

Prescribing Patterns and Risk of Adverse Effects of Lamotrigine in a Clinical Setting: A Survey-Based Study

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Background and Purpose

Lamotrigine is a second-generation antiepileptic medication used in the management of seizure or bipolar disorders. One of the limitations of lamotrigine is a black box warning for Stevens-Johnson Syndrome (SJS), a potentially life threatening rash, leading to a recommended dosing titration over 6 to 10 weeks.^{1,2}

Recently, Jang et al. (2021) explored the use of a novel, accelerated titration over 11 days to reach therapeutic doses. This resulted in an incidence of drug-related rash similar to literature using the standard lamotrigine titration. This raised the question if an accelerated titration can be, or is being utilized, more often in practice than expected.³ The re-titration speed after missed days of lamotrigine has been questioned due to patient's prior tolerance.

The purpose of this study was to better understand and describe the use, titration practices, and risks of lamotrigine in clinical practice.

Methods

This was a mixed-methods, survey-based descriptive study. Providers across the US and Canada who were members of relevant organizations were sent a link to complete a Qualtrics survey.

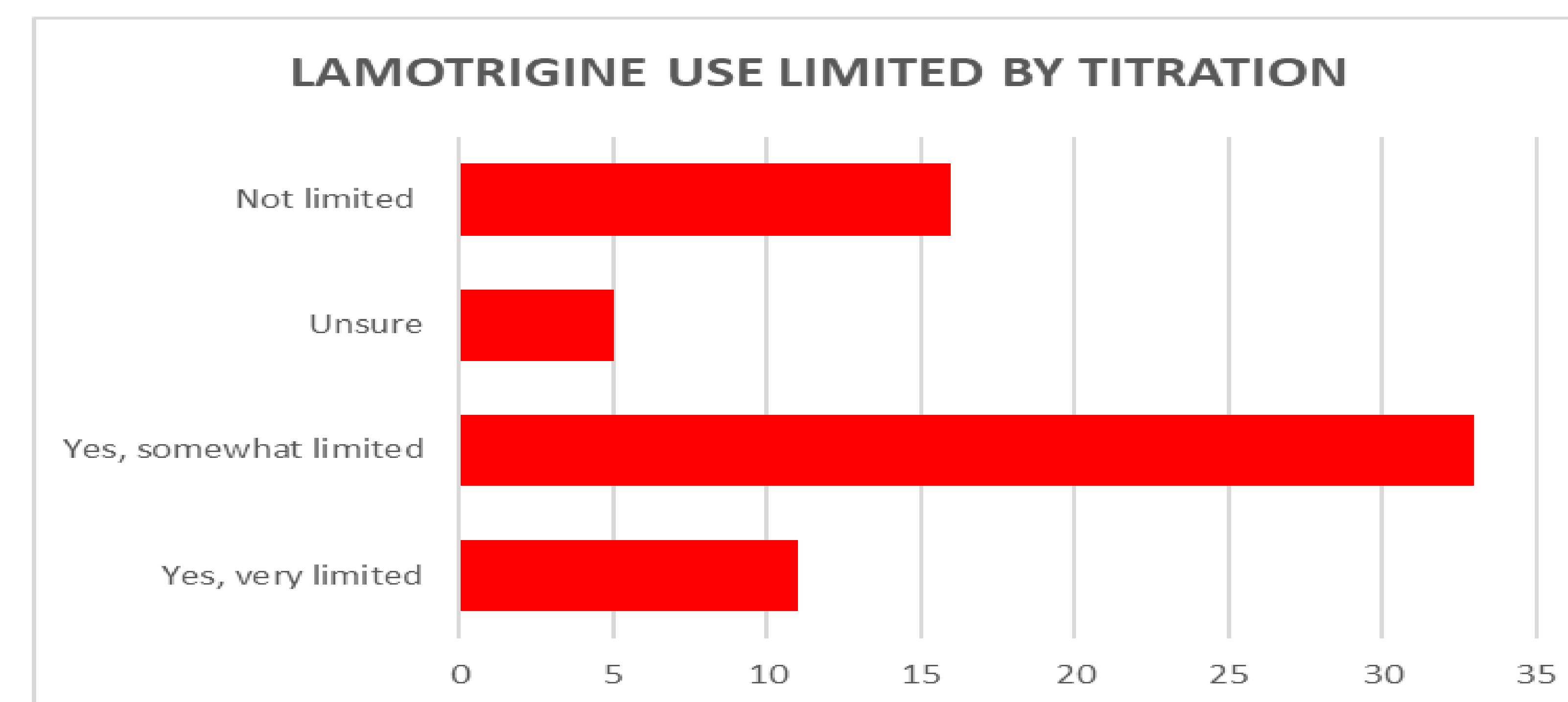
- Quantitative questions: frequency of lamotrigine prescribing, frequency of drug-related rash, and missed days until re-titration.
- Qualitative questions: titration schedule used for new and prior use lamotrigine, opinion of reported drug-related rash incidence, and openness to accelerated titrations.

