Reduction in inpatient resource utilization and costs associated with long-acting injectable antipsychotics across different age groups of Medicaid-insured schizophrenia patients

Siddhesh A Kamat1, Steve Offord1, John Docherty1, Jay Lin2, Anna Eramo3, Ross A Baker4, Benjamin Gutierrez5*, Craig Karson2

1Otsuka America Pharmaceutical, Inc., Princeton, NJ, USA; 2Novosys Health, Flemington, NJ, USA; 3Lundbeck, Deerfield, IL, USA
4Otsuka Pharmaceutical Development and Commercialization, Inc., Princeton, NJ, USA; 5CNK Consulting Group LLC, Delray Beach, FL, USA
*Current affiliation is GlaxoSmithKline, King of Prussia, PA, USA

Citation
Kamat SA, Offord S, Docherty J, Lin J, Eramo A, Baker RA, Gutierrez B, Karson C. Reduction in inpatient resource utilization and costs associated with long-acting injectable antipsychotics across different age groups of Medicaid-insured schizophrenia patients. Drugs in Context 2015; 4: 212267. doi: 10.7573/dic.212267

Copyright
Copyright © 2015 Kamat SA, Offord S, Docherty J, Lin J, Eramo A, Baker RA, Gutierrez B, Karson C. Distributed under the terms of the Creative Commons License Deed CC BY NC ND 3.0 which allows anyone to copy, distribute, and transmit the article provided it is properly attributed in the manner specified below. No commercial use without permission.

Correct attribution
Copyright © 2015 Kamat SA, Offord S, Docherty J, Lin J, Eramo A, Baker RA, Gutierrez B, Karson C. http://dx.doi.org/10.7573/dic.212267. Published by Drugs in Context under Creative Commons Attributions License Deed CC BY NC ND 3.0.

Article URL
http://www.drugsincontext.com/reduction-inpatient-resource-utilization-costs-associated-long-acting-injectable-antipsychotics-across-different-age-groups-medicaid-insured-schizophrenia-patients

Abbreviations
CCI, Charlson Comorbidity Index; LAI, long-acting injectable; SD, standard deviation

Correspondence
Siddhesh Kamat, MS, MBA, Health Economics & Outcomes Research, Otsuka America Pharmaceutical, Inc., Princeton, NJ, 08540, USA. Siddhesh.Kamat@otsuka-us.com

Provenance
Submitted, externally peer reviewed
Group Editor-in-Chief
Christopher M Blanchette, PhD, MBA
Associate Dean for Research & Public Engagement, Director of Data Sciences and Business Analytics, Associate Professor of Public Health Sciences, College of Health and Human Services, University of North Carolina at Charlotte, NC, USA

Expert Advisers – Epidemiology and biostatistics
Alex K Exuzides, PhD
Director, ICON Clinical Research Inc, San Francisco, CA, USA

Professor Scott L Friedman, MD
Fishberg Professor of Medicine, Dean for Therapeutic Discovery Chief, Division of Liver Diseases, Mount Sinai School of Medicine, New York, USA

Carl De Moor, PhD
Chief Technology Officer, Inform Genomics Inc, USA

Expert Adviser – Publication Ethics
Dr Elizabeth (Liz) Wager
Publications Consultant, Princes Risborough, UK; Visiting Professor, University of Split School of Medicine, Croatia; Former Chair (2009-2012), Committee on Publication Ethics (COPE)

Specialist editorial board members
Anthony Louder
Principal Researcher – Retrospective Research, Comprehensive Health Insights, Humana Inc, Cincinnati, OH, USA

Nick C Patel, PharmD, PhD, BCPP
Director and Practice Lead – Collaboration Research, Comprehensive Health Insights, Humana Inc, Spring, TX, USA

Dr Jill Rasmussen
General Practitioner, Merstham, Surrey, UK

To see the full Drugs in Context Editorial Board, please visit www.drugsincontext.com/editorial-board

Editor-in-Chief Emeritus
Dr George Kassianos, FRCPG, FBHS, FESC, FBGTHA, FAcadMed, FFTM RCPSPGlasg
General Practitioner, Bracknell, Berkshire, UK; President, British Global & Travel Health Association; Fellow of the European Society of Cardiology
Reduction in inpatient resource utilization and costs associated with long-acting injectable antipsychotics across different age groups of Medicaid-insured schizophrenia patients

Siddhesh A Kamat, Steve Offord, John Docherty, Jay Lin, Anna Eramo, Ross A Baker, Benjamin Gutierrez, Craig Karson

Otsuka America Pharmaceutical, Inc., Princeton, NJ, USA; Novosys Health, Flemington, NJ, USA; Lundbeck, Deerfield, IL, USA

Otsuka Pharmaceutical Development and Commercialization, Inc., Princeton, NJ, USA; CNK Consulting Group LLC, Delray Beach, FL, USA

Current affiliation is GlaxoSmithKline, King of Prussia, PA, USA

Abstract

Objective: Evaluate utilization of inpatient healthcare resources and associated costs after 12 months of treatment using long-acting injectable (LAI) antipsychotic medications among a large sample of Medicaid-insured patients categorized by different age groups.

