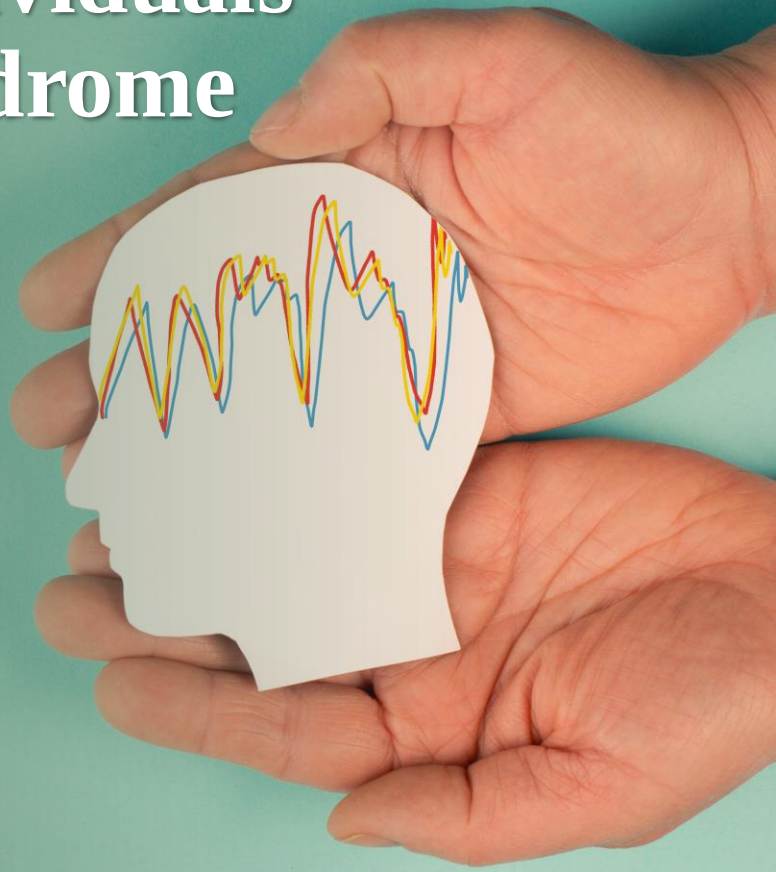
The Life-long Care of Individuals with Lennox-Gastaut Syndrome

Strategies for Outcomes Optimization from Childhood Through Adulthood



CME OUTFITTERS

This program is supported by an independent medical education grant from Jazz Pharmaceuticals.

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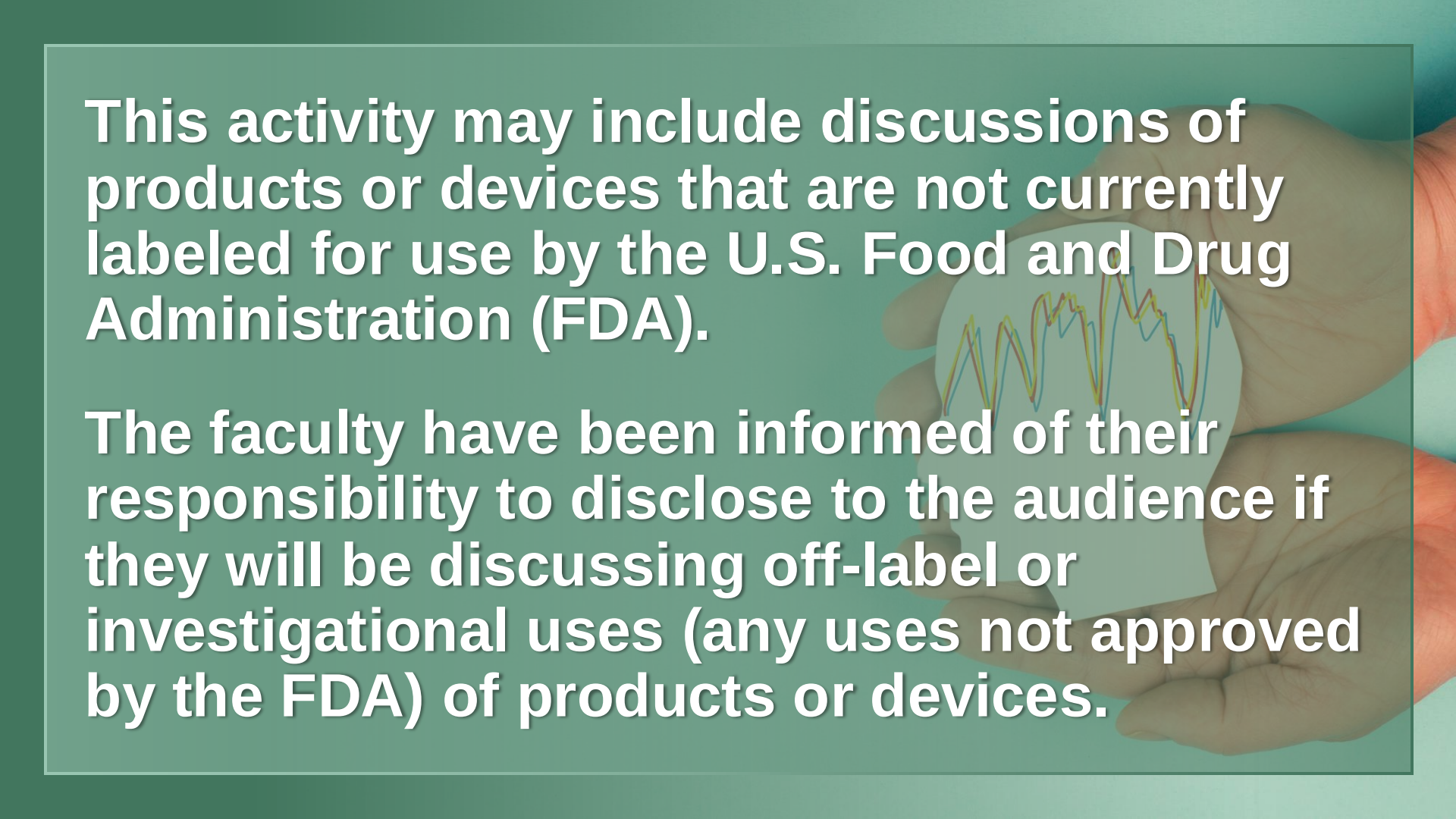
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Elaine Wirrell, MD
(Moderator)

