The Impact of the Clinical Antipsychotic Trials of Intervention Effectiveness (CATIE) on Prescribing Practices: An Analysis of Data From a Large Midwestern State

Rachel L. Berkowitz, MD; Urvashi Patel, PhD; Quanhong Ni, MS; Joseph J. Parks, MD; and John P. Docherty, MD

ABSTRACT

Background: The Clinical Antipsychotic Trials of Intervention Effectiveness (CATIE) was a series of effectiveness trials. The results of these trials began publication in September 2005. Among other findings, these studies were interpreted to suggest that (1) second-generation antipsychotics might have fewer advantages over first-generation antipsychotics than had been generally thought; (2) among the agents assessed, olanzapine had the best efficacy outcome; and (3) after treatment failure with a second-generation antipsychotic, the most efficacious second-line medication is clozapine. To examine the actual impact on practice of these publications, we looked at change in physician prescribing behavior based on these 3 conclusions before and after publication of CATIE.

Method: Rates of antipsychotic medication prescriptions to 51,459 patients with an *ICD-9* code of 295 for schizophrenia were extracted from a Missouri Medicaid claims database. χ^2 Tests were used to compare the rates of prescribing antipsychotic medications before and after each of 3 key CATIE publications (time 1 was September 2005, time 2 was December 2006, and time 3 was April 2006).

Results: At all time points, we demonstrated a decrease in prescriptions by all prescribers for olanzapine ($P < .0001$). One year after time 1, we found an increase in prescriptions by all prescribers for aripiprazole ($P < .0001$). No statistically significant increases in clozapine prescribing were observed. Also, a small but statistically significant increase was seen in prescriptions of perphenazine ($P < .02$ at time 3). However, this increase occurred only for prescriptions written by psychiatrists and not other prescribers.

Conclusions: We found some evidence in our sample that the publication of the results from CATIE had a small but statistically significant effect on prescribing habits of psychiatrists but not other physicians in our sample population. However, larger changes occurred in prescribing behavior that were largely unrelated to the CATIE trial. We propose a hypothesis to explain the direction of observed changes.

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Corresponding author: *Urvashi Patel, PhD, Outcomes Research Division, Care Management Technologies Inc, 1 Copley Pkwy, Ste 500, Morrisville, NC 27560 (urvashi76@aol.com).*

It is now recognized that clinically important research findings may take years to have any impact on clinical practice.[1–3] This delay of knowledge transfer has been recognized in multiple fields of medicine.[4] Furthermore, it is variable, and variability is dependent on multiple factors, including (1) difficulty of implementing change[5]; (2) divergent goals in industry and academic communities[6]; (3) barriers created by managed care practices[7]; (4) physician lack of confidence with new procedures; and (5) disagreement with research recommendations, poor awareness of new recommendations, and inertia of prior practice.[8]

Results from the Clinical Antipsychotic Trials of Intervention Effectiveness (CATIE) study began with a publication in the *New England Journal of Medicine* in September 2005.[9] The CATIE was designed as a multiphase effectiveness trial whose aim was to improve the use of antipsychotic medications in the treatment of schizophrenia. In the first phase of the study, CATIE compared the efficacy and tolerability of 4 second-generation antipsychotic (SGA) medications (olanzapine, risperidone, quetiapine, and ziprasidone) and 1 first-generation antipsychotic (FGA) medication (perphenazine). The main outcome measure was any-cause discontinuation. Phase 1 of the study found that patients with schizophrenia treated with olanzapine had a significantly longer number of months before medication discontinuation than patients on the other medications. However, the study also found that olanzapine had the highest rate of metabolic side effects of the drugs studied. Subsequent articles and commentaries suggest that CATIE failed to show any meaningful clinical advantage of the SGA medications over perphenazine and that FGA medications are more cost-effective.[10] This conclusion has been challenged.[11]

Published in April 2006, results from CATIE phase 2 demonstrated that, after initial treatment with an SGA medication failed for reasons of efficacy, a switch to clozapine would be more effective than a switch to another SGA medication (olanzapine, quetiapine, risperidone).[12]

The implications of CATIE for the treatment of patients with schizophrenia have been vigorously and widely discussed.[13–15] The fact that the studies were published in prestigious journals and have been widely discussed in the scientific literature, public policy forums, and press suggests that they should have some impact on clinical practice. One study,[16] however, has suggested that there is limited awareness among clinicians of the CATIE findings.

