# Relapse Rates in Patients With Schizophrenia Receiving Aripiprazole in Comparison With Other Atypical Antipsychotics

Karen E. Moeller, Pharm.D., B.C.P.P.;
Theresa I. Shireman, Ph.D., R.Ph.;
and Barry I. Liskow, M.D.

***Objective:*** Aripiprazole is the first of a new generation of antipsychotics that possesses a unique mechanism of action as a partial dopamine agonist. After the release of aripiprazole, case reports appeared conveying an acute psychosis/agitation reaction occurring after the initiation of treatment, most specifically after patients were switched from a previous antipsychotic to aripiprazole. The primary objective of this study was to compare relapse rates among patients with schizophrenia who were switched to aripiprazole with those who switched to a second-generation antipsychotic (SGA) from another antipsychotic.

***Method:*** The design was a retrospective cohort study based on Kansas Medicaid enrollees with an ICD-9-CM diagnosis code for schizophrenia during calendar year 2002 who switched antipsychotic agents. Six-month psychiatric relapse rates, defined as hospitalization for a psychiatric event, were compared between those subjects who switched to aripiprazole and those who switched to another SGA. Time to relapse was modeled using Cox proportional hazards, adjusting for demographic characteristics, major comorbid conditions, and prior psychiatric-related health care use.

***Results:*** Four hundred forty-four aripiprazole and 521 SGA switchers were comparable with respect to gender, race, comorbidities, and health care utilization, though the aripiprazole group was 4.5 years younger. Twenty percent of aripiprazole patients and 19.4% of patients receiving SGAs were hospitalized 6 months after being switched (relative risk = 0.92; 95% CI = 0.67 to 1.26). Mean times to psychiatric hospitalization for the aripiprazole and SGA groups were 65.7 and 73.8 days, respectively ($p > .05$). Factors associated with hospitalization were prior psychiatric hospitalizations and comorbid depression, substance abuse, and neurotic, personality, and nonpsychotic mental disorders.

***Conclusion:*** Our study found that rates of relapse and time to relapse with aripiprazole were comparable to other SGAs during a 6-month period. Thus, aripiprazole appears to be an appropriate first-line agent along with the other SGAs.

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*Corresponding author and reprints: Karen E. Moeller, Pharm.D., B.C.P.P., Department of Pharmacy Practice, University of Kansas Medical Center, Mail Stop 4047, 3901 Rainbow Blvd., Room B440, Kansas City, KS 66160 (e-mail: kmoeller@kumc.edu).*

Schizophrenia is a lifelong debilitating mental disorder characterized by frequent relapses and low rates of remission associated with poor long-term prognosis, rehospitalization, and high utilization of health care dollars.[1,2] Therefore, relapse prevention is an essential goal among the schizophrenia population. The advent of atypical antipsychotics or second-generation antipsychotics (SGAs) (i.e., clozapine, olanzapine, risperidone, quetiapine, ziprasidone) in the 1990s provided new hope for the prevention and delay of relapse and for maintaining schizophrenia patients on drug therapy with fewer adverse effects. Although recent studies have shown certain atypical agents to be superior to typical antipsychotics with respect to relapse prevention,[3–5] they are not without side effects. Long-term risks associated with atypical antipsychotics include weight gain, diabetes, elevated cholesterol, and QTc prolongation.[6] Thus, novel treatments for schizophrenia are aimed at minimizing these side effects as well as preventing relapse. Aripiprazole, released in November 2002, is the first of a new generation of antipsychotics that possess a unique mechanism of action as a partial dopamine agonist. Clinical studies of aripiprazole have shown minimal side effects with little effect on weight gain, serum lipid levels, prolactin levels, QTc interval, and extrapyramidal symptoms.[7]

The availability of new agents with minimal side effects often prompts clinicians to switch patients from their current antipsychotic drug therapy in hopes of minimizing side effects and improving quality of life. After the release of aripiprazole, however, case reports appeared suggesting an acute psychosis/agitation reaction following initiation of treatment[8–12] with the potential of precipitating relapse hospitalizations. A plausible cause of these psychoses was attributed to aripiprazole's unique mechanism as a partial dopamine agonist. These reports prompted the present study, which evaluates relapse rates and time to relapse in patients taking aripiprazole.