Professor and Chair
Child and Adolescent Neurology
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Tracy Dixon-Salazar, PhD
(Patient Advocate)

Executive Director
Lennox-Gastaut Syndrome (LGS) Foundation
San Diego, California



Bethany Thomas, DNP

Epilepsy Nurse Practitioner
Hospital of the University
of Pennsylvania
Philadelphia, Pennsylvania

Learning Objective 1

Evaluate the disease burden and impact of Lennox-Gastaut syndrome (LGS) on quality of life (QoL) for both patients and caregivers

Learning Objective 2

Utilize diagnostic criteria and distinguishing features of both early- and late-onset LGS to achieve early and accurate diagnosis in all patients

Learning Objective 3

Develop strategies to optimize management of LGS across patients' lifespans

The Burden of LGS on Patients and Their Caregivers

Tracy Dixon-Salazar, PhD



Audience Response



Which of the following is a common non-seizure symptom seen in LGS?

A. Sleep disorders
B. Eyelid ptosis
C. Reliance on parenteral nutrition
D. Hydrophobia
E. I don’t know

CME OUTFITTERS

Introduction: Savannah's LGS Journey (Age 1-5)

Unknown at birth





1st seizure

Age 2



Epilepsy

4 seizures at age 2 → 6 months without seizure → back with a vengeance at age 3



Treatment-resistant epilepsy

Age 3 years old

Other seizure types emerge

Developmental delay

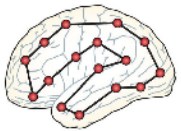


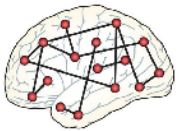
Frequent epileptiform activity



100s of seizures a day

Interplay leads to DEE

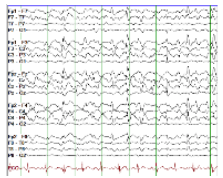


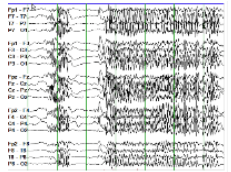


Toddler brain development

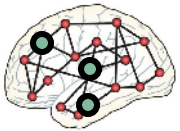
LGS

Diagnosed at age 5









ETIOLOGY | **EVOLUTION** | **BRAIN DAMAGE**

DEE = developmental and epileptic encephalopathy.

CME OUTFITTERS

Savannah's LGS Journey (Age 5-18)

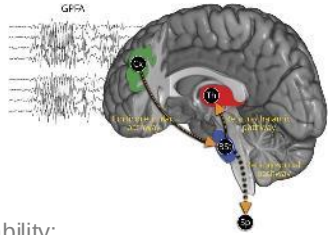


LGS

Age 5-18

# of Seizures: >40,000
 # Years to Get LGS Diagnosis: 3 years
 # Years to Find Etiology: 15
 # Neurologists: 7
 # Treatments Tried: 26
 # Hospitalizations: 15
 # Surgeries: 5
 # Rescue Med Uses/Month: 2-5
Monthly drug cost: $1,640
Emergency med use: $183/dose
Last stay: $53,475

LGS + DEE + IDD
+
Intractable Epilepsy
+
Unknown Etiology



Impact

Seizures (all the time!):
- Weekly status and clusters/SUDEP
- Frequent aspiration pneumonia
- Regular emergency room visits and hospitalizations
- Brain matter atrophy

Developmental Delay/Intellectual Disability (inability to safely navigate the world):
- **Behavior:**
  - Aggression
  - Temper tantrums
  - Inattention
  - OCD
- **Academic/Communications Issues:**
  - Can't read or write
  - Speech and language delayed/slurred
  - Inability to communicate needs
  - Memory issues/psychological slowing
- **Mobility and Physical Care Issues**
  - Severely off balance/low tone
  - Can't walk long distances
  - Doesn't dress/toilet/feed self

Sleep Issues:
- Excessive daytime sleepiness
- Nocturnal seizures
- Excessive nighttime waking

Constipation
Low Bone Density
Social Isolation
Weight Loss
Liver Issues

The Whole Family:
- Sibling issues
- Sleep issues
- Social isolation
- Financial challenges
- Access-to-care challenges
- Caregiver fatigue