To further study the actual impact of CATIE, we analyzed Medicaid prescription and services data covering 1.4 million people. We sought to understand what impact the CATIE study has had on prescribing practices of clinicians treating outpatients

with schizophrenia. Specifically, we hypothesized that, if CATIE did impact prescribing practices, the following changes would occur:

1. An increase in prescriptions for olanzapine based on the initial September 2005 report.[9]
2. An increase in prescriptions for the FGA medication perphenazine based on the initial September 2005[9] report and the subsequent cost-effectiveness study published in December 2006.[10]
3. An increase in prescriptions for clozapine based on the April 2006 CATIE publication in which clozapine was reported to have a superior efficacy effect to olanzapine, quetiapine, and risperidone in patients who had discontinued initial treatment with one of these SGA medications due to lack of efficacy.[12]

Clinical Points

- The Clinical Antipsychotic Trials of Intervention Effectiveness (CATIE) study was intended to provide antipsychotic medication effectiveness data to help clinicians make evidence-based decisions.
- An analysis of a large Medicaid claims database suggests that CATIE publications have not yet had a major impact on prescribing to patients with schizophrenia.
- It is important to increase efforts to help clinicians access, understand, and translate into clinical practice the findings of well-designed clinical trials.

METHOD

Data were extracted from Missouri's fee-for-service Medicaid administrative claims database 1 year before and after the publication of each of the 3 CATIE articles. The administrative claims database consists of medical and pharmacy utilization and expense information for all adult and child recipients of fee-for-service Medicaid. The time points in the study were September 2005, April 2006, and December 2006 (Figure 1). The articles from September 2005 and December 2006 both concern perphenazine and olanzapine and are designated time point 1 and time point 2. April 2006, the date of publication of the article concerning clozapine, is designated as time point 3. Medicaid claims for patients with schizophrenia for risperidone, olanzapine, ziprasidone, quetiapine, aripiprazole (an SGA not included in the initial CATIE study because it was not yet approved by the US Food and Drug Administration [FDA]), perphenazine, and clozapine were examined between January 2004 and December 2009. Patients with schizoaffective disorder or schizophreniform disorder were excluded, as they were in CATIE. Injectable forms of these medications and combination products were excluded. The data were analyzed for all prescribers and repeated by separating those prescriptions written by psychiatrists and nonpsychiatrists.

We used χ^2 tests to compare separately the rates of prescribing each medication 1 year, 6 months, and 3 months before and after the 3 time points. Changes were considered statistically significant when $P < .05$. The more conservative significance level $P < .0001$ provides additional control for experiment-wide type I error given the large number of comparisons made in this study.

RESULTS

A total of 51,459 patients were identified with an *ICD-9* diagnosis code 295 for schizophrenic disorders. Of these patients, 30,219 were diagnosed with schizoaffective disorder (*ICD-9* code 295.7) or schizophreniform disorder (*ICD-9* code 295.4); 2,483 patients did not have any pharmacy claims between January 1, 2004, and December 31, 2009. Therefore, 18,757 patients with schizophrenia who had at least 1 pharmacy claim were included in the analysis.

Time 1: September 2005

Time 1 was September 2005, when published results from the first CATIE trial[9] reported that the FGA perphenazine, measured by time to all-cause discontinuation, had equivalent effectiveness as all included SGAs except olanzapine.

Prescriptions rates 1 year before time 1 versus 1 year after. The dataset before time 1 (September 2004 to August 2005) included 13,381 patients with a diagnosis of schizophrenia; the dataset after time 1 (September 2005 to August 2006) included 13,046 patients. As denoted in Table 1, results for all prescribers showed a significant decrease in prescriptions for olanzapine and risperidone; significant increases in prescriptions for aripiprazole; and no significant change in prescriptions for clozapine, quetiapine, ziprasidone, or perphenazine.