Currently, there are no studies comparing relapse rates of patients taking aripiprazole with active controls among patients previously receiving other antipsychotics. The primary objective of this observational study was to compare relapse rates and time to relapse among patients with chronic schizophrenia who were switched to aripiprazole with those who were switched to a SGA from another antipsychotic using a retrospective analysis of claims data from the Kansas Medicaid population.

## METHOD

### Study Design

The design was a retrospective cohort study examining psychiatric relapse rates, defined as hospitalization for a psychiatric event, for persons with schizophrenia who switched antipsychotic agents. The study population consisted of all Kansas Medicaid enrollees with a diagnosis code for schizophrenia (International Classification of Diseases, 9th Revision, Clinical Modification [ICD-9-CM] code 295.xx) during the calendar year 2002. Subjects from this pool were included if they were 18 years of age or older, were continuously enrolled in Medicaid during the 12-month study period, and were switched from any antipsychotic to either aripiprazole (cases) or 1 of the other atypical antipsychotics (comparisons). For each eligible patient, 6 months of utilization data were collected and evaluated both prior to and after the switch.

### Data

A programmer from the Kansas Department of Social and Rehabilitative Services, Topeka, Kan. (now the Division of Health Planning and Finance or DHPF) extracted all paid (i.e., Kansas Medicaid) and crossover claims (initial claims paid by a secondary provider, e.g., Medicare) from in-state and out-of-state institutions, outpatient medical providers, and pharmacies for study subjects. Reversed claims and adjustments were removed or corrected. Claims data included dates and places of service; diagnosis, procedure, or drug codes; and Medicaid reimbursement amounts. The programmer also created a demographic file containing dates of birth, dates of death, gender, and race/ethnicity codes based upon the eligibility file. Age was determined as of Jan. 1, 2002. Race and ethnicity codes were cross-tabulated to create the following groups: white, non-Hispanic; black, non-Hispanic; and other. Subjects who died during the study period were excluded. Continuous eligibility was defined as at least 1 claim per month.

### Cases and Comparisons

From the date of the first antipsychotic prescription filled between July 1, 2002, and June 30, 2003, we looked back to determine if the patient had previously received an antipsychotic agent. If the prescription was for a new atypical antipsychotic medication, the patient was classified as a switcher. We then sorted switchers into the following groups: those switching to aripiprazole (cases) or those switching to one of the other SGAs (clozapine, olanzapine, quetiapine, risperidone, or ziprasidone) (comparisons). Patients receiving multiple antipsychotics prior to the switch were included in the analysis to help depict real-life prescribing practices. All other patients were excluded (e.g., those switched to typical antipsychotics or those who remained on the same antipsychotic).

### Outcome Variable

The principal outcome of interest was hospitalization for a psychiatric diagnosis within 6 months of the switch date. Psychiatric hospitalizations were defined as an ICD-9-CM primary diagnosis code of 290.xx through 299.xx for an inpatient claim lasting at least 1 day. We recorded the occurrence of any psychiatric-related admission, the time to admission (days since the switch occurred), and length of stay. Only the first postswitch psychiatric hospitalization was included in the analysis.

### Study Variables

We tabulated the number of psychiatric hospitalizations, psychiatric-related outpatient services, and psychotropic medications used in the 6 months prior to the switch as an indirect measure of psychiatric severity. Psychiatric-related outpatient services included specific psychiatric visits (i.e., psychotherapy and medication management; Current Procedure Terminology codes 90801–90821, 90862), community support (Healthcare Common Procedure Coding System [HCPCS] codes Y9118, Y9119, Y9544, Y9564), and case management (HCPCS code Y9117) based upon billed procedure codes. Prior psychotropic medication use was measured as the number of unique medications received within the 6 months prior to the switch. For example, if a patient received 2 antidepressants and 1 antipsychotic in the 6 months prior to the switch, prior medication use equaled 3 different psychotropic medications. Classification of psychotropic medications included antipsychotics, antidepressants, anxiolytics, benzodiazepines, mood stabilizers (both lithium and anticonvulsant medications), sedative-

hypnotics, stimulant and nonstimulant medications (e.g., atomoxetine), and drugs for the treatment of substance abuse (e.g., disulfiram, naltrexone).