Method: Adult patients with schizophrenia were identified from the Thomson Reuters MarketScan Research database (1/1/2006–12/31/2010) before initiation of treatment using LAI antipsychotic agents. Utilization of inpatient healthcare resources and associated direct medical costs were compared for 12-month baseline and 12-month follow-up periods.

Results: Among 3,094 Medicaid-insured patients with schizophrenia initiating treatment with LAIs, the mean number of all-cause hospitalizations and hospitalization days were reduced by 24% and 31% (p<0.0001) compared with baseline, respectively, with similar significant reductions among all age groups (18–30, 31–40, 41–50, and 51–60 years). During 12-month follow-up with LAIs, mean reductions in all-cause costs were $4,369 (18–30 years, p<0.0001), $3,681 (31–40 years, p<0.0001), $2,051 (41–50 years, p=0.1332), and $4,492 (51–60 years, p=0.0107). Subanalyses separating first-generation and second-generation medication groups resulted in mean reduction in all-cause costs of $3,561 and $3,645, respectively.

Conclusions: Results from this large cohort study provide naturalistic real-world evidence of the utility of LAIs in patients with schizophrenia and suggest that these agents may help to reduce the risk of relapse across all age groups (especially among younger patients). Given that relapse prevention is the ultimate goal of antipsychotic treatment, results from this large Medicaid patient population establish the value of LAIs for the management of schizophrenia.

Keywords: utilization of inpatient healthcare resources, inpatient costs, long-acting injectable agents, schizophrenia, mirror study, first-generation, second-generation, naturalistic study.

Introduction

Schizophrenia is a burden for patients and society. An estimated 1.1% of adults (2.6 million) in the USA are diagnosed with schizophrenia (one-year prevalence based on data from the 2010 census) with onset in early adulthood [1,2]. The overall cost of schizophrenia in the USA was estimated to be $22.7 billion in 2002 based on direct healthcare costs (drug acquisition; care in inpatient, outpatient, and long-term settings) for patients with schizophrenia, which was equivalent to $46.7 billion in 2012 (adjusted for inflation using the US Consumer Price Index Medical Care Category) [3].

Antipsychotic therapy remains the cornerstone of schizophrenia management. However, in the naturalistic real-world setting, adherence to antipsychotic agents given via the oral route is often low. Up to 74% of patients are non-adherent to prescribed oral antipsychotic agents [4].
Non-adherence to oral antipsychotics is associated with an increased risk of schizophrenia relapse as well as hospitalizations and associated costs [5–7]. Even short gaps in medication intake have been shown to increase the risk of relapse [8]. Early-intervention strategies are associated with successful treatment outcomes [9]. Discontinuation of antipsychotic therapy by patients with first-episode schizophrenia and schizoaffective disorder has been reported to carry the strongest correlation of risk factors for relapse [10], and is the biggest predictive factor of relapse after a first episode of psychosis [11].

Long-acting injectable (LAI) formulations of antipsychotic agents (‘depot antipsychotics’) were developed with the primary aim of improving treatment adherence in patients with schizophrenia. LAIs provide sustained drug coverage due to the drug-formulation benefits of long-acting dosage forms. In addition, patients treated with LAIs must visit the clinic every 1–6 weeks [12] where interactions with healthcare professionals can facilitate persistence and adherence to treatment, thereby reducing the risk of future relapses and hospitalizations [13].

Guidelines, such as those set by the American Psychiatric Association and the World Federation of Societies of Biological Psychiatry [14–19], support use of LAIs for patients with schizophrenia. However, in the naturalistic real-world setting, the effectiveness of LAIs compared with that of oral treatments is controversial. Controlled clinical studies have demonstrated that LAIs are at parity with oral treatments in terms of efficacy [20]. Specifically, a recent non-inferiority trial investigated three second-generation antipsychotic agents compared with an oral antipsychotic. The investigators found the oral antipsychotic to be non-inferior in both the 18-month intent-to-treat analysis and additional subanalyses [21]. Also, the Preventing Relapse Oral Antipsychotics Compared to Injectable Efficacy (PROACTIVE) study showed that differences between treatment use of LAIs and oral second-generation agents in time to first relapse and hospitalization were not significant [22]. In addition, a meta-analysis of randomized trials revealed that second-generation LAIs were similar to oral medications in terms of relapse prevention, though first-generation LAIs were superior to oral medications [23]. That study stated that randomized controlled trials are less representative of real-world patients, and that studies in real-world patients are needed to make a true comparison. Given that treatment non-adherence is most evident in the naturalistic real-world setting, results from controlled clinical studies may not be the most important consideration in understanding the value of LAIs in the management of schizophrenia. Several systematic reviews and meta-analyses of studies of LAIs compared with oral treatments have indicated that study design and practice setting play important parts, especially with regard to medication adherence, and that these naturalistic and/or mirror studies favor LAIs over oral therapies in terms of effectiveness and adherence [24–26].

