DIFFERENCES IN TREATMENT OUTCOMES AMONG PATIENTS WITH MAJOR DEPRESSIVE DISORDER WITH AND WITHOUT COMORBID SUBSTANCE ABUSE

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Background & Objectives

- Comorbid substance abuse (SA) blunts treatment response and is linked to worsened treatment outcomes in patients with major depressive disorder (MDD).[1,2]
- Adjunctive atypical antipsychotics (AAP) are treatment options for patients with more severe MDD, who are inadequately responding to first-line antidepressant therapy.[3]
- Current literature on comorbid SA in MDD has not examined overall healthcare resource utilization (HCRU) and associated costs in this population with more severe MDD receiving AAP.[4,5,6]
- The objective of this study was to compare HCRU and costs between MDD patients treated with adjunctive AAP with/without comorbid SA.

Methods

- Retrospective cohort study using the Truven Health Analytics MarketScan® Medicaid (M), Commercial (C), and Medicare Supplemental (MS) databases
- Patient identification **(Figure 1)**
  - The study included patients who
    - had existing or newly diagnosed MDD (≥1 inpatient or 2 outpatient claims for MDD with ICD-9-CM: 296.2x, 296.3x; ICD-10-CM: F32.0-F32.5, F32.9, F33.0x-F33.4x, F33.9x) during study period (1/1/15-12/31/16-M, 1/1/15-9/30/16-C and MS);
    - received a single oral AAP adjunctive to antidepressant (≥1 pharmacy claim for brexpiprazole, lurasidone, quetiapine) during the identification (ID) period (7/1/15-6/30/16-M, 7/1/15-3/31/16-C and MS);
      - Specifically patients were identified based on having
        - ≥1 antidepressant pharmacy claim 90 days prior to and 90 days after index date (index date defined as the first date of starting AAP monotherapy during ID period; therapy used on index date defined as index therapy);
        - ≥15 days of overlap of antidepressant with the index therapy; and
        - no index therapy use during the 6 months prior to index date (baseline), allowing non-index antipsychotic therapy during the baseline period.
    - had ≥6 months continuous enrollment during both baseline and follow-up (defined as 6 months after index date); and
    - were ≥18 years on the index date
  - The study excluded patients who
    - had ≥1 diagnosis of schizophrenia or bipolar I disorder (BD-I) during study period;
    - had Medicare and Medicaid dual eligibility; or
    - within the MS database
      - lacked pharmacy or mental health coverage information; or
      - had capitated plans
- Patients were stratified by with or without comorbid SA status
  - Presence of comorbid SA
    - Having ≥1 claim with relevant code* (ICD-9/10 diagnosis or procedure, CPT or HCPCS) during baseline
- Key outcomes of interest during the 6-month follow-up period
  - All-cause and psychiatric-specific (with a primary diagnosis of any mental disorder; ICD-9-CM code: 209.xx-311.xx; ICD-10-CM code: F01.xx-F99.xx)
    - Hospitalization
    - Medical cost (inpatient and outpatient, excluding outpatient pharmacy)
- Statistical analysis
  - Logistic regression models performed to examine the association between SA and hospitalizations (all-cause and psychiatric)
  - Linear regression models performed to understand the association between SA and medical costs (all-cause and psychiatric); all costs were adjusted to Y2016 USD
  - Models controlled for demographic and clinical characteristics, insurance type, baseline medication, and baseline hospitalization
  - All data transformations and statistical analyses performed using SAS© version 9.4

* ICD-9-CM: 291.xx, 292.xx, 303.xx, 304.xx, 305.0x, 305.2x-305.9x, 790.3, V65.42; ICD-10-CM: F10.10-F10.2x, F11.xx-F16.xx, F18.xx-F19.xx; CPT: 99408-99409, 4320F; HCPCS: H0005-H0015, H0020, H0047, H0050, H2034-H2036, S9475, T1006-T1012; ICD-9-CM procedure codes: 94.45-94.46, 94.53-94.54, 94.6x; ICD-10-CM procedures codes: HZ2.xxx-HZ9.xxx

Results

Baseline characteristics

- Of 4,862 identified patients with MDD who received AAP adjunctive to antidepressant, 853 (17.5%) had comorbid SA; the remaining 4,009 (82.5%) were without SA **(Figure 1; Table 1)**.
- At baseline, patients with SA were younger [mean (SD) 42.3 (14.3) years vs. 48.5 (16.3) years], had a higher hospitalization rate (55.6% vs. 19.2%) (p<0.001), and had a higher rate of anxiety (75.4% vs 60.9%) while receiving less anti-anxiety medication (52.5% vs 62.5%) than those without SA.