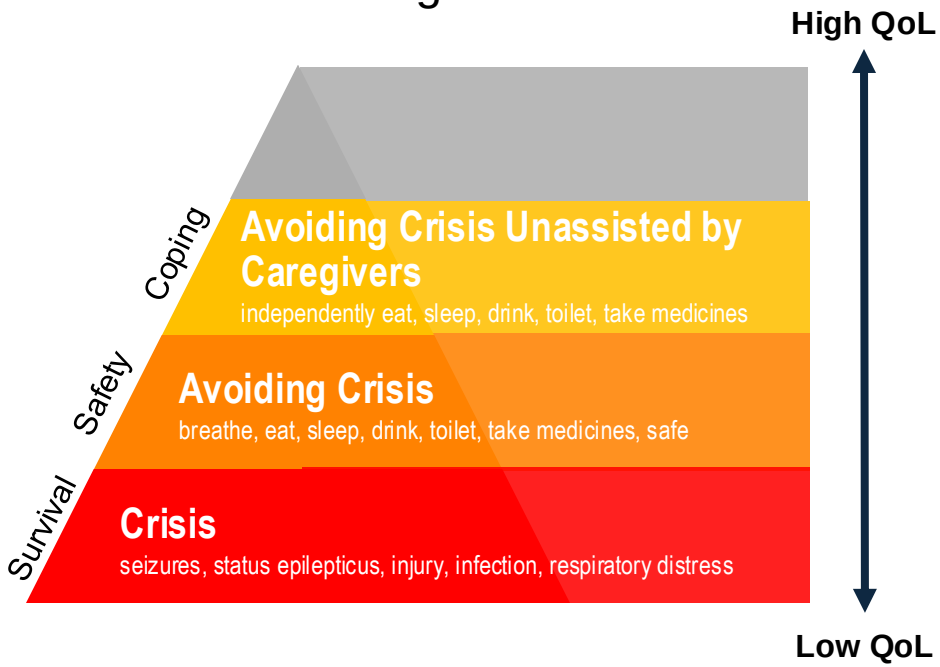
IDD = intellectual and developmental disability;
SUDEP = sudden unexpected death in epilepsy.
Warren AEL, et al. *Neurology*. 2019;93(3):e215-e226.

CME OUTFITTERS

Savannah's LGS Evolution (Age 18-29)

Our Hierarchy of Needs

Age 5-18



LGS

Age 18-31







Age 18
95% reduction in seizures on verapamil
99% reduction in clusters/status epilepticus
STARTED LEARNING AGAIN!!!
Savannah is now 31!

CME OUTFITTERS

Lennox-Gastaut Syndrome

Developmental epileptic encephalopathy characterized by multiple types of drug-resistant seizures and cognitive and behavioral abnormalities

Accounts for 1%-2% of all childhood epilepsies

Often evolves from other infantile epilepsy syndromes, such as infantile epileptic spasms syndrome (IESS)/West syndrome

Typically presents between 18 months and 8 years of age with peak age of onset between 3 to 5 years

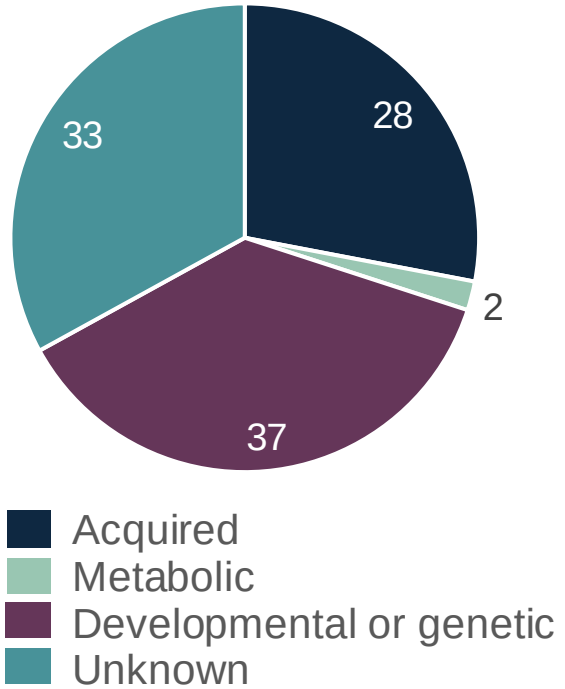
Persists into adulthood in nearly all cases

Asadi-Pooya AA. *Neurol Sci.* 2018;39(3):403-414.

CME OUTFITTERS

What Causes LGS?

- Broad range of causes!
- Likelihood of finding a cause depends on intensity of investigations
- Approximately 25%-35% are of unknown cause
- Both *syndrome* and *etiology* provide critical information to best manage the patient



Asadi-Pooya AA. *Neurol Sci.* 2018;39(3):403-414. Goldsmith IL, et al. *Epilepsia*. 2000;41(4):395-399. Cross JH, et al. *Front Neurol.* 2017;8:505.

CME OUTFITTERS

Seizures in LGS

Hallmark Seizures of LGS

- Tonic (predominantly at night)*
- Atonic
- Atypical absence

Other Associated Seizure Types

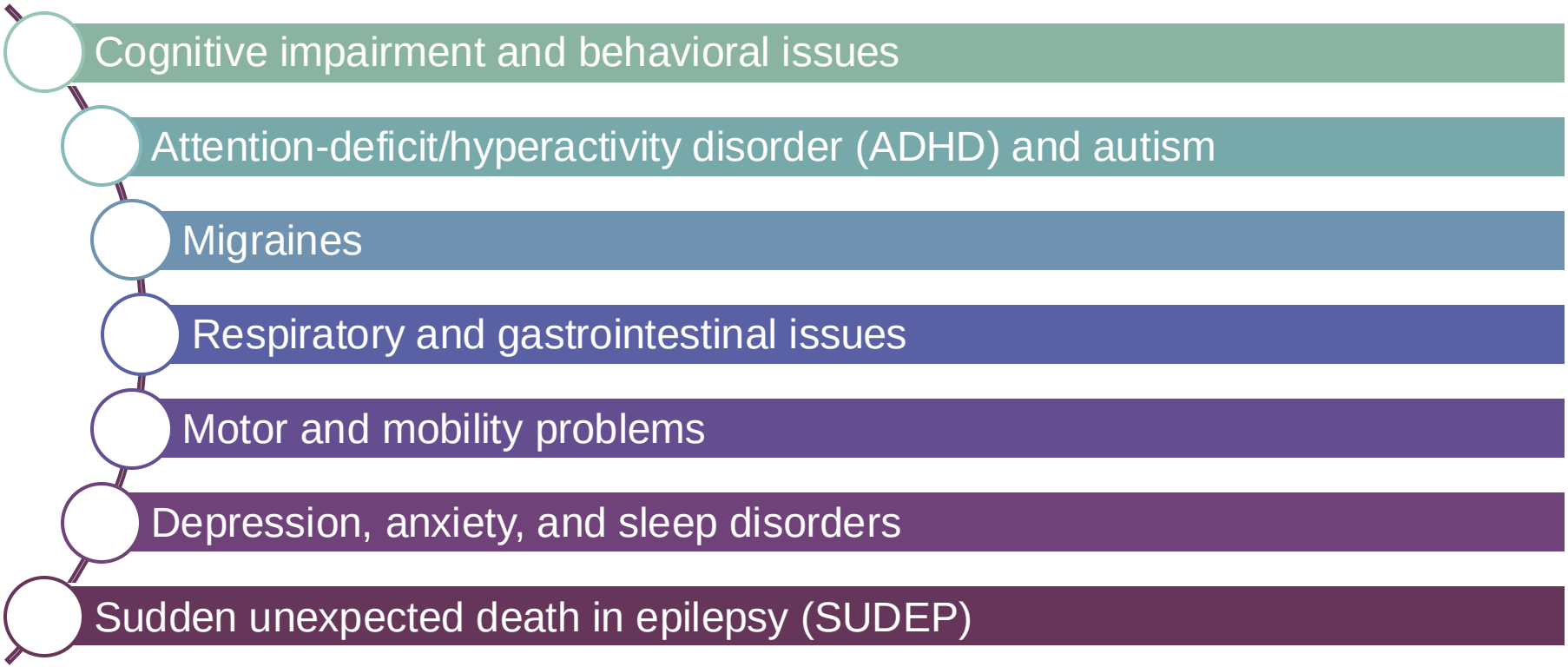
- Epileptic spasms
- Non-convulsive status epilepticus
- Focal motor
- Focal impaired awareness
- Tonic-clonic
- Myoclonic

