

## Brief Report

# Role of Patient Experience in Atypical Antipsychotic Adherence: A Retrospective Data Analysis

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### ABSTRACT

**Objective:** We report on differences in atypical antipsychotic adherence after the start of outpatient treatment with atypical antipsychotics in patients receiving routine clinical care, based on whether they had been dispensed antipsychotic medication during the previous 180 days. We hypothesized that prior receipt of an antipsychotic prescription would identify patients with a reduced risk for medication discontinuation, perhaps due to greater experience with illness and/or medication experience.

**Methods:** De-identified computerized pharmacy records of 406,032 patients from 1157 pharmacies throughout the United States were used to select patients who were dispensed a noninjectable atypical antipsychotic between October 1, 2003, and March 31, 2004. Patients receiving an atypical antipsychotic prescription during this enrollment period were divided into 2 groups. One group consisted of patients to whom antipsychotic medications had been dispensed in the 180-day period prior to the index outpatient fill. The other group was composed of individuals who had not been dispensed a conventional or atypical antipsychotic during this period. Adherence was measured using Kaplan-Meier time-to-discontinuation analysis during a 360-day follow-up period after the enrollment date. *Discontinuation* was defined as being 30 days late for a scheduled refill.

**Results:** Patients without receipt of an antipsychotic in the 180-day period prior to the index fill composed 32.6% of the total sample of patients (N = 406,432). Women composed 55.2% of the sample; men, 44.8%. The mean age was 43.7 years. In patients previously dispensed an antipsychotic medication, the median time to discontinuation was 125 days,

while in patients not previously dispensed an antipsychotic medication, this value was 34 days.

**Conclusions:** In this analysis of data from pharmacy records, past antipsychotic use appeared to be associated with atypical antipsychotic adherence. Patients without evidence of having been dispensed antipsychotic medication during the 180 days prior to the index antipsychotic prescription appeared to have a high risk for medication discontinuation in the first 30 days after the start of outpatient therapy. This finding suggests that close follow-up during that period in patients who are either new to antipsychotic medication or who are being restarted on an antipsychotic after a prolonged lapse in use may be beneficial. (*Clin Ther.* 2007;29:2768-2773) Copyright © 2007 Excerpta Medica, Inc.

**Key words:** risk for discontinuation, antipsychotic adherence.

### INTRODUCTION

Illness or medication inexperience has been linked to poor medication adherence in several prior studies of mental illness. In bipolar disorder, an increased risk for medication discontinuation was associated with first year of lithium treatment, fewer episodes of illness, and younger age.<sup>1</sup> Among patients with first-admission

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schizophrenia, 73% of the lapses in antipsychotic medication use are noted to be patient-initiated and to occur soon after hospital discharge.<sup>2</sup> Studies also have observed that patients prescribed conventional antipsychotics may experience levels of medication adherence that are better than those observed in patients prescribed atypical antipsychotics.<sup>3,4</sup> One possible explanation for this finding may be that conventional antipsychotic use may help to identify patients whose illness and medication management skills are better due to prior experience with illness and/or medication. Indeed, it was our clinical experience that many patients receiving long-term psychiatric care continued to receive conventional agents, treatment with which was started years, even decades, earlier, while newly diagnosed and less experienced patients often were prescribed newer atypical agents.

The objective of this brief report was to determine the extent to which prior medication experience affected the risk for medication discontinuation in patients prescribed atypical antipsychotics.

