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 Index[4] (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

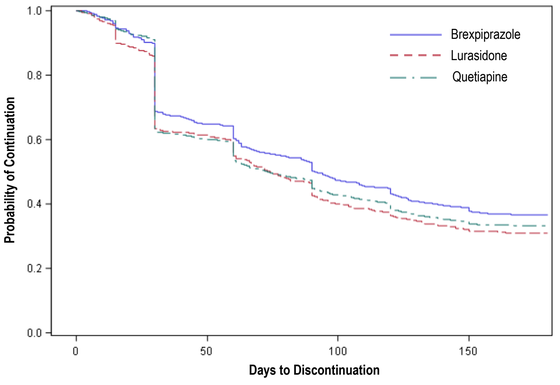
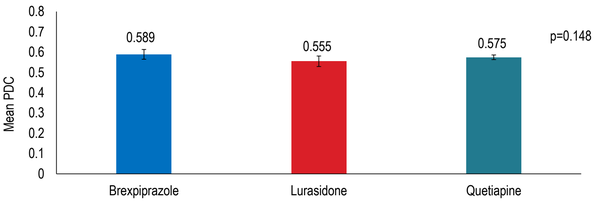


Figure 2. Adjusted[a,b] Medication Adherence

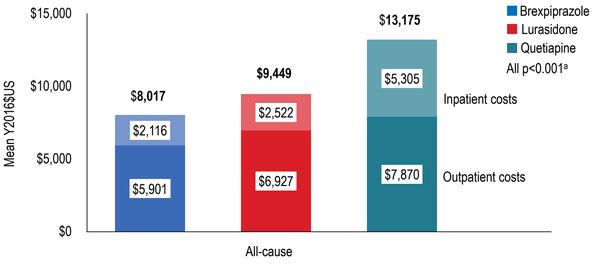


PDC: Proportion of days covered, number of days during year when medication was available/365.
[a] Adjusted by age group, gender, insurance type, and the following baseline characteristics: Charlson comorbidity (modified), no. of HCUP chronic conditions, psychiatric comorbidities (including anxiety, 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

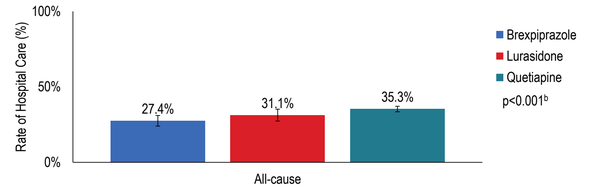
- Unadjusted rate of all-cause hospital care differed significantly across cohorts [brexpiprazole (25.8%), lurasidone (34.2%), quetiapine (37.6%); overall p<0.001)]
- Unadjusted mean all-cause medical (outpatient and inpatient) costs differed among the three cohorts (Overall p<0.001) **(Figure 3)**
-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

1. Greenberg PE, et al. *J Clin Psychiatry*. 2015;76(2):155–62. 2. Dieleman JL, et al. *JAMA*. 2017 Nov 7;318(17):1668–78. 3. Shah A. Int J Emerg Ment Health. 2015;17(2):476-480. 4. Charlson ME, et al. *J Chronic Dis*. 1987;40(5):373–383. 5. Agency for Healthcare Research and Quality. HCUP Chronic Condition Indicator. Healthcare Cost and Utilization Project (HCUP). www.hcup-us.ahrq.gov/toolssoftware/chronic/chronic.jsp. Published June 2015.

Disclosures: MG and RD are employees of Otsuka Pharmaceutical Development and Commercialization, Inc., Princeton, NJ. MSB, JTY, EC, and IY are employees of Partnership for Health Analytic Research, LLC, Beverly Hills, CA. AH is an employee of Lundbeck, Deerfield, IL. This study was sponsored by Otsuka Pharmaceutical Development and Commercialization, Inc. and Lundbeck; conducted by Partnership for Health Analytic Research, LLC.

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