Inpatient resource use and costs associated with switching from oral antipsychotics to aripiprazole once-monthly for the treatment of schizophrenia

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Abstract

Background: Schizophrenia is associated with high direct healthcare costs due to progression of disease and frequent occurrence of relapses. Aripiprazole once-monthly (AOM) has been shown to reduce total psychiatric hospitalizations among patients who switched from oral standard of care (SOC) therapy to AOM in a multicenter, open-label, mirror-image study of patients with schizophrenia. Because of the increasing need to improve patient outcomes while containing costs, it is important to understand the impact of AOM treatment initiation on medical costs associated with psychiatric hospitalizations and antipsychotic pharmacy costs.

Methods: In the current study, an economic model was developed using data from the AOM mirror-image study to evaluate the psychiatric hospitalization-related medical costs and antipsychotic pharmacy costs during a 6-month period before (retrospective period) and after (prospective period) the AOM treatment initiation. The economic model evaluated cost-saving potential of AOM among all patients (n=433) as well as a subset of patients with ≥1 prior hospitalization (n=165) who switched from oral SOC to AOM. Unit cost data were obtained from publicly available sources.

Results: Both hospitalizations and hospital days were reduced following a switch from oral SOC to AOM. As a result, psychiatric hospitalization-related costs were lower during the prospective period when compared with the retrospective period. Furthermore, the increase in antipsychotic pharmacy costs due to switching from oral SOC to AOM was offset by a reduction in psychiatric hospitalization-related medical costs. Per-patient costs were reduced by $1,046 (USD) in the overall population and by $20,353 in a subset of patients who had at least 1 psychiatric hospitalization during the retrospective period. Results were most sensitive to changes in hospitalization costs.

Conclusions: AOM is associated with reducing the risk of relapse among patients with schizophrenia. The increase in antipsychotic pharmacy costs due to switching from oral SOC to AOM was offset by a reduction in costs associated with psychiatric hospitalizations, thereby presenting a cost-saving opportunity for health plans.

Keywords: schizophrenia, long-acting injectable, economic model, aripiprazole once-monthly, relapse, healthcare cost.

Abbreviations: AOM, aripiprazole once-monthly; HCUP, Healthcare Cost and Utilization Project; HEDIS, Healthcare Effectiveness Data and Information Set; ICER, incremental cost-effectiveness ratio; LAI, long-acting injectable; LOS, length of stay; P, prospective; R, retrospective; SOC, standard of care.

Citation

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Introduction

Schizophrenia affects approximately 2.4 million people in the United States (about 1.1% of the population ≥18 years of age) and is associated with high direct healthcare costs, estimated at $22.7 billion in 2002 ($48.4 billion in 2014 when adjusted for inflation using the US Consumer Price Index Medical Care Category) [1–3]. The high cost of schizophrenia treatment is due to the chronic nature of the disease and the frequent occurrence of relapses [4,5]. Rates of schizophrenia relapse have been reported as high as 80% at 12 months following treatment discontinuation [6]. Relapses often require hospitalization, which contributes substantially to the total healthcare costs associated with this disease [5]. Overall,
relapse can account for the largest portion of schizophrenia costs [2,7,8].

Antipsychotic treatment benefits patients by reducing the risk of relapse, but even partial nonadherence increases the risk of relapse-related hospitalizations [9]. Despite the importance of adherence, 74% of schizophrenia patients are nonadherent to oral antipsychotics according to an 18-month study [10].

Long-acting injectable (LAI) formulations of antipsychotic agents were developed with the primary aim of improving the treatment adherence of patients with schizophrenia, and thus preventing relapse, by providing sustained medication coverage to patients over the duration of the injectable. LAI treatment reduced the risk of rehospitalization compared with oral medication in a pair-wise comparison following hospital discharge [11] and resulted in a reduction in hospitalizations and schizophrenia relapses following initiation of LAI compared with oral medication [12]. Patients who initiated LAIs have also been shown to incur lower healthcare costs as a result of fewer hospitalizations [13,14], an outcome that encompasses all age groups, including young adults [15]. However, there are conflicting data on the comparative effectiveness of oral medications compared with LAIs in reducing the risk of relapse. In a recent randomized clinical trial, LAI risperidone did not confer an advantage over oral medication for relapse or hospitalization but did provide some advantage for psychotic symptoms [16]. The conflicting data highlight the need for continued evidence generation on the value of LAIs over oral antipsychotic medications.

