Medication Adherence and Discontinuation in Medicaid Patients with Dual Diagnoses of Schizophrenia and Bipolar Who Initiated a Long-Acting Injectable Antipsychotic Versus Those Who Changed to a Different Oral Antipsychotic Monotherapy

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Introduction

- Medicaid is the predominant insurance program for the approximately 2.6 million adults with schizophrenia in the U.S.[1,2]
  - Approximately 0.3% of the U.S. population has schizoaffective disorder,[3] co-occurrence of schizophrenia and a mood disorder (major depressive or bipolar disorder).[4]
- Medication non-adherence is associated with greater risks of relapse of symptoms and repeated hospitalizations.[5,6]
- Long-acting injectable antipsychotics (LAIs) were developed to improve medication adherence;[7] however, existing studies have not examined medication adherence in schizophrenia patients with comorbid bipolar disorder.

Objective

To compare medication adherence and discontinuation in patients with dual diagnoses of schizophrenia and bipolar disorder who initiated a LAI to those who changed from an oral antipsychotic to a different oral antipsychotic monotherapy.

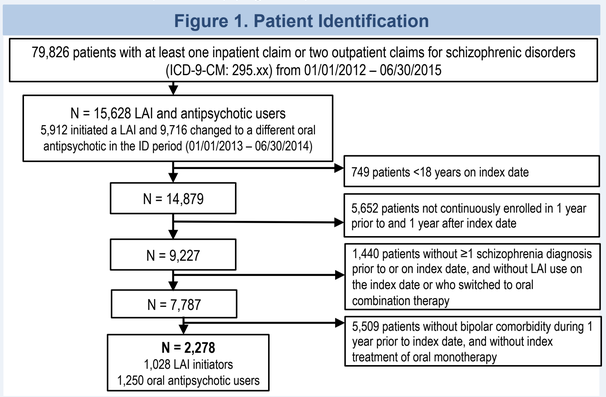
Methods

- Longitudinal cohort study using the Truven MarketScan® Medicaid Database
- Patient identification
  - Schizophrenia (≥1 inpatient or ≥2 outpatients claims) patients (existing or newly diagnosed) during the study period (01/01/2012 to 06/30/2015)
  - LAI cohort
    - Newly started one of the following LAIs during the identification period (01/01/2013 to 06/30/2014):
      - aripiprazole, haloperidol, paliperidone, risperidone, fluphenazine, olanzapine
    - Index date: first LAI use
    - No index LAI use 1 year prior to the index date (use of a different LAI was allowed)
  - Oral cohort
    - Schizophrenia patients, with no prior LAI use, who changed to a different oral antipsychotic monotherapy
    - Index date: date of use of new oral monotherapy
  - Dual Diagnoses: schizophrenia patients who had a diagnosis of bipolar disorder comorbidity within one year prior to the index date
  - Additional inclusion criteria
    - Schizophrenia diagnosis before index date
    - 1-year pre- (baseline) and post-index continuous enrollment
  - Exclusion criteria
    - ≤17 years old on index date
  - Patients followed for variable period until disenrollment from health plan or study end
- Medication adherence reported as proportion of days covered (PDC) during 1-year follow-up
  - PDC = number of days when index medication was available /365 days
- Discontinuation defined as switch or gap of ≥60 days of index treatment
- Statistical analysis
  - A multivariate, general linear regression model used to estimate medication adherence
  - A Kaplan-Meier Curve and a Cox regression model used to estimate time to discontinuation and risk of discontinuation
  - Both the general linear regression and Cox regression models were adjusted for patient demographic and clinical characteristics, baseline medication, and baseline emergency department (ED) visits or hospitalizations

Results

- 1,028 (45.1%) LAI initiators and 1,250 (54.9%) oral monotherapy users were identified (Figure 1).
- Compared with oral users, LAI initiators were younger [mean (SD) LAI vs. oral: 37.5 (12.8) years vs. 40.8 (12.5) years]. A higher percentage of LAI initiators were male (51.6% vs. 39.7%) and African American (44.6% vs. 34.2%) (Table 1).
- LAI initiators had lower psychiatric and somatic comorbid disease burden than oral users, but more ED or inpatient utilization during the baseline period (Table 1).
- Adjusting for covariates, LAI initiators had better medication adherence than oral users; the oral cohort discontinued treatment at a higher rate than LAI cohort (Table 2)
- Median time to discontinue the index LAI was 144 days vs. 109 days for the oral cohort (*P*=0.025) (Figure 2).

