

# ADJUNCTIVE ATYPICAL ANTIPSYCHOTIC CHOICE AFFECTS HEALTHCARE UTILIZATION IN MAJOR DEPRESSIVE DISORDER (MDD)

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## Background & Objectives

- Major depressive disorder (MDD) is associated with high costs—as much as \$200 billion (direct and indirect costs) per year in the US.<sup>1</sup> Despite available therapies, costs appear to have risen steadily over recent decades.<sup>2</sup>
- Adjunctive atypical antipsychotics (AAPs) are treatment options for patients with more severe MDD, who are inadequately responding to antidepressant therapies.<sup>3</sup>
- The objective of this study was to examine healthcare utilization and costs, as well as medication adherence among patients with severe MDD treated with adjunctive AAP.

## Methods

- Retrospective cohort study using the Truven Health Analytics MarketScan® Medicaid (M), Commercial (C), and Medicare Supplemental (MS) databases
- Included patients who
  - had ≥1 inpatient or ≥2 outpatient claims for MDD (ICD-9-CM: 296.2x, 296.3x; ICD-10-CM: F32.0-F32.5, F32.9, F33.0x-F33.4x, F33.9x) in any diagnosis field during the study period (1/1/15-12/31/16-M, 1/1/15-9/30/16-C and MS)
  - received a single adjunctive oral AAP (≥1 pharmacy claim for brexpiprazole, lurasidone, quetiapine [3 branded AAPs commonly used in MDD]) during the identification (ID) period (7/1/15-6/30/16-M, 7/1/15-3/31/16-C and MS) while on antidepressant therapy;
    - Specifically patients were identified based on having
      - ≥1 antidepressant pharmacy claim within +/-90 days after index date (defined as first date of single oral AAP during ID period; therapy used on index date defined as index therapy)
      - ≥15 days of overlap of antidepressant with first prescription of index therapy; and
      - no index therapy for 6 months before index date (baseline period)
    - had ≥6 months continuous enrollment during both baseline and follow-up (defined as 6 months after the index date); and
    - were ≥18 years on the index date
  - Excluded patients who
    - used multiple AAPs on index date;
    - had a claim for schizophrenia or bipolar I disorder any time during study period;
    - were Medicare and Medicaid dual eligible; or were in a capitated plan
  - Three cohorts, defined by index date:
    - Brexpiprazole
    - Lurasidone
    - Quetiapine
  - Outcome measures (all measured during the 6-month follow-up)
    - Adherence, measured by proportion of days covered (PDC; number of days during year when medication was available/365)
    - Discontinuation, defined by either switch or gap of ≥30 days supply
    - All-cause healthcare utilization and costs
      - Hospital care: hospitalization or emergency department (ED) visits
      - Medical cost: sum of outpatient and inpatient costs
  - Statistical analysis
    - Multivariable analyses
      - Linear regression models for PDC and costs; all costs adjusted to Y2016 USD
      - Cox regression models (survival analyses) for time to discontinuation
      - Logistic regression for hospital care
      - Models adjusted for baseline age group, gender, insurance type, Charlson Comorbidity Index<sup>4</sup> (excluding diabetes mellitus [DM] type 2, which was included separately), number of Healthcare Cost and Utilization Project (HCUP)<sup>5</sup> chronic conditions, obesity, type 2 DM, psychiatric comorbidities, inpatient hospitalization, ED visit, non-psychiatric medication use, and use of non-index antipsychotic medication
    - Data transformations and analyses performed using SAS® version 9.4. Comparisons were 2-sided with significance level 0.05.

## Results

### Patient characteristics on index date and during baseline period

- 4,862 patients with MDD who initiated atypical antipsychotic augmentation therapy: 778 (16.0%) initiated brexpiprazole; 626 (12.9%) lurasidone; and 3,458 (71.1%) initiated quetiapine (**Table 1**)
  - Mean (SD) age 47.2 (16.2) years
  - Majority female and had commercial health insurance
  - Significant differences in baseline demographic and clinical characteristics