The number of patients receiving their prescriptions from psychiatrists was 6,816 before time 1 and 6,413 after time 1. We found a significant decrease in prescriptions for olanzapine; significant increases in aripiprazole and perphenazine; and no statistically significant change in risperidone, quetiapine, ziprasidone, or clozapine.

The number of patients receiving their prescriptions from nonpsychiatrists was 12,718 before time 1 and 12,252 afterward. We found significant decreases in prescriptions for olanzapine and risperidone; significant increases in aripiprazole; and no statistically significant change in quetiapine, ziprasidone, perphenazine, or clozapine.

Prescription rates 6 months before and 6 months after time 1. In the 6 months before and 6 months after time 1, the number of patients with schizophrenia was 12,465 and 12,044, respectively. Data from these time periods showed a significant ($P < .0001$) decrease in olanzapine; a significant ($P = .01$) increase in aripiprazole; and no significant changes in risperidone, quetiapine, ziprasidone, perphenazine, or clozapine.

In the 6 months before time 1, the number of patients with schizophrenia who received their medication from a psychiatrist was 5,853 and, in the 6 months after time 1, the number was 5,550. In this group receiving prescriptions from

Figure 1. The Clinical Antipsychotic Trials of Intervention Effectiveness (CATIE) Study Timeline

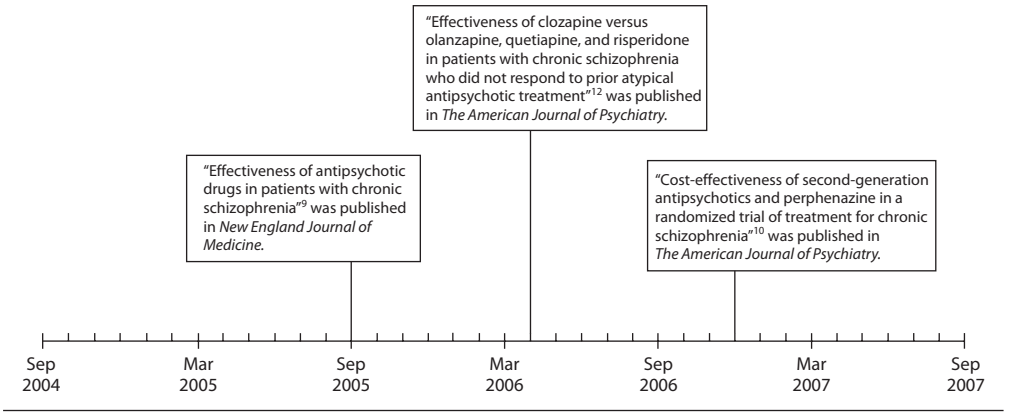

Table 1. Prescriptions 1 Year Before and 1 Year After September 2005 by Psychiatrists and Nonpsychiatrists

	All Prescribers			Psychiatrist			Nonpsychiatrist		
Drug	Before Sep 2005 (n = 13,381), Rx (%)	After Sep 2005 (n = 13,046), Rx (%)	*P* Value	Before Sep 2005 (n = 6,816), n Rx (%)	After Sep 2005 (n = 6,413), Rx (%)	*P* Value	Before Sep 2005 (n = 12,718), Rx (%)	After Sep 2005 (n = 12,252), Rx (%)	*P* Value
Olanzapine	2,507 (18.7)	1,947 (14.9)	< .0001	1,265 (18.6)	962 (15.0)	< .0001	1,700 (13.4)	1,237 (10.1)	< .0001
Quetiapine	2,519 (18.8)	2,392 (18.3)	.31	1,534 (22.5)	1,396 (21.8)	.31	1,575 (12.4)	1,430 (11.7)	.08
Aripiprazole	1,301 (9.7)	1,507 (11.6)	< .0001	896 (13.1)	1,007 (15.7)	< .0001	629 (4.9)	730 (6.0)	.0004
Ziprasidone	766 (5.7)	738 (5.7)	.81	504 (7.4)	417 (7.3)	.91	394 (3.1)	371 (3.0)	.75
Perphenazine	50 (0.4)	68 (0.5)	.07	23 (0.3)	47 (0.7)	.002	30 (0.2)	25 (0.2)	.59
Clozapine	338 (2.5)	345 (2.6)	.54	254 (3.7)	244 (3.8)	.81	163 (1.3)	154 (1.3)	.86
Risperidone	3,040 (22.7)	2,740 (21.0)	.0007	1,697 (24.9)	1,505 (23.4)	.06	1,900 (14.9)	1,652 (13.5)	.001

