (1=Yes)	(22.3)	(18.0)	(17.6)
Acute Hospital Services	1,812	749	1,045
Psychiatric Hospitalization (1=Yes)	(0.40)	(1.0)	(1.2)
Psychiatric Hospital Services	38	101	654
LTC (1=Yes)[1]	(1.9)	(2.3)	(2.0)
Nursing Home Costs[1]	351	418	413
Psychologist	49	16	3
Home Health	48	92	82
Hospice	4	0	22
Other	168	227	293
Net Costs[2]	12,285	12,080	14,377
Total Costs (1-Year Post)	15,193	16,752	18,738
Gap in Claims, Prior 6 months	(14.9)	(19.2)	(7.0)
Gap in Claims, 1-Year Post	(78.7)	(76.1)	(40.0)
Relative Change in Costs per Month			
Nursing Home (LTC) Costs		Undefined	
Net Costs[2]	(-4.6)	(-15.2)	(-10.9)
Total Costs	(+3.2)	(+1.4)	(-0.1)

[1] Not statistically significant difference across formulary access periods.

[2] Net cost = total cost – drug cost.

NOTE: Numbers in parentheses are percentages.

SOURCES: McCombs, J.S., University of Southern California, Mulani, P., Abbott Laboratories, and Gibson, P.J., Eli Lily and Company, 2003.

drug therapy in the closed access period experienced an 3.2 percent increase in total cost per month from their pre- to post-index periods, as compared to a 19.5-percent increase for all patients. As before, much of this increase was for prescription drugs, as total other costs per month actually decreased –4.6 percent (+13.3 percent for all patients). The post-treatment cost profile for restart episodes were significantly better in the open-access period. Average net monthly post-index costs decreased 10.9 percent and were sufficient to offset increased drug costs, resulting monthly costs in the post-treatment period remaining virtually unchanged relative to the prior 6 months.

The data in Table 6 summarize patient outcomes for restart episodes by ambulatory patients with schizophrenia, broken down by time period and initial drug. Several results are of interest. First, all three second-generation antipsychotic medications exhibit notably longer duration of therapy than conventional antipsychotics. Second, all four classes of antipsychotic exhibit a decrease in average duration of therapy in the open-access period. This suggests that the decline in duration under open access is related primarily to changes in the characteristics of the patient population, rather than specific drug characteristics. Third, the change in the average costs in the post-treatment

Table 6

Summary of Drug Therapy Outcomes and Changes in Relative Costs per Month Over Time, by Initial Therapy: Ampulatory Restart Patients with Schizophrenia

Patient Outcomes	Closed Access January 1994-September 1997	Transition October 1997-March 1998	Open Access April 1998-April 1999	*p*-Value
Conventional Antipsychotics[1]	*N*=17,825	*N*=1,429	*N*=768	
Duration on Initial Prescription	72	82	51	0.0001
Duration: All Drugs	104	114	62	0.0001
1 Year of Uninterrupted Therapy	(5.6)	(6.2)	(1.04)	0.0001
Added Second Antipsychotic within 1 Year	(44.0)	(50.2)	(49.35)	0.0001
Percent Change in Net Costs[2]	(-2.6)	(-18.2)	(-8.2)	—
Percent Change in Total Costs	(+2.2)	(-6.9)	(-1.0)	—
Olanzapine[1]	*N*=2,843	*N*=2,869	*N*=886	
Duration on Initial Prescription	110	125	74	0.0001
Duration: All Drugs	168	154.4	83	0.0001
1 Year of Uninterrupted Therapy	(16.0)	(15.2)	(2.83)	0.0001
Added Second Antipsychotic within 1 Year	(29.0)	(30.4)	(32.96)	0.2822
Percent Change in Net Costs[2]	(-7.2)	(-15.1)	(-14.3)	—
Percent Change in Total Costs	(+17.9)	(+4.8)	(+1.5)	—
Risperidone[1]	*N*=3,946	*N*=1,157	*N*=514	
Duration on Initial Prescription	88	109	68	0.0001
Duration: All Drugs	134	146	84	0.0001
1 Year of Uninterrupted Therapy	(9.8)	(11.93)	(2.9)	0.0001
Added Second Antipsychotic within 1 Year	(37.6)	(42.52)	(42.0)	0.0018
Percent Change in Net Costs[2]	(-14.0)	(-8.8)	(-13.6)	—
Percent Change in Total Costs	(-0.1)	(+8.2)	(-3.5)	—
Quetiapine[1]	*N*=0	*N*=222	*N*=336	
Duration on Initial Prescription	—	105	72	0.0001
Duration: All Drugs	—	130	82	0.0001
1 Year of Uninterrupted Therapy	—	(9.46)	(1.80)	0.0001
Added Second Antipsychotic within 1 Year	—	(37.39)	(42.36)	0.4883
Percent Change in Net Costs[2]	—	(-25.2)	(+4.1)	—
Percent Change in Total Costs	—	(-7.9)	(+3.3)	—

[1] $p<0.0001$ for all comparisons of duration of initial therapy, completion rates and switch rates, across drugs within each of the three time periods.