Aripiprazole once-monthly (AOM) is the first dopamine partial agonist available in a long-acting formulation and has been approved for treatment of schizophrenia by the US Food and Drug Administration [17,18]. In a recent study of patients with schizophrenia, AOM significantly delayed time to relapse compared with placebo [18]. Additionally, in a separate multicenter, open-label, mirror-image study of patients with schizophrenia, AOM was reported to reduce total psychiatric hospitalizations among patients who switched from oral standard of care (SOC) therapy to AOM (AOM mirror-image study; NCT01432444) [19]. In that study, hospitalization rates were reduced from 38.1% (165/433) during the SOC 6-month retrospective period, compared with 8.8% (38/433) during the AOM 6-month prospective period (p<0.0001) [19].

Given the increasing pressure from payers to improve patient outcomes while containing costs, it is important to understand the impact of AOM treatment initiation on medical costs related to psychiatric hospitalizations and antipsychotic pharmacy costs. In the current study, a decision model was developed to estimate costs associated with AOM treatment initiation using the clinical data gathered in the AOM mirror-image study [19]. Additionally, because previous hospitalizations are predictive of future schizophrenia-related hospital admissions [20], the decision model evaluated cost-saving opportunities among a subset of patients who had at least one psychiatric hospitalization prior to AOM treatment initiation.

### Methods

#### Patient population and comparators

The patient population for this analysis was the population investigated in the multicenter, open-label AOM mirror-image study; specifically, patients were 18–65 years of age with schizophrenia who switched from oral SOC antipsychotic therapy (retrospective period) to AOM (prospective period) in a naturalistic community setting in North America [19]. In both the retrospective and prospective phases, the majority of patients were male (73.5 and 69.5%) and approximately half of the patients were white (46.2 and 49.9%). At baseline for the 2 study phases, patients had a mean age of 42.7 and 42.1 years and a mean BMI of 30.4 and 30.8 kg/m². Patients entering the prospective period had moderate disease severity (CGI-S scale 3.9±0.8) at baseline for the prospective period [19].

A decision model was designed to compare costs based on data obtained from the retrospective period of the AOM mirror-image study with costs based on data obtained from the prospective period. In the full study population group, 433 patients received oral SOC treatment in the 6-month retrospective period and then switched to AOM for the 6-month prospective period. In addition to this full study population, a subset of 165 patients from the AOM mirror-image study who had ≥1 psychiatric hospitalization during the retrospective period was also analyzed; among all patients who relapsed during the retrospective SOC period (n=19), 11.5% relapsed during the prospective AOM treatment period.

#### Model structure and input

A Microsoft Excel-based decision model was developed to compare psychiatric hospitalization-related medical and antipsychotic treatment costs before and after AOM treatment initiation based on the results of the mirror-image study. Per-patient costs (drug costs and psychiatric hospitalization-related charged amounts) were estimated during the pre- and post-AOM initiation period: the 6-month retrospective period during which patients received oral SOC treatment and the 6-month prospective period during which patients received AOM after switching treatment from oral SOC to AOM (Figure 1).

#### Clinical input

The probability of psychiatric hospitalizations and number of hospitalizations (among those hospitalized) were obtained from the AOM mirror-image study. Complete data for the 6-month retrospective period were available for the full study population (433 patients) and for the subset of 165 patients who experienced at least one psychiatric hospitalization during the 6-month retrospective period (Table 1). Similar data were collected for patients in the 6-month prospective period while on AOM; however, due to discontinuations from the clinical trial during the 6-month prospective period, complete data on psychiatric
hospitalizations were not available for all patients during this period. During the prospective period, patients stayed on AOM for an average of 4.93 months prior to discontinuing from the study. Based on Kane et al. [19], 140 out of 433 patients (32.3%) discontinued AOM at the end of 6 months of the study. Because patients were not on AOM for the entire 6 months and remained on AOM for a mean of 4.93 months before discontinuing treatment or exiting the study, estimates of the probability of hospitalization and number of hospitalizations among those hospitalized were calculated for the remaining 1.07 months using data from the retrospective period as a proxy.

Specifically, the percentage of patients experiencing a psychiatric hospitalization after discontinuation of AOM (6.08%) was derived by multiplying the percentage of hospitalizations in the retrospective period (38.11%) [19] by 0.178 (1.07 months divided by 6 months). The number of psychiatric hospitalizations among those hospitalized after discontinuation of AOM was estimated to be 1.04 (Table 1).

