

# Depression Symptom Experience Among Patients with Epilepsy Reporting a Diagnosis of Focal Seizures (FS): A Patient-Reported Outcomes Study

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## BACKGROUND

- Depression in people with epilepsy (PwE) is often underrecognized, underdiagnosed, and undertreated<sup>1-3</sup>
  - Fewer than 50.0% of PwE with self-reported moderate to severe depression symptoms have a formal diagnosis<sup>1,4,5</sup>
- About one-third of PwE meet criteria for major depressive disorder (MDD), while many others experience significant depression symptoms that do not reach DSM-5 diagnostic thresholds<sup>6-8</sup>
- Depression in PwE may present differently than primary MDD, making recognition and diagnosis challenging
  - Symptoms may last only a few minutes to days<sup>9-11</sup>
  - Symptoms can occur episodically or in relation to seizures (e.g., post-ictal)<sup>9,11</sup>
- Anhedonia, a core feature of MDD, may represent a substantial additional burden for people with epilepsy (PwE), further impacting quality of life and daily functioning beyond seizure control<sup>12</sup>
- Despite growing evidence on the impact of depression in epilepsy, gaps remain in understanding PwE’s experiences with depression or anhedonia outside of a formal MDD diagnosis

## OBJECTIVES

- This study sought to assess the burden PwE reporting focal seizures (FS) experience with depression symptoms, even among those without a formal diagnosis of depression

## 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; the study was institutional review board (IRB)-exempt (Advarra, Columbia, MD)
- Patients were recruited via either a patient panel or their physician at the point of care, using the following criteria:

Inclusion Criteria	Exclusion Criteria
<ul style="list-style-type: none"><li>United States resident</li><li>Age 18 to 80-years-old</li><li>Self-reported, physician-confirmed diagnosis of FS for at least 1 year</li><li>Experiencing ≥ 1 seizure in a typical month</li><li>Have used (currently or previously) at least 2 ASMs and are currently taking at least 1 ASM for at least 1 month</li></ul>	<ul style="list-style-type: none"><li>Currently enrolled in a clinical trial for FS</li><li>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</li></ul>

- 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 ensure they fit the inclusion and exclusion criteria
- Physician at point of care:** Physicians were provided with the study inclusion and exclusion criteria, and they selected patients to recruit for the study. Patients then participated in the survey screener to verify they met the inclusion and exclusion criteria
- Patients completed a 30-minute web-enabled survey from July to September 2023 to assess seizure-related and non-seizure-related symptoms, comorbidities, and mental health burden
- Data was collected via a custom questionnaire that included the PHQ-9, a common screening tool for depression that has been previously validated and used in patients with epilepsy<sup>13</sup>
  - 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<sup>14</sup>
  - Using the PHQ-9, patients reported how often they were bothered by depression symptoms over the past two weeks
- Data were analyzed using descriptive statistics in Q Research Software 5.12.4.0

