Impact of Depression on Outcomes and Treatment Patterns in Patients with Newly Diagnosed Epilepsy: A Retrospective Claims Analysis

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BACKGROUND

- Meta-analyses and epidemiological studies consistently show elevated risk of depression in patients with epilepsy compared to the general population, highlighting its high prevalence in this population[1-2]
- In epilepsy, depression is a leading driver of reduced health-related quality of life (HRQOL)[3-4]
- Depression can also exacerbate adverse effects of antiseizure medications, reduce response to both pharmacological and surgical treatments, and increase likelihood of patients being resistant to anti-seizure medications (ASMs)[4-5]
- Despite the recognized burden, additional evidence may strengthen further understanding on how depression impacts outcomes and treatment patterns in newly diagnosed epilepsy

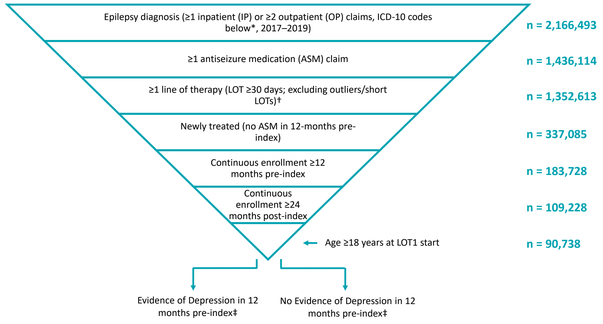
OBJECTIVES

- This study aimed to evaluate outcomes and treatment patterns among patients newly diagnosed with epilepsy, stratified by the presence or absence of depression

METHODS

- Study Design and Data Source:
  - Retrospective observational study using 100% U.S. Medicare Fee-for-Service (FFS) claims data and the Inovalon's Medical Outcomes Research for Effectiveness and Economics (MORE^2) Closed Claims Registry
  - Study period: January 1, 2016 to December 31, 2023 (only up to December 31, 2022 for FFS)
- The index date was defined as the first prescription during the study period that was part of a line of therapy (LOT) lasting at least 30 days
- Duration of therapy was measured as the time from the start to the end of each LOT
- LOTs ended at discontinuation (≥60-day gap in all treatment), switch (new agent with <30 days overlap), augmentation (new agent with ≥30 days overlap), or partial drop (discontinuation of one or more agents for ≥60 days)

Figure 1. Cohort Attrition Flow



*ICD-10 Codes: G40.0X, G40.1X, G40.2X, G40.5X, G40.80X, G40.89, G40.9X

†ASM classification by MOA[6-9]:
GABA – Vigabatrin, Primidone, Phenobarbital, Tiagabine, Clobazam
Sodium channel blockers – Phenytoin, Carbamazepine, Oxcarbazepine, Eslicarbazepine, Lamotrigine, Lacosamide
Calcium channel blockers – Ethosuximide, Gabapentin, Pregabalin
SV2A – Levetiracetam, Brivaracetam
AMPA – Perampanel
Other/mixed/multiple – Topiramate, Valproate, Zonisamide, Felbamate, Cenobamate

‡Evidence of Depression defined by (≥1 IP or ≥2 OP claims, ICD-10 Codes: F32-F33)

RESULTS

Table 1. Demographic Characteristics at Index Among Individuals Newly Diagnosed with Epilepsy