Concurrent psychiatric and medical conditions were documented from ICD-9-CM diagnosis codes recorded in the preswitch inpatient and outpatient claims. Specific psychiatric and medical conditions were included because of their prevalence as significant concurrent conditions likely to influence the risk for hospitalization for persons with schizophrenia: depression (code 311); substance abuse (codes 291.xx–292.xx, 303.xx–305.xx); neurotic, personality, and other nonpsychotic mental disorders (codes 300.xx–302.xx, 306.xx–316.xx); mental retardation (codes 317.xx–319.xx); diabetes (code 250.xx); cardiovascular diseases (codes 401.xx–405.xx, 410.xx–414.xx, 428.xx); hyperlipidemia (code 272.xx); metabolic disorders (codes 270.xx–272.xx); and cerebrovascular diseases (codes 430.xx–438.xx).

### Analysis

Cases and comparisons were compared with respect to basic demographic variables, concurrent conditions, and prior psychiatric-related health care use in bivariate analyses using appropriate descriptive statistics, including t tests for means and $\chi^2$ tests for distributions. Time to relapse was modeled using Cox proportional hazards and adjusted for demographic characteristics, major comorbid conditions, and prior psychiatric-related health care use. Data were manipulated and analyzed using Excel (Microsoft Corp., Redmond, Wash.) and SPSS (SPSS, Inc., Chicago, Ill.) for Windows. The study protocol was approved by the University of Kansas Medical Center Human Subjects Committee.

## RESULTS

### Patient Disposition and Demographics

A total of 5975 patients with a diagnosis of schizophrenia were identified from the Kansas Medicaid population, with 3576 patients continuously enrolled during 2002 to 2003. Overall, 965 patients (444 aripiprazole [cases], 521 SGAs [comparisons]) met eligibility requirements. Of the patients excluded, 91 were less than 18 years of age, 106 had no history of prior antipsychotic use, and 2414 either were continued on their antipsychotic during the time period or were switched to a typical antipsychotic.

Patient characteristics, demographics, comorbidities, and health care use are presented in Table 1. Aripiprazole patients were younger in comparison with patients receiving SGAs (42.6 vs. 47.1 years, respectively; $p < .001$). The study populations were comparable with respect to gender and race.

With respect to psychiatric comorbidities, neurotic, personality, and nonpsychotic mental disorders; substance abuse; and depression were the most frequent comorbidities in both treatment groups. Aripiprazole patients were less likely to suffer from depression than patients receiving SGAs (26.8% vs. 34.4%, respectively; relative risk (RR) = 1.43; 95% CI = 1.08 to 1.88). Cardiovascular diseases, lipid disorders, diabetes, and pulmonary diseases were the most commonly reported medical comorbidities, and rates did not differ between the groups.

Prior medication use and health care utilization differed slightly between treatment groups. In the 6 months prior to the switch, aripiprazole patients were more likely than the SGA group to have tried more antipsychotic medications (2.83 versus 2.60, respectively; $p < .001$). Patients receiving multiple antipsychotics did not differ between groups. However, more aripiprazole patients were switched from an atypical antipsychotic than patients in the SGA group (82.8% vs. 73.5%, respectively; RR = 0.58; 95% CI = 0.43 to 0.78). Use of other psychotropic medications (e.g., antidepressants, anticonvulsants) did not differ between the 2 groups. Previous psychiatric hospitalizations and outpatient visits were comparable, yet aripiprazole patients were more likely to receive community support and case management prior to the switch.

### Relapse/Time to Relapse

Rates of relapse based on psychiatric hospitalizations did not differ between groups. Twenty percent of aripiprazole patients and 19.4% of SGA patients were hospitalized 6 months after being switched from their previous antipsychotic regimen (RR = 0.92; 95% CI = 0.67 to 1.26). Among those hospitalized, time to relapse was not statistically different between groups. The mean times to psychiatric hospitalization postswitch for the aripiprazole and SGA groups were 65.7 and 73.8 days, respectively. Figure 1 illustrates the hazard function for time to hospitalization according to treatment cohorts.