Cost input

Costs were obtained from publicly available sources and were used to calculate cost for drug and hospitalization charged amounts (summarized in Table 2). Pharmacy acquisition costs for oral aripiprazole and AOM as well as oral SOC were obtained [22]; the cost used for oral SOC was a simple average of generic pricing for fluphenazine, olanzapine, risperidone, quetiapine, and ziprasidone. Average hospitalization charges for a psychiatric hospitalization were obtained [23], and the same
Sensitivity analysis

Sensitivity analysis was performed to test the robustness of the model’s assumptions and specific parameter estimates, given their uncertainty. One-way sensitivity analysis in which one parameter value is varied at a time while all others are held constant was performed for the following model parameters: time on AOM, cost per month on oral medication, percentage of patients with a psychiatric hospitalization in both the retrospective and prospective periods, number of psychiatric hospitalizations among those hospitalized in both the retrospective period and prospective period, hospital length of stay, and cost per psychiatric hospitalization. Variation in these parameter values was based on 95% CIs or assumption (where data did not exist) (Tables 1 and 2). Additionally, a probabilistic sensitivity analysis in which the impact of varying all of the above parameters simultaneously according to prespecified distributions was conducted. Specifically, a second-order Monte Carlo simulation was conducted, in which variability was examined over 10,000 iterations.

Table 1. Clinical input parameters.

| Parameter                                      | Full study value (range) | Subpopulation value (range) | Data source                                                                 |
|-----------------------------------------------|--------------------------|-----------------------------|-----------------------------------------------------------------------------|
| Duration of treatment, months                 |                          |                             |                                                                             |
| Retrospective                                 | 6                        | 6                           | Study design                                                                |
| Prospective while on AOM                      | 4.93 (4.67–5.19)         | 5.15 (4.92–5.38)            | AOM mirror-image study results [19]                                         |
| Prospective while off AOM                     | 1.07                     | 0.85                        | Calculated as 6 months minus time on AOM                                    |
| Percentage of patients with hospital stay     |                          |                             |                                                                             |
| Retrospective                                 | 38.11% (33.60–42.73%)    | 100.0%                      | AOM mirror-image study/subpopulation [19]                                   |
| Prospective while on AOM                      | 8.78% (6.30–11.62%)      | 11.52% (7.13–16.80%)        | AOM mirror-image study results [19]                                         |
| Prospective while off AOM                     | 6.80%                    | 14.17%                      | Estimated assuming uniform distribution of hospitalizations for SOC (1.41 months/6 months) |
| Total estimated prospective                   | 15.58%                   | 25.69%                      | Sum of the two percentages above                                           |
| Among patients with ≥1 hospitalization, mean number of hospitalizations per patient |                          |                             |                                                                             |
| Retrospective                                 | 1.23 (1.13–1.33)         | 2.23 (1.13–1.33)            | Mirror-image study results [19]                                             |
| Prospective while on AOM                      | 1.18 (1.02–1.36)         | 1.26 (1.00–1.60)            | Mirror-image study results [19]                                             |
| Prospective while off AOM                     | 1.04                     | 1.03                        | Calculated as (No. Hosp_{R}–1) × (6–X months)/(6 months) + 1³                |
| Average estimated number of hospitalizations per patient among patients hospitalized during the prospective period | 1.12                     | 1.13                        | Weighted average of prospective hospitalizations while on and off AOM       |
| Average length of stay, days                  | 11.16 (9.04–13.50)       | 11.16 (9.04–13.50)          | HCUP 2015 [22]; US BLS 2015 [32]                                            |

ICER = \frac{\text{total cost accrued when on SOC+AOM} - \text{total cost accrued when on SOC}}{\text{Hospital days when on SOC} - \text{hospital days when on SOC+AOM}}

**Adverse events**

In the Kane study, patients were first stabilized on oral aripiprazole during the oral conversion phase prior to initiating AOM [19]. Due to the unavailability of tolerability data during the retrospective period, this model did not compare adverse events experienced before and after AOM treatment initiation. However, during the prospective period, patients may have discontinued AOM treatment due to adverse events and this is factored into the calculation of hospitalization rates after AOM initiation.

