

# Evaluation of High vs Low Dose Levetiracetam for Early Post Traumatic Seizure Prophylaxis in Patients with Traumatic Brain Injury

Emilie Muvundamina, PharmD, Parth Parikh, PharmD, BCPS, Madalyn Kirkwood Brakel, PharmD, BCCCP



**OUR LADY OF THE LAKE**  
REGIONAL MEDICAL CENTER  
*Franciscan Missionaries of Our Lady Health System*

## Background



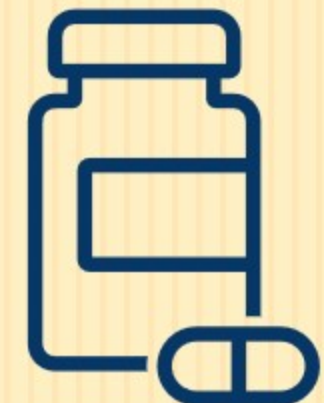
Annual Traumatic Brain Injury (TBI) statistics<sup>1</sup>

- 1.5 million TBIs
- 223,000 hospitalizations
- 50,000 deaths



TBI and Seizures

- In the 7 days following a severe TBI, there is a risk of Early Post Traumatic Seizures (EPTS)<sup>2</sup>
- Brain Trauma Foundation Guidelines for Management for Severe TBI recommends 7 days of phenytoin to prevent EPTS<sup>2</sup>



Levetiracetam for EPTS prophylaxis

- Not yet adopted by guidelines<sup>2</sup>
- Mild adverse effect profile
- Lesser need for therapeutic drug monitoring<sup>3</sup>
- Increased tolerability



EPTS prophylaxis at Our Lady of the Lake

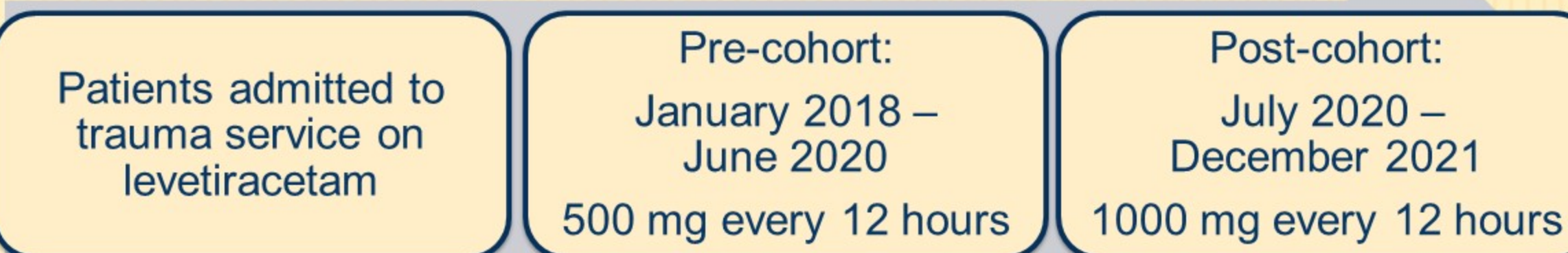
- Levetiracetam (preferred)
  - 1000 mg every 12 hours
  - 500 mg every 12 hours
- Fosphenytoin
  - Initial: 20 mg PE/kg
  - Maintenance: 100 mg PE every 8 hours

## Objective

To determine if levetiracetam 1000 mg every 12 hours will result in fewer clinical seizures in the 7 days following traumatic brain injury compared to levetiracetam 500 mg every 12 hours

## Methods

- Single-center, retrospective, pre/post- levetiracetam protocol implementation, cohort, chart review
- Franciscan Missionaries of Our Lady of the Lake Institutional Review Board (IRB) approved
- January 1, 2018 to December 31, 2021
- Levetiracetam high dose protocol implementation date: July 1, 2020