Naturalistic and/or mirror studies demonstrate the benefits of use of LAIs, including reduction of the risk of schizophrenia relapse, resource utilization, and cost. Use of LAIs has been shown to reduce the frequency of re-hospitalizations for patients with schizophrenia compared with oral formulations of the same treatment [27]. All-cause hospitalizations and schizophrenia-related hospitalizations were reduced by 41% and 56%, respectively, among patients who initiated therapy using LAIs in community mental health centers and Veterans Health Administration hospitals in the USA [28]. Utilization of inpatient healthcare resources and schizophrenia relapses declined significantly after patients initiated therapy using LAIs within the Veterans Health Administration [29], and the prevalence of hospitalization and related costs declined in commercially insured patients who initiated therapy using LAIs [12]. Two recent reports describe an improvement in patient outcomes based on fewer hospitalizations and relapses, and an associated reduction in healthcare costs for patients with schizophrenia who initiated therapy using LAI antipsychotic therapy [30,31]. Collectively, these data support use of LAIs as an important treatment option for patients with schizophrenia.

Medicaid is the largest payer of mental health services in the USA. It provides critical access to health and behavioral care for individuals with mental illnesses [32]. More than half of Medicaid beneficiaries are diagnosed with a mental illness, including schizophrenia and bipolar disorder [33], thereby underscoring the importance of understanding disease burden and best treatment options for patients reliant upon Medicaid.

Studies in commercially insured and Medicaid-insured patients suggest that LAIs are used more often among older patients, and also document the effectiveness of LAIs over a six-month timeframe [31]. However, data are limited on the effectiveness of LAIs among different age categories (especially younger patients) and the long-term benefits of LAIs observed over 12 months.

To advance our understanding of the effectiveness of LAIs in reducing hospitalizations among patients with schizophrenia in the USA, we evaluated utilization of inpatient healthcare resources and direct medical costs before and after initiation of use of LAIs among one of the largest available databases of Medicaid-insured patients with schizophrenia. The value of initiating LAIs for patients across different age categories was also assessed to evaluate treatment-related unmet need among younger patients.

**Methods**

**Data source and study design**

This was a retrospective study of Medicaid-insured patients who initiated therapy using LAIs. Patients (aged 18–60 years)
with at least one inpatient claim or two outpatient claims on separate dates with a primary or secondary diagnosis of schizophrenia (ICD-9-CM codes 295.0X, 295.1X, 295.2X, 295.3X, 295.5X, 295.6X, 295.8X, 295.9X) before initiation of treatment with LAI antipsychotic agents (index event) were identified for inclusion from the Thomson Reuters MarketScan Research database (1/1/2006–12/31/2010). It is a proprietary US research database providing fully integrated, de-identified patient data (inpatient, outpatient, drug, laboratory, health and productivity management; health-risk assessment; benefit design) from commercial, Medicare supplemental, and Medicaid populations. The index date was the date of initiation of LAIs. Patients were required to have 12 months of continuous enrolment in medical and pharmacy health plans before (baseline period) and after (follow-up period) initiation of LAI antipsychotic agents to ensure a balanced comparison in the two study periods. Utilization of inpatient healthcare resources and associated actual direct medical costs were compared for baseline and follow-up periods. The follow-up period for all endpoints was 12 months.

To assess the effectiveness of LAIs among different-aged patients with schizophrenia, patients from the full study group were divided into four age categories: 18–30, 31–40, 41–50, and 51–60 years.

Results

Demographics and clinical characteristics

A total of 3,094 Medicaid-insured patients with schizophrenia who initiated treatment using LAIs were included in these analyses. Baseline demographic and clinical characteristics are summarized in Table 1. Overall, the mean age was 38.7 years. Most patients were male (55.0%) and were African–American (58.3%) or Caucasian (32.5%). The most common LAI antipsychotic therapies initiated (index drugs) were haloperidol and risperidone (41.8% and 38.6%, respectively; Table 1).