Table 1. Baseline Demographics and Patient Characteristics

|  | Brexpiprazole<br>N = 778; 16.0% | Lurasidone<br>N = 626; 12.9% | Quetiapine<br>N = 3,458; 71.1% | P Value <sup>a</sup> |
|--|---------------------------------|------------------------------|--------------------------------|----------------------|
| Age, year, mean (SD)                     | 47.8 (13.2)                     | 44.2 (14.0)                  | 48.0 (17.1)                    | <0.001               |
| Female, n (%)                            | 576 (74.0)                      | 487 (77.8)                   | 2,325 (67.2)                   | <0.001               |
| Insurance type, n (%)                    |                                 |                              |                                | <0.001               |
| Medicaid                                 | 159 (20.4)                      | 193 (30.8)                   | 770 (22.3)                     |                      |
| Commercial                               | 566 (72.8)                      | 400 (63.9)                   | 2,237 (64.7)                   |                      |
| Medicare supplemental                    | 53 (6.8)                        | 33 (5.3)                     | 451 (13.0)                     |                      |
| Charlson Comorbidity Index, mean (SD)    | 0.7 (1.3)                       | 0.7 (1.4)                    | 1.0 (1.7)                      | <0.001               |
| No. chronic conditions (HCUP), mean (SD) | 3.5 (2.0)                       | 3.5 (2.0)                    | 3.7 (2.1)                      | 0.025                |
| Baseline healthcare service use          |                                 |                              |                                |                      |
| Any hospitalization, n (%)               | 81 (10.4)                       | 100 (16.0)                   | 1,062 (30.7)                   | <0.001               |
| Any ED visits, n (%)                     | 197 (25.3)                      | 196 (31.3)                   | 1,227 (35.5)                   | <0.001               |

<sup>a</sup> P value indicates overall differences among the three AAP cohorts.

### Medication adherence and discontinuation during the follow-up period

- Unadjusted medication adherence differed among the three cohorts [mean (SD) PDC: brexpiprazole users 0.600 (0.320), lurasidone 0.560 (0.320) and quetiapine 0.570 (0.330) (overall p=0.027)]
- Median time to discontinuation was longer for brexpiprazole users compared to lurasidone and quetiapine users (median days [95% CI]: 92 [88-107] vs 74 [64-90] and 73 [66-82], respectively; overall p=0.023) (**Figure 1**)
- After adjustment, mean PDC did not differ across the three cohorts (overall p=0.148) (**Figure 2**)
- Medication adherence did not differ when comparing quetiapine and lurasidone with brexpiprazole [Estimate (95% confidence interval): quetiapine -1.4% (-4.0% - 1.3%), p=0.313; lurasidone -3.4% (-6.9% - 0.0%), p=0.051]
- Risk of discontinuation was statistically higher for quetiapine than for brexpiprazole [Hazard ratio (95% CI): 1.13 (1.02 - 1.25); p=0.023], and numerically higher for lurasidone than brexpiprazole [1.14 (1.00 - 1.29); p=0.054]

## Results (continued)

Figure 1. Days to Discontinuation

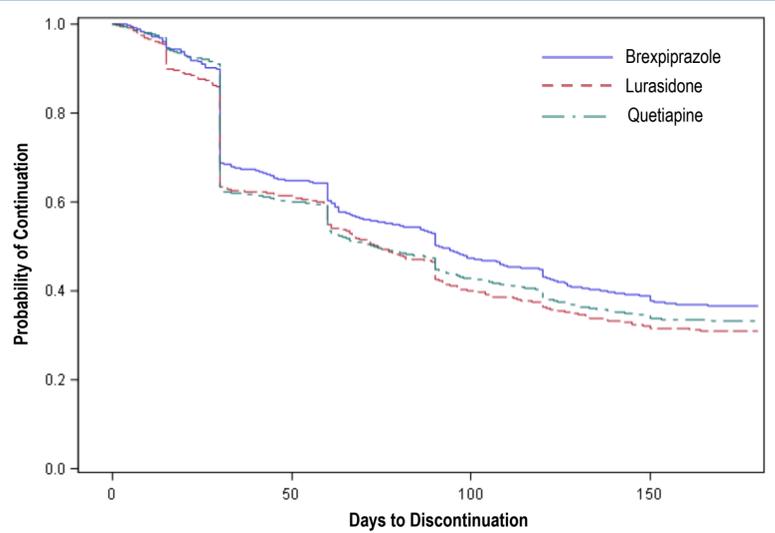
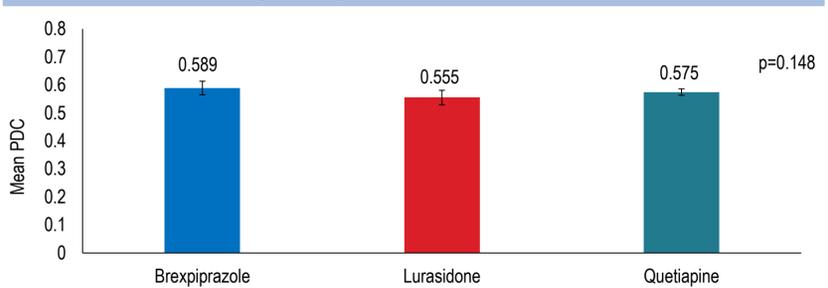


