# Impact of Initiating Long-Acting Injectables (LAI) on All-Cause and Psychiatric-Specific Hospitalization in Patients with Bipolar I Disorder

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## Introduction

- Bipolar I disorder (BD-I) places substantial economic burden on the US healthcare system.
  - Persons with BD-I incurred $200 billion in combined direct and indirect healthcare costs in 2015.[1]
  - Hospitalization is one of the major drivers of healthcare costs, contributing to over a quarter of the total direct costs of treating patients with BD-I.[1,2]
- Limited evidence suggests that aripiprazole once-monthly (AOM 400), one of the most recently approved long-acting injectables (LAIs) for BD-I[3], may be more effective in reducing all-cause hospitalization in BD-I patients.[4]
- Existing studies have not examined the clinical effectiveness impact of selecting one LAI vs another in reducing psychiatric hospitalization among patients with BD-I.[5,6]

## Objective

To evaluate and compare risk of all-cause and psychiatric-specific hospitalization in patients with bipolar I disorder (BD-I) initiating an LAI.

## Methods

- Retrospective cohort study using the Truven MarketScan® Medicaid, Commercial, Medicare Supplemental Databases
- Patient identification
  - BD-I patients during the study identification (ID) period between 01/01/2013 and 06/30/2015 with
  - ≥1 inpatient or ≥2 outpatient claims for BD-I [ICD-9-CM diagnosis codes: 296.0x, 296.1x, 296.4x, 296.5x, 296.6x, 296.7x, 296.8x (excluding 296.82) and ICD-10-CM diagnosis codes: F30.x and F31.x (excluding F31.81)]
  - Both existing and newly diagnosed patients eligible for inclusion
  - LAI cohort
    - At least one claim for one of the following LAIs and initiated one of the following LAIs during the ID period (01/01/2013-06/30/2015):
      - AOM 400, fluphenazine, haloperidol, paliperidone-4-week, risperidone
    - Index date: the earliest occurrence (the first date) of a claim for one of the above LAI therapies of interest during the ID period
    - No index LAI use 1-year prior to the index date (use of a different, non-index LAI was allowed)
  - Additional requirements
    - First diagnosis before or on the index date
    - 1-year pre-index (baseline) continuous enrollment
    - 1-year post-index continuous enrollment
  - Exclusion criteria
    - ≤17 years old on index date
    - Had prescription for clozapine during study period
    - Excluded patients who were Medicare and Medicaid dual eligible, did not have pharmacy coverage, did not have mental health coverage information, or had capitated plan
- Outcome measures
  - All-cause and psychiatric-specific hospitalization rates over 1-year post-index period
- Statistical analysis
  - A logistic regression model was used to estimate risks of all-cause and psychiatric-specific hospitalization across different LAIs during the 1-year post-index, adjusting for patient demographics, clinical characteristics, baseline medication use, and baseline hospitalization.

## Results

- Of the identified patients with BD-I, 413 initiated AOM 400, 154 fluphenazine, 476 haloperidol, 1,026 paliperidone-4-week, and 323 risperidone. **(Figure 1)**
  - Mean (SD) age of the total population was 37.8 (14.5) years, 49.6% were female, and 76.6% were insured through Medicaid. **(Table 1)**
- AOM 400 users had the lowest unadjusted all-cause (34.6%, p<0.001) and psychiatric-specific (25.9%, p=0.006) hospitalization rates when compared to other LAIs: fluphenazine - all-cause: 42.9%, psychiatric-specific: 35.1%; haloperidol - 47.5%, 38.4%; paliperidone-4-week - 38.6%, 32.1%; risperidone - 44.6%, 36.8%.
- Adjusting for differences in baseline characteristics, the odds of having both all-cause and psychiatric-specific hospitalization during the 1-year post-index period were significantly higher in the haloperidol-LAI [Odds Ratio (OR) (95% CI): 1.39 (1.03-1.87) (all-cause), p=0.029; 1.41 (1.03-1.93) (psychiatric-specific), p=0.0315] and risperidone-LAI [1.54 (1.12-2.13), p=0.009; 1.68 (1.20-2.37), p=0.003] cohorts compared with AOM 400 users. **(Figures 2a and 2b)**
  - Across LAIs, the lowest adjusted all-cause hospitalization rates were found in Paliperidone-4-week (35.9%) and AOM 400 users (36.0%) (p=0.004). **(Figure 3a)**
  - Across LAIs, AOM 400 users had the lowest adjusted psychiatric-specific (25.7%) (p=0.013) hospitalization rate. **(Figure 3b)**