## MATERIALS AND METHODS

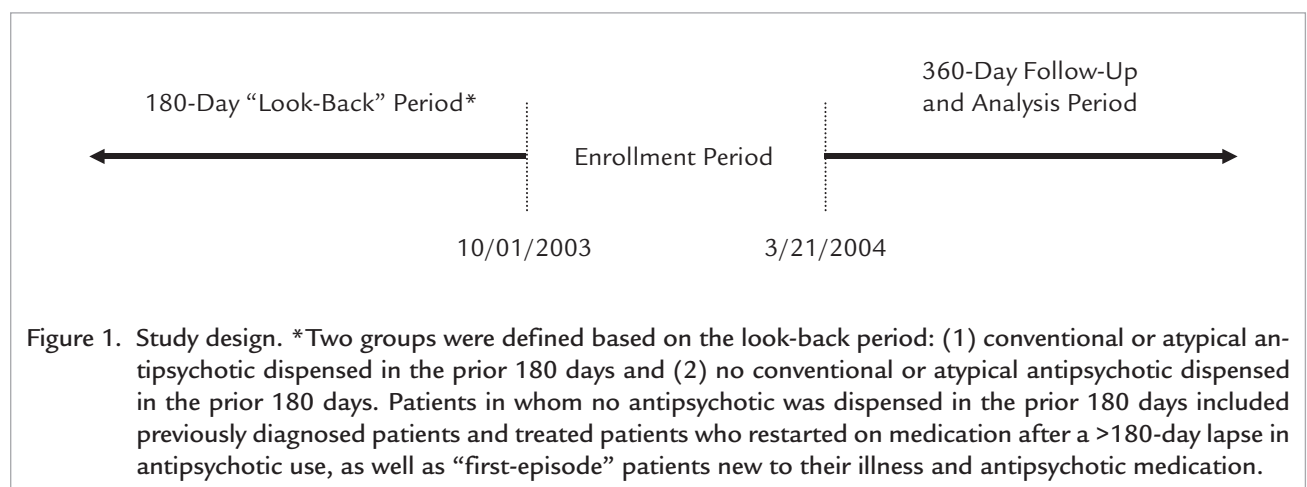
De-identified computerized pharmacy records from 1157 pharmacies throughout the United States were used to select patients who were dispensed a noninjectable atypical antipsychotic during a patient enrollment period that started on October 1, 2003, and ended on March 31, 2004. Data contained complete prescription histories of all patients regardless of the patient's health care plan. The date on which a prescription medication was dispensed during the enrollment period was called the *index*

*date*. Patients identified during this enrollment period were divided into 2 groups. One group (*antipsychotic previously dispensed*) consisted of patients to whom either a conventional or atypical antipsychotic had been dispensed during the 180-day period prior to the index date. The other group (*antipsychotic not previously dispensed*) was composed of patients to whom neither a conventional nor an atypical antipsychotic had been dispensed in the 180 days preceding the index date (Figure 1). Adherence was evaluated using Kaplan-Meier curves to compare the time to discontinuation between the 2 groups during a 360-day period after the index date. Patients were defined as having discontinued therapy once they were 30 days late for a scheduled refill. Patients who switched from the index antipsychotic to another antipsychotic were considered to have continued with therapy. Individuals who were prescribed 2 or more atypical antipsychotics were redefined as having received the atypical antipsychotic they were first dispensed. Due to the nature of the data (pharmacy records), adverse-events data were not available.

The New England Institutional Review Board approved the study and its methods.

## RESULTS

The distribution of patients in the total sample (N = 406,032) by treatment was as follows: ziprasidone (n = 121,607), risperidone (n = 98,257), olanzapine (n = 84,919), quetiapine (n = 78,873), aripiprazole (n = 20,279), and clozapine (n = 2097). Patients without receipt of an antipsychotic in the 180-day period