*Required for diagnosis.

Cross JH, et al. *Front Neurol.* 2017;8:505.

CME OUTFITTERS

Non-seizure Symptoms in LGS



Marchese F, et al. *SN Compr Clin Med*. 2021;3:2167-2179.

CME OUTFITTERS

Evolution of Comorbidities with Age

- Cognitive impairment worsens with age in most patients
  - 95% have variable cognitive impairment at 5 years after onset
  - 80% have a decline in IQ by ≥15 points over time
  - By adulthood, most have moderate to severe cognitive impairment
- Behavior and sleep issues often become more significant in adolescence
  - Hyperactivity, autistic traits, aggression
- 15%-20% have deterioration in gait – many need a wheelchair for longer distances
- Increased swallowing difficulties may be seen with age, and some patients need gastrostomy tube placement

Marchese F, et al. *SN Compr Clin Med*. 2021;3:2167-2179. Cross JH, et al. *Front Neurol*. 2017;8:505.

CME OUTFITTERS

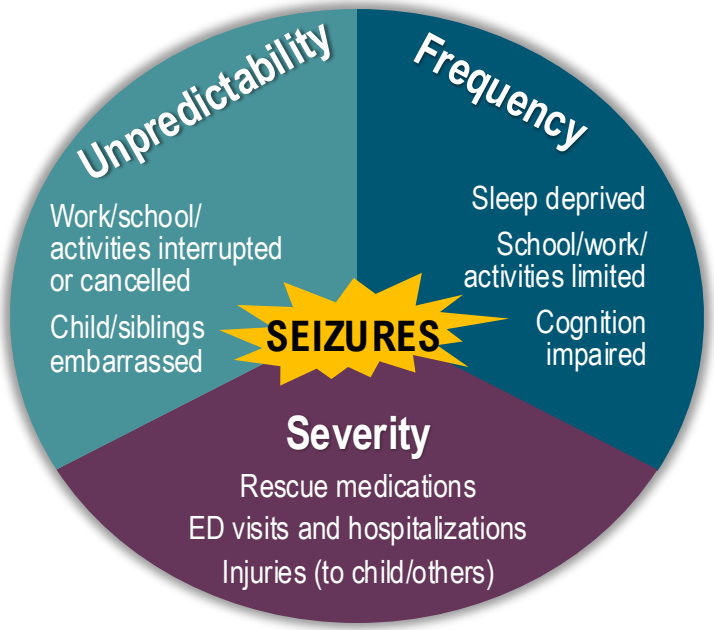
Impact on Patient QoL

Cognitive/behavioral	• Limited ability to communicate • Frustration, aggression
Physical	• Risk of falls with seizures • Need for a wheelchair
Social	• Limited social interactions • Limited recreational activities
Mortality	• Increased mortality compared to other children

Gallop K, et al. Seizure. 2010;19(1):23-30. Autry AR, et al. *J Child Neurol*. 2010;25(4):441-447.

CME OUTFITTERS

Impact on Caregiver/Family QoL



ED = emergency department.

Berg AT, et al. *Epilepsia Open*. 2019;4:293-301. Bailey LD, et al. *Epilepsy Behav.* 2020;112:107377.

CME OUTFITTERS

Impact on Caregiver/Family QoL

Inability to make plans

Managing complex medical care (appointments, specialists, medications, etc.)