Abbreviation: Rx = number of prescriptions.

a psychiatrist, a significant ($P = .04$) decrease in olanzapine and significant ($P = .03$) increase in aripiprazole was observed in the 6 months after time 1 compared to the 6 months before time 1; no significant changes were seen in risperidone, quetiapine, ziprasidone, perphenazine, or clozapine.

The number of patients who received their prescriptions from nonpsychiatrists 6 months before time 1 was 11,618, and, afterward, the number was 11,173. In this group receiving prescriptions from a nonpsychiatrist, results showed a significant ($P = .0004$) decrease in olanzapine and no significant change in risperidone, clozapine, quetiapine, aripiprazole, perphenazine, or ziprasidone in the 6 months after time 1 compared to the 6 months before time 1.

Prescription rates 3 months before versus 3 months after time 1. Three months before time 1 (June 2005 to August 2005), 11,608 patients were diagnosed with schizophrenia. Three months after time 1 (September 2005 to November 2005) 11,348 patients were diagnosed. A significant ($P = .04$) decrease in prescriptions for olanzapine was observed. No changes were noted for risperidone, clozapine, quetiapine, aripiprazole, ziprasidone, or perphenazine in the 6 months after time 1 compared to the 6 months before time 1.

Three months before time 1, the number of patients with schizophrenia who received their prescriptions from a psychiatrist was 5,101. Three months after time 1, the number of patients who received their prescriptions from a psychiatrist was 4,998. In this group receiving prescriptions from a psychiatrist, there was no change in all 7 drugs from preperiod to postperiod.

Three months before time 1, the number of patients with schizophrenia who received their prescriptions from a nonpsychiatrist was 10,609, and, after time 1, the number was 10,351. In this group receiving prescriptions from a nonpsychiatrist, no statistically significant change was observed for any of the 7 drugs in the 3 months before compared to the 3 months after time 1.

Time 2: December 2006

Time 2 was December 2006, when a cost-benefit analysis[10] regarding CATIE was published. This article argued that, if perphenazine is the drug used to initiate a program of treatment in previously treated non–first-episode schizophrenic patients, the course of treatment is less costly and generally equivalent in effectiveness to SGAs.

Prescription rates 1 year before and 1 year after time 2. The dataset before time 2 (December 2005 to November 2006) included 12,835 patients with schizophrenia; the dataset after time 2 (December 2006 to November 2007) included 12,336 patients. For all prescribers, there were significant decreases in olanzapine, ziprasidone, and risperidone; no significant changes were seen in quetiapine, aripiprazole, perphenazine, or clozapine. Results are presented in Table 2.

Before time 2, the number of patients who received their prescriptions from psychiatrists was 6,152, and, after time 2,

Table 2. Prescriptions 1 Year Before and 1 Year After December 2006 by Psychiatrists and Nonpsychiatrists

	All Prescribers			Psychiatrist			Nonpsychiatrist		
Drug	Before Dec 2006 (n = 12,835), Rx (%)	After Dec 2006 (n = 12,336), Rx (%)	*P* Value	Before Dec 2006 (n = 6,152), Rx (%)	After Dec 2006 (n = 5,834), Rx (%)	*P* Value	Before Dec 2006 (n = 12,026), Rx (%)	After Dec 2006 (n = 11,643), Rx (%)	*P* Value
Olanzapine	1,762 (13.7)	1,320 (10.7)	< .0001	867 (14.1)	740 (12.7)	.02	1,085 (9.0)	772 (6.6)	< .0001
Quetiapine	2,240 (17.5)	2,076 (16.8)	.19	1,285 (20.9)	1,231 (21.1)	.77	1,317 (11.0)	1,220 (10.5)	.24
Aripiprazole	1,488 (11.6)	1,439 (11.7)	.86	989 (16.1)	940 (16.1)	.96	710 (5.9)	741 (6.4)	.14
Ziprasidone	731 (5.7)	622 (5.0)	.02	455 (7.4)	389 (6.7)	.12	361 (3.0)	333 (2.9)	.52
Perphenazine	81 (0.6)	79 (0.6)	.93	54 (0.9)	55 (0.9)	.71	32 (0.3)	32 (0.3)	.90
Clozapine	341 (2.7)	294 (2.4)	.17	237 (3.9)	216 (3.7)	.67	145 (1.2)	112 (1.0)	.07
Risperidone	2,635 (20.5)	2,267 (18.4)	< .0001	1,447 (23.5)	1,274 (21.8)	.03	1,557 (12.9)	1,357 (11.7)	.002