### Predictors of Relapse

Results of the Cox proportional hazards model are reported in Table 2. Overall, significant variables in the model included other psychiatric diagnoses and past number of psychiatric-related hospitalizations. Comorbid diagnoses of depression (adjusted hazard ratio [AHR] = 1.44; 95% CI = 1.05 to 1.98), substance abuse (AHR = 1.80; 95% CI = 1.32 to 2.47), and neurotic, personality, and nonpsychotic mental disorders (AHR = 2.27; 95% CI = 1.58 to 3.26) all increased the risk of psychiatric hospitalizations. Prior psychiatric hospitalization also increased the risk of postswitch hospitalization (AHR = 1.38; 95% CI = 1.22 to 1.55). Use of aripiprazole versus other SGAs had no effect on the risk of hospitalization (AHR = 1.16; 95% CI = 0.86 to 1.56).

**Table 1. Baseline Demographics and Clinical Characteristics for Schizophrenia Patients Switching to Aripiprazole Versus Other Second-Generation Antipsychotic (SGA) Medications**

| Characteristic | Aripiprazole | Other SGAs |
|---|---|---|
| Subjects, N (%) | 444 (100) | 521 (100) |
| Age, mean ± SD (range), y* | 42.62 ± 12.9 (18–85) | 47.1 ± 14.9 (18–95) |
| Gender (male), N (%) | 199 (44.8) | 250 (48.0) |
| Race, N (%) | | |
| White, non-Hispanic | 344 (77.5) | 416 (79.8) |
| Black, non-Hispanic | 74 (16.7) | 77 (14.8) |
| Other | 26 (5.9) | 28 (5.4) |
| Comorbidities, N (%) | | |
| Psychiatric | | |
| Neurotic, personality, and nonpsychotic mental disorders | 218 (49.1) | 261 (50.1) |
| Substance abuse | 146 (32.9) | 183 (35.1) |
| Depression** | 119 (26.8) | 179 (34.4) |
| Mental retardation | 39 (8.8) | 63 (12.1) |
| Medical | | |
| Cardiovascular diseases | 187 (42.1) | 230 (44.1) |
| Lipid disorders | 102 (23.0) | 96 (18.4) |
| Diabetes | 87 (19.6) | 117 (22.5) |
| Pulmonary diseases | 84 (18.9) | 117 (22.5) |
| Metabolic disorders | 54 (12.2) | 69 (13.2) |
| Cerebrovascular diseases | 24 (5.4) | 27 (5.2) |
| Prior no. of medications received 6 mo prior to switch, mean ± SD | | |
| Psychotropics** | 5.31 ± 2.24 | 4.97 ± 2.14 |
| Antipsychotics* | 2.83 ± 0.93 | 2.60 ± 0.91 |
| Antidepressants | 1.10 ± 1.03 | 1.10 ± 1.08 |
| Mood stabilizers[a] | 0.86 ± 0.96 | 0.83 ± 0.95 |
| Sedatives/hypnotics[b] | 0.37 ± 0.54 | 0.33 ± 0.53 |
| Other[c] | 0.13 ± 0.41 | 0.09 ± 0.34 |
| Most recent antipsychotic prior to switch, N (%) | | |
| Olanzapine** | 115 (25.9) | 102 (19.6) |
| Quetiapine | 97 (21.8) | 90 (17.3) |
| Risperidone | 95 (21.4) | 112 (21.5) |
| Ziprasidone | 60 (13.5) | 48 (9.2) |
| Clozapine | 47 (10.6) | 64 (12.3) |
| Haloperidol** | 41 (9.2) | 67 (12.9) |
| Other typical antipsychotics** | 46 (10.4) | 83 (15.9) |
| Patients receiving 2 antipsychotics prior to switch, N (%) | 49 (11.0) | 40 (7.7) |
| Patients receiving 3 antipsychotics prior to switch, N (%) | 4 (0.9) | 2 (0.4) |
| Prior health-related services, mean ± SD | | |
| Psychiatric hospitalizations | 0.40 ± 0.90 | 0.45 ± 0.86 |
| Outpatient psychiatric visits | 5.75 ± 5.90 | 5.31 ± 5.74 |
| Case management visits** | 8.14 ± 12.15 | 6.26 ± 11.35 |
| Community support visits* | 35.4 ± 58.65 | 23.2 ± 45.70 |