## 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**

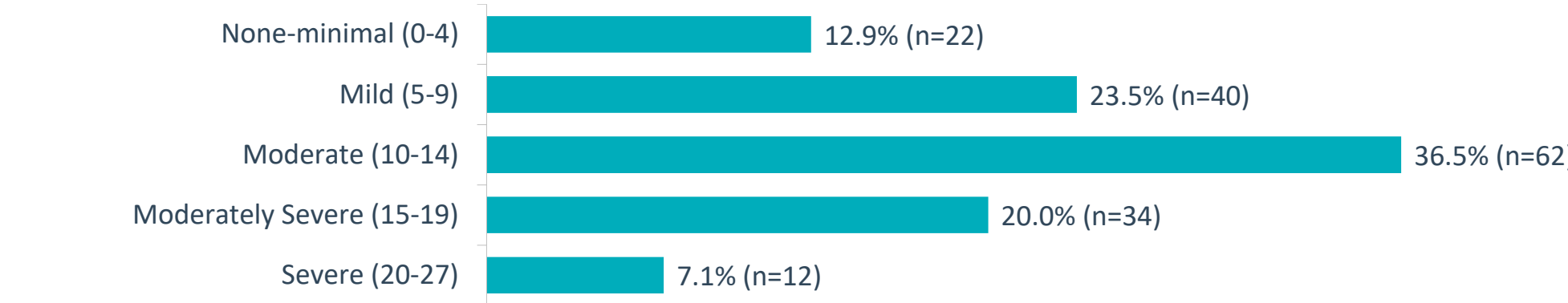
	Study Population (N=170)	No to Mild Depression* (n=62)	Moderate to Severe Depression* (N=108)
<b>Age, mean (SD)</b>	42.6 (10.9)	45.2 (12.1)	41.0 (9.9)
<b>Female, n (%)</b>	92 (54.1%)	41 (66.1%)	51 (47.2%)
<b>Race, n (%)</b>			
White	99 (58.2%)	38 (61.3%)	61 (56.5%)
Black	26 (15.3%)	14 (22.6%)	12 (11.1%)
Other	45 (26.5%)	10 (16.1%)	35 (32.4%)
<b>Employed Full- or Part-time, n (%)</b>	79 (46.5%)	23 (37.1%)	56 (51.9%)
<b>Annual Household Income &lt; \$60,000, n (%)</b>	74 (43.5%)	34 (54.8%)	40 (37.0%)
<b>Insurance status, n (%)</b>			
Private	77 (45.3%)	23 (37.1%)	54 (50.0%)
Public (e.g., Medicare, Medicaid)	102 (60.0%)	39 (62.9%)	63 (58.3%)
Government (e.g., VA, DOD)	9 (5.3%)	2 (3.2%)	7 (6.5%)
Uninsured	6 (3.5%)	2 (3.2%)	4 (3.7%)
<b>Number of Years Since Epilepsy Diagnosis, median (IQR)</b>	5.7 (3.6 – 14.8)	5.5 (2.4-15.6)	5.8 (4.0-14.8)
<b>Number of Prior Lines of Therapy, median (IQR)</b>	2 (2-4)	2 (1-4)	3 (2-4)
<b>Providers Currently Managing Epilepsy<sup>a</sup>, n (%)</b>			
Neurologist	64 (37.6%)	25 (40.3%)	39 (36.1%)
Primary Care Physician	23 (13.5%)	7 (11.3%)	16 (14.8%)
Epileptologist	113 (66.5%)	37 (59.7%)	76 (70.4%)
Psychiatrist	9 (5.3%)	1 (1.6%)	8 (7.4%)
Psychologist	6 (3.5%)	2 (3.2%)	4 (3.7%)
Other	3 (1.8%)	2 (3.2%)	1 (0.9%)

<sup>a</sup>The PHQ-9 was used to define no to mild depression (PHQ-9 < 10) and moderate to severe depression (PHQ-9 ≥ 10); <sup>a</sup>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; <sup>†</sup>Other provider types reported include primary physician, psychiatrist, psychologist, therapist, neurosurgeon, and neuro-oncologist

### Depression Symptom Experience

- Of the 170 respondents, 40.0% (n=68) reported physician-diagnosed depression
- 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)

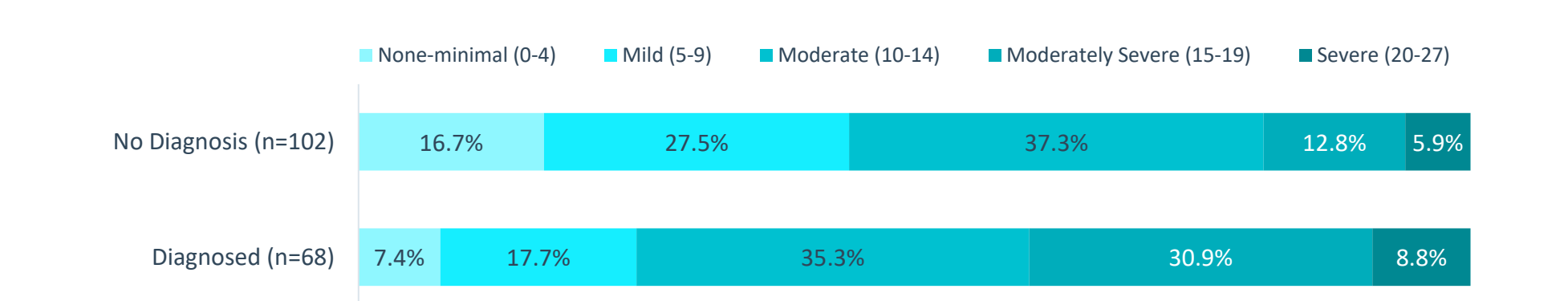
**Figure 1. PHQ-9 Score Distribution for PwE Reporting FS (N=170)**



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

- Of the 102 patients reporting no physician-diagnosed depression, 55.9% (57/102) reported moderate to severe depression symptoms via the PHQ-9 score (Figure 2)
- Among those reporting physician-diagnosed depression, 75.0% (51/68) reported moderate to severe depression symptoms via the PHQ-9 score (Figure 2)

