IMPACT OF COMORBID SUBSTANCE ABUSE ON HEALTHCARE UTILIZATION AND COSTS IN PATIENTS WITH BIPOLAR I DISORDER TREATED WITH ATYPICAL ANTIPSYCHOTICS

Mallik Greene, BPharm, PhD, DBA[1]; Jessie Tingjian Yan, PhD[2]; Eunice Chang, PhD[2]; Ann Hartry, PhD[3]; Irina Yermilov, MD, MPH, MS[2]

[1] Otsuka Pharmaceutical Development & Commercialization, Inc., Princeton, NJ, USA;
[2] Partnership for Health Analytic Research, LLC, Beverly Hills, CA, USA; [3] Lundbeck, Deerfield, IL, USA

Background & Objectives

- The rate of substance abuse (SA) is approximately three times higher in those with serious mental illness compared to the general US adult population.[1]
  - The lifetime prevalence rate of comorbid SA in patients with bipolar I disorder (BD-I) is 60.3%, which is the highest rate within mood disorders.[2]
- Comorbid substance abuse in BD-I negatively impacts prognosis and treatment adherence.[3]
- Adjunctive atypical antipsychotics (AAP) are a treatment option for patients with more severe BD.[4,5]
- Current literature on comorbid SA in BD has not examined overall healthcare resource utilization and associated costs in this population with more severe BD receiving AAP.[2,6,7]
- The objective of this study was to compare healthcare resource utilization (HCRU) and costs between patients with BD-I treated with AAP with/without comorbid SA.

Methods

- Retrospective cohort study using the Truven Health Analytics MarketScan® Medicaid, Commercial, and Medicare Supplemental databases
- Patient identification **(Figure 1)**
  - ≥1 inpatient or ≥2 outpatient claims for existing or newly diagnosed BD-I (ICD-9-CM: 290.0x, 296.1x, 296.4x-296.8x, excluding 296.82; ICD-10-CM: F30.x-F31.x, excluding F31.81) during the study period (1/1/15-12/31/16-Medicaid, 1/1/15-9/30/16-Commercial and Medicare Supplemental)
  - ≥1 pharmacy claim for new or additional atypical oral antipsychotic during the identification period (7/1/15-6/30/16-Medicaid, 7/1/15-3/31/16-Commercial and Medicare Supplemental)
    - To ensure newly started index therapy (atypical oral antipsychotic monotherapy used on the index date), no evidence of the index therapy during baseline (6 months prior to index date) allowed
    - Use of non-index therapy in baseline allowed
    - Index date defined as first day of treatment
  - ≥6 months continuous enrollment during both baseline and follow-up (defined as 6 months after the index date)
  - ≥18 years on the index date
  - Exclusion criteria:
    - ≥1 diagnosis of schizophrenia any time during study period;
    - Medicare and Medicaid dual eligibility; or
    - Within the Medicare Supplemental database
      - Lack of pharmacy or mental health coverage information; or
      - Had capitated plans
- Presence of comorbid SA
  - Having ≥1 claim with a relevant ICD-9/10 or procedure code during baseline*
- Outcome measures
  - HCRU and costs during the 6-month follow-up period compared between patients with SA and those without
    - 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)
    - Key outcomes of interest:
      - Hospitalization
      - Medical cost
- Statistical analysis
  - Multivariable regression models were conducted to estimate adjusted utilization and costs, controlling for demographic and clinical characteristics, insurance type, baseline medication, and baseline hospitalization.
    - 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 data transformations and statistical analyses performed using SAS© version 9.4.

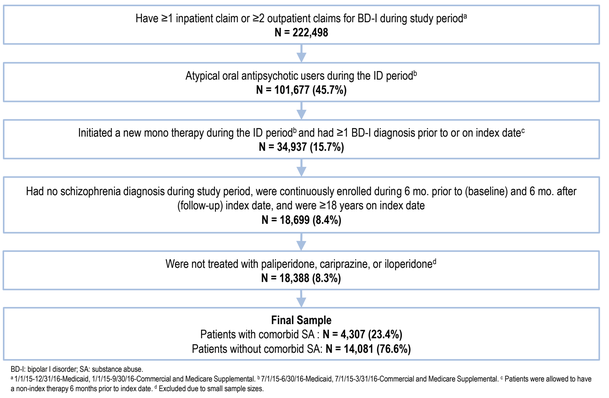
* (ICD-9-CM: 291.xx, 292.xx, 303.xx, 304.xx, 305.0x, 305.2x-305.9x, 790.3, V65.42; ICD-10-CM: F10.10-F10.2x, F11.xx-F16.xx, F18.xx-F19.xx; CPT: 99408-99409, 4320F; HCPCS: H0005-H0015, H0020, H0047, H0050, H2034-H2036, S9475, T1006-T1012; ICD-9-CM procedure codes: 94.45-94.46, 94.53-94.54, 94.6x; ICD-10-CM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

Results

Baseline characteristics

- Of 18,388 identified patients with BD-I who initiated atypical antipsychotics, 4,307 (23.4%) had comorbid SA; the remaining 14,081 (76.6%) were without SA **(Figure 1; Table 1)**.
- At baseline, patients with SA were younger [mean (SD) 38.0 (13.3) years vs. 41.0 (14.8) years], had a higher general disease burden measured by mean (SD) Charlson Comorbidity Index [0.9 (1.6) vs. 0.7 (1.4)], and higher unadjusted hospitalization rate (55.1% vs. 19.4%) than those without SA (p<0.001 for all).

