Treatment Experiences with Anti-Seizure Medications (ASMs): Patient and Clinician Perspectives on Titration Burden, Quality of Life, and No-Titration Options

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BACKGROUND

- Epileptic seizures are classified by onset and clinical presentation, including focal, generalized, unknown (whether focal or generalized), and unclassified.[1] In the United States (US), focal seizures (FS) account for approximately 60% of the ~3 million adults living with epilepsy.[2,3]
- Initiating most anti-seizure medications (ASMs) requires slow titration to improve tolerability, which may delay achievement of therapeutic doses and optimal seizure control.[4] When initiating treatment for FS, titration schedules can extend over several months and may be challenging for patients due to complex dosing regimens.[5]
- While prior studies have examined perceptions of ASM management and treatment goals[6] as well as the emotional impact of ASM use on patients,[7] evidence is limited regarding real-world experiences of ASM titration from both patient and healthcare provider (HCP) perspectives.

OBJECTIVE

- To compare the perspectives of patients with FS and HCPs regarding ASM experiences during titration, focusing on barriers encountered during ASM titration, quality of life (QoL) implications during ASM titration, and the value of ASMs that would not require titration.

METHODS

Participants: Patients with FS

- A cross-sectional, online survey was conducted in January 2025 among patients with a physician-confirmed diagnosis of FS. The study was approved by an institutional review board (IRB) (WCG IRB, Cary, NC).
- Participants completed a screening survey and were eligible if they had tried and failed ≥1 ASM within the past year and either:
  - had both an office visit and used an ASM requiring titration and/or dose escalation/modification* within the past year, or
  - were currently using or initiating an ASM requiring titration and/or dose escalation/modification.
- Participants with a history of psychogenic non-epileptic seizures, Dravet syndrome, Lennox–Gastaut syndrome, or other developmental and epileptic encephalopathies were excluded.
- Data collected included demographics, clinical history, and epilepsy-specific QoL measures.
- The survey also assessed factors influencing ASM selection, challenges encountered, and emotions experienced during titration.
- Outcomes were summarized using descriptive statistics, including means and standard deviations (SDs) for continuous variables and frequency counts and percentages for categorical variables.

Participants: Physician Experts

- A moderated physician roundtable was conducted in April 2025 among US board-certified physicians (MD/DO) who treat patients with FS and met the following eligibility criteria:
  - manage ≥25 FS patients per month (with ≥50% initiating or undergoing ASM titration or dose escalation/modification*);
  - currently manage ≥5 patients meeting the patient-survey inclusion criteria;
  - have current or prior experience prescribing ASMs requiring titration; and
  - are willing and able to complete a 30-minute interview on ASM switching and outcomes.
- Prior to the roundtable discussion, each physician participated in a 30-minute, semi-structured interview about their practices and perspectives across the titration process, including initial dosing strategies, monitoring techniques, adherence to prescribing guidelines, and challenges with drug–drug interactions (DDIs).
- Data from the patient survey and interviews with physician experts informed the roundtable agenda and discussion topics. During the roundtable, physicians compared their clinical perspectives with the patients' self-reported experiences of ASM titration.
- Roundtable discussions were transcribed and systematically reviewed to identify key themes via thematic analysis. The responses to live polling questions were summarized using basic descriptive statistics.

*Dose escalation/modification is considered different from titration, which is FDA-recommended to reach a therapeutic dose. Dose escalation/modification could be 1) increasing the dose after reaching a therapeutic dose, 2) reducing the dose over time, or 3) cross-titration, which indicates decreasing the dose of one drug while simultaneously increasing the dose of another drug.[8]

RESULTS

Participants: Patients with FS

- Demographic characteristics of the surveyed patients with FS (N=48) are summarized in **Table 1**.

Table 1. Patient Characteristics

Patient Characteristics	(N=48)
Age (N=45)[a]	
Mean (SD)	35 (13)
Median (Range)	32 (19–70)
Sex, n (%)	
Female	21 (44)
Male	27 (56)
Race/ethnicity, n (%)[b]	
White	20 (42)
Hispanic or Latino	13 (27)
Black or African American	9 (19)
Asian / Pacific Islander	5 (10)
Native American or American Indian	1 (2)
Age at diagnosis of epilepsy (N=45)[a]	
Mean (SD)	24 (16)
Median (Range)	22 (0–65)

SD=standard deviation
[a]Data regarding age and age at diagnosis of epilepsy are missing for n=3 patients.
[b]Respondents were able to select all response options that applied; therefore, the responses are not mutually exclusive.

Participants: Physician Experts

- Characteristics of the participating physicians (N=7) are summarized in **Table 2**.

Table 2. Physician Expert Characteristics

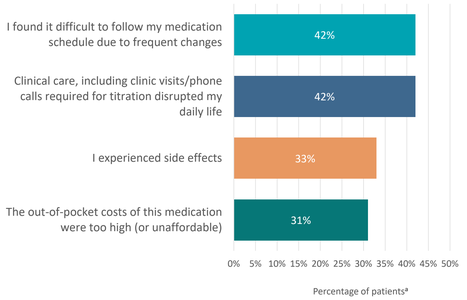
Physician Expert Characteristics	(N=7)
Primary specialty, n (%)	
Epileptologist	7 (100)
Setting of practice, n (%)	
Academic medical hospital	7 (100)
Years in practice since completing their education	
Mean (SD)	20 (7)
Median (Range)	25 (10–26)
Patients with FS treated per month	
Mean (SD)	95 (21)
Median (Range)	100 (70–120)

SD=standard deviation

Barriers Encountered During Titration

- Patients self-reported barriers encountered during titration, including difficulty following schedules due to frequent dose changes (42%) and disruptions to daily life from clinic visits and phone calls (42%) (**Figure 1**).