Figure 1. Patient identification

Had ≥1 inpatient claim or ≥2 outpatient claims for MDD and no schizophrenia or BD-I diagnoses during study period[a]
N = 779,733

↓

Received adjunctive oral AAP (brexpiprazole, quetiapine, or lurasidone) during the ID period[b,c] and had ≥1 MDD diagnosis prior to or on index date
N = 6,907 (0.8%)

↓

Were continuously enrolled during 6 mo. prior (baseline) and 6 mo. after (follow-up) index date, and were ≥18 years on index date
N = 4,862 (0.6%)

↓

Final Sample
Patients with comorbid SA
N = 853 (17.5%)
Patients without comorbid SA
N = 4,009 (82.5%)

AAP: atypical antipsychotics; BD-I: bipolar I disorder; MDD: major depressive disorder; SA: substance abuse.
[a] 1/1/15-12/31/16-Medicaid, 1/1/15-9/30/16-Commercial and Medicare Supplemental. [b] 7/1/15-6/30/16-Medicaid, 7/1/15-3/31/16-Commercial and Medicare Supplemental. [c] Non-index antipsychotics were allowed during baseline

Table 1. Baseline demographics and clinical characteristics

	Substance Abuse Disorders		
	Yes	No	P Value
N (%)	853 (17.5)	4,009 (82.5)	
Age, year, mean (SD) [median]	42.3 (14.3) [44]	48.5 (16.3) [50]	<.001
Female, n (%)	502 (58.9)	2,886 (72.0)	<.001
Insurance type, n (%)			<.001
Medicaid	268 (31.4)	854 (21.3)	
Commercial	556 (65.2)	2,647 (66.0)	
Medicare supplemental	29 (3.4)	508 (12.7)	
Charlson comorbidity index, mean (SD)	0.9 (1.6)	0.9 (1.6)	0.936
No. chronic conditions (HCUP), mean (SD)	3.7 (2.1)	3.6 (2.1)	0.715
Anxiety, n (%)	643 (75.4)	2,443 (60.9)	<.001
Personality disorder, n (%)	46 (5.4)	119 (3.0)	<.001
Somatic comorbidities,[a] n (%)	397 (46.5)	2,035 (50.8)	0.025
Any baseline inpatient hospitalization, n (%)	474 (55.6)	769 (19.2)	<.001
Antipsychotic use, n (%)	1,080 (26.9)	210 (24.6)	0.163
Anti-anxiety medications, n (%)	2,105 (52.5)	533 (62.5)	<.001
Sedatives or hypnotics, n (%)	1,117 (27.9)	219 (25.7)	0.194
Somatic medications,[b] n (%)	2,220 (55.4)	468 (54.9)	0.786

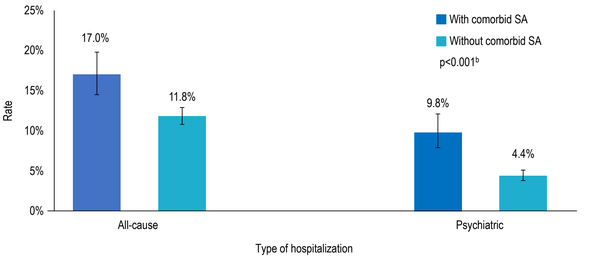
[a] Obesity, type 2 diabetes mellitus, hyperlipidemia, and hypertension.
[b] Anti-diabetic, lipid-lowering, and anti-hypertensive medications.

Results (continued)

Healthcare resource utilization

- During the 6-month follow-up period, the group of patients with MDD and SA had statistically higher use of unadjusted all-cause and psychiatric healthcare resources compared to patients without comorbid SA.
  - ≥1 hospitalization [23.2% vs. 12.6% (all-cause); 15.8% vs. 4.9% (psychiatric)],
  - ≥1 ED visit [40.1% vs. 25.6% (all-cause); 9.4% vs. 3.2% (psychiatric)], and
  - higher number of office visits [13.9 vs. 12.7 (all-cause); 8.7 vs. 6.8 (psychiatric)] (p<0.001 for all).
- Controlling for baseline differences, patients with SA had statistically significantly higher adjusted all-cause and psychiatric hospitalization rates [17.0% vs. 11.8% (all-cause); 9.8% vs. 4.4% (psychiatric)] compared to patients without comorbid SA **(Figure 2)**.