Figure 1. Patient Identification



BD-I: bipolar I 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] Patients were allowed to have a non-index therapy 6 months prior to index date. [d] Excluded due to small sample sizes.

Table 1. Baseline Demographics and Clinical Characteristics

	Substance Abuse Disorders		
	Yes	No	P Value
N (%)	4,307 (23.4)	14,081 (76.6)	
Age, year, mean (SD) [median]	38.0 (13.3) [37]	41.0 (14.8) [41]	<0.001
Female, n (%)	2,747 (63.8)	9,969 (70.8)	<0.001
Insurance type, n (%)			
Medicaid	2,245 (52.1)	5,235 (37.2)	<0.001
Commercial	1,982 (46.0)	8,106 (57.6)	
Medicare supplemental	80 (1.9)	740 (5.3)	
Charlson Comorbidity Index, mean (SD)	0.9 (1.6)	0.7 (1.4)	<0.001
No. chronic conditions (HCUP), mean (SD)	3.5 (2.1)	3.2 (2.0)	<0.001
Major depressive disorder, n (%)	1,879 (43.6)	4,044 (28.7)	<0.001
Anxiety, n (%)	2,767 (64.2)	6,699 (47.6)	<0.001
Personality disorder, n (%)	573 (13.3)	817 (5.8)	<0.001
Somatic comorbidities,[a] n (%)	1,841 (42.7)	6,030 (42.8)	0.927
Any baseline inpatient hospitalization, n (%)	2,375 (55.1)	2,735 (19.4)	<0.001
Antipsychotic use, n (%)	1,418 (32.9)	4,315 (30.6)	0.005
Anti-anxiety medications, n (%)	2,067 (48.0)	5,609 (39.8)	<0.001
Sedatives or hypnotics, n (%)	825 (19.2)	2,718 (19.3)	0.830
Somatic medications,[b] n (%)	1,767 (41.0)	5,895 (41.9)	0.329

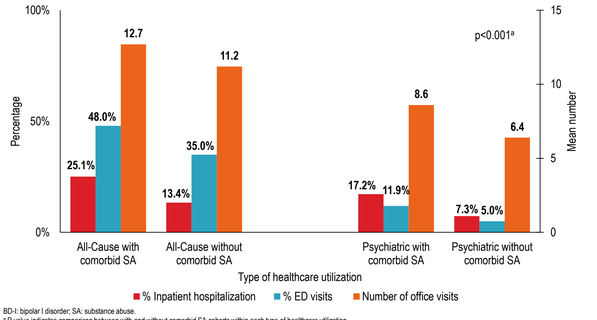
[a] Obesity, type 2 diabetes mellitus, hyperlipidemia, and hypertension.
[b] Anti-diabetic, lipid-lowering, and anti-hypertensive medications.

Results (continued)

Healthcare resource utilization

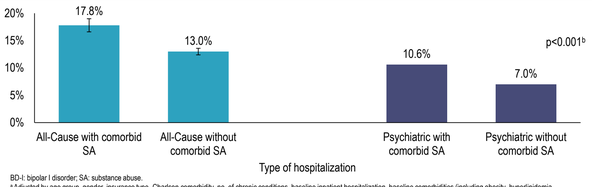
- The group of patients with BD-I and SA had statistically significantly higher use of unadjusted both all-cause and psychiatric healthcare resources.
  - ≥1 hospitalization [25.1% vs. 13.4% (all-cause); 17.2% vs. 7.3% (psychiatric)],
  - ≥1 ED visit [48.0% vs. 35.0% (all-cause); 11.9% vs. 5.0% (psychiatric)], and
  - Higher number of office visits [12.7 vs. 11.2 (all-cause); 8.6 vs. 6.4 (psychiatric)] (p<0.001 for all) during the 6-month follow-up **(Figure 2).**
- Controlling for baseline differences, patients with SA had statistically significantly higher adjusted all-cause and psychiatric hospitalization rates [17.8% vs. 13.0% (all-cause); 10.6% vs. 7.0% (psychiatric)] (p<0.001) **(Figure 3)**.