[a]Mood stabilizers include lithium preparations and all anticonvulsants.
[b]Sedative/hypnotics include benzodiazepines, barbiturates, and hypnotics.
[c]Other includes atomoxetine, buspirone, disulfiram, naloxone, and central nervous system stimulants.
*$p < .001$.
**$p < .05$.

## DISCUSSION

Recent reports have appeared that suggest worsened psychosis and agitation occurring with the initiation of aripiprazole. The reports led us to conduct this study comparing rates of relapse and time to relapse among patients with schizophrenia who switched to either aripiprazole or an SGA. Our study found that the prevalence of relapse and time to relapse in patients with schizophrenia were similar between patients receiving aripiprazole and SGAs. The results showed that approximately 20% of patients within each group relapsed within 6 months of treatment, which is consistent with other published reports.[13] Mean time to hospitalization postswitch was not significantly different between the 2 groups, although there was a trend to earlier time to hospitalization in the aripiprazole group compared with the SGA group (65.7 and 73.8 days, respectively). Clinical significance of this 8-day trend is questionable. Additionally, multivariable analysis also confirmed that there was no statistical difference between groups concerning time to hospitalization.

To the best of our knowledge, this is the first study to evaluate relapse associated with aripiprazole compared with other SGAs. One study compared aripiprazole to placebo resulting in relapse rates of 34% for aripiprazole and 57% for placebo,[14] which is higher than the 20% relapse rate of aripiprazole patients in our study. Our relapse rates, however, are consistent with other published studies evalu-

**Figure 1. Hazard Function for Time to Hospitalization for Aripiprazole Versus Second-Generation Antipsychotics (SGAs)**

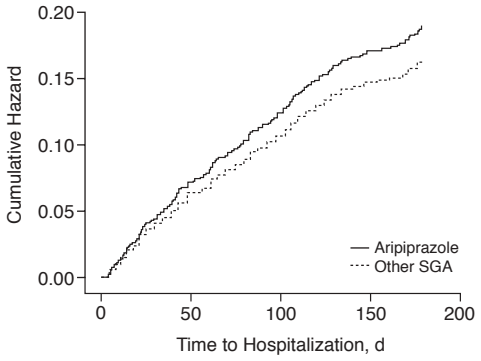


**Table 2. Cox Proportional Hazards Analysis of Time to Psychiatric Hospitalization for Schizophrenia Patients Switching to Aripiprazole Versus Other Second-Generation Antipsychotic (SGA) Medications**

| Predictor | Adjusted Hazard Ratio | 95% Confidence Interval |
|---|---|---|
| Demographics | | |
| Age | 1.00 | 0.98 to 1.01 |
| Female | 0.87 | 0.65 to 1.18 |
| White, non-Hispanic | 1.00 | |
| Black, non-Hispanic | 1.22 | 0.82 to 1.82 |
| Other | 0.82 | 0.41 to 1.61 |
| Comorbidities | | |
| Neurotic, personality, and nonpsychotic mental disorders* | 2.27 | 1.58 to 3.26 |
| Depression* | 1.44 | 1.05 to 1.98 |
| Substance abuse* | 1.80 | 1.32 to 2.47 |
| Prior psychiatric health services | | |
| Inpatient admissions | 1.38 | 1.22 to 1.55 |
| Outpatient psychiatry | 1.00 | 0.98 to 1.03 |
| Community support | 1.00 | 0.997 to 1.002 |
| Case management | 1.00 | 0.993 to 1.017 |
| Antipsychotics | 0.96 | 0.82 to 1.11 |
| Other psychoactive agents | 1.00 | 0.93 to 1.08 |
| Aripiprazole vs other SGAs | 1.16 | 0.86 to 1.56 |

*$p < .05$.