Figure 1. Patient-Reported Barriers Encountered During Titration (N=48)



[a]Respondents were able to select all response options that applied; therefore, the responses are not mutually exclusive.
Question: During the titration (the time when your doctor gradually adjusts your medication dose to find the right amount that works best for you) of [index ASM], did you encounter any of the following barriers that made it difficult to continue taking the medication? Please select all that apply.

- All physician experts (100%) identified DDIs as a key titration barrier and reported difficulty managing cross-titration when switching ASMs to mitigate interaction risks.

Figure 2. Physician Expert Reports of Challenges Related to DDIs

DDI-Informed Monitoring & Patient Education

- DDIs are a key consideration when selecting ASMs and managing treatment transitions.
- Physicians often need to educate patients about potential interactions and monitoring requirements.

Time to Therapeutic Dose

- Achieving a therapeutic dose can be challenging due to variability in patient response and pharmacokinetics.
- Titration often requires multiple adjustments, which can delay time to efficacy.

Concomitant Medications Influence Ease of Titration

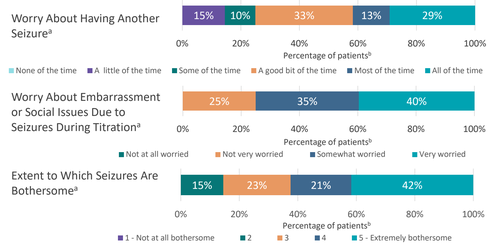
- DDIs are a major factor influencing titration decisions.
- Concomitant therapies can complicate dosing and require additional monitoring or adjustment.

DDI = drug-drug interaction

QoL Impacts

- Among patients, 86% reported being a very nervous person at least "some of the time" during titration; almost 80% of patients reported feeling downhearted and blue at least "some of the time" during the titration period.
- At least 40% of patients selected "none of the time" or "a little of the time" on each question about feeling calm and peaceful and about feeling happy during the titration period.
- 85% of patients reported worrying about having another seizure at least "some of the time" during the titration period (**Figure 3**).
- 42% of patients reported that seizures during the ASM titration period were "extremely bothersome" (**Figure 3**).

Figure 3. Patient-Reported Experiences of Worry or Bother During Titration (N=48)



[a]Items were adapted from the QOLIE-31-P (v2; Quality of Life in Epilepsy Inventory–31 Problems).
[b]Due to rounding, the sum of percentages within a row may not equal 100%.
Question: (1) Have you worried about having another seizure? (2) How worried were you about embarrassment or other social problems resulting from having a seizure during the titration period? (3) How much do seizures bother you?
Notes: Response options on the left side indicate better QoL. For negative concepts (e.g., worried about having another seizure), options begin with 'none of the time'.

- Physician experts identified two key themes that contribute to stress for both patients and physicians (**Figure 4**).

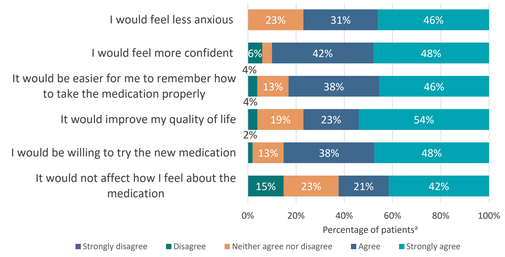
Figure 4. Physician Expert Reports of Patient and Provider Stress During Titration

1. **Efficacy/Safety Trade-offs**
   - Physician experts noted frustration with having to reduce the dose of a concomitant ASM when titrating a new ASM because of potential pharmacokinetic/pharmacodynamic DDIs, which may reduce efficacy and increase the risk of breakthrough seizures.
2. **Different Patient Characteristics**
   - Physician experts noted different patient characteristics may make titration very complicated; someone with cognitive disability or socioeconomic challenges may be more at risk of nonadherence due to complex titration schedules.

Value of Initiating an ASM Without Titration Requirements

- Most patients agree/strongly agree that initiating an ASM without needing to titrate to a stable dose would boost their confidence, reduce anxiety, and improve adherence (**Figure 5**).

Figure 5. Patient Perspectives on Initiating an ASM Without Titration Requirements (N=48)



[a]Due to rounding, the sum of percentages within a row may not equal 100%.
Question: The following questions are about a new treatment option that does not require titration, which allows you to achieve a stable dose immediately. In a scenario where a new treatment option like this was available, please select the extent to which you agree with the following statements (one response was selected for each line).

- Physician experts identified two key benefits for initiating an ASM without titration requirements (**Figure 6**).

Figure 6. Physician Expert Perspectives on the Benefits of Initiating an ASM Without Titration Requirements

1. **Less Stress for Both Physicians and Patients**
   - Physician experts noted less stress as a potential benefit for both HCPs and patients when there is no titration; it is one less barrier for patients.
2. **Simplicity for Both Physicians and Patients**
   - Physician experts noted that many patients are already on complex drug regimens, and that there is a benefit to adding new ASMs with minimal complexity.

CONCLUSIONS

- Patient and HCP perspectives suggest that ASM titration imposes a meaningful burden on both groups, with patients reporting challenges related to medication schedules and daily life during titration and physician experts reporting challenges related to treatment complexity and cross-titration.
- These perspectives suggest that ASMs that do not require titration may offer benefits and underscore the potential value of avoiding a titration period to reduce stress and simplify FS management for both patients and physician experts.
- Collectively, these findings highlight the real-world impact of ASM titration from both patient and HCP perspectives and suggest an opportunity to further simplify care and integrate the patient voice into treatment decision-making.

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