Provider Demographics (n=61)

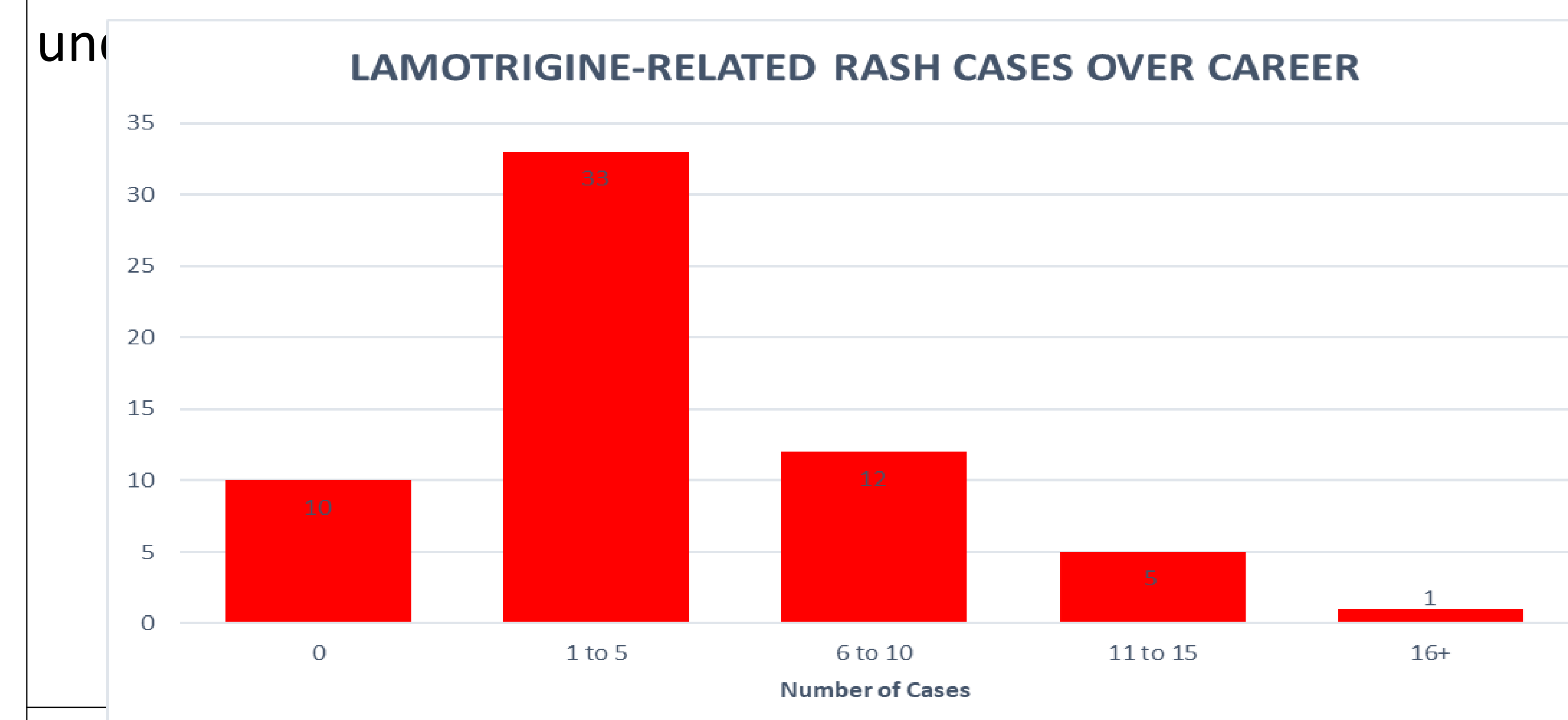
Area of Practice	Length of Practice		Practice Site		
Psychiatry	52 (85.3%)	Less than 5 years	12 (19.7%)	Inpatient	31 (50.8%)
Neurology	2 (3.3%)	5-10 years	19 (31.2%)	Outpatient	22 (36.1%)
Epileptology	3 (4.9%)	11-15 years	17 (27.9%)	Both in- and outpatient	7 (11.5%)
Family Medicine	1 (1.6%)	16-20 years	3 (4.9%)	Residential	1 (1.6%)
Other	3 (4.9%)	20+ years	10 (16.4%)		