Figure 2. Adjusted<sup>a,b</sup> Medication Adherence

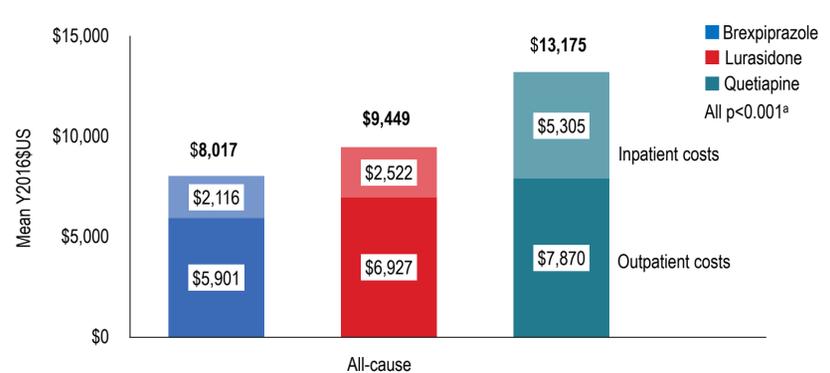


PDC: Proportion of days covered, number of days during year when medication was available/365.  
<sup>a</sup> Adjusted by age group, gender, insurance type, and the following baseline characteristics: Charlson comorbidity (modified), no. of HCUP chronic conditions, psychiatric comorbidities (including anxiety, personality disorder, substance abuse disorder), obesity, type 2 DM, hospitalization, ED visit, non-psychiatric medication use, and any use of non-index antipsychotic in baseline. <sup>b</sup> General linear regression model.

### Hospital care and medical cost during the 6-month follow-up period

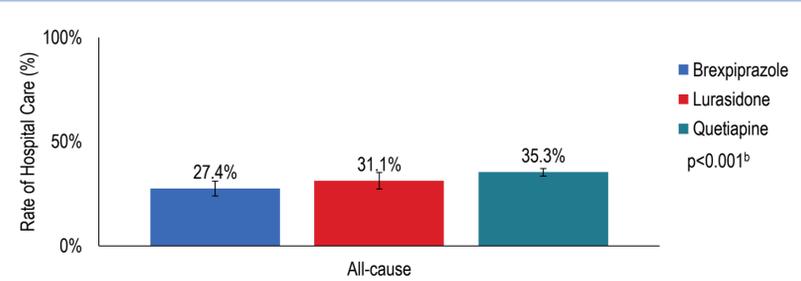
- Unadjusted rate of all-cause hospital care differed significantly across cohorts [brexpiprazole (25.8%), lurasidone (34.2%), quetiapine (37.6%); overall p<0.001]
- Unadjusted mean all-cause medical (outpatient and inpatient) costs differed among the three cohorts (Overall p<0.001) (**Figure 3**)
- After adjustment, the rate of all-cause hospital care remained statistically significantly different (**Figure 4**); however, adjusted mean all-cause medical costs were no longer significant
- The risk of all-cause hospital care was higher in quetiapine compared to brexpiprazole users [Odds ratio (95% CI): 1.45 (1.19 - 1.76); p<0.001], but did not differ between lurasidone and brexpiprazole users [1.20 (0.03 - 1.54); p=0.153]
- Quetiapine users had increased all-cause costs compared to brexpiprazole users [Estimate (95% CI): \$2,309 (31 - 4,587); p=0.047]; all-cause costs did not differ between lurasidone and brexpiprazole [\$913 (-2,033 - 3,859); p=0.543]

Figure 3 Components of Medical Costs (unadjusted) During the 6-Month Follow-Up Period



<sup>a</sup> P value indicates overall differences among the three AAP cohorts within each type of medical cost.

Figure 4. Adjusted<sup>a</sup> Rates of Hospital Care (Hospitalization/ED) During 6-Month Follow-Up Period



<sup>a</sup> Adjusted by age group, gender, insurance type, and the following baseline characteristics: Charlson comorbidity (modified), no. of HCUP chronic conditions, psychiatric comorbidities (including anxiety, personality disorder, substance abuse disorder), obesity, type 2 DM, hospitalization, ED visit, non-psychiatric medication use, and any use of non-index antipsychotic in baseline.  
<sup>b</sup> P value indicates overall differences among the three AAP cohorts.

## Limitations

- The study was limited by its design and data source; as we relied on insurance claims for our data, we cannot know why a particular adjunctive therapy was selected.

## Conclusions

- In patients with MDD and a variety of insurance types, augmentation with brexpiprazole was associated with lower
  - risks of discontinuation,
  - rates of hospital care (hospitalization and ED visits), and
  - medical costs
 compared to adjunctive quetiapine.
- AAP treatment choice may impact subsequent healthcare utilization.

## References

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