Demographics	All Study Patients N = 90,738	Depression Cohort N =21,388	No Depression Cohort N = 69,350	p-value
Age at Index				
Median (IQR)	58 (40-72)	59 (43-71)	58 (39-72)	
Age group, years (n, %)				n.s.
18-64	54,565 (60.1%)	12,800 (59.8%)	41,765 (60.2%)	
≥65	36,173 (39.9%)	8,588 (40.2%)	27,585 (39.8%)	
Sex (n, %)				<0.05
Female	49,749 (54.8%)	13,347 (62.4%)	36,402 (52.5%)	
Male	40,989 (45.2%)	8,041 (37.6%)	32,948 (47.5%)	
Race/ethnicity (n, %)				<0.05
White	54,967 (60.6%)	14,605 (68.3%)	40,362 (58.2%)	
Black	15,240 (16.8%)	2,988 (14.0%)	12,252 (17.7%)	
Hispanic or Latino	7,804 (8.6%)	1,535 (7.2%)	6,269 (9.0%)	
Asian	1,712 (1.9%)	257 (1.2%)	1,455 (2.1%)	
Other/Unknown	11,015 (12.1%)	2,003 (9.4%)	9,012 (13.0%)	
Payer Channel (n, %)				<0.05
Medicare FFS	49,676 (54.7%)	13,165 (61.6%)	36,511 (52.6%)	
Managed Medicaid	22,366 (24.6%)	4,719 (22.1%)	17,647 (25.4%)	
Commercial	10,034 (11.1%)	1,609 (7.5%)	8,425 (12.1%)	
Medicare Advantage	8,662 (9.5%)	1,895 (8.9%)	6,767 (9.8%)	

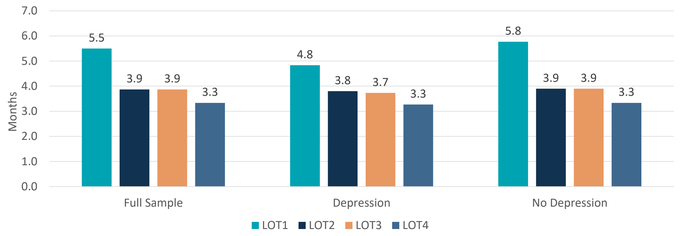
- A total of 90,738 patients met inclusion criteria, with 21,388 (24%) classified into the depression cohort and 69,350 (76%) into the no depression cohort
- The median age was 59 (Q1, 43; Q3 71) years for the depression group and 58 (Q1, 39; Q3, 72) years for the no depression group
- Compared with the no depression group, the depression group had a higher proportion of females (62% vs. 53%) and White patients (68% vs. 58%)

Table 2. Clinical Characteristics during Baseline Among Individuals Newly Diagnosed with Epilepsy

Clinical Characteristics	All Study Patients N = 90,738	Depression Cohort N =21,388	No Depression Cohort N = 69,350	p-value
Deyo Charlson Comorbidity Index (CCI) score				<0.05
Mean (SD)	2.7 (3.0)	3.5 (3.3)	2.5 (2.9)	
Deyo CCI Categories (n, %)				<0.05
0	26,675 (29.4%)	3,811 (17.8%)	22,864 (33.0%)	
1	16,381 (18.1%)	3,718 (17.4%)	12,663 (18.3%)	
2	11,353 (12.5%)	2,766 (12.9%)	8,587 (12.4%)	
3	8,714 (9.6%)	2,259 (10.6%)	6,455 (9.3%)	
4+	27,615 (30.4%)	8,834 (41.3%)	18,781 (27.1%)	
Individual Comorbidities (n, %)				
Anxiety Disorders	30,427 (33.5%)	13,902 (65.0%)	16,525 (23.8%)	<0.05
Neuropathy/Neuropathic pain associated condition	26,575 (29.3%)	8,444 (39.5%)	18,131 (26.1%)	<0.05
Sleep Disorder	23,752 (26.2%)	8,909 (41.7%)	14,843 (21.4%)	<0.05
Stroke	20,828 (23.0%)	5,954 (27.8%)	14,874 (21.4%)	<0.05
Psychosis	9,854 (10.9%)	4,180 (19.5%)	5,674 (8.2%)	<0.05
Bipolar Disorder	9,115 (10.0%)	3,772 (17.6%)	5,343 (7.7%)	<0.05
Select Deyo CCI Components (n, %)				
COPD	25,656 (28.3%)	8,523 (39.8%)	17,133 (24.7%)	<0.05
Diabetes without Complications	22,116 (24.4%)	6,450 (30.2%)	15,666 (22.6%)	<0.05
Peripheral Vascular Disease	15,502 (17.1%)	4,830 (22.6%)	10,672 (15.4%)	<0.05
Congestive Heart Failure	14,135 (15.6%)	4,530 (21.2%)	9,605 (13.9%)	<0.05