Results

Most respondents saw between 0-10 patients on lamotrigine each month (59.0%), though some did see upwards of 30 (4.9%). All but one respondent indicated using the manufacturer recommended titration schedule when starting new patients on lamotrigine (98.4%). Respondents were slightly more likely to deviate from this titration when restarting a patient on lamotrigine after a lapse in therapy (16.4%). The number of days before re-titration was deemed necessary varied across the sample, but most respondents indicated 4-6 days (57.4%), followed by 1-3 (29.5%).

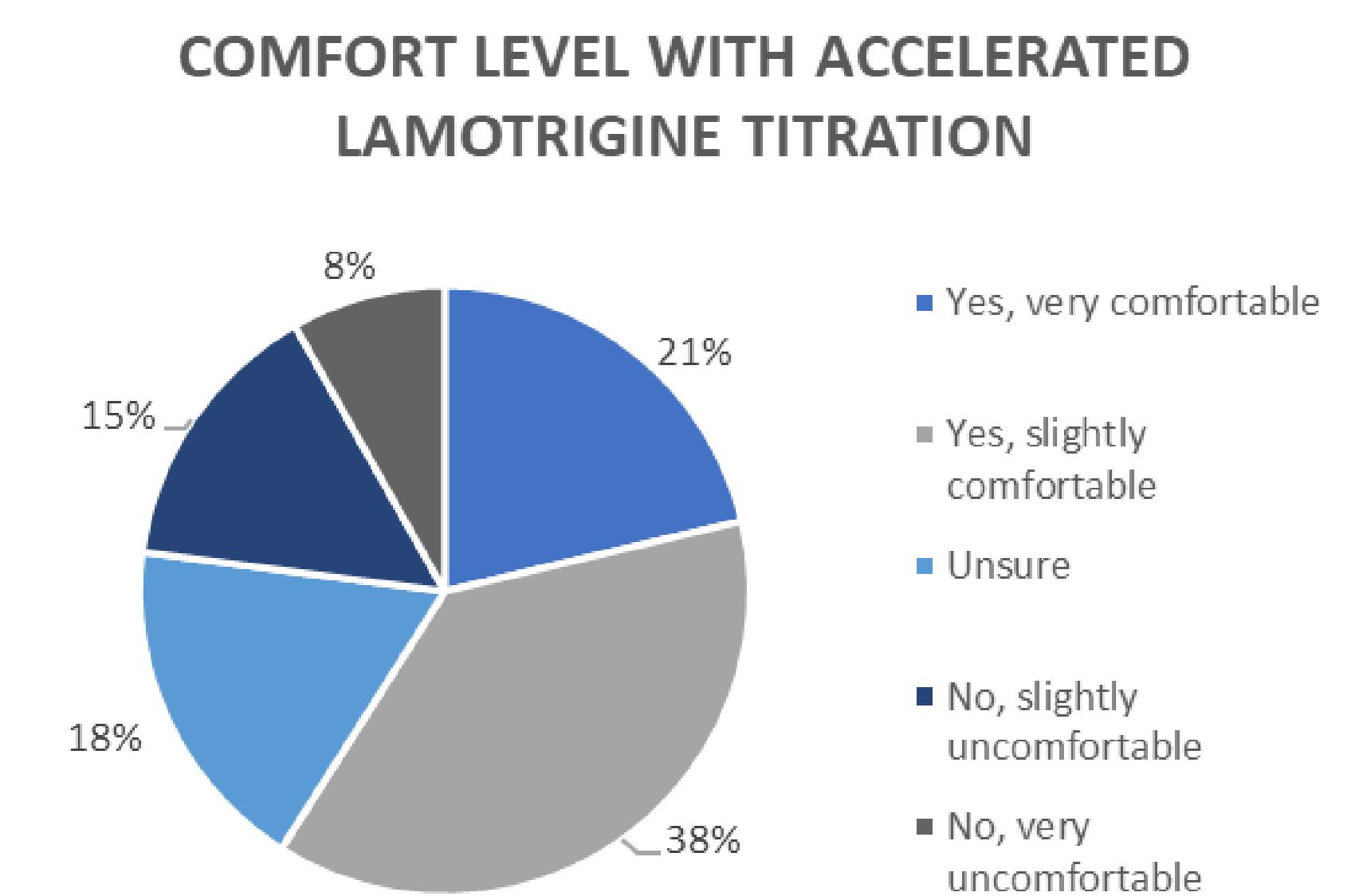


A majority of respondents reported that all (32.8%) or most (29.5%) of the cases of drug-rash were among patients who were newly starting lamotrigine. Most respondents (52.3%) stated the risk of drug-related rash was overestimated in the literature, followed by 43.1% stated correctly estimated and 4.6% stated



Results (cont)

Providers mostly were not using genetic testing at all (83.6%). It was indicated when testing was used, it often did not change the drug choice or titration (66.6%).



Strengths

- Use of open-ended and ranking questions
- Inquired about nuances in practices (ex. genetics)
- Sample consisted of current practitioners

Weaknesses

- Very small sample size
- Predominantly one provider group (psychiatry)
- Analyses restricted to descriptive statistics