Figure 2. Components of All-cause and Psychiatric Healthcare Utilization (unadjusted) in the 6-Month Post-Index Period in Patients with BD-I with/without Comorbid SA



BD-I: bipolar I disorder; SA: substance abuse.
[a] P value indicates comparison between with and without comorbid SA cohorts within each type of healthcare utilization.

Figure 3. Adjusted[a] All-Cause and Psychiatric Hospitalization Rates in Follow-Up Period in Patients with BD-I with/without Comorbid SA

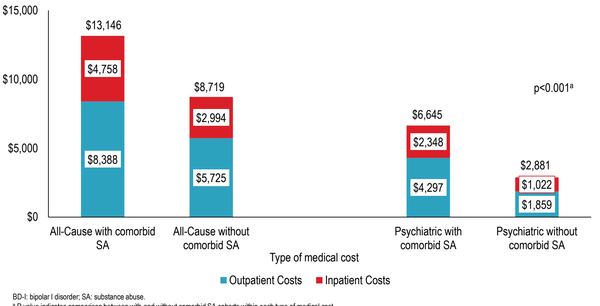


BD-I: bipolar I disorder; SA: substance abuse.
[a] Adjusted by age group, gender, insurance type, Charlson comorbidity, no. of chronic conditions, baseline inpatient hospitalization, baseline comorbidities (including obesity, hyperlipidemia hypertension, major depressive disorder, anxiety, and personality disorder), baseline non-index antipsychotic 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.

Costs

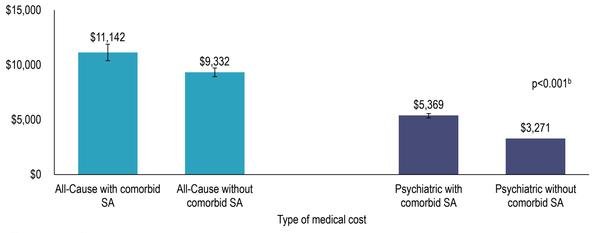
- The group of patients with BD-I and SA had higher unadjusted all-cause and psychiatric medical costs [$13,146 vs. $8,719 (all-cause); $6,645 vs. $2,881 (psychiatric) (p<0.001)] **(Figure 4)**.
- Controlling for baseline differences, during the follow-up period patients with SA had statistically significantly higher adjusted medical costs [$11,142 vs. $9,332 (all-cause); $5,369 vs. $3,271 (psychiatric)] (p<0.001) **(Figure 5).**

Figure 4. Components of All-Cause and Psychiatric Medical Costs (unadjusted) in Follow-Up Period in Patients with BD-I with/without Comorbid SA



BD-I: bipolar I disorder; SA: substance abuse.
[a] P value indicates comparison between with and without comorbid SA cohorts within each type of medical cost.

Figure 5. Adjusted[a] All-Cause and Psychiatric Medical Costs in Follow-Up Period in Patients with BD-I with/without Comorbid SA



BD-I: bipolar I 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, major depressive disorder, anxiety, and personality disorder), baseline non-index antipsychotic 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 medical cost.

Conclusions

- Patients with BD-I and comorbid SA had higher all-cause and psychiatric specific hospitalization rates and costs.
- Efforts to address comorbid SA in BD-I patients may help reduce HCRU and costs.
- The prevalence of SA, which may have been underestimated as not all patients with SA receive a claims-based diagnosis, is a limitation of this study.

References

1. The NSDUH Report - Substance Use and Mental Health Estimates from the 2013 National Survey on Drug Use and Health: Overview of Findings. Rockville, MD: Substance Abuse and Mental Health Services Administration, Center for Behavior Health Statistics and Quality; 2014.
2. Pettinati HM, et al. *Am J Psychiatry*. 2013;170(1):23–30.
3. Messer T, et al. *Psychiatry Res*. 2017;253:338–50.
4. Shah N, et al. *Indian J Psychiatry*. 2017;59(5):51
5. Hirschfeld RMA, et al. *FOCUS J Lifelong Learn Psychiatry*. 2003;1(1)-64-110.
6. Cloutier M, et al. *J Affect Disord*. 2017;226:45–51.
7. Bergeson JG, et al. *Am Health Drug Benefits*. 2012 Sep;5(6):379–86.

Disclosures: M. Greene is an employee of Otsuka Pharmaceutical Development and Commercialization, Inc., Princeton, NJ. J. Yan, E. Chang, and I. Yermilov are employees of Partnership for Health Analytic Research, LLC, Beverly Hills, CA. A. Hartry is an employee of Lundbeck, Deerfield, IL. TThis study was sponsored by Otsuka Pharmaceutical Development and Commercialization, Inc. and Lundbeck; conducted by Partnership for Health Analytic Research, LLC.

ISPOR Asia Pacific,
September 8-11, 2018, Tokyo, Japan