Is the Mental Health Burden of Epilepsy Under-Recognized in Patients Reporting Focal Onset Seizures? A Patient-Reported Outcomes Study

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BACKGROUND

- Approximately 3 million adults in the U.S. have epilepsy and an estimated 60% of the total epilepsy population experiences focal onset seizures (FOS) [1-5]
- Patients with FOS are primarily treated with antiseizure medications (ASMs); however, nearly one third of patients are not well controlled on treatment and high rates of adverse events (ranging from 7-31%) have been reported [6-8]
- The burden of epilepsy can negatively impact quality of life (QoL) as patients may experience challenges with their employment status, maintaining independence, and managing activities of daily living [9]
- Anxiety and depression are common comorbidities in epilepsy that further exacerbate the burden of epilepsy and may require additional care or support [10]
- The Patient Health Questionnaire-9 (PHQ-9) and Generalized Anxiety Disorder-7 (GAD-7) are common screening tools for depression and anxiety, respectively, that have been previously validated and used in patients with epilepsy [11,12]
- Despite existing information on the burden of patients living with epilepsy, a knowledge gap remains in the understanding of the real-world experiences of patients with epilepsy reporting FOS, including the mental health burden that persists despite ongoing treatment with ASMs

OBJECTIVES

- This study sought to assess the self-reported disease burden, QoL, health care resource utilization (HCRU), and work productivity in patients reporting FOS

METHODS

- A cross-sectional study employing a 30-minute, customized, web-enabled survey was conducted from July to September 2023 to assess symptomology, comorbidities, and mental health burden among patients reporting FOS; the study was institutional review board (IRB)-exempt (Advarra, Columbia, MD)
- Mental health was assessed using validated patient-reported outcome measures; the PHQ-9 and GAD-7 were used to assess depression and anxiety-related symptom severity, respectively [13,14]
  - PHQ-9 is a 9-item instrument that assesses depression-related symptom severity, with scores ranging from 0 to 27 and higher scores indicating more severe symptoms [13]
  - GAD-7 is a 7-item instrument that assesses anxiety-related symptom severity, with scores ranging from 0 to 21 and higher scores indicating more severe symptoms [14]
- Cognitive interviews (n=4) were conducted to ensure the survey was clear and understandable for patients reporting FOS
- Patients were recruited via either a patient panel or their physician at the point of care, using the following criteria:

Inclusion Criteria	Exclusion Criteria
▪ At least 18 years of age and residing in the United States ▪ A physician-confirmed diagnosis of FOS 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 FOS ▪ 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 were analyzed using descriptive statistics in Q Research Software 5.12.4.0

RESULTS

Sample Description

Table 1. Demographics and Baseline Characteristics of Patients Reporting FOS

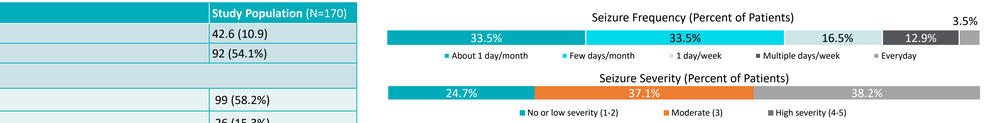
	Study Population (N=170)
Age, mean (SD)	42.6 (10.9)
Female, n (%)	92 (54.1%)
Race, n (%)	
White	99 (58.2%)
Black	26 (15.3%)
Other	45 (26.5%)
Employed Full- or Part-time, n (%)	79 (46.5%)
Annual Household Income < $60,000 USD, n (%)	74 (43.5%)
Number of Years Living with Epilepsy, mean (SD)	11.3 (12.4)
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%)
Seizure Types and Epilepsy Syndromes Reported[b], n (%)	
FOS	170 (100.0%)
Primary Generalized Seizures (PGS)[c]	79 (46.5%)
Non-epileptic Psychogenic Seizures	19 (11.2%)
Lennox-Gastaut Syndrome (LGS)	19 (11.2%)
Developmental and Epileptic Encephalopathy (DEE)	14 (8.2%)
Combination of Seizure Types and Epilepsy Syndromes Reported, n (%)	
FOS only	74 (43.5%)
FOS + PGS	54 (31.8%)
FOS + PGS + other*	25 (14.7%)
FOS + other*	17 (10.0%)

[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; [b] Patients were asked, "Has a neurologist ever diagnosed you with any of the following seizure types?" and allowed to report physician diagnosis for more than one type of epilepsy/seizure type; [c] Primary Generalized Seizures was defined as, "Seizures that start on both sides of the brain at the same time and cause loss of awareness from the start of the seizure. Primary generalized seizures are sometimes called grand mal seizures. This type of seizure has no warning or confusion at the start of it.", *Other seizure types and epilepsy syndromes reported include non-epileptic psychogenic seizures, Lennox-Gastaut Syndrome (LGS), and Developmental and Epileptic Encephalopathy (DEE)

