

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.¹ Despite available therapies, costs appear to have risen steadily over recent decades.²
- Adjunctive atypical antipsychotics (AAPs) are treatment options for patients with more severe MDD, who are inadequately responding to antidepressant therapies.³
- 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 Index⁴ (excluding diabetes mellitus [DM] type 2, which was included separately), number of Healthcare Cost and Utilization Project (HCUP)⁵ 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 N = 778; 16.0% | Lurasidone N = 626; 12.9% | Quetiapine N = 3,458; 71.1% | P Value ^a |
|------------------------------------------|---------------------------------|------------------------------|--------------------------------|----------------------|
| 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 |

^a 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

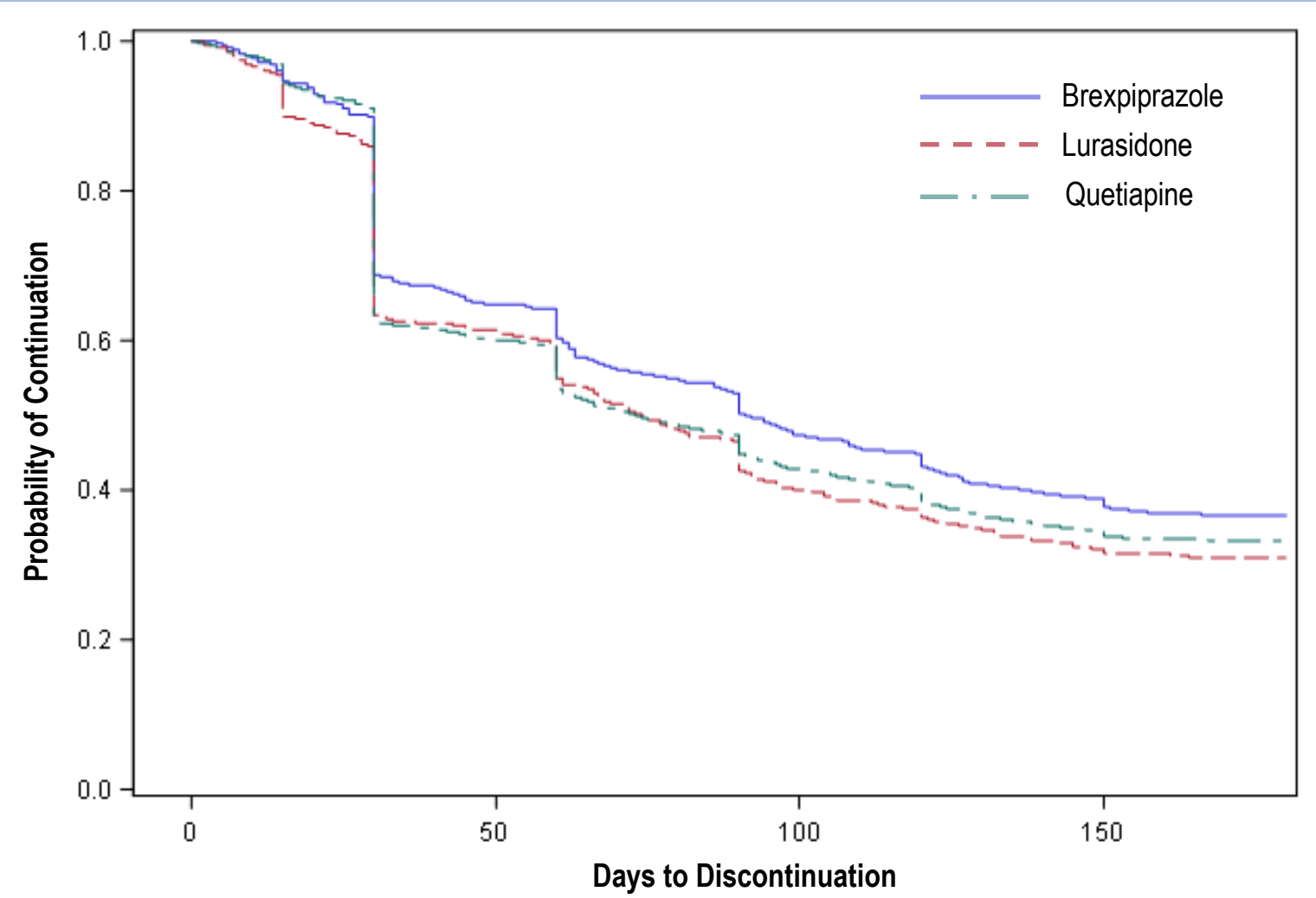
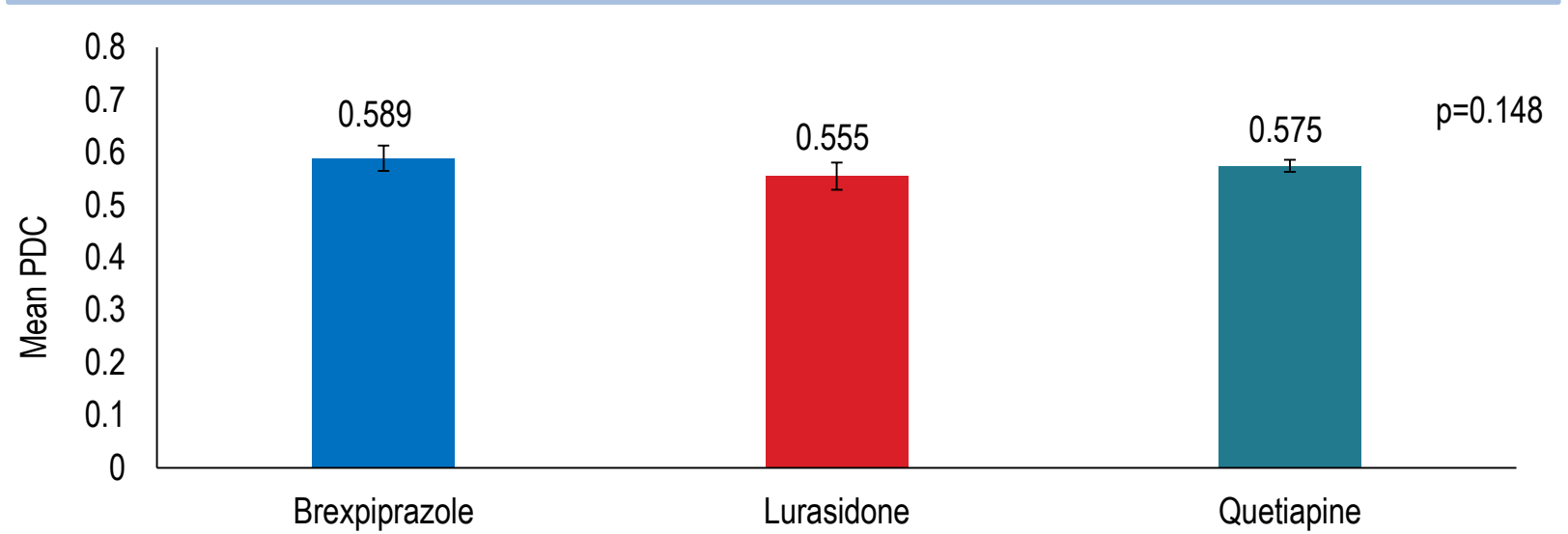