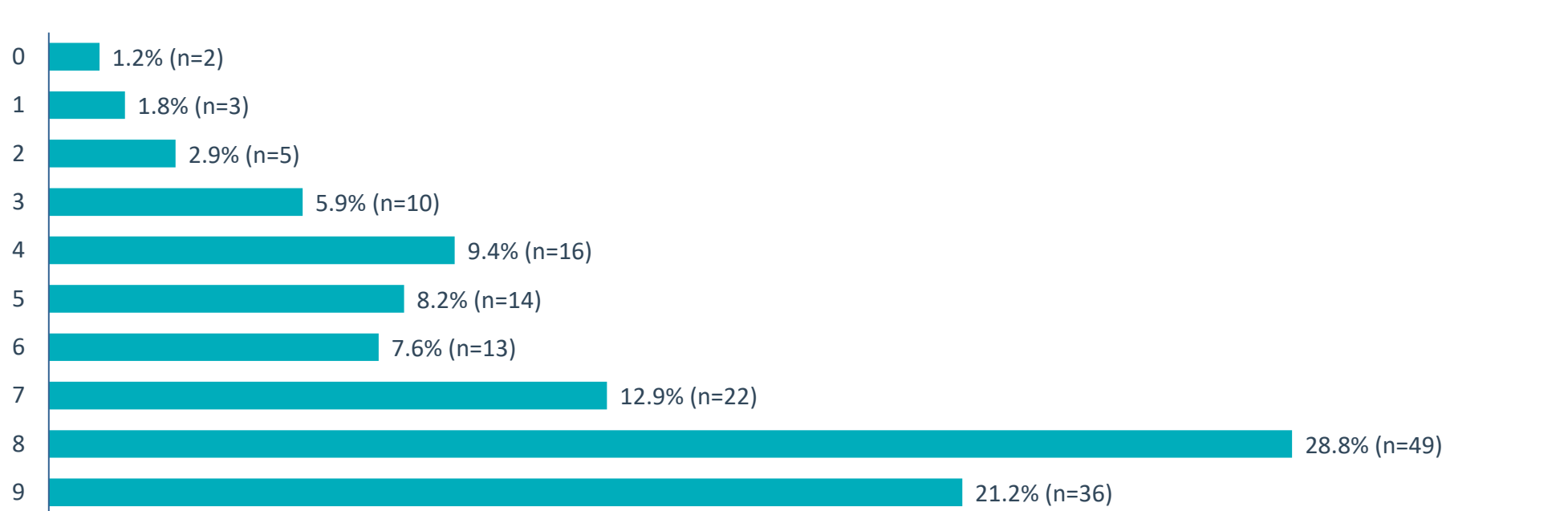
**Figure 2. PHQ-9 Score Distribution among Patients With and Without a Self-reported Physician-Diagnosis of Depression**



<sup>\*</sup>Diagnosis of depression by a physician was self-reported by the patients (Question: Other than epilepsy, which of the following conditions have you been diagnosed with by a doctor? Please think about all diagnoses you have received to present date.)

- 50% of patients exhibited ≥8 depression symptoms for at least several days a week during the past 2 weeks (Figure 3)

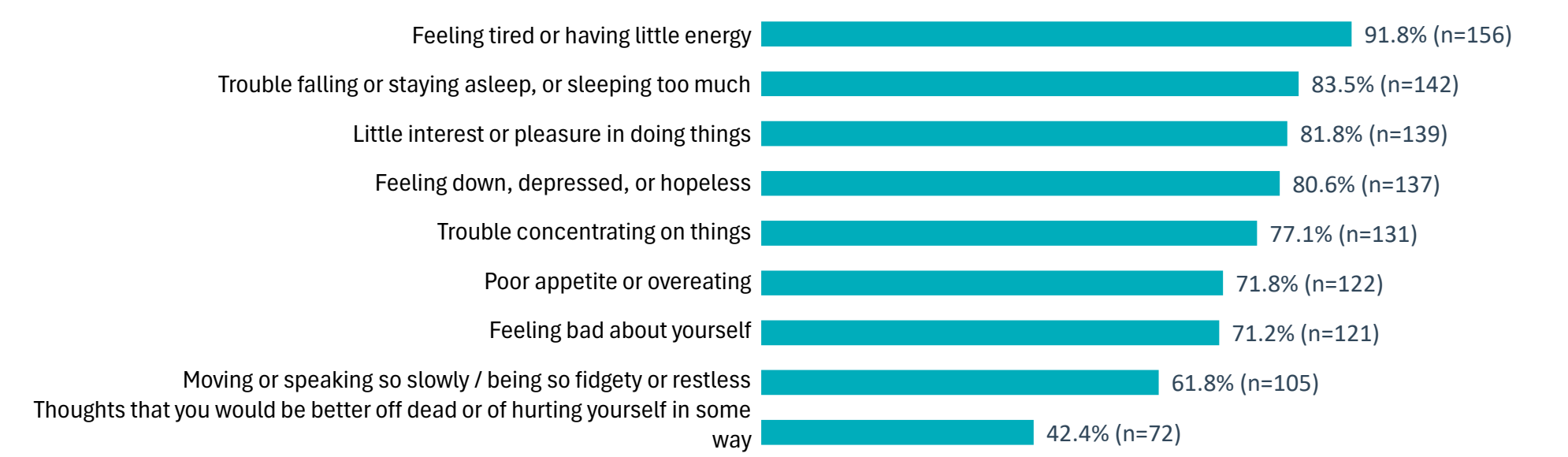
**Figure 3. Number of PHQ-9 Symptoms Reported for at least Several Days per Week (N=170)**