**Model calculations**

Costs and outcomes per patient over 6 months were estimated for the retrospective period and the prospective period (Figure 1). Per-patient model results were presented as drug costs, hospital charges, total costs (drug costs plus hospital charges), number of hospitalizations, and hospitalization days. Additionally, incremental cost-effectiveness ratio (ICER) per hospital day avoided over a 6-month period was calculated as:

\text{cost per hospitalization was applied to hospitalizations in both the retrospective and prospective periods. Charges represent the amount per hospitalization charged to the payer, whereas actual reimbursement may vary by health plan.}
### Table 2. Cost input parameters.

| Parameter                                             | Parameter estimate                                      | Plausible range for sensitivity analysis | Data source                                                                 |
|-------------------------------------------------------|--------------------------------------------------------|------------------------------------------|----------------------------------------------------------------------------|
| Drug cost amounts                                      |                                                        |                                          |                                                                            |
| AOM (per patient per month)                            | $1,61 (for full-cohort)                                | NA                                      | Redbook (2015) [22] and overall distribution of AOM doses during the prospective period in Kane (2015) [19] |
|                                                       | $1,619 (for subset of patients with at least 1 psychiatric hospitalization at baseline) |                                          |                                                                            |
| Cost of concomitant oral aripiprazole treatment at the time of AOM initiation | $349                                                   | NA                                      | Redbook (2015) [22]                                                        |
| Oral SOC (per month)                                   | $73                                                    | $59–$89                                 | Redbook (2015) [22]                                                        |
| Hospitalization charges                                |                                                        |                                          |                                                                            |
| Average charge\(^b\) per hospitalization            | $30,536                                                | $17,227–$47,591                         | HCUP 2015 [22]                                                             |

\(^a\)Oral antipsychotics include generically available antipsychotics, such as fluphenazine, olanzapine, risperidone, quetiapine, and ziprasidone. For the SOC-treatment cost calculation, it was assumed that patients were receiving lower-priced generic antipsychotics; hence, aripiprazole and paliperidone were excluded from this calculation.

\(^b\)Charges represent the amount per hospitalization charged to the payer; actual reimbursement may vary by health plan.

AOM, aripiprazole once-monthly; HCUP, Healthcare Cost and Utilization Project; NA, not applicable; SOC, standard of care.

Parameter uncertainty was varied based on available data. For example, 95% CIs were estimated for the number of psychiatric hospitalizations, given standard error and assuming a gamma distribution. Given the sample size and assuming a beta distribution, 95% CIs were also calculated for the percentage of patients with psychiatric hospitalizations. For time on therapy, 95% CI was estimated assuming a normal distribution and using the standard error from the clinical trial. Cost of oral antipsychotics and average hospital length of stay were varied by ±20% of base-case values while average hospital charges were varied by ±50%. For the one-way sensitivity analysis, the impact on the incremental cost per hospital day avoided for each parameter was then ranked from most sensitive to least sensitive and plotted in the form of a tornado diagram. For the probabilistic sensitivity analysis, the impact on the incremental total costs was presented in a histogram.

### Results

#### Deterministic results

In the overall population, the proportion of patients experiencing psychiatric hospitalization was reduced in the prospective phase compared with the retrospective phase, the mean number of hospitalizations per patient was reduced from 0.47 to 0.17 after AOM initiation, and mean hospital days per patient decreased from 5.23 to 1.95. As a result, the increase in drug costs in the prospective period ($7,943) was offset by a reduction in hospitalization charges ($–8,990) (Figure 2). Total cost in the prospective period ($13,708) was lower than that in the retrospective period ($14,754) by $1,046 per patient, and the incremental cost per hospital day avoided for the overall population was $–319, where AOM was dominant (more effective and less costly).

For the subset of 165 patients who had ≥1 prior hospitalization, the mean number of hospitalizations per patient was reduced from 1.23 to 0.29 after AOM initiation and the mean number of hospital days per patient decreased from 13.72 to 3.25. As with the full population, increased drug costs in the prospective period ($8,308) were offset by a reduction in hospital charges ($–28,660) (Figure 3). Total cost in the prospective period ($17,647) was 54% ($20,353) lower than the cost per patient in the retrospective period ($38,000), and the incremental cost per hospitalization day avoided was $–1,943, where AOM was again dominant.

#### Sensitivity analyses

For the one-way sensitivity analysis, the tornado diagram for the base population shows that the results were most sensitive to the costs per psychiatric hospitalization (Figure 4a). Specifically, decreasing the cost per psychiatric hospitalization to its lower bound increased the cost to avoid a hospital day up to $874. Decreasing the number of hospitalizations or the percentage of patients with a hospital stay in the retrospective period to their lower bounds also resulted in slightly positive
Figure 2. Estimated 6-month costs per patient before and after switching from SOC to AOM: base-case analysis.

| Cost Component | Retrospective | Prospective |
|----------------|--------------|-------------|
| Hospitalization | $14,314 | $5,324 |
| Drug | $8,384 | $441 |
| Total | $22,708 | $5,765 |

AOM, aripiprazole once-monthly; SOC, standard of care.