Abbreviation: Rx = number of prescriptions.

Table 3. Prescriptions 1 Year Before and 1 Year After April 2006 by Psychiatrists and Nonpsychiatrists

	All Prescribers			Psychiatrist			Nonpsychiatrist		
Drug	Before Apr 2006 (n = 13,330), Rx (%)	After Apr 2006 (n = 11,874), Rx (%)	*P* Value	Before Apr 2006 (n = 6,728), Rx (%)	After Apr 2006 (n = 5,580), Rx (%)	*P* Value	Before Apr 2006 (n = 12,600), Rx (%)	After Apr 2006 (n = 11,133), Rx (%)	*P* Value
Olanzapine	2,210 (16.6)	1,311 (11.0)	< .0001	1,122 (16.7)	725 (13.0)	< .0001	1,441 (11.3)	755 (6.8)	< .0001
Quetiapine	2,540 (19.1)	1,916 (16.1)	< .0001	1,539 (22.9)	1,151 (20.6)	.003	1,566 (12.4)	1,093 (9.8)	< .0001
Aripiprazole	1,461 (11.0)	1,369 (11.5)	.15	978 (14.5)	926 (16.6)	.002	725 (5.8)	658 (5.9)	.61
Ziprasidone	779 (5.8)	624 (5.3)	.04	495 (7.4)	405 (7.3)	.83	409 (3.2)	316 (2.8)	.07
Perphenazine	62 (0.5)	81 (0.7)	.02	38 (0.6)	61 (1.1)	.001	28 (0.2)	26 (0.2)	.86
Clozapine	346 (2.6)	284 (2.4)	.3	246 (3.7)	216 (3.9)	.53	169 (1.3)	109 (1.0)	.01
Risperidone	2,905 (21.8)	2,168 (18.3)	< .0001	1,611 (23.9)	1,294 (23.2)	.33	1,808 (14.3)	1,218 (10.9)	< .0001

Abbreviation: Rx = number of prescriptions.

the number was 5,834. In this group, we found significant decreases in olanzapine and risperidone; no significant changes were seen in aripiprazole, perphenazine, quetiapine, ziprasidone, or clozapine.

Before time 2, the number of patients who received their prescriptions from nonpsychiatrists was 12,026, and, after time 2, the number was 11,643. In this group, significant decreases were observed in olanzapine and risperidone; no significant changes were seen in quetiapine, aripiprazole, clozapine, ziprasidone, or perphenazine. Similar results were obtained at 6 months (except that quetiapine and aripiprazole prescriptions increased significantly in total sample and nonpsychiatrist prescriber sample) and at 3 months (except that quetiapine prescriptions increased in the total sample and the nonpsychiatrist prescriber sample, clozapine prescriptions increased slightly in the total sample and psychiatrist prescriber sample, and aripiprazole and ziprasidone increased in total sample) after time 2.

Time 3: April 2006

Time 3 was April 2006, when published results of the CATIE phase 2E trial[10] demonstrated that clozapine had superior effectiveness compared to olanzapine, quetiapine, or risperidone based on time to discontinuation for inadequate therapeutic response in patients who did not respond to a prior trial with 1 of these SGA medications.

Prescription rates 1 year before and 1 year after time 3. Before time 3 (April 2005 to March 2006), the dataset included 13,330 patients and, after time 3 (April 2006 to March 2007), 11,874. For all prescribers, there were significant decreases in olanzapine, risperidone, quetiapine, and ziprasidone; a significant but small increase was observed in perphenazine; and no changes were seen in aripiprazole or clozapine. Results are displayed in Table 3.

