Clinical Practice and Patient Burden Associated With Antiseizure Medication Titration: A Thematic Analysis

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INTRODUCTION

- Epileptic seizures are classified by onset and clinical presentation, including focal, generalized, unknown (whether focal or generalized), and unclassified.[1] Of these, focal seizures (FS) account for approximately 60% of the ~3 million adults with epilepsy in the US[2,3]
- Most antiseizure medications (ASMs) recommend slow titration to improve tolerability, potentially delaying therapeutic dosing and optimal seizure control.[4] The titration of ASMs for FS can take months, and patients may struggle with complex titration schedules[5]
- While ASMs include US Food and Drug Administration (FDA)-recommended titration instructions, the titration process is often individualized on various factors including patient characteristics and ASM-specific factors[4,5]
- Although the challenges of ASM titration have been described, there remains a gap in understanding how patients with FS and healthcare providers (HCPs) experience this process in real-world practice

OBJECTIVE

- To assess both patient and HCP perspectives on the practical realities of ASM titration, focusing on identifying key unmet needs and defining the burden on both patients with FS and HCPs who directly treat these patients

METHODS

Participants: Patients With FS

- A cross-sectional, web-based 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 stopped ≥1 ASM within the past year and either (a) had both an office visit and used an ASM requiring titration and/or dose escalation/modification[a] within the past year, or (b) were currently using or initiating an ASM requiring titration and/or dose escalation/modification and had no history of psychogenic nonepileptic seizures, Dravet syndrome, Lennox-Gastaut syndrome, or other developmental and epileptic encephalopathies
- Data collected included demographics, clinical history, and epilepsy-specific quality-of-life measures. The survey also assessed factors influencing ASM selection, adherence, side effects, dose modifications, healthcare resource utilization (HCRU), and challenges 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

[a]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 1 drug while simultaneously increasing the dose of another drug.[8]

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 patients with FS per month (with ≥50% initiating or undergoing ASM titration or dose escalation/modification[a]), currently manage ≥5 patients meeting the patient-survey inclusion criteria, have current or prior experience prescribing titration-requiring ASMs, 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, semistructured 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 physician interviews informed the roundtable agenda and discussion topics
- The roundtable discussion was transcribed and analyzed using thematic analysis; analysts independently coded the transcript, reconciled discrepancies by consensus, and organized salient themes

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)
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)

[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.
SD, standard deviation.

Participants: Physician Experts

- Characteristics of the participating physicians (N=7) are summarized in **Table 2**; all were epileptologists treating a mean of 95 patients with FS per month

Table 2. Physician Expert Characteristics

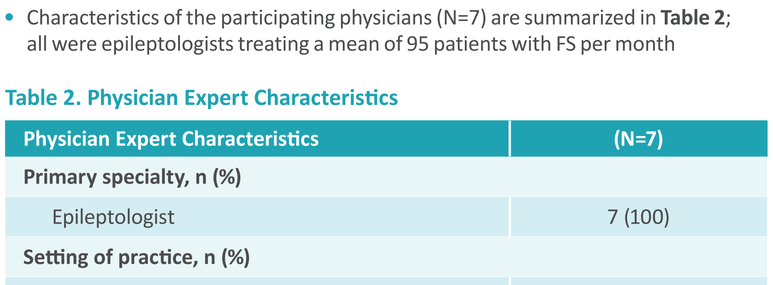
Physician Expert Characteristics	(N=7)
Primary specialty, n (%)	
Epileptologist	7 (100)
Setting of practice, n (%)	
Academic medical hospital	7 (100)
Years in practice since completing their education	
Mean (SD)	20 (7)
Median (range)	25 (10-26)
Patients with FS treated per month	
Mean (SD)	95 (21)
Median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

FS, focal seizures; SD, standard deviation.

Thematic Analysis

- The main theme and emerging subthemes from the roundtable are shown in **Figure 1**

Figure 1. Main Theme and Subthemes Emerging From the Roundtable

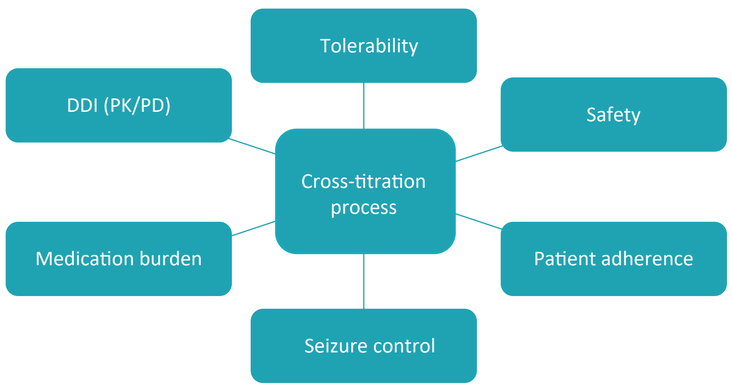


ASM, antiseizure medication; HCP, healthcare provider.