Comorbidities and concomitant medications

Most patients had a CCI score of 0 (total mean score of 0.8; Table 1), which suggested a low comorbidity burden and

| Table 1. Demographics and clinical characteristics of patients at baseline. |
|---------------------------------------------------------------|
| **Variable** | **Full study group (N=3,094)** |
|---------------|---------------------------------|
| **Continuous variables** |                                |
| Age, years    | Mean 38.7 SD 12.0               |
| Charlson Comorbidity Index | 0.79 SD 1.33 |
| **Charlson Comorbidity Index group** | N % |
| 0             | 1,816 58.7                     |
| 1–2           | 1,002 32.4                     |
| 3–4           | 198 6.4                        |
| ≥5            | 78 2.5                         |
| **Categorical variables** | N % |
| Sex               |                                |
| Male             | 1,702 55.0                     |
| Female           | 1,392 45.0                     |
| Race             |                                |
| Caucasian        | 1,006 32.5                     |
| African–American | 1,803 58.3                     |
| Hispanic         | 42 1.4                         |
| Other/unknown    | 243 7.9                        |
| **Index drug, n (%)** |                |
| Fluphenazine     | 395 12.8                       |
| Haloperidol      | 1,294 41.8                     |
| Paliperidone     | 212 6.9                        |
| Risperidone      | 1,193 38.6                     |

*Cut-off for patient age was >60 years.

Patient and treatment-related characteristics of interest

**Baseline characteristics.** Demographic/clinical characteristics and comorbidities assessed by the Charlson Comorbidity Index (CCI) [34], as well as utilization of healthcare resources and associated costs, were reported. Inpatient costs were acquired from the MarketScan Research database representing the payment amount recorded in the claims database.

**Outcomes of interest over the follow-up period.** The change in the number of all-cause hospitalizations, the change in the number of all-cause inpatient days, and direct inpatient costs were reported.

Statistical analyses

Descriptive statistics were used to evaluate differences for baseline and follow-up with p-values provided by chi-squared test, analysis of variance, and Student’s t-tests (when appropriate). Statistical analyses were carried out using SAS® 9.2 software; p=0.05 was considered significant. Repeated measures in the study design provided additional statistical power to the overall analyses.

*SAS Institute, Inc., Cary, NC, USA.*
Utilization of healthcare resources

Compared with baseline, initiation of therapy using LAI antipsychotic agents resulted in significant reductions in utilization of all-cause inpatient resources during 12-month follow-up regardless of age.

For the full study group, the mean number of all-cause hospitalizations before and after initiation of therapy using LAI antipsychotic agents was reduced significantly by 24.2%, from 1.28 (standard deviation [SD] 2.19) to 0.97 (SD 1.97); p<0.0001 (Figure 1a). Specific age-group analyses of the full study group also showed that the mean number of all-cause hospitalizations before and after initiation of therapy using LAI antipsychotic agents was reduced significantly. The mean number of hospitalizations was reduced by 21.7%, from 1.38 (SD 2.13) to 1.08 (SD 2.26); p<0.0001 (18–30 years); 29.5%, from 1.22 (SD 1.91) to 0.86 (SD 1.74); p<0.0001 (31–40 years); 26.0%, from 1.23 (SD 2.24) to 0.91 (SD 1.93); p<0.0001 (41–50 years); and 23.8%, from 1.26 (SD 2.45) to 0.96 (SD 1.72); p=0.0021 (51–60 years). Subanalyses separating first-generation and second-generation medication groups showed similar reductions for the overall age group (Figure 1b) and individual age groups (data not shown). In subanalyses of data for mental health-related hospitalizations, the mean number of hospitalizations was also reduced significantly by 24.2%, from 1.24 (SD 2.07) to 0.94 (SD 1.93).

The mean number of hospitalization days before and after initiation of therapy using LAI antipsychotic agents was reduced significantly by 31.0%, from 11.52 (SD 20.33) to 7.95 (SD 19.72) days; p<0.0001 (Figure 2a). The mean number of hospitalization days was also reduced by 32.4%, from 13.10 (SD 23.37) to 8.85 (SD 22.16); p<0.0001 (18–30 years); by 38.9%, from 10.36 (SD 18.00) to 6.33 (SD 14.15); p<0.0001 (31–40 years); by 25.5%, from 10.34 (SD 18.43) to 7.70 (SD 20.08); p=0.0001 (41–50 years); and by 28.4%, from 11.85 (SD 19.73) to 8.48 (SD 19.79); p=0.0003 (51–60 years). Subanalyses separating first-generation and second-generation medication groups showed similar reductions for the overall age group (Figure 2b) and individual age groups (data not shown). In subanalyses of the data for mental health-related hospitalizations, the total length of stay was reduced by 31.6% from 11.35 (SD 20.07) to 7.76 (SD 19.40). As for full-study data, age-group data had similar reductions.