Before time 3, we found 6,728 patients who received their prescriptions from psychiatrists, and, after time 3, we identified 5,580 patients who received their prescriptions from psychiatrists. In this group, significant decreases were found in olanzapine, quetiapine, and aripiprazole; significant increases in perphenazine; and no significant changes in ziprasidone, clozapine, or risperidone.

Before time 3, we identified 12,600 patients who were given their prescriptions by nonpsychiatrists, and 11,133 afterward. In this group, we found significant decreases in olanzapine, quetiapine, clozapine, and risperidone and no significant changes in aripiprazole, ziprasidone, or perphenazine. Similar results were obtained at 6 months after time 3, except that no statistically significant increases were found in perphenazine prescriptions in the total sample and psychiatrist prescriber sample or in aripiprazole in the psychiatrist prescriber sample. No significant changes were observed for all groups at 3 months after time 3.

In addition, the overlapping periods of the studies were analyzed to assess the impact of these several studies on prescribing behavior. The change between 12 months before publication of the CATIE studies (September 2004 to August 2005) was compared to 12 months after CATIE studies (December 2006 to November 2007). Results of this analysis were similar to the results described above. There were significant ($P < .0001$) decreases in certain SGAs,

including olanzapine; increases in aripiprazole; no change in clozapine; and a small but significant ($P < .0001$) increase in perphenazine.

DISCUSSION

The very large sample sizes involved in these analyses can make very small changes reach conventional levels of statistical significance. Nevertheless, several consistent and possibly informative patterns emerged. Over the course of the time periods analyzed, prescriptions for olanzapine decreased, prescriptions for aripiprazole increased, prescriptions for the FGA perphenazine increased by a small but statistically significant number and continued to be prescribed at rates of 1% or less, and prescription rates for clozapine did not show sustained changes. Few differences were seen in these patterns between psychiatrist and nonpsychiatrist prescribers.

A recent study[17] performed using data from hospitals operated by the New York State Office of Mental Health looked at perphenazine and clozapine prescriptions before and after the publication of CATIE results. The results of this study also demonstrated limited impact of the CATIE trial. Among about 2,000 patients, the investigators found small but significant increases in use of both of these medications after the publication of CATIE (perphenazine: 1.2% [before], 2.6% [after]; clozapine: 20.6% [before], 24.9% [after]). The investigators concluded that CATIE did, in fact, have a measureable but small impact on prescribing habits in this specialized and controlled setting. An important difference between the studies is that the present one looked at outpatients prescribed medications by both psychiatrists and nonpsychiatrists, while the New York State study looked only at psychiatric inpatients. This probably accounts for the much higher rates of clozapine use in the Citrome et al[17] study, but it is very interesting to see somewhat similar and very small increases in perphenazine use between the 2 studies.

How, then, might we understand these results? The phase 1 CATIE trial demonstrated that olanzapine was superior to other SGAs on the main outcome measure of any-cause discontinuation, and Positive and Negative Syndrome Scale scores decreased. As a result, an increase in olanzapine prescriptions based on the efficacy results of the trial might have been predicted. Instead, olanzapine prescriptions decreased consistently and significantly at all time points in this population of patients with schizophrenia. Why should this have been the case? It may be hypothesized that these results are due to the confirmatory finding in CATIE that olanzapine causes more weight gain and adverse metabolic effects than other SGA medications, as well, perhaps, as the numerous academic and popular media reports and lawsuits related to growing awareness and concern regarding the long-term effect of metabolic syndrome and diabetes associated with olanzapine.[18–23] If this hypothesis is correct, why did these adverse effect concerns supersede the superior efficacy results?

In 2 of the 3 time periods analyzed (period 1 and period 3) there was a statistically significant increase in prescriptions for perphenazine only among psychiatrists. This increase was very small, and at all points perphenazine was prescribed to a maximum of 1.2% of the patients with schizophrenia. It is plausible that the CATIE findings stimulated some interest among psychiatrists into prescribing an FGA. The question remains, however, why such a small increase?