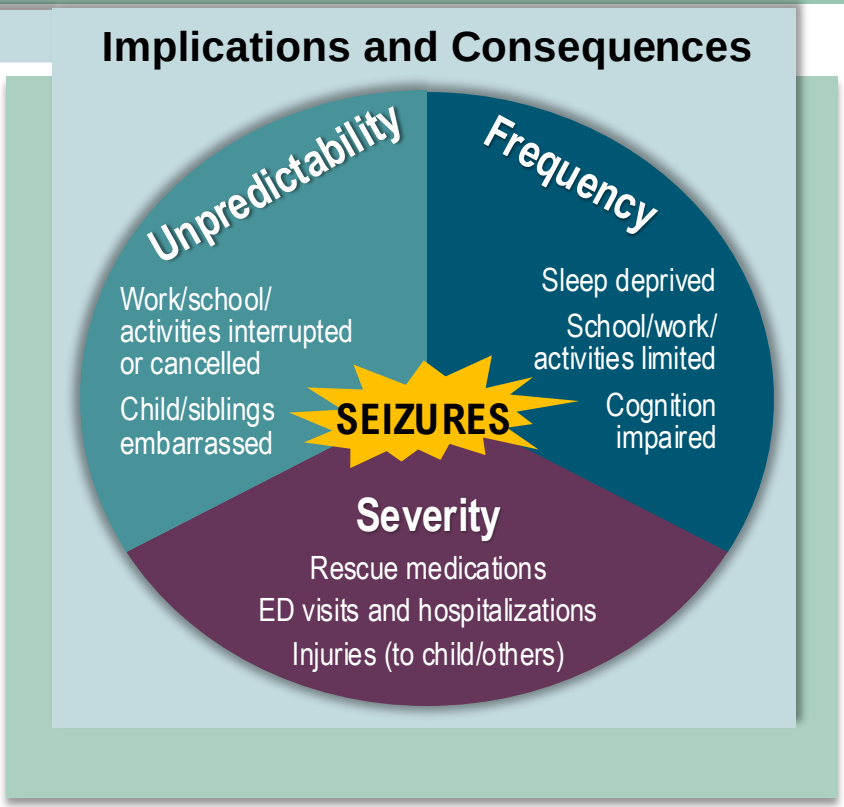
Battling system-level barriers (insurance, finances, advocacy)

Educating self, family, outside caregivers (school, home nurse)

Balancing impacts/needs of other family members

Stranger in home (home nurse)

Monitoring seizures, behavior, cognition, sleep (SUDEP), diet



Berg AT, et al. *Epilepsia Open*. 2019;4:293-301. Bailey LD, et al. *Epilepsy Behav*. 2020;112:107377.

CME OUTFITTERS

Impact on Caregiver/Family QoL

Inability to make plans

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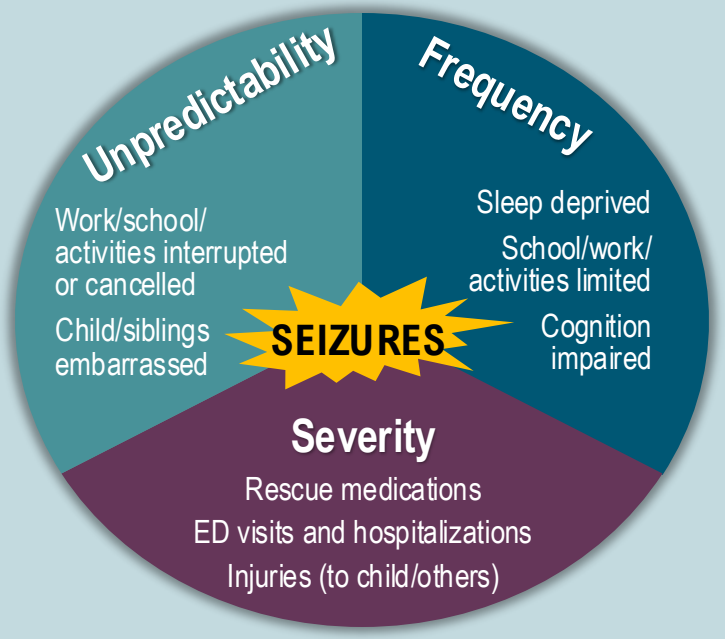
Educating self, family, outside caregivers (school, home nurse)

Balancing impacts/needs of other family members

Stranger in home (home nurse)

Monitoring seizures, behavior, cognition, sleep (SUDEP), diet

Implications and Consequences



Chronic Traumatic Stress

Constant stress overload

Constant fear/anxiety/worry

Self-sacrifice and guilt about not doing enough

Chronic sleep deprivation, 24/7 exhaustion

Wear on relationships (marriage, siblings, friends)

Isolation and depression

Loss of hope

Fear for the future

"*Surviving–Not thriving*"

SUDEP = sudden unexpected death in epilepsy.

Berg AT, et al. *Epilepsia Open*. 2019;4:293-301. Bailey LD, et al. *Epilepsy Behav*. 2020;112:107377.

CME OUTFITTERS

Discussion:

Impact of LGS on Patients and Caregivers





Catching It Early: Recognition and Diagnosis of LGS

Elaine Wirrell, MD



Patient Case: Connor



Connor is a 4-year-old male presenting with drug-resistant tonic seizures, focal seizures, and atypical absences



First seizures occurred at 10 months of age and Connor was initially diagnosed with non-syndromic focal epilepsy

Prior to first seizure development was normal



Behavior issues, including hyperactivity and self-injurious behavior

Increasing cognitive impairment with limited ability to speak

Video EEG with sleep confirms frequent tonic seizures with paroxysmal fast activity and interictal generalized slow spike-and-wave complexes

EEG = electroencephalogram.