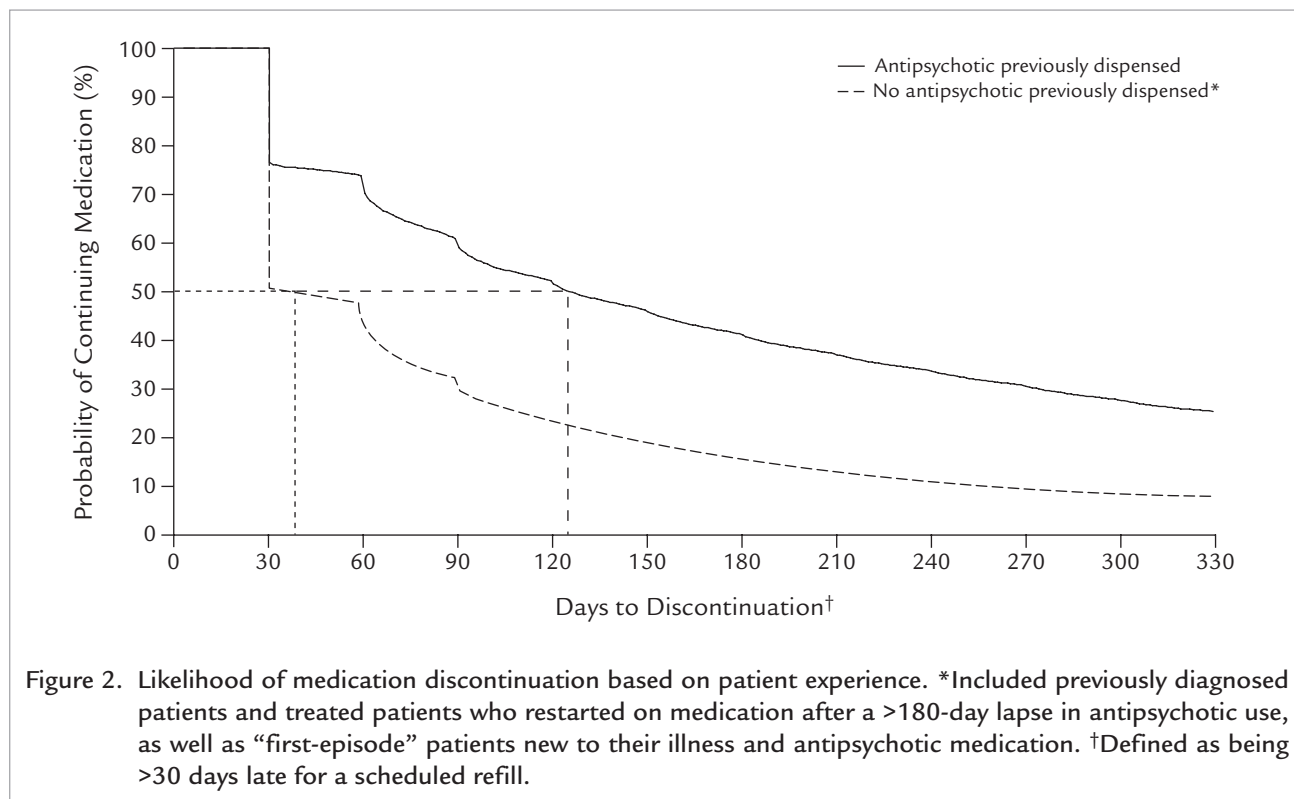
prior to the index fill composed 32.6% of the sample. Women composed 55.2% of the sample; men, 44.8%. The mean age was 43.7 years.

The median numbers of days until half of the patients who started therapy had discontinued were 125 in patients who had previously been dispensed an antipsychotic and 34 in patients who had not previously been dispensed an antipsychotic (Figure 2). Among patients previously dispensed an antipsychotic, the median (95% CI) number of days to discontinuation were: ziprasidone, 142 (133–150); risperidone, 132 (130–136); olanzapine, 123 (121–125); quetiapine, 121 (120–123); aripiprazole, 119 (113–122); and clozapine, 267 (263–271). Among patients not previously dispensed an antipsychotic, these values were: ziprasidone, 40 days (32–48); risperidone, 48 (44–51); olanzapine, 30 (26–34); quetiapine, 42 (36–46); aripiprazole, 33 (30–41); and clozapine, 108 (33–252) (Figure 3). Switching from one atypical to another medication in the class was observed in 6.3% of the patients. For every patient who switched to another agent, 13 patients appeared to have discontinued treatment with atypical antipsychotic medications outright.