The PHQ-9 is a 9-item instrument that assesses depression-related symptom severity; patients provide scores for the frequency of each symptom ranging from 0 (not at all) to 3 (nearly every day) for each item.

- Depressed mood (“feeling down, depressed, or hopeless”) and anhedonia (“little interest or pleasure in doing things”) were reported by 80.6% (137/170) and 81.8% (139/170), respectively (Figure 4)
- Suicidal ideation or thoughts of self-harm for at least several days a week was reported by 42.4% (72/170) of patients
- 61.8% (105/170) to 91.8% (156/170) of patients reported being bothered by other depression symptoms captured by the PHQ-9 for at least several days a week

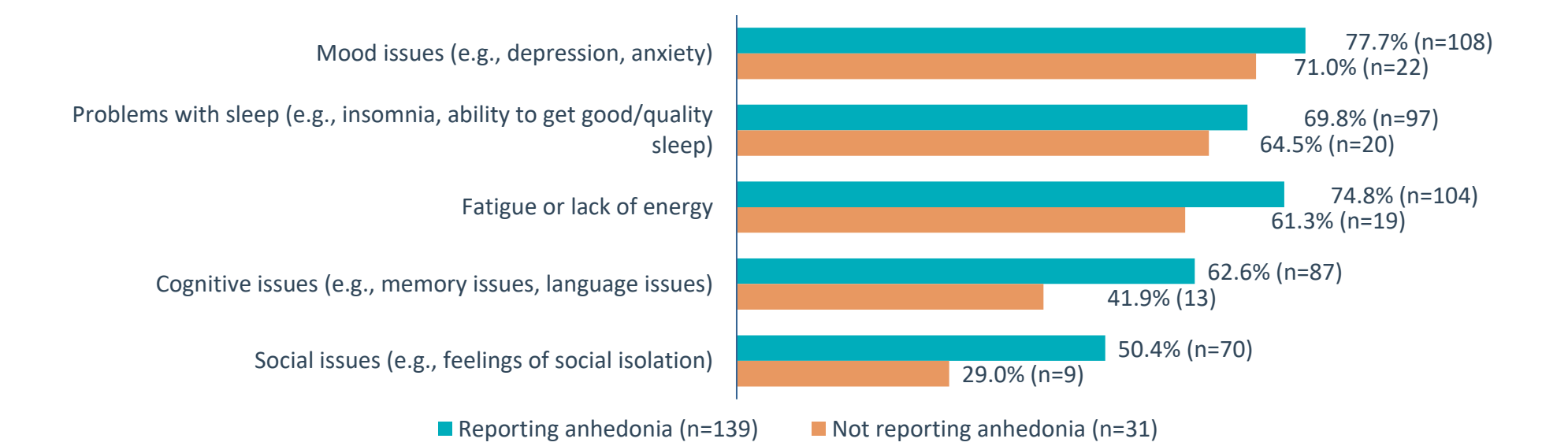
**Figure 4. Proportion of PwE Reporting FS Reporting Each Symptom from PHQ-9 (N=170)**



This graph represents the number of symptoms for which patients selected 1 or more, indicating at least experiencing several days a week, for each symptom.

- Patients reporting anhedonia (n=139) were more likely to report experiencing non-seizure symptoms such as cognitive issues (62.6% [87/139] vs 41.9% [13/31]) and social issues (50.4% [70/139] vs 29.0% [9/31]) (Figure 5)

**Figure 5. Non-Seizure Symptoms Experienced by PwE Reporting FS, Stratified by Experiencing Anhedonia**



Patients reporting anhedonia were those who selected 1 to 3 for little interest or no pleasure in doing things in PHQ-9 while those not reporting anhedonia selected 0; Questions: 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?

## CONCLUSION

- PwE reporting FS experience considerable mental health burden, including those reporting no formal diagnosis of depression
- Most patients reported depressed mood and anhedonia, core depression features that may be independent of the adverse effects of medication
- These findings support recent guidelines for the routine screening of depression in clinical practice and highlight the potential unrecognized burden of depression in PwE reporting FS

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

**DISCLOSURES** AO, 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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