Annual healthcare costs

As a result of the decline in the mean number of hospitalizations and hospitalization days for inpatients, hospital costs were collectively significantly lower during 12-month follow-up compared with baseline for most ages, with the exception of patients aged 41–50 years (Figure 3).

Mean reduction in all-cause costs for the full study group was $3,599 (p<0.0001) during 12-month follow-up compared with baseline. For specific age groups, mean reductions in all-cause costs were $4,369 (18–30 years; p<0.0001), $3,681 (31–40 years; p<0.0001), $2,051 (41–50 years; p=0.1332), and $4,492 (51–60 years; p=0.0107) during 12-month follow-up compared with baseline. Annual healthcare costs were also assessed in the subanalyses separating first-generation and second-generation medication groups, and demonstrated similar results (Figure 3b); mean reduction in all-cause costs for the first-generation medication group was $3,561, and was $3,645 for the second-generation medication group. In subanalyses focusing on mental health-related hospitalizations, the mean reduction in total costs was $3,587 (p<0.0001), and for the specific age groups was $4,270 (18–30 years; p<0.0001), $3,846 (31–40 years; p<0.0001) and $3,128 (41–50 years; p<0.0001) for the second-generation medication group.
p<0.0001), $2,154 (41–50 years; p=0.0878), and $4,275 (51–60 years; p=0.0090) during 12-month follow-up compared with baseline.

**Discussion**

Observational studies have provided naturalistic real-world evidence that therapy using LAI antipsychotic agents can improve management of schizophrenia. Such study designs are more representative of the population of schizophrenia patients. They also provide information on treatment patterns and resource utilization observed in these patients in routine clinical practice. This retrospective mirror study involving >3,000 Medicaid-insured patients with schizophrenia in the USA is one of the largest cohorts studied to evaluate outcomes associated with LAIs over a 12-month follow-up period. Results showed that compared with baseline, during the 12-month follow-up after initiation of treatment using LAI antipsychotic agents, a reduction in healthcare utilization and associated annual healthcare costs was clearly evident. Utilization of all-cause inpatient healthcare and costs for the full study group were reduced significantly during the 12-month follow-up after initiation of treatment using LAI antipsychotic agents compared with baseline. Specific age-group analyses of the full study population indicate that LAIs are as effective in younger patient groups as they are for older patients.

Our findings on the reduction in the utilization of healthcare resources and costs are consistent with previous analyses of US claims documenting reductions among patients with schizophrenia who initiated treatment of LAIs in the naturalistic real-world setting [12,30,31]. While consistent with the overall reduction in utilization of healthcare resources, the magnitude of cost savings was higher in earlier studies, possibly due to smaller cohorts and shorter time horizons [12] or inclusion of commercial populations [31]. Differences in cost savings between the present study and those reported...
by Bera and colleagues [30] in a similar study of Medicaid-insured patients with schizophrenia may be due to the variable follow-up period in the Bera study after initiation of LAIs, which ended when the patient was disenrolled from Medicaid coverage, or at the end of the study period, whichever came first. For patients who were not taking antipsychotic medications at baseline (n=821; Figure 1), reductions in resource utilization and healthcare costs may be because patients are receiving LAIs and because of initiating treatment with antipsychotic agents.

The comprehensive body of evidence from naturalistic and mirror studies should be considered in addition to controlled clinical studies that indicate that LAIs are at parity in terms of effectiveness compared with oral treatments [20]. Non-adherence to treatment is more likely in the naturalistic real-world setting than in clinical trials. Hence, it may be more appropriate to consider the results from these naturalistic and mirror studies instead of extrapolating findings on adherence and effectiveness from clinical studies to the naturalistic real-world setting. Evidence suggests that patients in the real-world setting are less likely to engage with physicians and health-service providers [24,25]. No clinical studies have shown that oral therapies are better than LAIs in terms of effectiveness, suggesting that LAIs may be considered for use based on the preferences of physicians, patients, or caregivers.

Research design is different in randomized controlled trials compared with naturalistic and mirror studies. While both are valid approaches, it can be argued that naturalistic and mirror studies offer more appropriate conditions for evaluation of the benefits of LAIs. However, conducting such studies presents a unique set of methodological challenges because, in the real world, LAIs are used among patients with more severe schizophrenia. Multivariable analyses and statistical matching...
may consider use of LAIs even in younger patients with schizophrenia. In such patients, prevention may have the greatest long-term impact in terms of patient outcomes and reduced utilization of healthcare resources.