Figure 3. Estimated 6-month costs per patient before and after switching from SOC to AOM: subset of patients who had ≥1 prior hospitalization.

| Cost Component | Retrospective | Prospective |
|----------------|--------------|-------------|
| Hospitalization | $37,559 | $8,899 |
| Drug | $8,748 | $441 |
| Total | $46,307 | $13,340 |

AOM, aripiprazole once-monthly; SOC, standard of care.

Figure 4. Tornado diagram results of one-way sensitivity analysis for the full study population (a) and for patients with at least one hospitalization in the retrospective period (b).

Parameter

- Resource-use costs—Psychiatric hospitalization ($17,227−$47,591)
- Percentage with hospital stay—Retrospective (33.60%−42.73)
- Number of hospitalizations—Retrospective (1.13−1.33)
- Percentage with hospital stay—Prospective (6.30%−11.62)
- Number of hospitalizations—Prospective (1.02−1.36)
- Length of stay (days)—Psychiatric hospitalization (9.04−13.5)
- Months on maintenance—Prospective (4.67−5.19)

Parameter

- Resource-use costs—Psychiatric hospitalization ($17,227−$47,591)
- Length of stay (days)—Psychiatric hospitalization (9.04−13.5)
- Number of hospitalizations—Retrospective (1.13−1.33)
- Percentage with hospital stay—prospective (7.13%−16.80)
- Number of hospitalizations—Prospective (1−1.6)
- Cost per month on medication—retrospective ($59.47−$88.81)
- Months on maintenance—Prospective (4.92−5.38)
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Utilizing the patient information provided by the Kane mirror-image study, which evaluated hospitalizations during the retrospective phase (Figure 5a), AOM was cost saving in all iterations for the full study population (a) and for patients with at least one hospitalization in the retrospective period (b).

Discussion

Initiation of LAI treatment has been shown to reduce schizophrenia relapses [24,25] and hospitalizations [11–14]. Kane et al. have demonstrated that AOM delayed time to relapse [17] and that switching to AOM from oral SOC reduced hospitalizations in patients with schizophrenia [19]. In addition to its clinical benefits, prevention of relapse in patients with schizophrenia may also reduce the economic burden of this costly disease. Due to the need to improve patient outcomes while minimizing costs, it is important to understand the impact of AOM treatment on psychiatric hospitalization-related costs as evaluated in the Kane et al. study [19].

Utilizing the patient information provided by the Kane mirror-image study, which evaluated hospitalizations during a 6-month time frame in patients 18–65 years of age with schizophrenia who switched from oral SOC antipsychotic therapy (retrospective period) to AOM (prospective period), we have shown that AOM treatment may result in a cost-of-care savings opportunity. Although schizophrenia is a chronic, debilitating condition and a 6-month observation window does not evaluate the long-term impact of AOM, these data are important given that health plans, physicians, and hospital networks focus on Healthcare Effectiveness Data and Information Set (HEDIS) quality measures of 30-day readmission rates for patients with schizophrenia. Drug costs and psychiatric-hospitalization costs associated with AOM as a treatment strategy for preventing relapse are less than corresponding costs associated with oral SOC therapy. Additionally, hospitalizations and hospital days were both reduced following a switch from oral SOC to AOM.

When considering parameter uncertainty, the model was most sensitive to the cost of psychiatric hospitalizations. Even when the cost of hospitalizations was at its extreme values and disadvantaged AOM treatment, the incremental cost per hospital day avoided was less than the cost of being in the hospital for an additional day. In addition, in all cases of parameter variation, AOM remained the more effective treatment.

Similar to our study, other cost studies have shown a cost benefit of using LAIs. A Hong Kong study reporting a predictive model using linear regression based on generalized estimating equations showed that risperidone LAI was associated with reductions in hospitalization costs of 24.7% and hospitalization days of 10.1% [26], compared with a decrease of 40% for both hospitalizations and hospitalization days in the current study. Other recent risperidone mirror-image studies in Finland, Taiwan, and New Zealand have shown cost benefit in starting...
LAI treatment [27–29], although benefits were compromised by longer bed stay [29] and increased utilization of outpatient services [28]. All of the patients in the current study switched from oral antipsychotics to AOM, which was not necessarily the case in the other LAI mirror-image cost studies that have been reported. As a result, this analysis may provide a better approximation of the impact of switching to AOM that a patient may observe as compared with previous mirror-image studies, which may have had a proportion of patients already on LAIs.

