HOSPITALIZATION RISK AMONG ADULTS WITH BIPOLAR I DISORDER TREATED WITH ORAL ATYPICAL ANTIPSYCHOTICS: A LONG-TERM RETROSPECTIVE ANALYSIS OF MEDICAID CLAIMS DATA

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KEY FINDINGS

- In a Medicaid population, lurasidone-treated adults with bipolar I disorder had significantly lower risk of all-cause hospitalization than those treated with olanzapine and quetiapine, lower risk of psychiatric hospitalization than quetiapine, and lower risk of bipolar I disorder-related hospitalization than quetiapine and risperidone, during the 24-month follow-up period.
- Lurasidone was associated with significantly shorter bipolar I disorder-related hospital stays (average of 3.97 days) compared to quetiapine (average of 8.42 days).
- Risks of all-cause, psychiatric and bipolar I disorder-related hospitalization were numerically lower for lurasidone compared to all other AAPs.

INTRODUCTION

- Bipolar disorder is a chronic psychiatric mood disorder that affects approximately 2.8% of adults in the US[1].
- Treatment recommendations for bipolar disorder vary depending on the specific phase (mania, depression, maintenance). Atypical antipsychotics (AAPs) lurasidone (Latuda®) and quetiapine are generally recommended first-line treatments for bipolar depression[2].
- Earlier studies have demonstrated that lurasidone was associated with significantly lower risk of hospitalization in a cohort of treatment-naïve adults with bipolar disorder, however, that study focused on commercially-insured population only and did not examine outcomes beyond a 12-month follow-up period[3].

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OBJECTIVE

- To compare the risk of hospitalization for adult Medicaid beneficiaries with bipolar I disorder when treated with lurasidone compared to other AAPs as monotherapy.

METHODS

Data Source

- The study utilized the IBM MarketScan Multi-state Medicaid Database from January 1, 2014 to June 30, 2019.
  - The Multi-state Medicaid database includes complete medical, outpatient pharmacy, and enrollment data for patients with Medicaid insurance.
  - The database represents 5-13 states on an annual basis.

Study Population

- The study sample was comprised of adults with bipolar I disorder (ICD-9-CM: 296.0X-296.7X, 296.80-296.81; ICD-10-CM: F30.X, F31.X) who initiated an AAP (index date) as monotherapy and continuously enrolled in a Medicaid plan for 12 months pre- and 24 months after-index date.
- Patients were excluded if they had a diagnosis of schizophrenia, had used mood stabilizers (i.e., carbamazepine, lamotrigine, lithium, oxcarbazepine, valproate) for ≥8 days within the first 30 days after index date, had used long-acting injectables, or were pregnant during study time period.

Treatment Categorization:

- The primary unit of analysis was the patient treatment-month.
- The post-index period was divided into twenty-four 30-day intervals (months).
- Patients were assigned to one of seven mutually exclusive monotherapy treatment categories in each month: lurasidone, aripiprazole, olanzapine, quetiapine, risperidone, no/minimal treatment (≤7 days of any AAP therapy) and other treatment (asenapine, brexpiprazole, cariprazine, ziprasidone, iloperidone, paliperidone, clozapine, multiple AAPs, AAPs with 8-23 days of coverage).
- Monotherapy was defined as ≥24 days of an AAP during that treatment month with no treatment with other AAP or mood stabilizers.

Outcomes:

- The primary outcome variables were a binary indicator for a hospital admission and length of stay (LOS) in each post-index month. All-cause, psychiatric and bipolar I disorder-related hospitalization rate and LOS were reported. Hospitalization rates were converted to per 100 patient months.

Statistical Analysis:

- Marginal structural models (MSM) were used to assess the effects of AAP treatment on the hospitalization risks.
  - Stabilized inverse probability of treatment weighting (IPTW) was calculated for each month in the post-index period using a multinomial logistic regression adjusting for the fixed pre-index (age, gender, race, CCI score, comorbidities, pre-index dependent variable, and index year) and time-varying covariates (prior month dependent variable, prior month office visits, month indicator and prior month substance abuse indicator).
  - All-cause, psychiatric and bipolar I disorder-related hospitalization rates were modeled with generalized estimating equations with a logit link. Adjusted odds ratios (aORs) and corresponding 95% confidence interval (CI) were reported.
  - Hospital LOS were modeled with zero-inflated Poisson regression model. Adjusted incidence risk ratios (aIRRs) and corresponding 95% CI were reported.

RESULTS

- The analysis included 8262 adults with bipolar I disorder at month 1 of the study period. Patients were assigned to AAP treatment groups: lurasidone (14%), aripiprazole (17%), olanzapine (8%), quetiapine (29%), risperidone (10%), no/minimal (1%) or other (21%). Patient baseline characteristics were reported in **Table 1**.
- Over a 24-month follow-up period, the unadjusted all-cause and psychiatric hospitalization rates were significantly lower for lurasidone, compared to olanzapine and quetiapine (**Table 2**).
- After applying the MSM, aORs for all-cause hospitalization were significantly higher for olanzapine and quetiapine, compared to lurasidone (**Figure 1**).
- The average bipolar I disorder-related hospital stay was more than twice as high for quetiapine (8.42 days), compared to lurasidone (3.97 days). **Figure 2** included the aIRRs of LOS for other AAPs compared to lurasidone.
- Risks of all-cause, psychiatric and bipolar I disorder-related hospitalization were numerically lower for lurasidone compared to all other AAPs.