Figure 2. Adjusted[a] all-cause and psychiatric hospitalization rates during the 6-month follow-up period in patients with MDD with/without comorbid SA



MDD: major depressive disorder; SA: substance abuse.
[a] Adjusted by age group, gender, insurance type, Charlson comorbidity, no. of chronic conditions, baseline inpatient hospitalization, baseline comorbidities (including obesity, hyperlipidemia hypertension, anxiety, and personality disorder), baseline non-index anti-psychotic use, baseline psychiatric medication use, and type 2 diabetes mellitus. [b] P value indicates comparison between with and without comorbid SA cohorts within each type of hospitalization.
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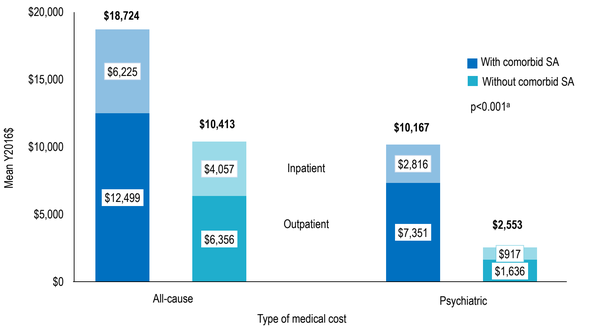
Costs

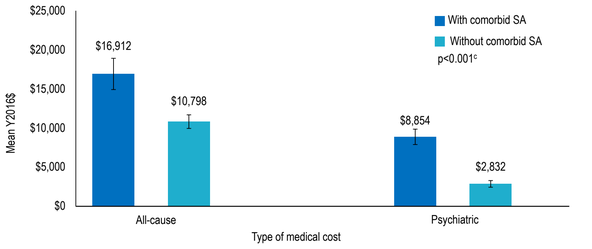
- The group of patients with MDD and SA had higher unadjusted all-cause and psychiatric medical costs [$18,724 vs. $10,413 (all-cause); $10,167 vs. $2,553 (psychiatric) (p<0.001 for all)] **(Figure 3)**.
- Controlling for baseline differences, the group of patients with MDD and SA had higher adjusted all-cause and psychiatric medical costs [$16,912 vs. $10,798 (all-cause); $8,854 vs. $2,832 (psychiatric)] (p<0.001) during the follow-up period **(Figure 4)**.

Figure 3. Components of all-cause and psychiatric medical costs (unadjusted) during the 6-month follow-up period in patients with MDD with/without comorbid SA



MDD: major depressive disorder; SA: substance abuse.
[a] P value indicates comparison between with and without comorbid SA cohorts within each type of medical cost.

Figure 4. Adjusted[a] all-cause and psychiatric medical costs[b] during the 6-month follow-up period in patients with MDD with/without comorbid SA



MDD: major depressive disorder; SA: substance abuse.
[a] Adjusted by age group, gender, insurance type, Charlson comorbidity, no. of chronic conditions, baseline inpatient hospitalization, baseline comorbidities (including obesity, hyperlipidemia hypertension, anxiety, personality disorder, and type 2 diabetes mellitus), baseline non-index antipsychotic use, and baseline psychiatric medication use. [b] Inpatient and outpatient costs (all costs except pharmacy costs). [c] P value indicates comparison between with and without comorbid SA cohorts within each type of medical cost.

Limitations

- All diagnoses were based on health insurance claims data, thus misclassification or coding errors were possible.
- The prevalence of SA may have been underestimated as not all patients with SA received a diagnosis of SA on their insurance claims.

Conclusions

- In patients with MDD being treated with adjunctive AAP, comorbid SA was associated with higher all-cause and psychiatric-specific hospitalization rates and costs.
- Although difficult, addressing comorbid SA in patients with MDD may help improve treatment outcomes, specifically reducing healthcare utilization and costs, following successful treatment.

References

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