Patients with schizophrenia have a known high risk of nonadherence to treatment, and LAIs were developed to improve treatment adherence in these patients. In addition to the sustained drug coverage of long-acting dosage forms, patients treated with LAIs are closely monitored because they must visit the clinic every 1–6 weeks [13]. Interaction with healthcare professionals during these visits may facilitate treatment adherence, which may reduce the risk of future relapses and hospitalizations [30]. Previous clinical trials have matched outcomes among patients receiving LAIs compared with oral antipsychotics. Because treatment nonadherence is greater in the real-world setting than in a controlled clinical-trial setting in which patients are closely monitored and have several incentives to adhere to their study medications, head-to-head clinical trials of LAIs compared with oral antipsychotics may not provide insight into the value of LAIs in the presence of patient nonadherence [31]. On the other hand, real-world observational studies comparing LAIs with oral antipsychotics pose challenges related to study design due to the selection bias of sicker schizophrenia patients, who are likely to receive LAIs compared to oral antipsychotics. Comparative effectiveness studies using multivariable analyses and statistical matching techniques may not be sufficient to account for the inherent clinical and disease-severity differences between patients initiating treatment with LAIs or oral therapies.

Mirror-image study designs that evaluate the change in patient outcomes before and after LAI initiation may be useful for understanding the value of LAIs; however, it is important to note the limitations of the AOM mirror-image study design in that each patient served as his or her own control with a parallel active-control group. As a result, it cannot be determined if other treatments (other LAIs, oral antipsychotics) may have a similar effect. Another limitation is that in this study design, it can be difficult to separate drug treatment effects from trial effects. Therefore, results may be influenced by independent factors, including admission patterns, insurance coverage, hospital bed availability, and community support. Additionally, as the study was not blinded, any influence of the study design on the clinical decision to hospitalize or not to hospitalize a given patient cannot be determined. It is unknown what the impact of these limitations may be and it may be possible to focus future studies to resolve these limitations.

In addition to limitations due to study design, the analysis evaluated only two aspects of the cost of care for patients with schizophrenia: those for antipsychotic medication and those for hospitalization. Although the prices of drugs and hospitalizations are expected to be the largest cost drivers in this patient population, due to lack of data on resource utilization such as emergency room visits, physician visits, and occurrence of adverse events during the retrospective and prospective phases, costs for these parameters were not included in the economic model.

**Conclusions**

Results from this economic model estimating the costs associated with psychiatric hospitalizations indicate that AOM treatment presents a potential cost-saving opportunity for health plans. The higher cost of drug is more than offset by cost savings due to fewer psychiatric hospitalizations, especially in a subset of patients with ≥1 previous psychiatric hospitalization. The use of AOM to prevent relapses may reduce the cost of care. As such, AOM treatment may be an appropriate clinical strategy for health plans.

**Contributions:** Michele Wilson, Siddhesh A. Kamat, Benjamin Gutierrez, Steve J. Offord, and Stephanie Earnshaw contributed to the conception and design of this study. This study’s statistical analyses were made by Michele Wilson; supervisory contributions were made by Siddhesh A. Kamat, Steve J. Offord, Anna Eramo, and Stephanie Earnshaw; and contributions related to administrative, technical, or material support were made by Christopher M. Blanchette. Michele Wilson, Anna Eramo, and Siddhesh A. Kamat contributed to the acquisition of data, and all authors contributed to the analysis and interpretation of the data as well as the writing, review, and revision of the manuscript.

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References

1. National Institute of Mental Health. Numbers count: mental disorders in America. Bethesda, MD; 2013 [cited 2013 Nov 17]. Available from: http://www.nimh.nih.gov/health/publications/the-numbers-count-mental-disorders-in-america/index.shtml#Schizophrenia

2. Wu EQ, Birnbaum HG, Shi L, Ball DE, Kessler RC, Moulis M, Aggarwal J. The economic burden of schizophrenia in the United States in 2002. J Clin Psychiatry 2005;66(9):1122–9. http://dx.doi.org/10.4088/JCP.v66n0906

3. U.S. Department of Labor. Bureau of Labor Statistics. Measuring price change for medical care in the CPI. Washington, D.C.; April 12, 2010 [cited 2014 Nov 17]. Available from: http://www.bls.gov/cpi/cpifact4.htm

4. Carr VJ, Lewin TJ, Neil AL, Halpin SA, Holmes S. Premorbid, psychosocial and clinical predictors of the costs of schizophrenia and other psychoses. Br J Psychiatry. 2004;184:517–25. http://dx.doi.org/10.1192/bjp.184.6.517