ating rehospitalization rates with SGAs.[15,16] Rabinowitz and colleagues[16] reported relapse rates of 21% with olanzapine and risperidone at 6 months of treatment, which increased to approximately 30% at 12 months of treatment (28% olanzapine and 31% risperidone). In contrast, studies evaluating relapse rates with conventional antipsychotics have shown ranges of around 30% to 50%.[1,3,13]

There were some differences observed between the aripiprazole group and the SGA group in this study. Patients in the aripiprazole group were younger (42.6 vs. 47.1 years of age, respectively) and received more community support visits, case management, and antipsychotic medications. These differences could illustrate that aripiprazole patients, who were younger, had better access to services or, conversely, that the aripiprazole group possessed a more severe form of schizophrenia than the patients in the SGA group. In evaluating psychiatric comorbidities, a significantly greater proportion of patients in the SGA group suffered from comorbid depression in comparison with the aripiprazole group (34.4% versus 26.8%, respectively); these rates are significantly higher than overall published rates of 25% for depression of schizophrenia.[17] The incidence of depression in schizophrenia is typically associated with poorer outcomes and higher rates of relapse and rehospitalization.[18–20] The rates of psychiatric and medical comorbidities in our patient population were similar to those in other published reports of schizophrenia patients. The major comorbidities that occurred in our study population were cardiovascular diseases (43%), substance abuse (34%), depression (30%), diabetes (21%),and lipid disorders (20%). These comorbidities are consistent with other published studies reporting up to 50% of schizophrenia patients suffering from coronary heart disease,[21] 40% from substance abuse,[22,23] 25% from depression,[17] 16% from diabetes,[24] and 14% from hyperlipidemia.[25]

The main limitation of this study was that the results were drawn from a single state's Medicaid plan and may not be generalizable to other populations. As with any analysis of claims data, we were unable to examine the medical records and therefore relied heavily on accurate coding of health care services and diagnoses. However, claims data analyses and validation projects have demonstrated higher validity for more severe mental health conditions such as schizophrenia than have been noted for other conditions.[26,27] Finally, we were unable to determine the severity of the patients' illness, as well as reasons for physician visits and discontinuation of medication (e.g., adverse drug reaction).

Another limitation of our study was that the comparator group contained a mixture of SGAs instead of comparing individual SGAs with aripiprazole. Although the newer agents are typically classified as a group, their side effects and receptor-binding profiles differ. These effects could produce differences in relapse and efficacy warranting direct comparison in future analyses. Also, our study did include patients who may have been receiving multiple antipsychotics after the switch and does not necessarily represent monotherapy with either aripiprazole or SGAs. This study design was chosen to portray real-life prescribing practices.

Our study found that rates of relapse with aripiprazole were comparable to those with other SGAs in a 6-month period. On these grounds, aripiprazole appears to be an appropriate first-line agent along with the other SGAs. Further long-term studies (1 year or greater) are needed to determine if this similarity is maintained and to examine adverse drug events. In addition, more studies are needed to determine relapse rates in both the bipolar and refractory schizophrenia population.

*Drug names:* aripiprazole (Abilify), atomoxetine (Strattera), clozapine (FazaClo, Clozaril, and others), disulfiram (Antabuse), haloperidol (Haldol and others), lithium (Eskalith, Lithobid, and others), naloxone (Suboxone, Narcan, and others), naltrexone (Vivitrol, ReVia, and others), olanzapine (Zyprexa), quetiapine (Seroquel), risperidone (Risperdal), ziprasidone (Geodon).