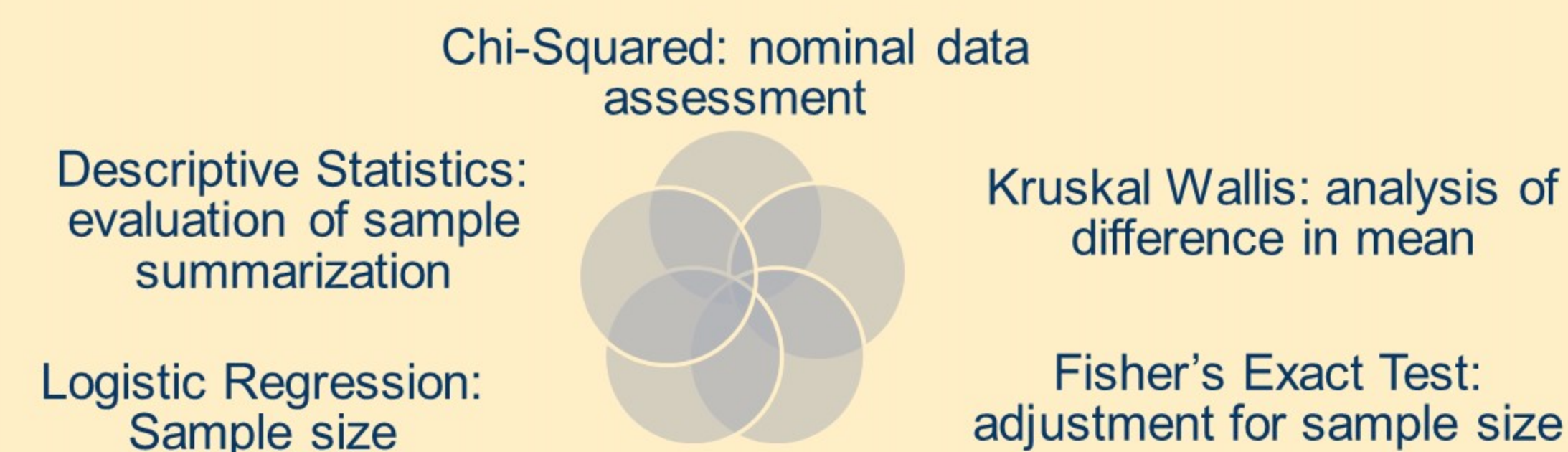
### Inclusion criteria

- Patients admitted to the trauma service and initiated on levetiracetam
- Patients diagnosed with TBI per imaging

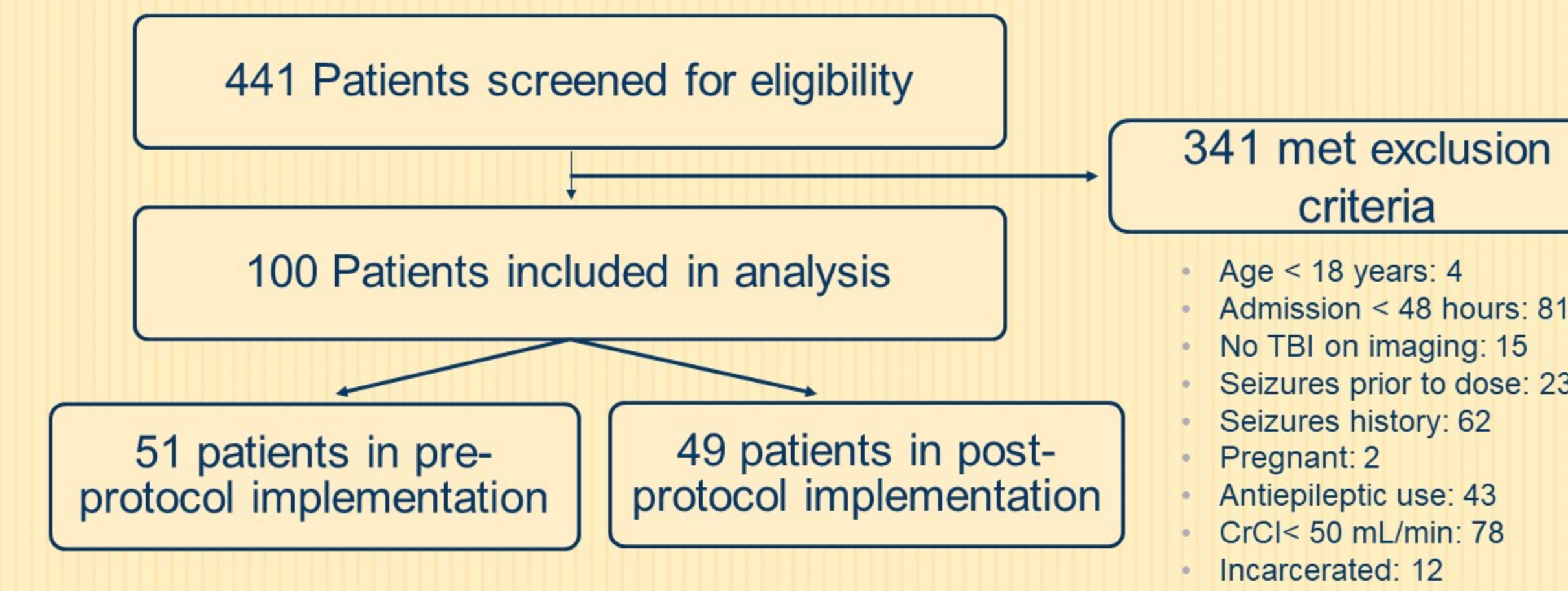
### Exclusion criteria

- Age < 18 years old
- Patients discharged within 48 hours of admission to unit
- Patients with history or development of seizures prior to first dose of levetiracetam
- Anti-epileptic drug use prior to first levetiracetam dose
- Allergies to levetiracetam or contraindication to its use
- Pregnant patients
- Patients with creatinine clearance < 50 mL/min