**Limitations**

The baseline compared with the follow-up study design lacks a comparable control patient population and regression to the mean. The effects of regression to the mean have been explored via age-category analyses, which show consistency in the finding that reduction in resource use and cost is similar across the four age groups. In addition, the fact that the baseline period may have contained a possible ‘index’

Figure 3. Reduction in costs for all-cause inpatient healthcare.

![Graph showing reduction in costs for all-cause inpatient healthcare](image)

- **A**
  - Full study group (N=3,094)
  - 18–30 years (n=983)
  - 31–40 years (n=617)
  - 41–50 years (n=877)
  - 51–60 years (n=617)

- **B**
  - First generation (n=1,689)
  - Second generation (n=1,405)

| Total mean hospital payment ($) | Pre-LAI initiation | Post-LAI initiation |
|--------------------------------|--------------------|--------------------|
| 20,000                         | $18,000            | $16,000            |
| 16,000                         | $14,000            | $12,000            |
| 12,000                         | $10,000            | $8,000             |
| 8,000                          | $6,000             | $4,000             |
| 4,000                          | $2,000             | $0                 |

*p*-values were determined by the paired t-test. *p*<0.0001. **p=0.1332. ***p=0.0107.

LAI, long-acting injectable.
hospitalization may have confounded the results. Furthermore, adherence was not assessed in the follow-up period, and so there was no control for adherence in the study. Some patients may have not continued administration of LAIs in the follow-up period, which may have affected the results. However, limiting the patient population to only those with high adherence would be too restrictive on the analyses and would enrich the sample with a specific population.

The LAI antipsychotic agents evaluated in this study included typical and atypical types, and the efficacy, safety, and outcomes may differ by class. Further study is needed to evaluate the outcomes of patients with schizophrenia treated with a particular LAI antipsychotic agent.

The MarketScan Medicaid database comprises claims submitted by healthcare providers. Such claims are subject to possible coding errors, coding for the purpose of exclusion rather than the actual disease, and undercoding (either by the healthcare provider or due to the limitations imposed by the database). Also, obtaining complete medical histories based on data from Medicaid claims is difficult. Changes in the status of Medicaid eligibility, disenrollment, and the likelihood of multiple insurance plans for some individuals may have confounded the results of this study. In addition, the MarketScan Medicaid database is based on a large convenience sample. The sample is not random, so it may contain biases or fail to generalize well to other populations, particularly those who have alternate healthcare coverage, such as commercial insurance.

Conclusions

This is one of the largest mirror studies of Medicaid-insured patients with schizophrenia. It showed a significant reduction in all-cause hospitalizations and overall healthcare costs during the 12-month follow-up after initiation of treatment with LAI antipsychotic medications. Age-specific analyses also suggest that use of LAIs in younger patients with schizophrenia may be beneficial for the prevention of relapse and for reducing costs. These results provide naturalistic real-world evidence of the utility of LAI antipsychotic medications in the treatment of schizophrenia.

Contributions

Drs. Gutierrez, Baker, Offord, Lin, and Karson contributed to the conception and design of this study. Contributions to statistical analyses were made by Mr. Kamat and Dr. Lin; supervisory contributions were made by Mr. Kamat and Dr. Offord; and contributions related to administrative, technical or material support were made by Dr. Lin. All authors contributed to the analysis and interpretation of the data as well as the writing, review, and revision of the manuscript.

Potential conflicts of interest

The International Committee of Medical Journal Editors’ (ICMJE) Potential Conflicts of Interests forms for the authors are available for download at: http://www.drugsincontext.com/wp-content/uploads/2015/03/dic.212267-COI.pdf

Mr. Kamat, Dr. Offord, and Dr. Docherty are employees of Otsuka America Pharmaceutical, Inc., and Dr. Gutierrez was employed at Otsuka during the time of the study. Dr. Docherty is also an Adjunct Professor of Psychiatry at Weill Cornell Medical College and a board member of Care Management Technologies. Dr. Baker is an employee of Otsuka Pharmaceutical Development and Commercialization, Inc. Dr. Eramo is an employee of Lundbeck. Dr. Lin is an employee of Novosys Health, which received research grant funds from Otsuka America Pharmaceutical, Inc., in connection with conduction of this study. Dr. Karson is an employee of CNK Consulting Group LLC, and is a paid consultant for Otsuka America Pharmaceutical, Inc.

Funding declaration

This study was sponsored by Otsuka America Pharmaceutical, Inc., Otsuka Pharmaceutical Development and Commercialization, Inc., and Lundbeck. Editorial support for the preparation of this manuscript was provided by Scientific Connexions, Inc., an Ashfield Company, funded by Otsuka America Pharmaceutical, Inc., and Lundbeck.