CME OUTFITTERS

Audience Response



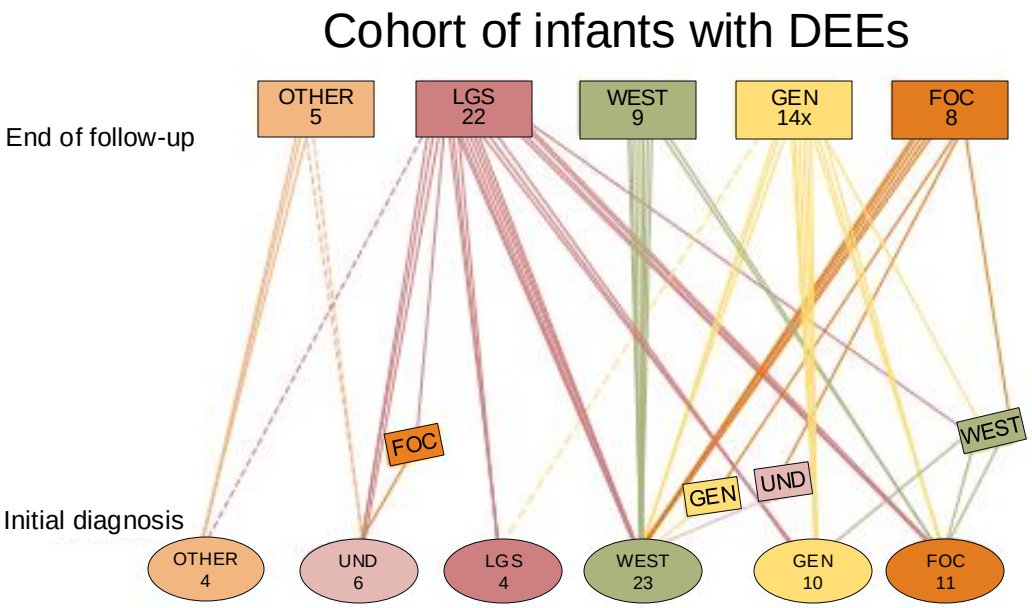
Which result of Connor's examination would be most likely to indicate LGS?

A. Inability to speak at a developmentally appropriate level
B. Paroxysmal fast activity during sleep
C. Recurring focal seizures
D. Initial diagnosis of non-syndromic focal epilepsy
E. I don't know

CME OUTFITTERS

Evolution of LGS

- LGS often evolves from other infantile epileptic disorders
- Up to 20% of epilepsies beginning in infancy will evolve into LGS
- Evolution to LGS takes a median of 1.9 years



22 of 58 had a final diagnosis of LGS

FOC = non-syndromic focal epilepsy; GEN = non-syndromic generalized epilepsy; UND = non-syndromic epilepsy of undetermined nature.

Berg AT, et al. *Epilepsia*. 2018;59(11):2096-2105.

CME OUTFITTERS

LGS Diagnostic Triad

Multiple seizure types	• Tonic*, atypical absence, tonic and atonic drop attacks, non-convulsive status epilepticus
Abnormal EEG	• Interictal slow spike waves (<2.5 Hz) • Paroxysmal fast rhythms (10-20 Hz) that are mainly during non-REM sleep
Cognitive impairment	• Developmental delay and/or intellectual slowing/regression or disability

*Required for diagnosis.
REM = rapid eye movement.
Specchio N, et al. *Epilepsia*. 2022;63(6):1398-1442.

CME OUTFITTERS

Differential Diagnosis

Syndrome	Age of Onset	EEG	Tonic Seizure	Atonic Seizure	Intellect Impaired
LGS	1-8 years	<2.5 Hz spike wave and GPFA in sleep	Mandatory, most common in sleep	Common	Yes
EMAtS/Doose	1-5 years	Parietal theta and GPSW	+/-	++	Rarely
Dravet	<20 months Convulsive with fever	Nonspecific, often normal at onset	Rare	Rare	Normal at onset but delay seen over time
IESS/West	Usually <1 year	Hypsarrhythmia common but not universal	May evolve to tonic with time	No	Usually impaired
DEE-SWS	2-10 years	Marked sleep activation	No	Yes	26%-56%

DEE-SWS = developmental epileptic encephalopathy with spike-wave activation in sleep; EMAtS = epilepsy with myoclonic-atonic seizures; GPFA = generalized paroxysmal fast activity; GPSW = generalized polyspike wave; IESS = infantile epileptic spasm syndrome.
Adapted and updated from Bourgeois BFD, et al. *Epilepsia*. 2014;55(4):4-9.

CME OUTFITTERS

Strategies for an Early Diagnosis

High degree of suspicion

- Awareness of the presenting features and diagnostic criteria is key
- Maintain a high degree of suspicion, particularly in children with previously diagnosed DEE or infantile epilepsy syndromes

Appropriate diagnostic workup

- Video EEG with sleep
- High-resolution neuroimaging when available
- Genetic investigations

Periodic review of diagnosis

- Heterogeneity of LGS presentation means the diagnostic features may not be present at onset and evolve over time
- Regularly review diagnosis of children presenting with DEEs to establish a diagnosis of LGS

Pujar S, et al. *Expert Rev Neurother.* 2024;24(4):383-389.

CME OUTFITTERS

Audience Response



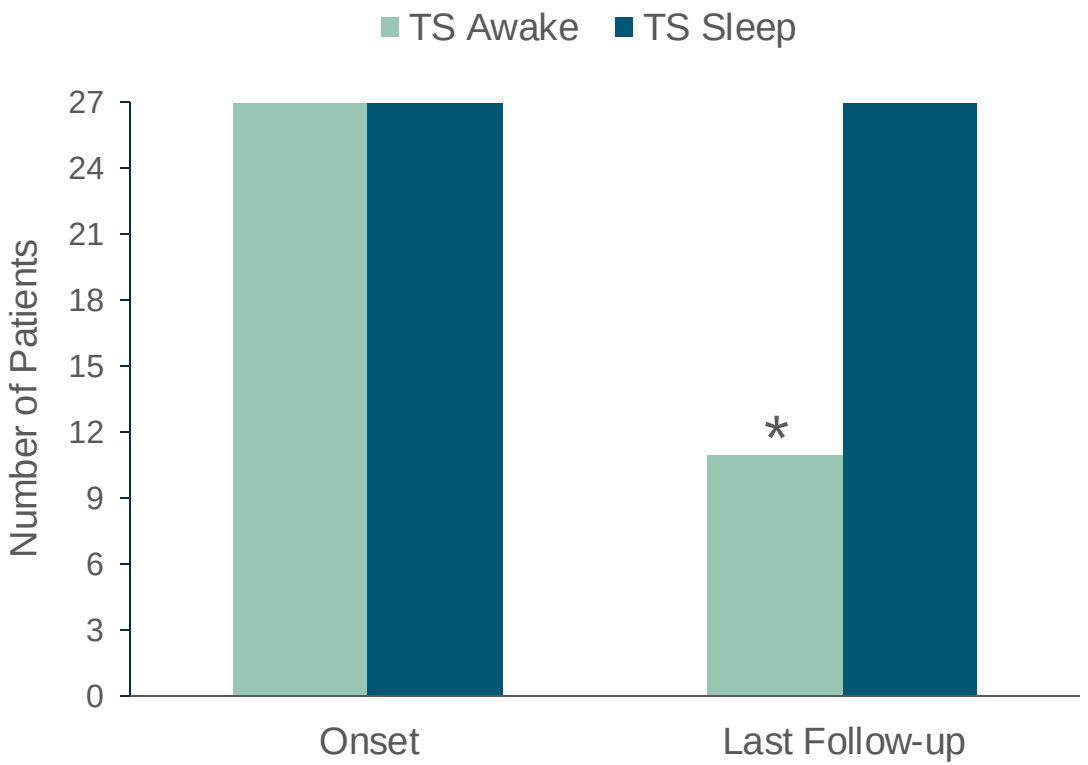
Which change in Connor's presentation might you expect to see if he presented in his teenage years?

