Multivariable Models Reporting Increased Economic and Humanistic Burden Among Patients With Epilepsy Reporting Focal Seizures (FS) Experiencing Moderate to Severe Depression Symptoms

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BACKGROUND

- Approximately 3 million adults in the U.S. have epilepsy and an estimated 60% of the total epilepsy population experience focal seizures (FS)[1-5]
- People with epilepsy (PwE) have a 2-3 times higher risk of depression than people without epilepsy[6]
- Previous research elucidated the holistic clinical, humanistic, and economic disease burden that affects PwE, but gaps remain in our understanding of how mental health challenges can exacerbate the humanistic and economic burden of the disease among PwE after accounting for patient- and disease-related factors

OBJECTIVES

- This study used multivariable regression analyses to quantify the independent relationship between depression symptoms and healthcare resource utilization (HCRU) or quality of life (QoL)

METHODS

- A quantitative, cross-sectional, web-enabled survey was conducted from July to September 2023 to understand the burden of illness for PwE reporting FS
- Patients were recruited via either a patient panel or their physician at the point of care, using the following criteria:

Inclusion Criteria	Exclusion Criteria
• United States resident • Age 18 to 80-years-old • Self-reported, physician diagnosis of FS for at least 1 year • Experiencing ≥ 1 seizure in a typical month • Have used (currently or previously) at least 2 ASMs and are currently taking at least 1 ASM for at least 1 month	• Currently enrolled in a clinical trial for FS • Experiencing seizures secondary to drug or alcohol use, ongoing infection, neoplasia, demyelinating disease, degenerative neurological disease, metabolic illness, progressive structural lesion, encephalopathy, or progressive central nervous system disease

- **Patient panel:** Patients applied to be part of the third-party vendor panel based on having a diagnosis of epilepsy. The vendor validated the epilepsy diagnosis before confirming panel enrollment. These patients then participated in the survey screener to verify they met the inclusion and exclusion criteria
- **Physician at point of care:** Physicians were provided with the study inclusion and exclusion criteria and used them to select patients to recruit for the study. Patients then participated in the survey screener to verify they met the inclusion and exclusion criteria
- Data was collected via a custom questionnaire and validated tools including the Patient Health Questionnaire-9 (PHQ-9) and the Quality of Life in Epilepsy Inventory-10 (QOLIE-10)
  - The PHQ-9 is a 9-item instrument that assesses depression-related symptom severity based upon the DSM-5 criteria for MDD, with scores ranging from 0 to 27 and higher scores indicating more severe symptoms[7,8]
  - The QOLIE-10 is a 10-item questionnaire that evaluates epilepsy-specific and general quality of life across domains such as energy, mood, daily activities, and medication effects with higher scores indicating better functioning[9]
- Multivariable regression analyses, including linear (QOLIE-10 outcome), Poisson (emergency room [ER] and inpatient visits outcomes), and logistic (treatment adherence outcome) regressions, were conducted to assess the association between moderate to severe depression (PHQ-9 ≥ 10) vs. no to mild depression (PHQ-9 < 10) and QoL (QOLIE-10), inpatient visits, ER visits, and treatment adherence. Stepwise Akaike information criterion (AIC) models were employed to identify the optimal model covariates. The variance inflation factor (VIF) was used to identify collinear covariates; variables with a VIF over 4 were excluded from the final multivariate model
- Disease-related (e.g., seizure frequency, severity, adverse effects (AEs), locus of control, lines of therapy, current medications, caregiver support, non-seizure symptoms, comorbidities, anxiety) and demographic covariates (e.g., sex, age, race/ethnicity, income, education, employment, insurance, region) were considered for the multivariable models, and a subset of these covariates were selected into the model for each outcome

RESULTS

Sample Description

- The average number of years living with epilepsy was 11.3 years, and the majority of patients (66.5%) were currently managed by an epileptologist (Table 1)

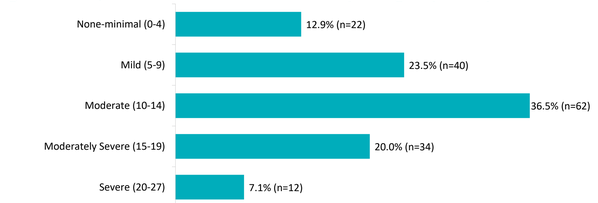
Table 1. Demographics and Baseline Characteristics of PwE Reporting FS

	Study Population *(N=170)*
Age, mean (SD)	42.6 (10.9)
Female, n (%)	92 (54.1%)
Race, n (%)	
White	99 (58.2%)
Black	26 (15.3%)
Other	45 (26.5%)
Employed Full- or Part-time, n (%)	79 (46.5%)
Annual Household Income < $60,000, n (%)	74 (43.5%)
Insurance status, n (%)	
Private	77 (45.3%)
Public (e.g., Medicare, Medicaid)	102 (60.0%)
Government (e.g., VA, DOD)	9 (5.3%)
Uninsured	6 (3.5%)
Number of Years Since Epilepsy Diagnosis, median (IQR)	5.7 (3.6 – 14.8)
Number of Prior Lines of Therapy, median (IQR)	2 (2-4)
Providers Currently Managing Epilepsy[a†], n (%)	
Neurologist	64 (37.6%)
Primary Care Physician	23 (13.5%)
Epileptologist	113 (66.5%)
Psychiatrist	9 (5.3%)
Psychologist	6 (3.5%)
Other	3 (1.8%)