- Not able to fully evaluate relationships or correlations

Discussion and Conclusion

This study intended to provide additional information regarding lamotrigine use in clinical practice. Providers in this study primarily used lamotrigine for bipolar disorder and infrequently saw drug-related rashes. Manufacturer suggested titration was almost exclusively used, which many felt restricted use. However, prior tolerance to lamotrigine may be factor when determining re-titration speed. Many providers would be open to quicker titration in lower risk patients with more supporting data. Future research should aim for larger and more diverse practice site samples to gain better insight into lamotrigine usage in a variety of clinical practices.

References:
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 2) Edinoff, A.N., Nguyen, L.H., Fitzgerald, M.J., Crane, E., Lewis, K., St Pierre, S., Kaye, A.D., Kaye, A.M., Kaye, J.S., Kaye, R.J., Gennuso, S.A., Varrasi, G., Viswanath, O., and Urtis, I., (2021). Lamotrigine and Stevens-Johnson Syndrome Prevention. *Psychopharmacology Bulletin*. 51(2): 96-114.
 3) Jang, Y., Moon, J., Kim, N., Kim, T.J., Jun, J.S., Shin, Y.W., Chang, H., Kang, H.R., Lee, S.T., Jung, K.H., Park, K., Jung, K.Y., Chu, K., and Lee, S.K. (2021). A new rapid titration protocol for lamotrigine that reduces the risk of skin rash. *Epilepsia Open*. 6, pp.394-401.