Figure 2. Adjusted^{a,b} Medication Adherence

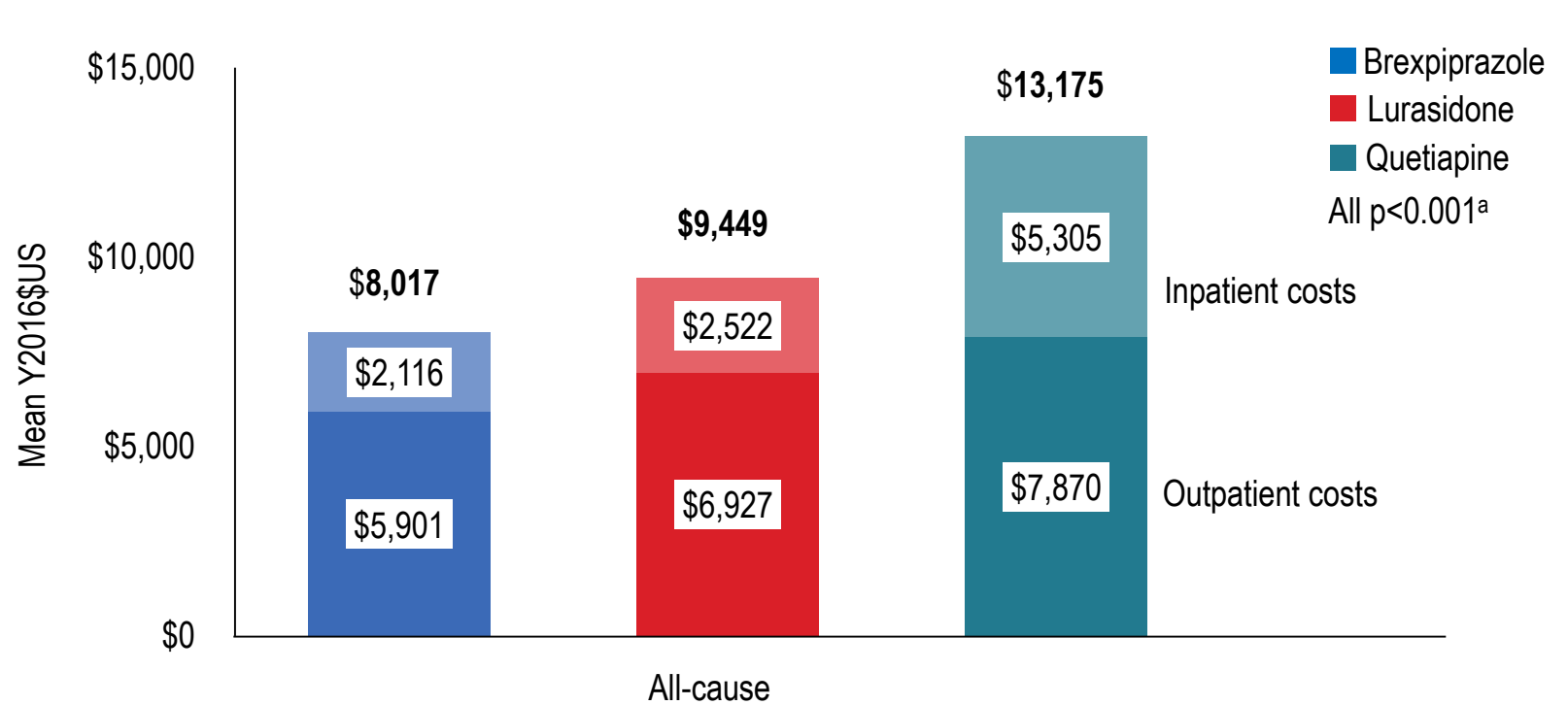


PDC: Proportion of days covered, number of days during year when medication was available/365.
^a Adjusted by age group, gender, insurance type, and the following baseline characteristics: Charlson comorbidity (modified), no. of HCUP chronic conditions, psychiatric comorbidities (including anxiety, personality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

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

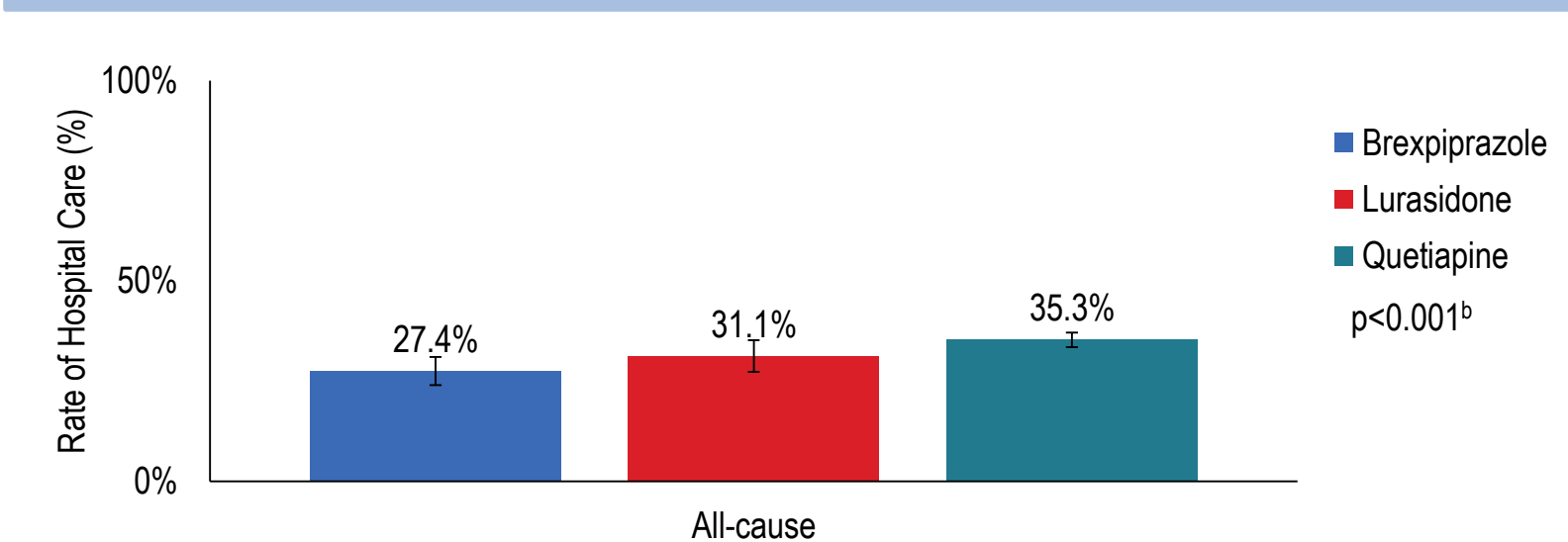
- Unadjusted rate of all-cause hospital care differed significantly across cohorts [brexpiprazole (25.8%), lurasidone (34.2%), quetiapine (37.6%); overall p<0.001]
- Unadjusted mean all-cause medical (outpatient and inpatient) costs differed among the three cohorts (Overall p<0.001) (**Figure 3**)
- 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



^a P value indicates overall differences among the three AAP cohorts within each type of medical cost.

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



^a 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.
^b 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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