### Figure 1. Patient Identification

Have ≥1 inpatient claim or ≥ 2 outpatient claims for BD-I during study period[a]
**N = 521,450**

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LAI and oral antipsychotic users
**N = 64,361 (12.3%)**
Initiated an LAI: 6,700 (10.4%)
Changed to a different oral antipsychotic: 57,661 (89.6%) in the ID period[b]

↓

Had mono index therapy, no use of clozapine, & ≥1 BD-I diagnosis prior to or on index date
**N = 40,781 (63.4%)**

↓

LAI users
**N = 4,955 (12.2%)**

↓

≥18 years on index date & continuously enrolled in 1-year prior to and 1-year after index date
**N = 2,446 (49.4%)**

↓

**LAI cohort**
AOM 400: 413 (17.3%)
Other LAIs: Fluphenazine: 154 (6.4%); Haloperidol: 476 (19.9%); Paliperidone, 4-week: 1,026 (42.9%); Risperidone: 323 (13.5%)

[a] Study period is defined as 01/01/2012 – 06/30/2016
[b] Identification period is defined as 01/01/2013 – 06/30/2015

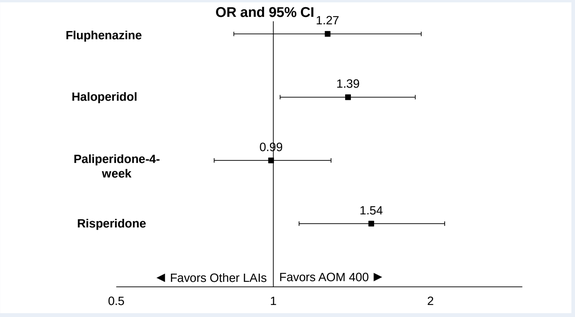
## Results (cont'd)

### Table 1. Patient Baseline Characteristics

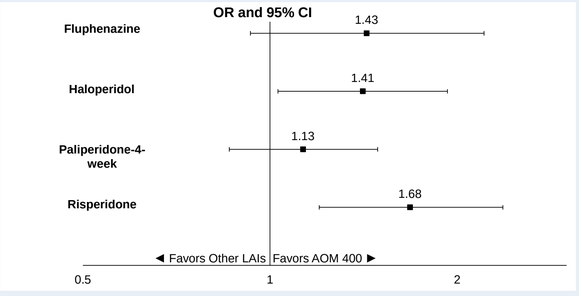
| | AOM 400 N = 413; 17.3% | Fluphenazine N = 154; 6.4% | Haloperidol N = 476; 19.9% | Paliperidone, 4-week N = 1,026; 42.9% | Risperidone N = 323; 13.5% | P Value |
|---|---|---|---|---|---|---|
| Age in years, mean (SD) | 34.0 (12.9) | 44.4 (15.9) | 39.3 (14.6) | 37.0 (13.8) | 39.7 (16.1) | <.001 |
| Female, n (%) | 217 (52.5) | 82 (53.2) | 239 (50.2) | 479 (46.7) | 169 (52.3) | <.149 |
| Insurance type, n (%) | | | | | | |
| Medicaid | 301 (72.9) | 102 (66.2) | 382 (80.3) | 830 (80.9) | 217 (67.2) | <.001 |
| Commercial | 107 (25.9) | 37 (24.0) | 71 (14.9) | 171 (16.7) | 87 (26.9) | |
| Medicare supplemental | 5 (1.2) | 15 (9.7) | 23 (4.8) | 25 (2.4) | 19 (5.9) | |
| Charlson comorbidity index, mean (SD) | 1.1 (1.7) | 1.7 (2.1) | 1.4 (1.9) | 1.1 (1.7) | 1.3 (2.0) | <.001 |
| Any hospitalization, n (%) | 218 (52.8) | 99 (64.3) | 341 (71.6) | 676 (65.9) | 197 (61.0) | <.001 |
| Use of any atypical and typical antipsychotics, n (%) | 369 (89.3) | 133 (86.4) | 432 (90.8) | 895 (87.2) | 290 (89.8) | .238 |
| Psychiatric comorbidities[a], n (%) | 332 (80.4) | 121 (78.6) | 424 (89.1) | 886 (86.4) | 269 (83.3) | <.001 |
| Somatic comorbidities[b], n (%) | 235 (56.9) | 106 (68.8) | 311 (65.3) | 583 (56.8) | 186 (57.6) | .002 |