## DISCUSSION

Two main conclusions emerge from this study. First, patients who had not filled a prescription for an antipsychotic during the 180-day period prior to the index date had a greater risk for medication discontinuation, and this risk was greatest in the first 30 days after initiating treatment. While 48.8% of patients without prior medication experience discontinued within 30 days after filling their index prescriptions, the rate of discontinuation in the subsequent months averaged only 4.3%. This 10-fold increase in the risk for medication discontinuation at the start of therapy suggests the presence of a crucial window of time when alliance building and patient follow-up may be especially important.

Patients who had not had a prescription for an antipsychotic filled during the 180 days prior to the index date would have included previously diagnosed and treated patients who were being restarted on medication after a 6-month lapse in antipsychotic use, as well as “first-episode” patients, who were new to their illness and antipsychotic treatment. Due to the limitations associated with using a pharmacy database, we were not able to specify the proportion of patients in each of



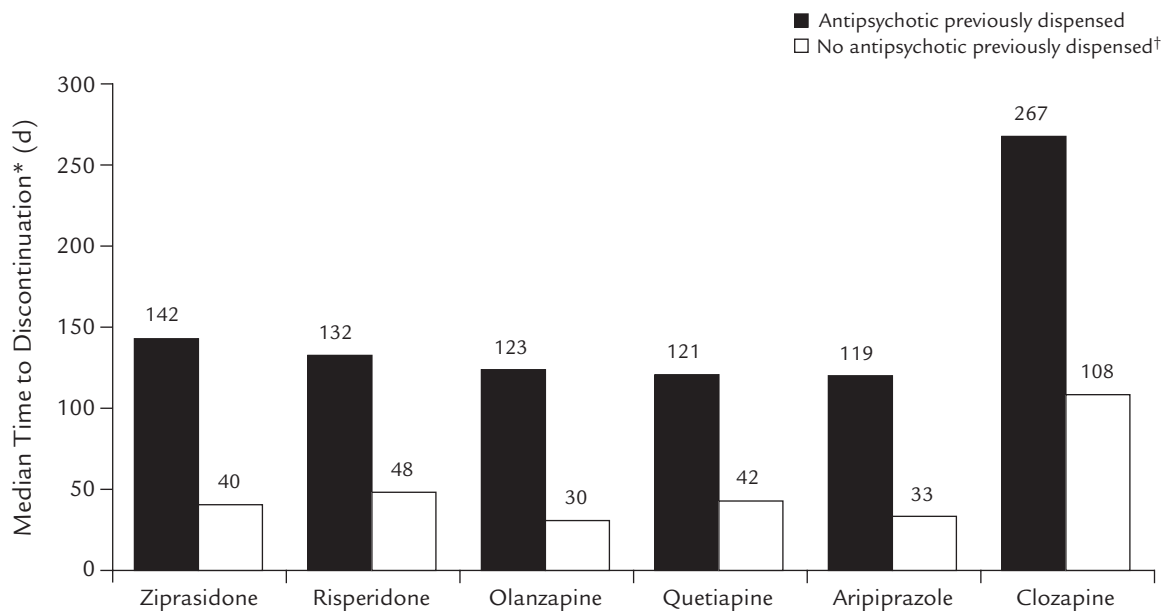


Figure 3. Median days to medication discontinuation (Kaplan-Meier estimates). \*Defined as being >30 days late for a scheduled refill. †Included previously diagnosed patients and treated patients who restarted on medication after a >180-day lapse in antipsychotic use, as well as “first-episode” patients new to their illness and antipsychotic medication.

these groups. However, clinical experience suggests that a far greater proportion of these patients would be those restarting medication after a lapse in use.

Second, past antipsychotic use (conventional or atypical) rather than receipt of a specific medication was most associated with future antipsychotic adherence. Far greater differences in adherence were observed between patients in receipt of the same medication but who had different degrees of medication experience (eg, patients receiving quetiapine who were previously dispensed an antipsychotic versus patients receiving quetiapine who were not previously dispensed an antipsychotic) than between patients receiving different medications who shared similar levels of medication experience (eg, patients receiving quetiapine previously dispensed an antipsychotic and patients receiving olanzapine previously dispensed an antipsychotic). Such data suggest that what patients know and do as a result of prior medication or illness experience (or lack of it) is a more robust predictor of future adherence than the receipt of a specific medication. Such data also suggest that researchers need to consider the role that past medication use plays in the likelihood of future adherence.

