

# Assessment of Extrapyramidal Symptoms in a Medicaid Population with Schizophrenia Newly Prescribed Second-Generation Antipsychotic Medications

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## CONCLUSIONS

- Nearly 1 in 8 patients in this study had evidence of extrapyramidal symptoms (EPS) within one year of initiating a second-generation antipsychotic (SGA) medication.
- Patients with EPS had significantly more healthcare resource utilization (HRU) and higher expenditures than those without evidence of EPS.
- Strategies should be implemented to mitigate the risk of EPS during the first year of SGA utilization and beyond.

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## INTRODUCTION

- Though more commonly associated with first generation antipsychotic (FGA) medications, extrapyramidal symptoms (EPS) have been reported in people taking second-generation antipsychotic (SGA) medications.<sup>1,2</sup>
- SGAs are associated with side effects, including EPS, that may affect medication utilization and treatment costs.
- EPS are involuntary movement disorders including dystonia, akathisia, Parkinsonism, tardive akathisia, and tardive dyskinesia.<sup>1,3</sup>
- EPS is associated with medication nonadherence, costly hospitalizations, and decreased quality of life.<sup>3,4</sup>

## OBJECTIVES

- To describe the 1-year incidence of EPS in patients with schizophrenia newly initiated on an SGA medication within a Medicaid population
- To examine utilization patterns of medications to treat EPS and compare healthcare resource utilization (HRU) and expenditures between those with and without evidence of EPS

## RESULTS

### BASELINE CHARACTERISTICS

- 16,346 patients diagnosed with schizophrenia and newly started on an SGA were included.
- 2,184 (13.4%) patients had evidence of EPS during the 12-month post-index period following SGA initiation.
  - 674 (30.9%) had a documented EPS diagnosis code
  - 1,558 (71.3%) had claims for EPS medications
- Patients with evidence of EPS were more likely to be male and Hispanic compared to those without evidence of EPS.
- Demographics and baseline clinical characteristics are presented in **Table 1** comparing patients with and without evidence of EPS.

**Table 1. Demographics and Clinical Characteristics of Patients with and without Evidence of EPS**

Characteristic	EPS N=2,184	No EPS N=14,162	P
Age, mean (sd)	37.8 (13.0)	38.7 (12.8)	0.004
Males, n (%)	1,370 (62.7)	8,083 (57.1)	<0.001
Race/Ethnicity, n (%)			<0.001
Black	771 (35.3)	5,260 (37.1)	
White	598 (27.4)	4,715 (33.3)	
Hispanic	268 (12.3)	1,269 (9.0)	
Other	47 (2.2)	257 (1.8)	
Unknown	500 (22.9)	2,661 (18.8)	
Charlson Comorbidity Index Score*, mean (sd)	0.6 (1.4)	0.7 (1.6)	<0.001
Other Severe Mental Disorders, n (%)			
Bipolar	900 (41.2)	5,610 (40.6)	0.156
Major Depressive Disorder	547 (25.0)	3,744 (26.4)	0.169

\* Charlson Comorbidity Index with Deyo adaptation

### HEALTH RESOURCE UTILIZATION & EXPENDITURES

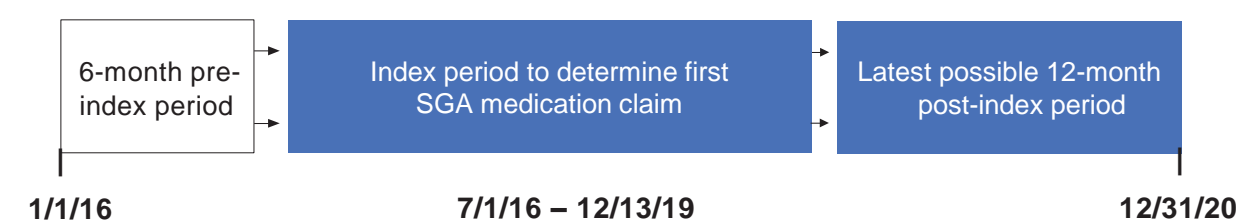
- For those with evidence of EPS, mean time between SGA initiation and evidence of EPS was 150.6 ± 108.4 days.
- A greater proportion of patients with evidence of EPS had all-cause inpatient and ED visits compared to those without evidence of EPS (inpatient: 53.9% vs. 42.7%, p<0.001; ED: 72.5% vs. 69.9%, p=0.016). (**Figure 2**) There was a similar trend in schizophrenia-related HRU prevalence.
- Patients with EPS had significantly more all-cause inpatient (1.5 vs. 0.9; p<0.001), ED (4.5 vs. 3.5; p<0.001), and outpatient (47.5 vs. 44.8; p=0.045) visits compared to those without EPS.