### Statistical Analysis



## Results



Baseline Characteristics	500 mg (N = 51)	1000 mg (N = 49)
Mean age, y ± SD	54 ± 21	44 ± 21
Male, n (%)	38 (74.5)	37 (75.5)
Race, n (%)		
White	30 (58.8)	23 (46.9)
Black	16 (31.4)	22 (44.9)
Mechanism of Injury		
Motor Vehicle Crash	14 (27.5)	23 (46.9)
Fall	22 (43.1)	9 (18.4)
Blunt Force Trauma	8 (15.7)	7 (14.3)

Outcomes	500 mg (N = 51)	1000 mg (N=49)	p-value
<b>Primary Outcome, n (%)</b>			
Seizure Incidence	4 (8)	3 (6)	0.373
<b>Secondary Outcomes, n (%)</b>			
Incidence of loading dose	10 (19.6)	5 (10.2)	-
Treatment duration > 7 days	7 (13.7)	9 (18.4)	0.228
Mortality during admission	12 (23.5)	9 (18.4)	0.525
<b>Secondary Outcomes, days</b>	Mean; (95% CI)	Mean; (95% CI)	
Time to first dose	0.92 (-0.31 - 2.15)	2.3 (-26.7 - 31.35)	0.432
Hospital length of stay	10.8 (8.0 - 13.53)	15.9 (9.07 - 22.7)	0.316
ICU length of stay	7.37 (5.2 - 9.49)	10.26 (5.34 - 15.17)	0.245
Time to seizure onset	1.29 (-1.39 - 3.93)	8.76 (-41.2 - 58.7)	0.086

## Discussion

- Study showed seizure incidence consistent with historical findings
- Variances from the 2019 evaluation are likely due to patient selection despite similar inclusion/ exclusion criteria
- Variability in time to drug initiation between groups did not result in a higher seizure incidence
- In the high dose group, patients with lower seizure incidence had a higher TBI severity

### Limitations

- Power was not met
- Limited follow-up due to short lengths of stay
- Patients had varying GCS scores during the first 24 hours

## Conclusion

High dose levetiracetam may be associated with lower incidence of post-traumatic seizures, however the findings were not statistically significant therefore warranting a larger clinical assessment to establish a dosing protocol

## References

1. National Center for Injury Prevention and Control . Report to Congress on Mild Traumatic Brain Injury in the United States: Steps to Prevent a Serious Public Health Problem. Centers for Disease Control and Prevention; Atlanta, GA, USA: 2003
2. Carney N, Totten AM, O'Reilly C, et al. Guidelines for the Management of Severe Traumatic Brain Injury, Fourth Edition. Neurosurgery. 2017;80(1):6-15.
3. Levetiracetam. Lexi-Drugs. Lexicomp. Wolters Kluwer Health, Inc. Waltham, MA. Accessed August 23, 2022. <https://online.lexi.com>.
4. Phenytoin. Lexi-Drugs. Lexicomp. Wolters Kluwer Health, Inc. Waltham, MA. Accessed August 23, 2022. <https://online.lexi.com>.
5. Heider C, Thibodeaux L, Parikh P. Evaluation of Levetiracetam for Early Post Traumatic Seizure Prophylaxis in Traumatic Brain Injury Patients in a Trauma Critical Care Unit.
6. Harris L, Hateley S, Tsang KT, Wilson M, Seemungal BM. Impact of anti-epileptic drug choice on discharge in acute traumatic brain injury patients. J Neurol. 2020;267(6):1774-1779
7. DJohn J, Ibrahim R, Patel P, DeHoff K, Kolbe N. Administration of Levetiracetam in Traumatic Brain Injury: Is it Warranted?. Cureus. 2020;12(7):e9117
8. Zampella B, Patchana T, Wiginton JG 4th, et al. Seizure Prophylaxis in Traumatic Brain Injury: A Comparative Study of Levetiracetam and Phenytoin Cerebrospinal Fluid Levels in Trauma Patients with Signs of Increased Intracranial Pressure Requiring Ventriculostomy. Cureus. 2019;11(9):e5784. Published 2019 Sep 27
9. Klein P, Herr D, Pearl PL, et al. Results of phase II pharmacokinetic study of levetiracetam for prevention of post-traumatic epilepsy. Epilepsy Behav. 2012;24(4):457-461.
10. Chen YH, Kuo TT, Yi-Kung Huang E, et al. Profound deficits in hippocampal synaptic plasticity after traumatic brain injury and seizure is ameliorated by prophylactic levetiracetam. Oncotarget. 2018;9(14):11515-11527. Published 2018 Jan 4.