- Of the 170 patients reporting FOS who participated in the survey, only 43.5% of patients reported having only FOS; Primary Generalized Seizures (PGS) was the most reported concomitant seizure type (46.5%) (Table 1)
- Patients reported being diagnosed with epilepsy for an average of 11.3 years (SD 12.4)

Seizure-Related Symptom Burden in Patients Reporting FOS

Figure 1. Self-Reported Seizure Frequency and Severity for Patients Reporting FOS

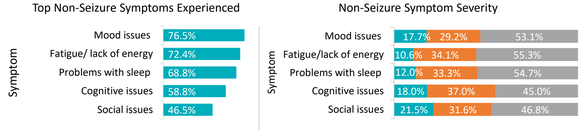


Questions: For each symptoms you currently experience, please indicate how often you experience it; For each symptoms you currently experience, please indicate the current severity of each symptoms (rating scale 1-5; 1=not at all severe, 5=extremely severe)

- 66.5% of patients reported seizures more than once a month, and 75.3% of patients indicated their seizures were moderate to highly severe (Figure 1)

Non-Seizure Related Symptom Burden in Patients Reporting FOS

Figure 2. Self-Reported Non-Seizure Symptoms and Severity for Patients Reporting FOS

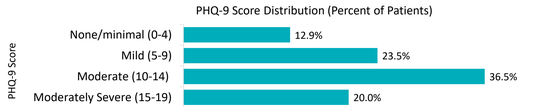


Footnotes. Mood issues were not explicitly defined in the survey instrument, but depression and anxiety were provided exempli gratia (e.g.); Questions: (Figure 2) People diagnosed with epilepsy report experiencing some of the symptoms listed below, outside of experiencing a seizure. Which of the following symptoms do you currently experience? (Figure 3) For each symptom you currently experience, please indicate how often you experience it; (Figure 4) For each symptom you currently experience, please indicate the current severity of each symptom (rating scale 1-5; 1 = not at all severe, 5 = extremely severe).

- 72.9% of patients reported experiencing at least 3 non-seizure symptoms despite current treatment with ASMs
- Mood issues (e.g., depression, anxiety) were the most common non-seizure symptoms, with 76.5% of patients reporting symptoms and 53.1% indicating them to be highly severe (Figure 2)
- 20.6% of patients reported having suicidal ideation or thoughts of self-harm in more than half of the days over the past two weeks; 4.7% reported having these thoughts every day

Depression Burden in Patients Reporting FOS

Figure 3. PHQ-9 Score Distribution for Patients Reporting FOS

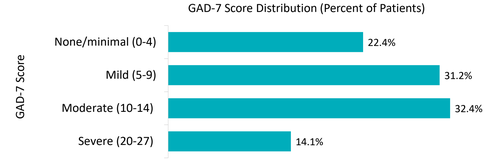


Footnotes. PHQ-9 assesses and monitors depression symptom severity; scores range from 0 to 27 and higher scores indicate more severe depression or depressive symptoms

- Mean (SD) PHQ-9 depression severity score for all patients was 11.2 (5.2) out of 27
- 63.5% of patients had a PHQ-9 score ≥10, suggestive of moderate to severe depression (Figure 3), although 47.2% (51/108) of those patients did not report prior physician diagnosis of depression

Anxiety Burden in Patients Reporting FOS

Figure 4. GAD-7 Score Distribution for Patients Reporting FOS



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

- Mean (SD) GAD-7 score for all patients was 8.9 (4.8) out of 21
- 46.5% had a GAD-7 score of ≥10, suggestive of moderate to severe generalized anxiety (Figure 4), yet 40.5% (32/79) of those patients reported no prior physician diagnosis of anxiety
- 37.7% of patients reported their anxiety symptoms made it very difficult or extremely difficult to do their work, take care of things at home, or have a good relationship with other people

CONCLUSION

- Patients with epilepsy reporting FOS experience considerable mental health burden in addition to their recurring seizure burden
- Most patients experienced ≥3 non-seizure symptoms despite ongoing treatment with existing ASMs, with most experiencing mood issues (e.g., depression, anxiety) that ranged from moderate to highly severe
- The high positive screening rates for depression and anxiety, in contrast to lower self-reported physician-diagnosed depression and anxiety, suggest mental health burden may be under-recognized in patients with epilepsy reporting FOS

FUNDING

This study was funded by Xenon Pharmaceuticals Inc. Vancouver, BC, Canada

DISCLOSURES

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

ACKNOWLEDGEMENTS

The authors would also like to acknowledge Devin McKinney, Feng (Johnson) Qian, and Austin Arnold from Trinity Life Sciences for their contributions to data analysis and medical writing.

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