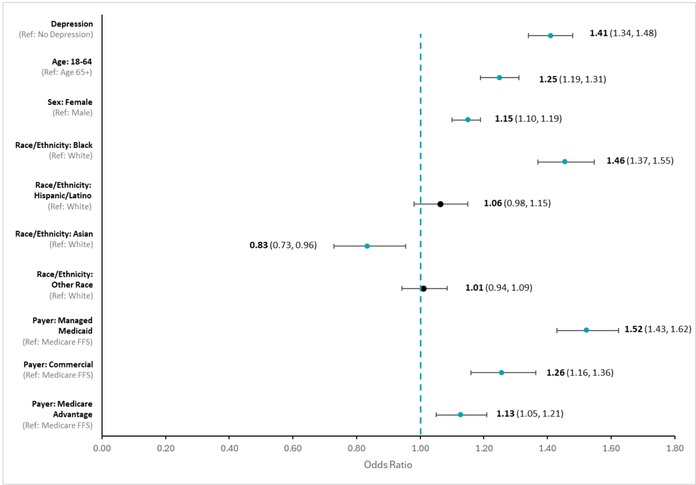
- Comorbidity burden was higher among epilepsy patients with depression, reflected by a higher mean Deyo Charlson Comorbidity Index (CCI) score (3.5 vs. 2.5) and a larger proportion with CCI score ≥4 (41% vs. 27%)
- Depression frequently occurred with multiple psychiatric conditions, with more than half also having anxiety disorders and over 40% having sleep disorders
- The depression cohort had higher prevalence of chronic cardiometabolic and systemic diseases such as COPD, diabetes, heart failure, and peripheral vascular disease

Figure 2. Median Duration of Therapy by LOT



- Epilepsy patients with depression remained on LOT1 for a shorter time compared to those without depression (median 4.8 months vs. 5.8 months)
- Durations across subsequent LOTs (LOTs 2–4) were similar between both cohorts, with modest declines over time

Figure 3. Forest Plot for Factors Associated with Treatment Failure* in Multivariable Logistic Regression Model



*Treatment failure defined as LOT discontinuation (≥60-day gap in all treatment), switch (new agent with <30 days overlap), augmentation (new agent with ≥30 days overlap), or partial drop (discontinuation of one or more agents for ≥60 days)

- Logistic regression analysis, adjusted for age, sex, race/ethnicity, and payer, demonstrated significantly higher odds of treatment failure (LOT1 termination) among epilepsy patients with depression (OR 1.41; 95% CI 1.34–1.48) compared to those without depression. (Fig. 3)

CONCLUSIONS

- Patients with epilepsy and depression exhibited a higher prevalence of psychiatric and systemic comorbidities, suggesting a more complex clinical profile and greater vulnerability across both mental and physical health domains
- Depression was also associated with shorter duration of initial therapy and an increased risk of treatment failure, underscoring the importance of tailored treatment strategies for this subgroup

LIMITATIONS

- Depression status was identified using claims in the pre-index period, which may not reflect follow-up status, and is overall subject to underreporting in administrative data
- Claims datasets generally lack clinical detail (e.g., toxicity, lack of effectiveness), limiting the ability to determine reasons for treatment discontinuation and reasons for subsequent lines of therapy
- More than 60% of the study population were Medicare beneficiaries, which may limit generalizability to other populations, such as those with commercial insurance (11% of the cohort)

FUNDING

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DISCLOSURES

TD, AY, and YH are employees of Inovalon, which was contracted by Xenon Pharmaceuticals Inc. for this study. ST has been a paid consultant for Jazz Pharmaceuticals, Inc. and is currently a paid consultant for Xenon Pharmaceuticals Inc. He is an employee of the University of Michigan and is supported by the National Institutes of Health K23 AG081463. AO, CP, and DT are employees and equity holders of Xenon Pharmaceuticals Inc.

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