Greater Complexity of Clinical Management

- Physicians reported that cross-titration, the process of decreasing the dose of 1 drug while simultaneously increasing the dose of another drug when switching between medications or initiating combination therapy, is largely guided by expert consensus and associated with unpredictable outcomes
- During cross-titration, physicians shared that they balance multiple, often competing considerations, including DDIs that add complexity, particularly when complications arise (**Figure 2**)
- Physicians also reported that complex dosing schedules (eg, multiple daily administrations and variable day-to-day doses) can negatively impact adherence

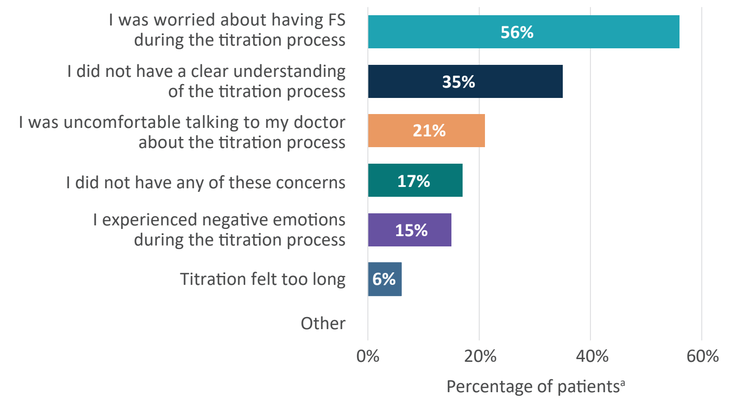
Figure 2. Cross-Titration Considerations



DDI, drug-drug interaction; PD, pharmacodynamics; PK, pharmacokinetics.

- Patients with FS reported concerns they experienced during the titration of their ASM, including worry about having FS during the titration process (56%) and not having a clear understanding of the titration process (35%) (**Figure 3**)

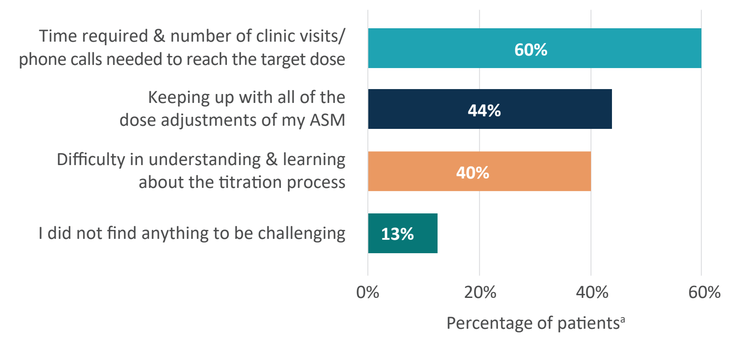
Figure 3. Patient-Reported Concerns Experienced During Titration (N=48)



[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 have any of the following concerns? Please select all that apply.
ASM, antiseizure medication; FS, focal seizures.

- Patients with FS also reported that the time and number of clinic visits/phone calls needed to reach the target dose (60%) and keeping up with multiple ASM dose adjustments (44%) were challenges they encountered during ASM titration (**Figure 4**)

Figure 4. Patient-Reported Challenges Encountered During Titration (N=48)

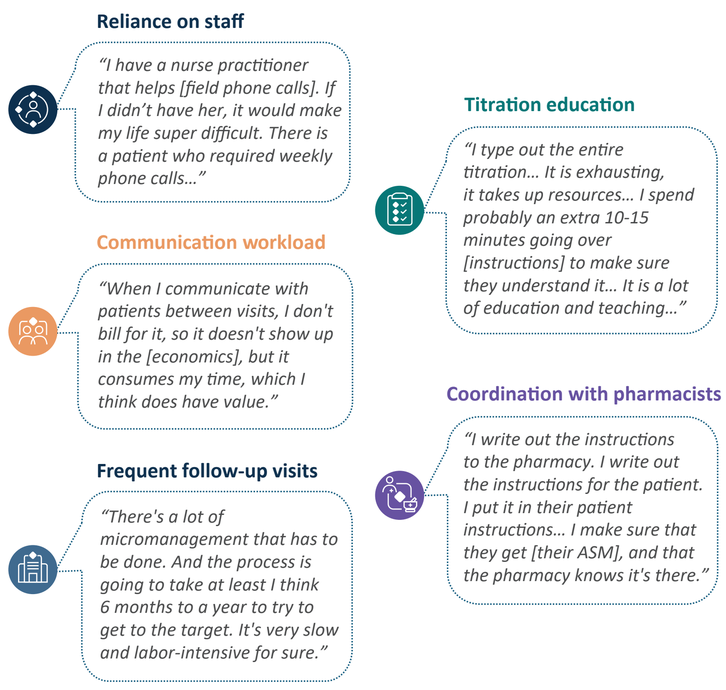


[a]Respondents were able to select all response options that applied; therefore, the responses are not mutually exclusive.
Question: During the titration (the time when your doctor gradually adjusts your medication dose to find the right amount that works best for you) of [index ASM], what challenges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