Figure 1. Patient Identification



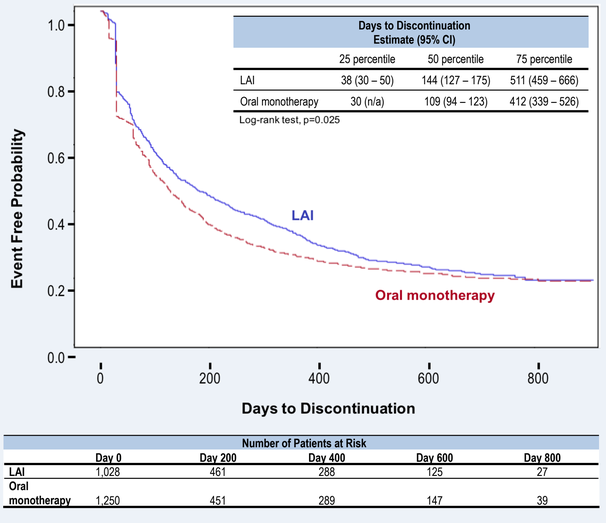
Results (cont'd)

Table 1. Patient Characteristics

	LAIs N=1,028; 45.1%	Oral Monotherapy N=1,250; 54.9%	All N=2,278	*P* Value
Demographics				
Age in years, mean (SD)	37.5 (12.8)	40.8 (12.5)	39.3 (12.7)	<.001
Female, n (%)	498 (48.4)	754 (60.3)	1,252 (55.0)	<.001
Race, n (%)				
White	405 (39.4)	607 (48.6)	1,012 (44.4)	<.001
African American	459 (44.6)	427 (34.2)	886 (38.9)	
Other	164 (16.0)	216 (17.3)	380 (16.7)	
Comorbidities				
Charlson comorbidity index, mean (SD)	1.4 (2.1)	1.9 (2.4)	1.7 (2.2)	<.001
No. chronic conditions, mean (SD)	4.4 (2.4)	4.9 (2.3)	4.6 (2.4)	<.001
Psychiatric comorbidities, n (%)	919 (89.4)	1,124 (89.9)	2,043 (89.7)	0.683
Depression	638 (62.1)	851 (68.1)	1,489 (65.4)	0.003
Anxiety	538 (52.3)	754 (60.3)	1,292 (56.7)	<.001
Personality disorder	260 (25.3)	268 (21.4)	528 (23.2)	0.030
Substance abuse disorders	691 (67.2)	841 (67.3)	1,532 (67.3)	0.975
Somatic comorbidities[a], n (%)	652 (63.4)	838 (67.0)	1,490 (65.4)	0.071
Baseline[b] medication and healthcare service use				
Use of any oral antipsychotic medication, n (%)	929 (90.4)	1,250 (100.0)	2,179 (95.7)	n/a
Any use of selected psychiatric medications, n (%)	833 (81.0)	1,117 (89.4)	1,950 (85.6)	<.001
Somatic medications, n (%)	512 (49.8)	690 (55.2)	1,202 (52.8)	0.010
Any inpatient hospitalization or ED visit, n (%)	886 (86.2)	1,067 (85.4)	1,953 (85.7)	0.574

[a] Obesity, diabetes mellitus, hyperlipidemia, hypertension. [b] One year prior to the index date.

Figure 2. Time to Discontinuation of Index Treatment



Number of Patients at Risk	Day 0	Day 200	Day 400	Day 600	Day 800
LAI	1,028	461	288	125	27
Oral monotherapy	1,250	451	289	147	39

Table 2. Multivariate[a] Results: Risk of Discontinuation and Adjusted Medication Adherence (PDC) Estimates

	Risk of discontinuation of index treatment in the 1-year follow-up period[b]		Index treatment PDC in the 1-year follow-up period[c,d]	
	HR (95% CI)	*P* Value	Estimate (95% CI)	*P* Value
Oral monotherapy (Ref: LAI)	1.14 (1.03 – 1.25)	0.010	-0.038 (-0.072 - -0.005)	0.023

[a] Adjusted for age groups, gender, race (White vs. non-White), Charlson comorbidity index, number of chronic conditions, any baseline inpatient hospitalization or ED visit, depression, anxiety, any baseline psychiatric medication use, and any baseline somatic medication use. [b] Cox regression model. [c] General linear regression model. [d] Adjusted mean (95% CI) PDC of index treatment in 1-year follow-up period: mono oral antipsychotic 0.480 (0.458 – 0.502); LAI 0.519 (0.495 – 0.543).

Limitations

- Clinical differences unmeasurable in this database may have been responsible for the choice of LAI vs. oral antipsychotics, and these differences may be responsible for some of the adherence advantage observed.
- Results may not be generalizable to non-Medicaid patient populations.

Conclusions

- Medicaid patients with dual diagnoses of schizophrenia and bipolar disorder initiating LAIs had slightly, but statistically significantly better medication adherence and lower medication discontinuation risk than patients who changed to a different oral antipsychotic monotherapy.
- Payers and clinicians treating patients with schizophrenia and bipolar disorder should consider LAIs as treatment options for patients with known or suspected poor adherence.

References

1. The National Institute of Mental Health. Schizophrenia [Internet]. Available from: http://www.nimh.nih.gov/health/statistics/prevalence/schizophrenia.shtml
2. Marcus SC, et al. J Manag Care Spec Pharm. 2015;21(9):754-68.
3. The National Alliance on Mental Illness. schizoaffective disorder [Internet]. Available from: http://www.nami.org/Learn-More/Mental-Health-Conditions/Schizoaffective-Disorder
4. Abrams, DJ, et al. Neuropsychiatr Dis Treat. 2008 Dec; 4(6): 1089–1109.
5. Weiden PJ, et al. Psychiatr Serv. 2004;55(8):886-891.
6. Lang K, et al. Psychiatr Serv. 2010;61(12):1239-47.
7. Sacchetti E, et al. Evidence-based Psychiatric Care. 2015;1:27-36.

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