Table 1. Patient Demographic and Clinical Characteristics

	Lurasidone (reference)	Aripiprazole	Olanzapine	Quetiapine	Risperidone
Sample size at index, N (%)	1,145 (13.9%)	1,407 (17.0%)	632 (7.7%)	2,381 (28.8%)	845 (10.2%)
Age (years), mean (SD)	38.2 (11.3)	38.3 (11.9)	39.4 (12.1)	39.3 (11.9)	39.2 (12.3)
Female, N (%)	891 (77.8%)	1056 (75.1%)	395 (62.5%)	1664 (69.9%)	584 (69.1%)
Race, N (%)					
White	815 (71.2%)	971 (69.0%)	407 (64.4%)	1486 (62.4%)	475 (56.2%)
African American	200 (17.5%)	259 (18.4%)	127 (20.1%)	563 (23.6%)	252 (29.8%)
Hispanic	24 (2.1%)	22 (1.6%)	**	33 (1.4%)	**
Other/Missing	106 (9.2%)	155 (11.0%)	**	299 (12.5%)	**
Index year, N (%)					
2015	486 (42.4%)	667 (47.4%)	262 (41.5%)	1,154 (48.5%)	411 (48.6%)
2016	565 (49.3%)	618 (43.9%)	298 (47.2%)	1,023 (43.0%)	359 (42.5%)
2017	94 (8.2%)	122 (8.7%)	72 (11.4%)	204 (8.6%)	75 (8.9%)
Charlson Comorbidity Index, mean (SD)	0.8 (1.2)	0.7 (1.2)	0.8 (1.5)	0.9 (1.4)	0.7 (1.2)
Psychiatric Comorbidities, N (%)					
Anxiety	656 (57.3%)	789 (56.1%)	336 (53.2%)	1350 (56.7%)	417 (49.3%)
Bipolar II disorder	116 (10.1%)	118 (8.4%)	44 (7.0%)	158 (6.6%)	50 (5.9%)
Major Depressive Disorder	656 (57.3%)	821 (58.4%)	329 (52.1%)	1334 (56.0%)	452 (53.5%)
Substance abuse*	370 (32.3%)	457 (32.5%)	278 (44.0%)	944 (39.6%)	302 (35.7%)
Physical Comorbidities, N (%)					
Hypertension	410 (35.8%)	501 (35.6%)	205 (32.4%)	889 (37.3%)	311 (36.8%)
Hyperlipidemia	277 (24.2%)	345 (24.5%)	107 (16.9%)	529 (22.2%)	179 (21.2%)
Obesity	324 (28.3%)	368 (26.2%)	90 (14.2%)	515 (21.6%)	156 (18.5%)
Hospitalization in pre-index period, per 100 patient months					
All-cause	2.53	2.89	3.67	3.28	3.23
Psychiatric	2.22	2.58	3.53	3.04	2.99
Bipolar I disorder-related	1.74	1.91	2.99	2.32	2.46

Highlighted cells indicate significant differences between lurasidone and AAP at *P<0.05*; Cells with ** indicate the numbers in that cell <11, thus not reported according to CMS cell size suppression policy; SD: standard deviation; *Substance abuse includes alcohol, opioids, cannabis, cocaine, hallucinogens, sedatives, inhalants and other stimulants (amphetamine and psychostimulant) abuse.

Table 2. Unadjusted Hospitalizations and Hospital Length of Stay Over 24-Month Follow-up Period

	Lurasidone (reference)	Aripiprazole	Olanzapine	Quetiapine	Risperidone
Treatment months	7,964	9,600	3,555	16,178	4,461
Hospitalizations, per 100 patient months					
All-cause	2.11	2.41	3.46	3.54	2.60
Psychiatric	1.88	2.09	2.98	3.01	2.15
Bipolar I disorder-related	1.02	1.06	1.43	1.52	1.39
Hospital length of stay (LOS), mean days					
All-cause	10.75	11.34	20.48	19.88	15.22
Psychiatric	9.33	9.25	16.40	15.82	11.43
Bipolar I disorder-related	4.55	4.30	6.95	7.80	8.03

Highlighted cells indicate significance of outcomes in comparison to lurasidone at p<0.05

LIMITATIONS

- This analysis of Medicaid patients may not be generalizable to patients with other types of insurance (eg. Commercial) or the uninsured population.
- Administrative claims are collected for billing purposes; thus there is potential for misclassification or data coding limitations.
- Marginal structural models control for pre-index and time-varying confounding variables, but unmeasured confounders could still be different between treatments.

Figure 1. Marginal Structural Model-adjusted Risk of Hospitalization Over 24-Month Follow-up Period

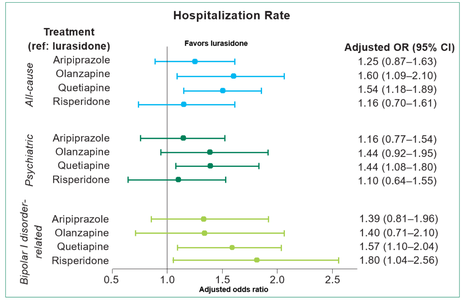
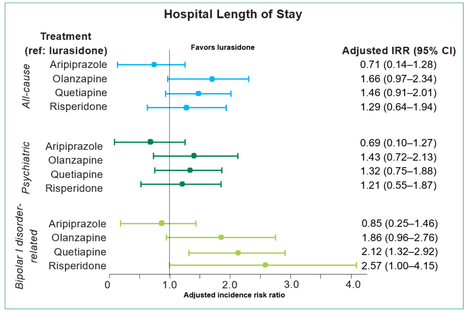


Figure 2. Marginal Structural Model-adjusted Hospital Length of Stay Over 24-Month Follow-up Period



DISCLOSURES

X. Niu, C. Dembek, K. Laubmeier, and GR. Williams are employees of Sunovion. P. Veeranki, S. Dennen, Y. Liu, and J. Shafrin are employed by PRECISIONheor who received funding from Sunovion to conduct this analysis.

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