We also did not observe any significant change in the rate of prescriptions for clozapine. Why, despite repeated recommendations that clozapine be prescribed to otherwise treatment-refractory patients, is this the case?

Finally, although aripiprazole was not part of the CATIE study, because it had not yet been approved by the FDA when the study was planned and initiated, the most consistent and robust increase in prescription rates in this time period occurred for aripiprazole. These increases were far larger than those found for perphenazine; almost 20% of the patients with schizophrenia in this sample were prescribed aripiprazole.

How then might we understand these results? The hypothesis that avoidance of long-term risk is a greater motivator in choice of medication than short-term gain in cost or effectiveness is consistent with all these findings. Although olanzapine was more effective than the other drugs tested by CATIE, prescriptions for this drug fell substantially, consistent with the long-term risk of diabetes and metabolic syndrome; clozapine prescribing did not increase, consistent with the shorter-term risk of agranulocytosis (1 case of which occurred in the relatively small sample of 49 patients who received clozapine in CATIE) and the long-term risk of weight gain, diabetes, and metabolic syndrome; perphenazine prescribing increased by a very small number, which is consistent with a continuing concern among physicians regarding adverse extrapyramidal symptoms (EPS) effects of the FGAs. Because perphenazine is often prescribed along with an anticholinergic medication to prevent or abort acute dystonia and parkinsonian adverse effects, it could be that clinicians have been reluctant to prescribe perphenazine more often because of concerns about the risk of tardive dyskinesia associated with a drug that has a greater propensity to induce EPS. In addition the most recent review[24] of the relative risk of tardive dyskinesia in FGAs versus SGAs reports that the rate of tardive dyskinesia in patients treated with FGAs may be almost 3 times as high.

What singularly unites all these observations is that clinicians may be selecting medications that they use with a recognition that, in treating schizophrenia, they are treating patients suffering from a life-long illness. As a result, consideration of the full range of a drug's effect dominates clinical decision making and prescribing behavior. The observed increase in aripiprazole use is also consistent with this hypothesis due to the perception of reduced risk of metabolic syndrome and tardive dyskinesia associated with this drug.

Our analysis has several limitations. First, patients were drawn from Missouri Medicaid's program. It is possible that CATIE had more influence on prescribing here than in other segments of the country. Second, we only looked

for evidence of the influence of the CATIE articles during a period of time extended to 1 year after publication. Longer time frames might afford a greater chance of finding greater impact.

Following CATIE, academics and administrators have concluded that there needs to be more emphasis and resources invested in improving how antipsychotic medications are utilized[13,25–27] and how knowledge transfer occurs because, as mentioned previously, it is affected by multiple factors. With new federal funds recently allocated for comparative efficacy studies like CATIE, there will be increasing need to determine how to translate subsequent findings into clinical reality.[28] Among other considerations, it will be important to address the concern that long-term effects are more persuasive in determining what physicians prescribe than shorter-term benefits. The feasibility limits of study designs, such as CATIE, which do not address that long-term time horizon, strongly suggest that new methods of comparative effectiveness evaluations, such as examination of large databases that have been collected over many years' time, may be needed to help address the issue of antipsychotic prescribing practices.

Drug names: aripiprazole (Abilify), clozapine (FazaClo, Clozaril, and others), olanzapine (Zyprexa), quetiapine (Seroquel), risperidone (Risperdal and others), ziprasidone (Geodon).

Author affiliations: Department of Psychiatry, Mt Sinai School of Medicine (Dr Berkowitz); Department of Psychiatry, Weill Cornell Medical College (Dr Docherty), New York, New York; Outcomes Research Division, Care Management Technologies, Inc, Morrisville, North Carolina (Dr Patel and Ms Ni); and Missouri Department of Mental Health, Jefferson City (Dr Parks).

Potential conflicts of interest: **Dr Parks** is an employee of the State of Missouri; has been a consultant to Care Management Technologies; and has served on speakers or advisory boards for Janssen. **Dr Docherty** has served on speakers or advisory boards for Bristol-Myers Squibb, AstraZeneca, Janssen, and Merck. **Drs Berkowitz** and **Patel** and **Ms Ni** report no conflicts of interest related to the subject of this article.

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