5. Ascher-Svanum H, Zhu B, Faries DE, Salkever D, Slade EP, Peng X, Conley RR. The cost of relapse and the predictors of relapse in the treatment of schizophrenia. BMC Psychiatry. 2010;10:2. http://dx.doi.org/10.1186/1471-244X-10-2

6. Emsley R, Chiliza B, Asmal L, Harvey BH. The nature of relapse in schizophrenia. BMC Psychiatry. 2013;13:50. http://dx.doi.org/10.1186/1471-244X-13-50

7. Feldman R, Bailey RA, Muller J, Le J, Dirani R. Costs of schizophrenia in the Medicare program. Popul Health Manag. 2014;17(3):190–6. http://dx.doi.org/10.1089/pop.2013.0062

8. Theida P, Beard S, Richter A, Kane J. An economic review of compliance with medication therapy in the treatment of schizophrenia. Psychiatr Serv. 2003;54(4):508–16. http://dx.doi.org/10.1176/appi.ps.54.4.508

9. Weiden PJ, Kozma C, Grogg A, Locklear J. Partial compliance and risk of rehospitalizations among California Medicaid patients with schizophrenia. Psychiatr Serv. 2004;55(8):886–91. http://dx.doi.org/10.1176/appi.ps.55.8.886

10. Lieberman JA, Stroup TS, McEvoy JP, Swartz MS, Perkins DO, Keefe RS, Davis SM, Davis CE, Lebowitz BD, Severe J, Hsiao JK. Clinical Antipsychotic Trials of Intervention Effectiveness (CATIE) Investigators. Effectiveness of antipsychotic drugs in patients with chronic schizophrenia. N Engl J Med. 2005;353(12):1209–23. http://dx.doi.org/10.1056/NEJMoa051688

11. Tiihonen A, Haukka J, Taylor M, Haddad PM, Patel MX, Korhonen P. A nationwide cohort study of oral and depot antipsychotics after first hospitalization for schizophrenia. Am J Psychiatry. 2011;168(6):603–9. http://dx.doi.org/10.1176/appi.ajp.2011.10081224

12. Offord B, Wong B, Mirski D, Baker RA, Lin J. Healthcare resource usage of schizophrenia patients initiating long-acting injectable antipsychotics vs oral. J Med Econ. 2013;16(2):231–9. http://dx.doi.org/10.3111/13696998.2012.751025

13. Peng X, Ascher-Svanum H, Faries D, Conley RR, Schuh KJ. Decline in hospitalization risk and health care cost after initiation of depot antipsychotics in the treatment of schizophrenia. Clinicoecon Outcomes Res. 2011;3:9–14. http://dx.doi.org/10.2147/CEOR.S16061
14. Bera R, Offord S, Zubek D, Lau G, Lin J, Baker RA, Karson C. Impact on healthcare resource usage and costs among Medicaid-insured schizophrenia patients after initiation of treatment with long-acting injectable. J Med Econ. 2013;16(4):522–8. http://dx.doi.org/10.3111/13696998.2013.771641

15. Karson C, Offord S, Baker RA, Eramo A, Lin J, Kamat S. Inpatient resource utilization and cost-related benefits of long-acting injectable antipsychotics across different age groups of Medicaid-insured schizophrenia patients. Presented at: the 52nd Annual Meeting of the American College of Neuropsychopharmacology; December 8–12, 2013; Hollywood, FL. Abstract W105.

16. Buckley PF, Schooler NR, Goff DC, Hsiao J, Kopelowicz A, Lauriello J, Manschreck T, Mendelowitz AJ, Miller del D, Severe JB, Wilson DR, Ames D, Bustillo J, Mintz J, Kane JM. PROACTIVE Study. Comparison of SGA oral medications and a long-acting injectable SGA: the PROACTIVE study. Schizophr Bull. 2015;41(2):449–59. http://dx.doi.org/10.1093/schbul/sbu067

17. Otsuka Pharmaceutical Co, Ltd. ABILIFY (aripiprazole) [prescribing information]. 2012. Tokyo, Japan.

18. Kane J, Sanchez R, Perry P, Jin N, Johnson BR, Forbes RA, McQuade RD, Carson WH, Fleischhacker WW. Aripiprazole intramuscular depot as maintenance treatment in patients with schizophrenia: a 52-week multicenter, randomized, double-blind, placebo-controlled study. J Clin Psychiatry. 2012;73(5):617–24. http://dx.doi.org/10.4088/JCP.11m07530