## METHODS

### STUDY DESIGN

- This retrospective observational study used 2016 - 2020 paid claims data from multiple state Medicaid programs. The index date was defined as the first SGA claim between 7/1/16 and 12/31/19. The study timeline included a 6-month pre-index period and all patients were followed for 12 months post-index. (**Figure 1**)

**Figure 1. Study Timeline**



- Evidence of EPS:** presence of an EPS diagnosis code or medication to treat EPS<sup>3</sup>
  - EPS ICD-10: G21.1x, G21.2, G21.8, G24.01, G24.02, G24.2-G24.9, G25.1-G25.4, G25.61, G25.7x, G25.89, G25.9, R25.xx
  - EPS medications: amantadine, biperiden, deutetrabenazine, tetrabenazine, trihexyphenidyl, valbenazine

### Inclusion Criteria

- ≥ 2 claims for oral SGAs during the post-index period
- Schizophrenia diagnosis (ICD-10: F20.xx) associated with ≥1 inpatient claims or ≥2 outpatient claims
- 18-63 years of age at index
- Continuously enrolled in Medicaid during the pre- and post-index periods

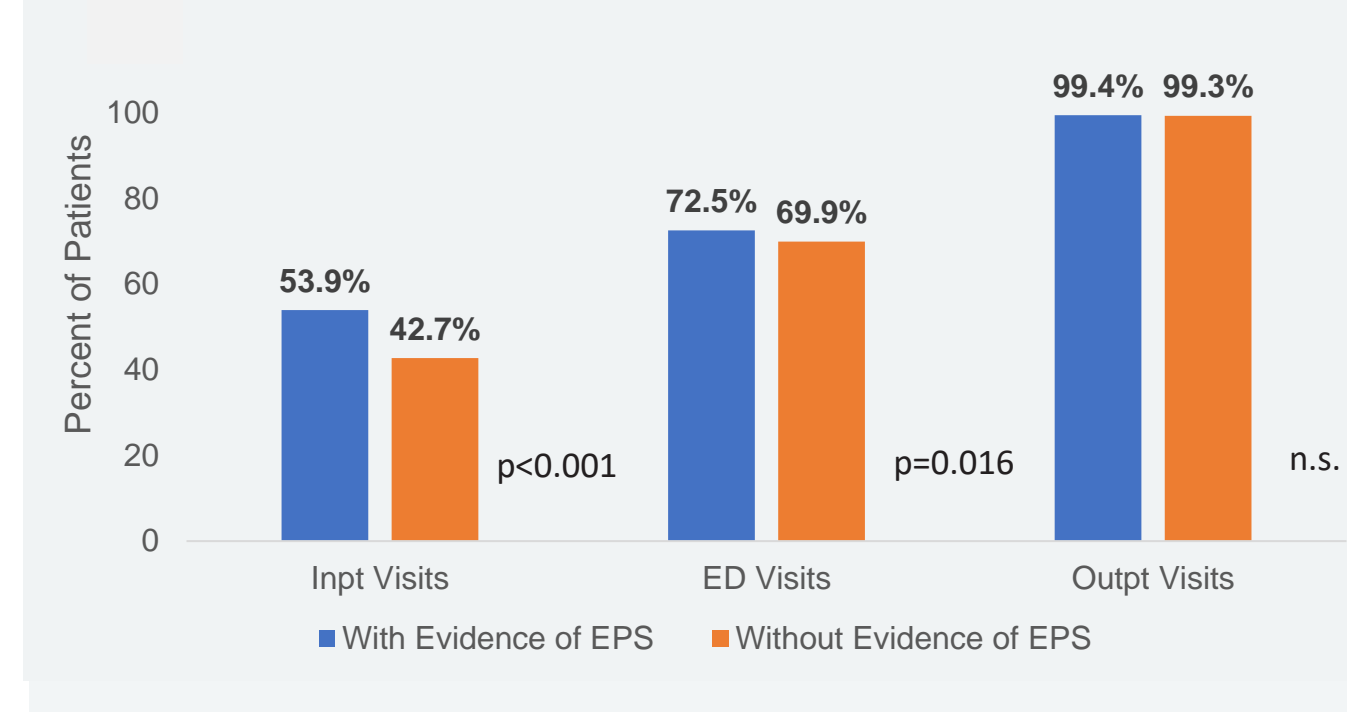
### Exclusion Criteria

- Claims for FGAs or SGAs during the pre-index period
- Dually eligible for Medicaid and Medicare at any time pre- or post-index
- Pre-index evidence of EPS
- Parkinson's disease diagnosis (ICD-10: G20) pre- or post-index

### Analyses

- Bivariate analyses were conducted using t- and X<sup>2</sup> tests.
- Logistic regression assessed the odds of inpatient and ED visits.
- Generalized linear model (GLM) regression using a gamma distribution and a log-link function assessed medical and total expenditures.
- Regression independent variables: EPS status, age, sex, CCI score, presence of other severe mental disorders (race not included due large % of unknowns)