Acknowledgements

The authors would like to acknowledge Scientific Connexions, Inc., for their assistance in preparation of this manuscript for submission.

References

1. Regier DA, Narrow WE, Rae DS, Manderscheid RW, Locke BZ, Goodwin FK. The de facto US mental and addictive disorders service system. Epidemiologic catchment area prospective 1-year prevalence rates of disorders and services. Arch Gen Psychiatry 1993;50:85–94. http://dx.doi.org/10.1001/archpsyc.1993.01820140007001
2. US Census Bureau. Age and Sex Composition: 2010 (C2010BR-03). Washington, DC, US Census Bureau, 2011. Available at: http://www.census.gov/prod/cen2010/briefs/ch1/ch1br-03.pdf [Last accessed: November 11, 2014].
3. Wu EQ, Birnbaum HG, Shi L et al. The economic burden of schizophrenia in the United States in 2002. J Clin Psychiatry 2005;66:1122–9. http://dx.doi.org/10.4088/JCPv66n0906
4. Lieberman JA, Stroup TS, McEvoy JP et al. Clinical Antipsychotic Trials of Intervention Effectiveness (CATIE)
Investigators. Effectiveness of antipsychotic drugs in patients with chronic schizophrenia. N Engl J Med 2005;353:1209–23. Erratum in: N Engl J Med 2010;363:1092–3.
5. Sun SX, Liu GG, Christensen DB, Fu AZ. Review and analysis of hospitalization costs associated with antipsychotic nonadherence in the treatment of schizophrenia in the United States. Curr Med Res Opin 2007;23:2305–12. http://dx.doi.org/10.1185/030079907X226050
6. Masand PS, Roca M, Turner MS, Kane JM. Partial adherence to antipsychotic medication impacts the course of illness in patients with schizophrenia: a review. Prim Care Companion J Clin Psychiatr 2009;11:147–54. http://dx.doi.org/10.4088/PCC.08r00612
7. Dilla T, Ciudad A, Alvarez M. Systematic review of the economic aspects of nonadherence to antipsychotic medication in patients with schizophrenia. Patient Prefer Adherence 2013;7:275–84. http://dx.doi.org/10.2147/PPA.S41609
8. Weiden PJ, Kozma C, Grogg A, Locklear J. Partial compliance and risk of rehospitalization among California Medicaid patients with schizophrenia. Psychiatr Serv 2004;55:886–91. http://dx.doi.org/10.1176/appi.ps.55.8.886
9. Harrison G, Hopper K, Craig T et al. Recovery from psychotic illness: a 15- and 25-year international follow-up study. Br J Psychiatry 2001;178:506–17. http://dx.doi.org/10.1192/bjp.178.6.506
10. Robinson DG, Woerner MG, Alvir JM, Bilder RM, Hinrichsen GA, Lieberman JA. Predictors of medication discontinuation by patients with first-episode schizophrenia and schizoaffective disorder. Schizophr Res 2002;57:209–19. http://dx.doi.org/10.1016/S0920-9964(01)00312-7
11. Caseiro O, Pérez-Iglesias R, Mata I et al. Predicting relapse after a first episode of non-affective psychosis: a three-year follow-up study. J Psychiatr Res 2012;46:1099–1105. http://dx.doi.org/10.1016/j.jpsychires.2012.05.001
12. 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.
13. Olsson M, Marcus SC, Ascher-Svanum H. Treatment of schizophrenia with long-acting fluphenazine, haloperidol, or risperidone. Schizophr Bull 2007;33:1379–87. http://dx.doi.org/10.1093/schbul/sbm033
14. Lehman AF, Lieberman JA, Dixon LB et al. American Psychiatric Association; Steering Committee on Practice Guidelines. Practice guideline for the treatment of patients with schizophrenia, second edition. Am J Psychiatry 2004;161(2 Suppl):1–56.
15. Lehman AF, Kreynenbuhl J, Buchanan RW et al. The Schizophrenia Patient Outcomes Research Team (PORT): updated treatment recommendations 2003. Schizophr Bull 2004;30:193–217. http://dx.doi.org/10.1093/oxfordjournals.schbul.a007071
16. McEvoy JP, Scheifler PL, Frances A. The expert consensus guideline series: treatment of schizophrenia. J Clin Psychiatry 1999;60(Suppl 11):1–80.
17. International Psychopharmacology Algorithm Project. IPAP Web site, 2006. Available at: http://www.ipap.org [Last accessed November 11, 2014].
18. Moore TA. Schizophrenia treatment guidelines in the United States. Clin Schizophr Relat Psychoses 2011;5:40–9.
19. Hasan A, Falkai P, Wobrock T et al. WFSBP Task force on Treatment Guidelines for Schizophrenia. World Federation of Societies of Biological Psychiatry (WFSBP) guidelines for biological treatment of schizophrenia, part 2: update 2012 on the long-term treatment of schizophrenia and management of antipsychotic-induced side effects. World J Biol Psychiatry 2013;14:2–44.
20. Rosenheck RA, Krystal JH, Lew R et al. CSP555 Research Group. Long-acting risperidone and oral antipsychotics in unstable schizophrenia. N Engl J Med 2011;364:842–51. Erratum in: N Engl J Med 2011;364:1281. http://dx.doi.org/10.1056/NEJMoa1005987
21. Rosenheck R, Liu H. Noninferiority of perphenazine vs. three-second-generation antipsychotics in chronic schizophrenia. J Nerv Ment Dis 2014;202:18–24. http://dx.doi.org/10.1097/NMD.0000000000000065
22. Buckley PF, Schooler NR, Goff DC et al. the PROACTIVE Study. Comparison of SGA oral medications and a long-acting injectable SGA: the PROACTIVE study. Schizophr Bull 2014 [Epub ahead of print]. DOI: 10.1093/schbul/sbu067. http://dx.doi.org/10.1093/schbul/sbu067
23. Kishimoto T, Robenzadeh A, Leucht S et al. Long-acting injectable vs oral antipsychotics for relapse prevention in schizophrenia: a meta-analysis of randomized trials. Schizophr Bull 2014;40:192–213. http://dx.doi.org/10.1093/schbul/sbs150
24. Zhornitsky S, Stip E. Oral versus long-acting injectable antipsychotic in the treatment of schizophrenia and special populations at risk for treatment nonadherence: a systematic review. Schizophr Res Treatment 2012;2012:407171. http://dx.doi.org/10.1155/2012/407171
25. Kirson NY, Weiden PJ, Yermakov S et al. Efficacy and effectiveness of depot versus oral antipsychotics in schizophrenia: synthesizing results across different research designs. J Clin Psychiatry 2013;74:568–75. http://dx.doi.org/10.4088/JCP.12r08167
26. Kishimoto T, Nitta M, Borenstein M, Kane JM, Correll CU. Long-acting injectable versus oral antipsychotics in schizophrenia: a systematic review and meta-analysis of mirror-image studies. J Clin Psychiatry 2013;74:957–65. http://dx.doi.org/10.4088/JCP.13r08440
27. 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;168:603–9. http://dx.doi.org/10.1176/appi.ajp.2011.10081224