19. Kane JM, Zhao C, Johnson BR, Baker RA, Eramo A, McQuade RD, Duca AR, Sanchez R, Peters-Strickland T. Hospitalization rates in patients switched from oral antipsychotics to aripiprazole once-monthly: final efficacy analysis. J Med Econ. 2015;18(2):145–54. http://dx.doi.org/10.3111/13696998.2014.979936

20. Yussuf AD, Kuranga SA, Balogun OR, Ajiboye PO, Issa BA, Adegunloye Q, Parakoyi MT. Predictors of psychiatric readmissions to the psychiatric unit of a tertiary health facility in a Nigerian city – a 5-year study. Afr J Psychiatry (Johannesburg). 2008;11(3):187–90. http://dx.doi.org/10.4314/afrpsy.v11i3.30267

21. Kamat SA, Blanchette CM, Wilson M, Tangirala M, Earnshaw S, Offord S, Gutierrez B, Eramo A, Baker RA. Health care cost savings associated with aripiprazole once-monthly (AOM) treatment among schizophrenia patients with psychiatric hospitalizations prior to AOM treatment initiation. Value Health. 2014;17(3):A216. http://dx.doi.org/10.1016/j.jval.2014.03.1262

22. Micromedex. Red Book Online. Accessed through Micromedex 2.0. Thomson Reuters September, 2015.

23. Healthcare Cost and Utilization Project (HCUP). Agency for Healthcare Research and Quality; 2012; Rockville, MD [cited 2015 Sep]. Available from: http://www.ahrq.gov/research/data/hcup/index.html

24. Gaebel W, Schreiner A, Bergmans P, de Arce R, Rouillon F, Cordes J, Eriksson L, Smeraldi E. Relapse prevention in schizophrenia and schizoaffective disorder with risperidone long-acting injectable vs quetiapine: results of a long-term, open-label, randomized clinical trial. Neuropsychopharmacology. 2010;35(12):2367–77. http://dx.doi.org/10.1038/npj.2010.111

25. Leucht C, Heres S, Kane JM, Kissling W, Davis JM, Leucht S. Oral versus depot antipsychotic drugs for schizophrenia—a critical systematic review and meta-analysis of randomised long-term trials. Schizophr Res. 2011;127(1–3):83–92. http://dx.doi.org/10.1016/j.schres.2011.10.020

26. Wu DB, Lee EH, Chung WS, Chow DP, Lee VW, Wong MC, Lee KK. Cost analysis of risperidone long-acting injection in the treatment of schizophrenia and schizoaffective disorders in Hong Kong: an approach using generalised estimating equations. Psychiatry Res. 2013;210(3):745–50. http://dx.doi.org/10.1016/j.psychres.2013.07.012

27. Asseburg C, Willis M, Löthgren M, Seppälä N, Hakala M, Persson U. Hospitalisation utilisation and costs in schizophrenia patients in Finland before and after initiation of risperidone long-acting injection. Schizophr Res Treatment. 2012;2012:791468 http://dx.doi.org/10.1155/2012/791468

28. Chang HC, Tang CH, Huang ST, McCrone P, Su KP. A cost-consequence analysis of long-acting injectable risperidone in schizophrenia: a one-year mirror-image study with national claim-based database in Taiwan. J Psychiatr Res. 2012;46(6):751–6. http://dx.doi.org/10.1016/j.jpsychires.2012.02.019

29. Carswell C, Wheeler A, Vanderpyl J, Robinson E. Comparative effectiveness of long-acting risperidone in New Zealand: a report of resource utilization and costs in a 12-month mirror-image analysis. Clin Drug Invest. 2010;30(11):777–87. http://dx.doi.org/10.2165/11537680-000000000-00000

30. Olsson M, Marcus SC, Ascher-Svanum H. Treatment of schizophrenia with long-acting fluphenazine, haloperidol, or risperidone. Schizophr Bull. 2007;33(6):1579–87. http://dx.doi.org/10.1093/schbul/sbm033

31. Kirson NY, Weiden PJ, Yermakov S, Huang W, Samuelson T, Offord SJ, Greenberg PE, Wong BJ. Efficacy and effectiveness of depot versus oral antipsychotics in schizophrenia: synthesizing results across different research designs. J Clin Psychiatry. 2013;74(6):568–75. http://dx.doi.org/10.4088/JCP.12r08167

32. U.S. Department of Labor, U.S. Bureau of Labor Statistics, US city average, not seasonally adjusted medical care services [cited 2015 Sept]. Available from: http://data.bls.gov/DPD/outside.jsp?survey=cu