[a] Major depressive disorder, anxiety, personality disorder, substance abuse disorders, schizophrenia
[b] Obesity, diabetes mellitus type 2, hyperlipidemia, hypertension

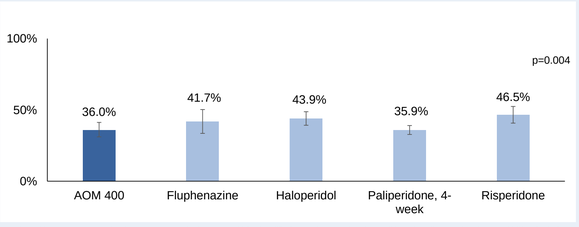
### Figure 2a. Risk of All-Cause Hospitalization in 1-Year Follow-Up Period




### Figure 2b. Risk of Psychiatric-Specific Hospitalization in 1-Year Follow-Up Period

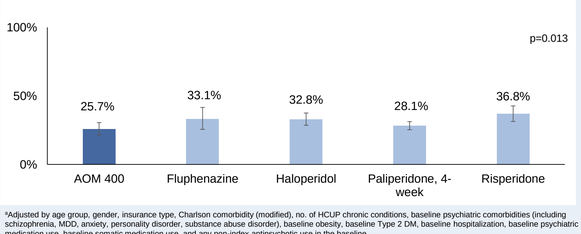



### Figure 3a. Adjusted[a] Rate of All-Cause Hospitalization During the 1-Year Follow-Up




[a] Adjusted by age group, gender, insurance type, Charlson comorbidity (modified), no. of HCUP chronic conditions, baseline psychiatric comorbidities (including schizophrenia, MDD, anxiety, personality disorder, substance abuse disorder), baseline obesity, baseline Type 2 DM, baseline hospitalization, baseline psychiatric medication use, baseline somatic medication use, and any non-index antipsychotic use in the baseline.

### Figure 3b. Adjusted[a] Rate of Psychiatric-Specific Hospitalization During the 1-Year Follow-Up




[a] Adjusted by age group, gender, insurance type, Charlson comorbidity (modified), no. of HCUP chronic conditions, baseline psychiatric comorbidities (including schizophrenia, MDD, anxiety, personality disorder, substance abuse disorder), baseline obesity, baseline Type 2 DM, baseline hospitalization, baseline psychiatric medication use, baseline somatic medication use, and any non-index antipsychotic use in the baseline.

## Conclusions

- Aripiprazole-LAI may be more beneficial at reducing the risk of both all-cause and psychiatric-specific hospitalizations in patients with BD-I in a real-world setting as compared to haloperidol-LAI and risperidone-LAI.
- Limitations
  - During the study period, AOM 400 had not yet been approved for treatment of BD and may have been used off-label.
  - BD-I was identified in healthcare claims, which is designed for reimbursement, not research.
  - Confounding variables, such as direct measures of disease severity, are not captured in claims.

## References

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