Failure to do so may cause investigators to conclude that a specific medication, rather than an imbalanced percentage of experienced patients, is the reason for apparent increased adherence.<sup>5</sup>

Despite the use of different patient population samples and study methods, the results reported here are similar to those obtained in the Clinical Antipsychotic Trials of Intervention Effectiveness (CATIE) study<sup>6</sup> for 3 of the atypical medications. Median times to discontinuation in patients continuing medication in this study and in patients in the CATIE study, who had, on average, 14 years of illness experience, were, respectively: ziprasidone, 4.7 and 3.5 months; risperidone, 4.4 and 4.8 months; and quetiapine, 4.0 and 4.6 months.<sup>6</sup> Only for olanzapine were the results markedly different (4.1 vs 9.2 months). The median time to discontinuation in patients newly initiating antipsychotic medication, a group not included in the CATIE study, ranged from 1.0 to 1.5 months.

Studies suggest that individuals with experience in a task differ from novices in the same role by being able to use prior experience to make more advantageous personal decisions.<sup>7,8</sup> Such a “learning curve”

might also apply to patients using medication to manage a chronic illness. We speculate that prior receipt of an antipsychotic prescription may have identified patients whose prior illness experience helped reinforce medication use, either due to the painful experiences associated with medication discontinuation or beneficial effects of continued use.<sup>9</sup> In bipolar disorder, a distinguishing feature of patients with good relative to poor medication adherence is the total number of past illness episodes experienced, especially depressive ones.<sup>10,11</sup> Behaviors that develop to avoid harmful situations in the future based on painful experiences in the past are examples of fear-conditioned or emotional learning.<sup>12</sup> Future studies would do well to examine the specific illness experiences and kinds of reinforcement associated with patients achieving high levels of medication adherence.

Limitations of this study included an inability to link pharmacy records to collateral clinical and diagnostic information; thus, the intended duration of antipsychotic use cannot be inferred. Patients identified as not having received an antipsychotic in the prior 180 days may have, in fact, been previously diagnosed and treated and lapsed on antipsychotic medication prior to a restart of their medication, or may have been first-episode patients receiving antipsychotic medication for the first time. Due to the limitations with our data, we could not make such a distinction. Patients receiving clozapine would necessarily have had more illness and medication experience than patients receiving other atypical antipsychotics due to clozapine's indication for use after other agents have failed. These patients might have benefited from a structured program of medication administration that served to improve adherence.<sup>3</sup> Reasons for medication discontinuation were not known and may have included hospitalization and/or discontinuation associated with short-term use. Differences in the insurance coverage and medication copayments were not available and might have affected the results. However, it is likely that they were similar among patients who took the same medication and who differed only in whether they had or had not filled a prescription for an antipsychotic in the prior 180 days. While refill rates from closed pharmacy systems (eg, health maintenance organizations) are known to provide good measures of overall adherence,<sup>13,14</sup> the data used here were drawn from retail pharmacy chains. However, the estimated rate at which individuals transfer in and out of retail chains is 0.5%.<sup>15</sup>

Two strengths of this study were its large sample size and use of data that reflected patterns of antipsychotic adherence observed under conditions of routine clinical practice across specialty and general practice settings, at academic and community sites, and among many geographic regions and payers throughout the United States.

## CONCLUSIONS

Based on the results of this data analysis, past antipsychotic use appears to be associated with future antipsychotic adherence more than does receipt of a particular medication. Patients who had not been dispensed an antipsychotic during the 180 days prior to an index fill were roughly twice as likely to discontinue their prescribed antipsychotic as were patients who had previously filled a prescription. This risk for discontinuation was greatest during the first 30 days of treatment. The degree to which antipsychotic medication adherence can be improved through better alliance building, patient education, and follow-up during the first 30 days of outpatient medication use merits further study.

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