28. Crivera C, DeSouza C, Kozma CM, Dirani RD, Mao L, Macfadden W. Resource utilization in patients with schizophrenia who initiated risperidone long-acting therapy: results from the Schizophrenia Outcomes Utilization Relapse and Clinical Evaluation (SOURCE). BMC Psychiatry 2011;11:168. http://dx.doi.org/10.1186/1471-244X-11-168

29. Ren XS, Crivera C, Sikirica M, Dirani R, Qian S, Kazis LE. Evaluation of health services use following the initiation of risperidone long-acting therapy among schizophrenia patients in the veterans health administration. J Clin Pharm Ther 2011;36:383–9. http://dx.doi.org/10.1111/j.1365-2710.2010.01211.x

30. Bera R, Offord S, Zubek D et al. Impact on healthcare resource usage and costs among Medicaid-insured schizophrenia patients after initiation of treatment with long-acting injectable. J Med Econ 2013;16:522–8. http://dx.doi.org/10.3111/13696998.2013.771641

31. Offord S, 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;16:231–9. http://dx.doi.org/10.3111/13696998.2012.751025

32. Brown JD, Barrett A, Ireys H, Caffery E, Hourihan K. Evidence-based practices for Medicaid beneficiaries with schizophrenia and bipolar disorder. Washington, DC, US Department of Health and Human Services, Office of Disability, Aging and Long-Term Care Policy, 2012. Available at: http://aspe.hhs.gov/daltcp/reports/2012/ebpsbd.pdf [Last accessed: November 11, 2014].

33. Kronick RG, Bella M, Gilmer TP. The faces of Medicaid III: refining the portrait of people with multiple chronic conditions. Edited by Martin LF. Hamilton, NJ, Center for Health Care Strategies, Inc., 2009. Available at: http://www.chcs.org/usr_doc/Faces_of_Medicaid_III.pdf [Last accessed: November 11, 2104].

34. Charlson ME, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. J Chronic Dis 1987;40:373–83. http://dx.doi.org/10.1016/0021-9681(87)90171-8