Increased Strain on Healthcare Resources

- Physicians reported that ASM titration is associated with increased HCRU, spanning both quantifiable events (eg, emergency department visits) and less easily measured burden (eg, communication workload)
- During titration, physicians identified the following increases in HCRU (**Figure 5**):
  - Increased reliance on clinic staff to triage calls and provide patient support
  - Higher volume of patient communication (emails and portal messages)
  - More frequent follow-up clinic visits to monitor patients during titration
  - Additional time spent developing/updating titration schedules and educational materials
  - Greater coordination with pharmacists to convey titration instructions and confirm prescriptions

Figure 5. Physician Expert Reports of Increased HCRU Related to Titration

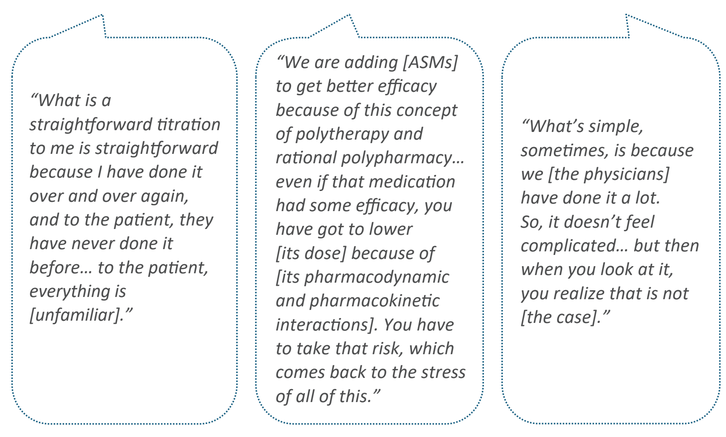


ASM, antiseizure medication; HCRU, healthcare resource utilization.

Underrecognized Burden of Titration

- Physicians previously viewed titration as routine and may not have fully appreciated the challenges experienced by patients and nonspecialist HCPs. All (100%) agreed that the burden of titration is greater than what is generally recognized (**Figure 6**)
- Patient-reported data were consistent with physician observations that titration burden may be underrecognized during titration; patients worried about breakthrough seizures (**Figure 3**) and reported difficulty keeping up with ASM dose adjustments and understanding the titration steps (**Figure 4**)

Figure 6. Physician Expert Insights on the Burden of Titration



ASM, antiseizure medication.

CONCLUSIONS

- This patient and physician research revealed titration is rarely part of the dialogue among physicians, despite titration's effect on clinical management complexity and increased strain on healthcare resources
- These findings underscore the substantial and potentially overlooked burden associated with ASM titration on patients and physicians, highlighting the need for improved communication between patients and physicians, as well as the need for ASMs that require simplified or no titration
- Increasing awareness of the burden of titration within the wider epilepsy community may improve shared decision-making through recognition of titration-related factors that may negatively impact the patient experience with ASMs

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ACKNOWLEDGMENTS: The authors would like to thank Diane Ito, Josephine Li-McLeod, and Ava Maurillo from Stratevi for their contributions to data analysis, medical writing, and editorial support of this poster. Additional editorial support was provided by Heidi Reinholdt, MS, MA, CMPP, of Helios Global Group and was funded by Xenon Pharmaceuticals Inc. (Vancouver, BC, Canada). Xenon Pharmaceuticals Inc. reviewed and provided feedback on the poster. The authors had full editorial control of the poster and provided their final approval of all content.

DISCLOSURES: **John M. Stern** has been a consultant and speaker for Ceribell, Jazz Pharmaceuticals, LivaNova, Neurelis, SK Life Science, UCB, and Xenon Pharmaceuticals Inc. (advisory board). **Danielle A. Becker** has been a consultant and speaker for Jazz Pharmaceuticals, LivaNova, Neurelis, NeuroPace, SK Life Science, and Xenon Pharmaceuticals Inc. (advisory board). **Steve S. Chung** has been a speaker for Neurelis, and a consultant and speaker for Jazz Pharmaceuticals, SK Life Science, UCB, and Xenon Pharmaceuticals Inc. (advisory board). **Micheál Macken** has been a consultant and speaker for Jazz Pharmaceuticals, SK Life Science, UCB, and Xenon Pharmaceuticals Inc. (advisory board). **David King-Stephens** has been a speaker for Neurelis, NeuroPace, SK Life Science, UCB, and Xenon Pharmaceuticals Inc. (advisory board). **Andrew J. Zillgitt** has been a speaker for Jazz Pharmaceuticals and SK Life Science, and a consultant and speaker for Catalyst, UCB, and Xenon Pharmaceuticals Inc. (advisory board). **Mohamad Z. Koubeissi** has been a speaker for SK Life Science and Xenon Pharmaceuticals Inc. (advisory board). **Brad Padilla** is an employee of Stratevi, a research consulting company, receiving funding from Xenon Pharmaceuticals Inc. to conduct this study. **Alvin Ong** is an employee of and owns stock or stock options in Xenon Pharmaceuticals Inc.

FUNDING: This study is funded by Xenon Pharmaceuticals Inc.

These data were previously presented at the American Epilepsy Society Annual Meeting, December 5-9, 2025, Atlanta, GA, USA.