[a]Patients were asked, "Which type of healthcare provider is currently managing/ treating your epilepsy?" and allowed to reported more than one type of healthcare provider; †Other provider types reported include primary physician, psychiatrist, psychologist, therapist, neurosurgeon, and neuro-oncologist

- Mean (SD) PHQ-9 score was 11.3 (5.5) out of 27, and 63.5% had a score ≥ 10, suggestive of moderate to severe depression (Figure 1)

Figure 1. PHQ-9 Score Distribution for PwE Reporting FS (N=170)

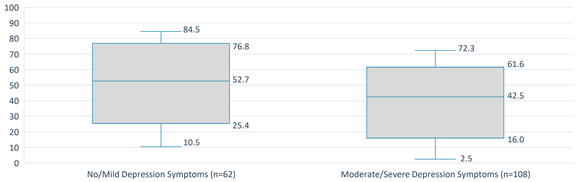


PHQ-9 assesses and monitors depression symptom severity; scores range from 0 to 27 and higher scores indicate more severe depression or depressive symptoms.

Burden among PwE Reporting FS by Depression Severity

- Patients with moderate to severe depression symptoms were more likely to have a reduced QoL compared to those with no to mild symptoms (Figure 2)

Figure 2. Quality of Life among PwE Reporting FS with Moderate to Severe Depression Symptoms and with No to Mild Symptoms



QOLIE-10 scores were converted to 0-100; higher scores indicate fewer problems related to epilepsy and better overall QoL.

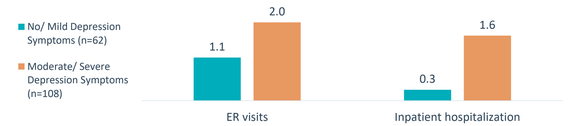
- After adjusting for covariates and consistent with unadjusted results (Figure 2), individuals with moderate to severe depression symptoms had a QOLIE-10 score that was 12 points lower than those with no to mild depression (p<0.001), reflecting a worse QoL (Figure 3)

Figure 3. Associations between Depression Symptoms and QOLIE-10 Using Linear Regression

Effect size of 0 = no difference between moderate to severe vs. no to mild depression symptoms
Model adjusted for age, sex, race, ethnicity, seizure frequency, anxiety, comorbidities, locus of control, number of non-seizure symptoms, seizure severity, number of AEs.

- Patients with moderate to severe depression symptoms had, on average, more ER visits and inpatient visits compared to patients with no to mild depression symptoms (Figure 4)

Figure 4. HCRU among PwE Reporting FS with Moderate to Severe Depression Symptoms vs. No to Mild Depression Symptoms



Question: How many ER visits and inpatient stays/hospitalizations have you experienced because of your epilepsy, in the last 12 months?

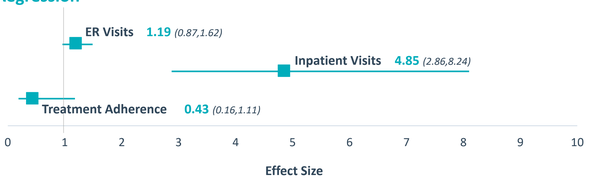
- Patients with moderate to severe depression symptoms are more likely to be less adherent to their treatment compared to those with no to mild depression symptoms (Figure 5)

Figure 5. ASM Adherence among PWE Reporting FS with Moderate to Severe Depression Symptoms vs. No to Mild Depression Symptoms

Question: How many days in the past week have you taken your chronic medication(s) as prescribed by your doctor?

- Compared to those with no to mild depression symptoms, individuals with moderate to severe depression symptoms reported 5 times more inpatient visits (p<0.001), even after controlling for covariates (Figure 6)
- Patients with moderate to severe depression symptoms had approximately 19% more ER visits and 57% lower treatment adherence, although the associations were non-significant (Figure 6)

Figure 6. Associations between Depression Symptoms with ER and Inpatient Visits using Poisson Regression, and Treatment Adherence using Logistic Regression



Effect size of 1 = no difference between moderate to severe vs. no to mild depression symptoms

All models adjusted for age, sex, race, ethnicity, and seizure frequency. The following variables were additionally adjusted for: region (ER visits, inpatient visits), insurance (inpatient visits), employment status (inpatient visits, adherence), locus of control (inpatient visits, adherence), # of non-seizure symptoms (adherence), seizure severity (ER visits, inpatient visits), # of AEs (ER visits, inpatient visits), # of inpatient visits (adherence), # current medications (inpatient visits), and # of prior lines (inpatient visits).

CONCLUSION

- Patients with epilepsy reporting FS with moderate to severe depression symptoms experience heightened disease burden
- Even after controlling for covariates, PwE reporting FS with depression symptoms experienced significantly lower QoL and higher HCRU, suggesting that depression may be a key contributor to the added humanistic and economic burden
- Findings underscore the need for recognition of depression among PwE reporting FS, supporting holistic care beyond seizure control through routine screening of depression symptoms

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DISCLOSURES BO, BS, and AA, are employees of Trinity Life Sciences, which was contracted for this study by Xenon Pharmaceuticals Inc. AA and BO hold equity in Trinity Life Sciences. JMW, AO, and CH are employees and equity holders of Xenon Pharmaceuticals Inc.

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