[2] Net costs = total costs – drug cost.

NOTES: Numbers in parentheses are percentages. Quetiapine not available prior to October 1997.

SOURCES: McCombs, J.S., University of Southern California, Mulani, P., Abbott Laboratories, and Gibson, P.J., Eli Lily and Company, 2003.

year relative to the 6 pre-treatment months is smaller for olanzapine, risperidone, and the conventional antipsychotics under open access. The cause of this result is likely due to the changes in the characteristics of patients, especially in light of reduced duration of therapy.

Open access greatly expanded access to second generation antipsychotics for black patients, with smaller increases for other minorities, as indicated in Table 7. When they received antipsychotic medications under closed access, black patients were less likely than white patients to get second-generation antipsychotics (22 versus 30 percent). Under open access, this situation was reversed, with black patients being more likely than white patients to be prescribed second-generation antipsychotics (72.7 versus 67.7 percent). Other racial minorities saw similar changes, though the disparities versus white patients were not as great. Quetiapine, which only became available during this study's transition period, remained relatively more likely to be used among white patients during the open-access period (14.2 percent) versus 11.6 percent for black patients and 13.5 percent for other races.

DISCUSSION

This study traced the impact of providing open access to second-generation antipsychotic medications under the Medi-Cal

Table 7

Conventional Versus Second-Generation Antipsychotic Use Over Time, by Race: Ambulatory Restart Patients with Schizophrenia

Initial Drug Used	White	Black	Other
		Percent	
Closed Access Period[1]			
Conventional Antipsychotic	70.0	78.1	73.4
Second Generation Antipsychotic	30.0	21.9	26.6
Olanzapine	12.6	8.2	11.4
Risperidone	17.4	13.2	15.2
Quetiapine	N/A	N/A	N/A
Transition Period[2]			
Conventional Antipsychotic	24.0	27.7	25.6
Second Generation Antipsychotic	76.0	72.3	74.4
Olanzapine	51.1	48.0	51.0
Risperidone	20.3	21.5	20.0
Quetiapine	4.6	2.8	3.4
Open Access Period[3]			
Conventional Antipsychotic	32.3	27.3	30.3
Second Generation Antipsychotic	67.7	72.7	69.7
Olanzapine	33.9	37.5	36.2
Risperidone	19.6	23.6	20.0
Quetiapine	14.2	11.6	13.5

[1] January 1994-September 1997.

[2] October 1997-March 1998.

[3] April 1998-April 1999.

NOTES: $p<0.0001$ for the cross tabulations of race by drug in each of the three time periods. NA is not available.

SOURCES: McCombs, J.S., University of Southern California, Mulani, P., Abbott Laboratories, and Gibson, P.J., Eli Lily and Company, 2003.

formulary. This policy change triggered a rapid, but temporary influx of patients restarting antipsychotic therapy. This access effect is consistent with meeting pent-up demand for an alternative treatment to conventional antipsychotics. Several changes in the characteristics of the patient population are also consistent with the access effect hypothesis. First, the increase in the number of episodes initiated per month were patients restarting therapy. Moreover, the average gap between treatment episodes for ambulatory patients restarting antipsychotic therapy increased from 270 days under closed access to 644 days during the transition period, then dropped to 388 days average under open access. The increased time off therapy for patients restarting therapy may explain the drop in the proportion of patients with a schizophrenia diagnosis in the transition and open-access period. Specifically, the mental health status of these patients may have been relatively stable, resulting in a lower rate of use of services for which a mental heath diagnosis would be recorded. A second explanation of the observed change in diagnostic mix is that physicians may have been less likely to record the potentially stigmatizing diagnosis of schizophrenia under open access, as it was no longer required for access to second-generation antipsychotics.

The increased use of antipsychotic medications by patients in nursing homes is also consistent with the hypothesis of a temporary access effect. Open access made it easier to prescribe second-generation in the nursing home environment as prescription drugs used during nursing home days not covered by Medicare are paid for by Medi-Cal and recorded in the prescription paid claims file. Consulting pharmacists and physicians supervise nursing home care, increasing the likelihood that a patient with a history of responding

poorly to conventional antipsychotics would be restarted on antipsychotics soon after the second-generation medications were available. Nursing home patients may have been particularly sensitive to the side effects associated with conventional antipsychotic medications, thus increasing the demand for alternative medications disproportionately in the frail elderly.