## REFERENCES


1. Hogarty GE. Prevention of relapse in chronic schizophrenic patients. J Clin Psychiatry 1993;54(3, suppl):18–23
2. Siris SG. Suicide and schizophrenia. J Psychopharmacol 2001;15: 127–135
3. Csernansky JG, Mahmoud R, Brenner R. A comparison of risperidone and haloperidol for the prevention of relapse in patients with schizophrenia. N Engl J Med 2002;346:16–22
4. Davis JM, Chen N, Glick ID. A meta-analysis of the efficacy of second-generation antipsychotics. Arch Gen Psychiatry 2003;60:553–564
5. Lindstrom E, Eriksson B, Hellgren A, et al. Efficacy and safety of risperidone in the long-term treatment of patients with schizophrenia. Clin Ther 1995;17:402–412
6. Freedman R. Schizophrenia. N Engl J Med 2003;349:1738–1749
7. Marder SR, McQuade RD, Stock E, et al. Aripiprazole in the treatment of schizophrenia: safety and tolerability in short-term, placebo-controlled trials. Schizophr Res 2003;61:123–136
8. Barnas ME, Hussain N, Petrides G. Treatment-emergent psychosis with aripiprazole [letter]. J Clin Psychiatry 2005;66:1339
9. DeQuardo JR. Worsened agitation with aripiprazole: adverse effect of dopamine partial agonism [letter]? J Clin Psychiatry 2004;65:132–133
10. Ramaswamy S, Vijay D, William M, et al. Aripiprazole possibly worsens psychosis. Int Clin Psychopharmacol 2004;19:45–48
11. Reeves RR, Mack JE. Worsening schizoaffective disorder with aripiprazole [letter]. Am J Psychiatry 2004;161:1308
12. Glick ID, Duggal V, Hodulik C. Aripiprazole as a dopamine partial agonist: positive and negative effects. J Clin Psychopharmacol 2006;26:101–103
13. Weiden PJ, Olfson M. Cost of relapse in schizophrenia. Schizophr Bull 1995;21:419–429
14. Pigott TA, Carson WH, Saha AR, et al. Aripiprazole for the prevention of relapse in stabilized patients with chronic schizophrenia: a placebo-controlled 26-week study. J Clin Psychiatry 2003;64:1048–1056
15. Dellva MA, Tran P, Tollefson GD, et al. Standard olanzapine versus placebo and ineffective-dose olanzapine in the maintenance treatment of schizophrenia. Psychiatr Serv 1997;48:1571–1577
16. Rabinowitz J, Lichtenberg P, Kaplan Z, et al. Rehospitalization rates of chronically ill schizophrenic patients discharged on a regimen of risperidone, olanzapine, or conventional antipsychotics. Am J Psychiatry 2001;158:266–269
17. Siris SG. Depression in schizophrenia: perspective in the era of "atypical" antipsychotic agents. Am J Psychiatry 2000;157:1379–1389
18. Birchwood M, Mason R, MacMillan F, et al. Depression, demoralization and control over psychotic illness: a comparison of depressed and non-depressed patients with a chronic psychosis. Psychol Med 1993;23: 387–395
19. Johnson DA. The significance of depression in the prediction of relapse in chronic schizophrenia. Br J Psychiatry 1988;152:320–323
20. Roy A, Thompson R, Kennedy S. Depression in chronic schizophrenia. Br J Psychiatry 1983;142:465–470
21. Hennekens CH, Hennekens AR, Hollar D, et al. Schizophrenia and increased risks of cardiovascular disease. Am Heart J 2005;150: 1115–1121
22. Kavanagh DJ, McGrath J, Saunders JB, et al. Substance misuse in patients with schizophrenia: epidemiology and management. Drugs 2002;62:743–755
23. Regier DA, Farmer ME, Rae DS, et al. Comorbidity of mental disorders with alcohol and other drug abuse: results from the Epidemiologic Catchment Area (ECA) Study. JAMA 1990;264:2511–2518
24. Subramaniam M, Chong SA, Pek E. Diabetes mellitus and impaired glucose tolerance in patients with schizophrenia. Can J Psychiatry 2003;48:345–347
25. Lieberman JA, Stroup TS, McEvoy JP, et al. Effectiveness of antipsychotic drugs in patients with chronic schizophrenia. N Engl J Med 2005;353:1209–1223
26. Schwartz AH, Perlman BB, Paris M, et al. Psychiatric diagnoses as reported to Medicaid and as recorded in patient charts. Am J Public Health 1980;70:406–408
27. Rawson NS, Malcolm E, D'Arcy C. Reliability of the recording of schizophrenia and depressive disorder in the Saskatchewan health care datafiles. Soc Psychiatry Psychiatr Epidemiol 1997;32:191–199