**Figure 2. Prevalence of All-Cause Inpatient, ED, and Outpatient Resource Utilization of Patients with and without Evidence of EPS**



- Annual all-cause and schizophrenia-related total expenditures were \$4,358 and \$2,387 higher, respectively, for the EPS cohort compared to those with no evidence of EPS (p<0.001). (**Table 2**)

**Table 2. Healthcare Expenditures for Patients with and without Evidence of EPS**

Expenditures	EPS N=2,184	No EPS N=14,162	P
<b>All-Cause, mean (sd)</b>			
Inpatient	\$10,209 (37,630)	\$7,647 (40,351)	0.005
ED	\$1,356 (3,744)	\$1,055 (2,556)	<0.001
Outpatient	\$7,033 (10,751)	\$6,512 (10,166)	0.027
Subtotal - Medical	\$18,598 (41,367)	\$15,213 (43,390)	<0.001
Prescriptions	\$6,277 (11,547)	\$5,303 (14,815)	0.003
<b>TOTAL</b>	<b>\$24,875 (43,553)</b>	<b>\$20,517 (46,377)</b>	<b>&lt;0.001</b>
<b>Schizophrenia-Related*, mean (sd)</b>			
Inpatient	\$1,657 (6,722)	\$664 (3,976)	<0.001
ED	\$44 (243)	\$27 (196)	<0.001
Outpatient	\$1,199 (3,294)	\$866 (3,013)	<0.001
Subtotal - Medical	\$2,900 (7,747)	\$1,558 (5,143)	<0.001
Prescriptions	\$3,410 (6,144)	\$2,364 (5,037)	<0.001
<b>TOTAL</b>	<b>\$6,309 (10,316)</b>	<b>\$3,922 (7,480)</b>	<b>&lt;0.001</b>

\* F20.xx in the primary position for medical claims; antipsychotic prescription claims

### EPS MEDICATION UTILIZATION & EXPENDITURES

- Of those with evidence of EPS, 1,558 (71.3%) were dispensed medication to treat EPS. (**Table 3**)
- Almost 95% of patients (N=1,475; 94.7%) with EPS treatments were prescribed biperiden.
- Few patients (~1.4%) were prescribed vesicular monoamine transporter 2 (VMAT2) inhibitors (i.e., deutetrabenazine, valbenazine), but these medications accounted for 92.8% of EPS treatment expenditures (~\$628K).

**Table 3. EPS Treatments and Expenditures**

EPS Medication	Number of Patients (%)	Number of Rx Claims (%)	Total Expenditures (%)	Mean Expenditure per Rx (sd)
Amantadine	37 (2.4%)	157 (3.1%)	\$9,436 (1.4%)	\$60 (32)
Biperiden	1,475 (94.7%)	4,643 (91.9%)	\$38,691 (5.7%)	\$8 (5)
Deutetrabenazine	*	22 (0.4%)	\$127,186 (18.8%)	\$5,781 (2,152)
Trihexyphenidyl	17 (1.1%)	146 (2.9%)	\$919 (0.1%)	\$6 (4)
Valbenazine	49 (3.1%)	82 (1.6%)	\$500,534 (74.0%)	\$6,104 (1,044)
<b>TOTAL</b>	<b>1,558 (100.0%)</b>	<b>5,050 (100.0%)</b>	<b>\$676,766 (100.0%)</b>	<b>\$134 (877)</b>

\*N is less than 11, thus not reported

### MULTIVARIABLE ANALYSES

#### HRU Prevalence

- Compared to patients with no evidence of EPS and controlling for covariates, those with EPS had:
  - 66.3% and 108.5% higher odds of an all-cause and schizophrenia-related inpatient visit, respectively
    - All-Cause – OR: 1.663, 95%CI: 1.512-1.830, p<0.001
    - Schiz-Related – OR: 2.086, 95%CI: 1.852-2.347, p<0.001
  - 18.5% and 68.0% higher odds of an all-cause and schizophrenia-related ED visit, respectively
    - All-Cause – OR: 1.185, 95%CI: 1.067-1.316, p=0.002
    - Schiz-Related – OR: 1.680, 95%CI: 1.453-1.942, p<0.001

#### Expenditures

- Compared to patients with no evidence of EPS and controlling for covariates, those with EPS had:
  - 26.9% and 79.1% higher all-cause and schizophrenia-related medical (inpatient + ED + outpatient) expenditures, respectively
    - All-Cause – 1.269, 95%CI: 1.137-1.416, p<0.001
    - Schiz-Related – 1.791, 95%CI: 1.544-2.078, p<0.001
  - 27.8% and 56.9% higher all-cause and schizophrenia-related total (medical + prescription) expenditures, respectively
    - All-Cause – 1.278, 95%CI: 1.166-1.402, p<0.001
    - Schiz-Related – 1.569, 95%CI: 1.443-1.707, p<0.001