Patients treated in psychiatric hospitals and psychiatric units of community hospitals frequently enjoyed open access to second-generation antipsychotics. However, to continue to use these medications on an outpatient basis required that their community-based physician obtain prior authorization. Anecdotal data suggest that prior authorization resulted in many physicians switching patients back onto older antipsychotics on discharge. As a result, patients often discontinued drug therapy after discharge based on their previous experience with these older medications. If this is true, open access may have made it easier for physicians and patients to continue the use of second-generation antipsychotics in the ambulatory setting, thus increasing the likelihood that patients treated under open access would have a history of prior institutionalizations.

The trends toward the increased use of the newer antipsychotic medications by nursing home patients and patients discharged after a psychiatric admission continued beyond the temporary transition period. The increased use of the newer medications by these high-risk patients represents the desired substitution effects envisioned by policymakers. More importantly, these substitution effects may have resulted in significant reductions in health care costs for patients initiating drug therapy in the open access period primarily due to reductions in nursing home use in the year following the initiation of the drug treatment episode.

The potential benefits from open access are not limited to patients with a history of institutionalization. The same pattern of results is found for the population of patients restarting therapy without any history of nursing home or hospice use in the 6 months prior to treatment (Table 5) that were found for the larger population (Table 4). It is also interesting to note that the pattern of smaller increases/larger reductions in cost per month in these ambulatory patients in the open-access period were independent of the medication used, including conventional antipsychotics (Table 6). This result is not necessarily inconsistent with the desired substitution effects of open access. Under open access, clinicians may have effectively matched medications to patients, using conventional medications for those patients who had a history of favorable treatment response.

A disappointing outcome under open access was that persistence with initial therapy among those using the newer antipsychotics was no better, and perhaps slightly worse, than persistence with initial therapy among those treated with conventional antipsychotics under closed access. Again, this may have been influenced by other changes in the population characteristics. It is also possible that open access made it easier to change drugs, thus reducing duration of therapy on the initial medication used in the treatment episode. The proportion of patients using a second antipsychotic within 1 year did increase significantly under open access across all medications (Table 6).

Limitations

Policymakers must be careful when they evaluate open-access policies to account for changes in the characteristics of patients being treated. In this case, these changes

confounded simple attempts to measure the impact of open access using average treatment costs or by comparing changes in relative costs over time. Future research will apply multivariate statistical modeling techniques to these data in an effort to generate more reliable estimates of the impact of open access on health care costs.

Data on the absolute level of health care costs reported here may be inaccurate as the methods used to estimate missing Medicare payments for patients dually eligible for Medicare and Medi-Cal can be questioned. For example, the per diem cost of $1,035 per day of hospital care may understate the true cost of a day of psychiatric hospital care and may not correspond well to the costs experienced in other State Medicaid Programs. However, the direction and statistical significance of any estimated impact of open access on health care costs are not affected significantly by these methodologies. A sensitivity analysis comparing patterns of health care costs over time for dually eligible and Medi-Cal-only patients found similar results across both groups (data not shown).

Medi-Cal depends heavily on nursing homes to provide institutional care for patients with severe mental illnesses. Other States may depend more heavily on State psychiatric hospitals or community-based services (Lyu et al., 2001). Even factors such as weather can limit the external validity of our results beyond California. For example, we observed a significant spike in the total number of episodes of drug therapy initiated in January 1998 that was observed across all drug types and across all types of episodes except switching/ augmentation (Figures 1 and 2). This may be explained by the El Nino rains experienced in California during January 1998 that likely force mentally ill homeless persons into shelters and back on drug therapy.

Future Research

Like most research, our results generate more questions than answers, particularly concerning the separate impacts of substitution and access effects. Additional research using multivariate statistical techniques is required to separate and quantify the effects of Medi-Cal's formulary expansion. This will not be a simple task given the significant temporary and permanent access effects generated by open access that are confounded with more permanent substitution effects across drugs. The potential overlap of episodes, and contribution of several episodes by one patient creates significant statistical challenges that must also be addressed in any complete analysis of the impact of open access on patient outcomes.

CONCLUSIONS

Providing unrestricted access to second-generation antipsychotics had a diverse and complicated impact on the Medi-Cal program. Two of the added medications quickly became the most expensive drugs covered by the Medi-Cal program in terms of total expenditures. Our data indicate that the average monthly cost of treating patients prescribed antipsychotics increased dramatically across all types of services. Worse yet, persistence on the initial medication used decreased under open access. Taken at face value, these unadjusted results could mislead Medi-Cal administrators to conclude that open access was a failure. However, a more careful analysis found that open access caused high-cost, previously treated patients to restart antipsychotic drug therapy using the newer products, especially patients who were institutionalized in a nursing home within the prior 6 months. Moreover, cost per month actually declined for patients

treated under open access whereas costs per month increased in the closed access period after treatment was initiated. Specifically, reductions in the future use of nursing home care and psychiatric hospitalizations were sufficient to offset the increased cost of the newer antipsychotics. More research is needed to verify the result reported here using methods that adjust for the difference in patient populations over time.

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