A. Increase in daytime seizure frequency
B. Greater predominance of tonic-clonic seizures
C. Reduced slow spike-wave activity
D. Absence of paroxysmal fast activity
E. I don't know

CME OUTFITTERS

Evolution of Seizures in LGS: Tonic

- The characteristics of seizures in LGS change with age
- Most patients continue to have daily to weekly seizures
- Tonic seizures decrease in wakefulness but persist in sleep

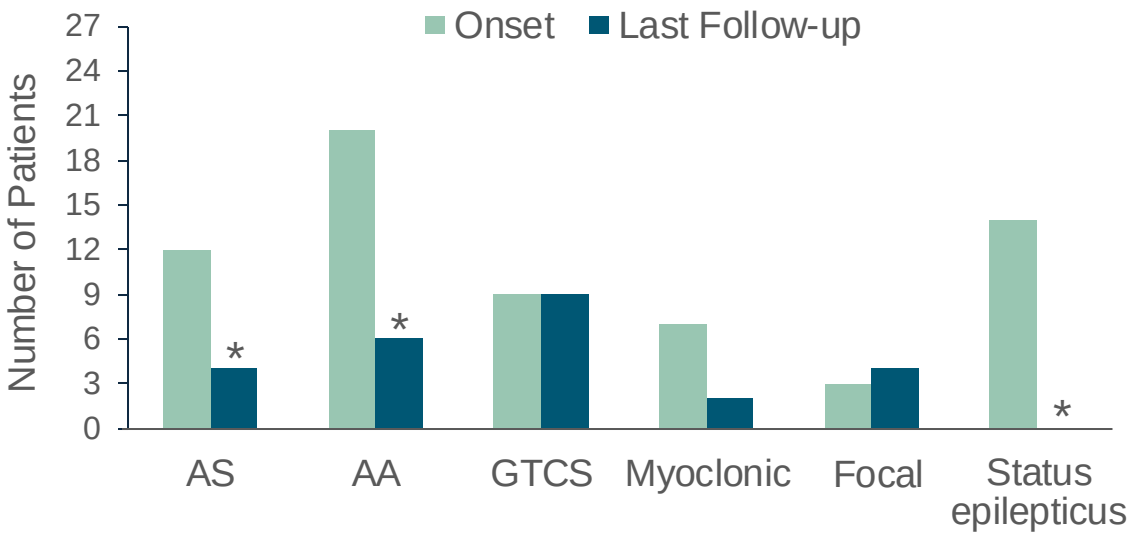


*$P < .05$.
TS = tonic seizure.
Ferlazzo E, et al. *Epilepsy Res.* 2010;89(2-3):271-277.

CME OUTFITTERS

Evolution of Seizures in LGS: Types

- The types of seizures seen in patients with LGS also change
- With increasing age:
  - Atonic seizures, atypical absences, and myoclonic seizures decrease
  - Focal seizures often increase



*$P < .05$.
Ferlazzo E, et al. *Epilepsy Res.* 2010;89(2-3):271-277.

CME OUTFITTERS

Challenges in Diagnosing LGS in Adults

- When diagnosis of LGS in childhood is missed, there are many challenges to diagnosing LGS in adults
  - Absence of early life and medical history
  - Difficulty obtaining records
  - Often very large volumes of records
  - Some characteristic features may be absent
  - Investigations are often incomplete
- Early diagnosis is best

Pina-Garza JE, et al. *Epilepsy Behav Case Rep.* 2016;5:38-43.

CME OUTFITTERS

Discussion:

Importance of an Early and Accurate Diagnosis





Providing Life-Long Care for Patients with LGS

Bethany Thomas, DNP



Audience Response

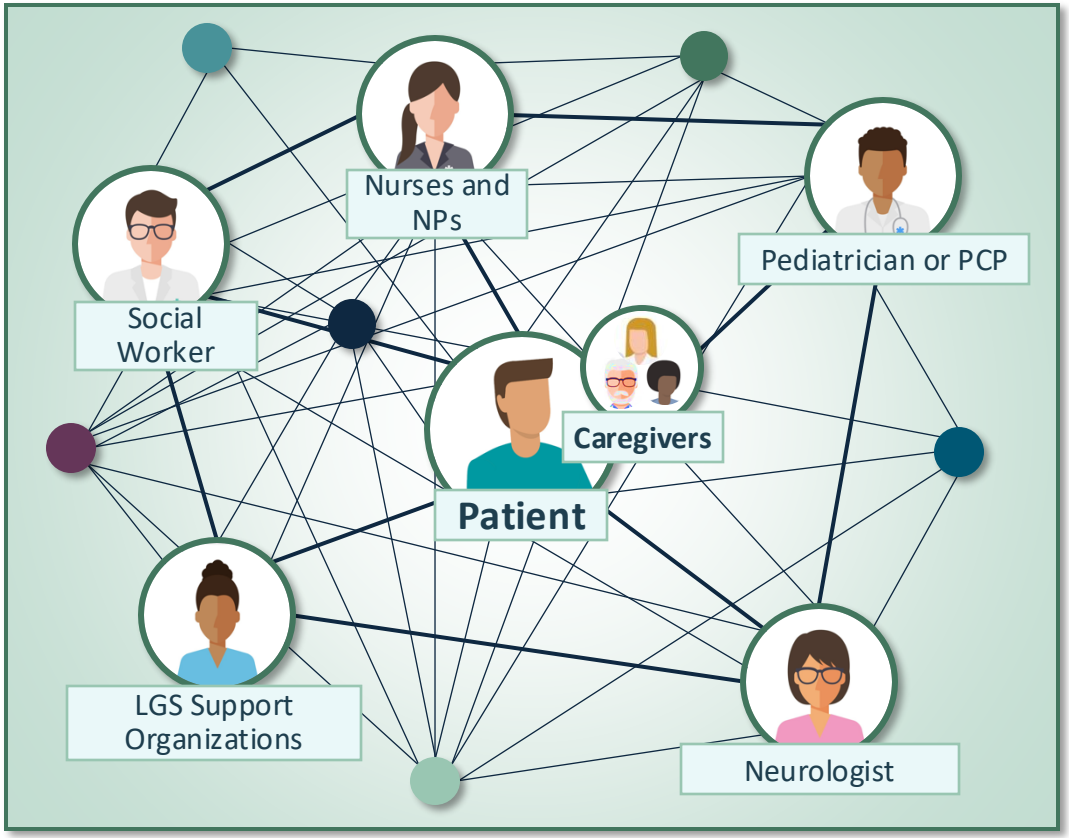


What is a key treatment goal in LGS?

A. Achieve seizure freedom
B. Regain patient motor skills
C. Prevent behavioral issues
D. Reduce seizure frequency and severity
E. I don’t know

CME OUTFITTERS

Importance of Nurses in the Multidisciplinary LGS Management Team



PCP = primary care practitioner.

CME OUTFITTERS

Treatment Goals in LGS

Seizure control

- Target most problematic seizures
- Reduce seizure frequency and severity
- **Seizure freedom is not an achievable goal**
- If significant *epileptic encephalopathy* component, more urgent and aggressive measures should be considered

Manage comorbidities and improve QoL

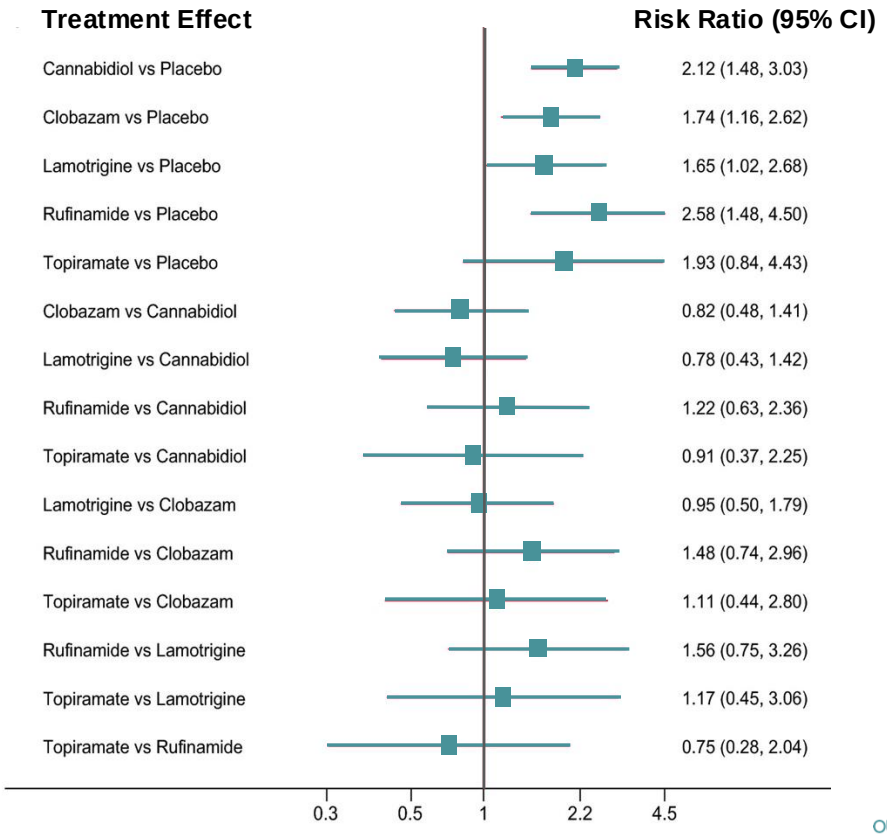
- **Minimize adverse effects** of anti-seizure medications
- Use rational polypharmacy
- Manage the **non-seizure symptoms**!

Auvin S, et al. *Epilepsia Open.* 2024;10(1):85-106.

CME OUTFITTERS

Efficacy of ASMs for LGS: Systematic Review and Network Meta-Analysis

- Total of eight RCTs; 1,171 patients included
- Six of the FDA approved ASMs were evaluated (felbamate and fenfluramine were not included)
- Outcome measure: 50% reduction in drop seizure rate



ASMs = anti-seizure medications; CI = confidence interval
RCTs = randomized controlled trials.
Zhang L, et al. *Dev Med Child Neurol.* 2022;64(3):305-313.

CME OUTFITTERS

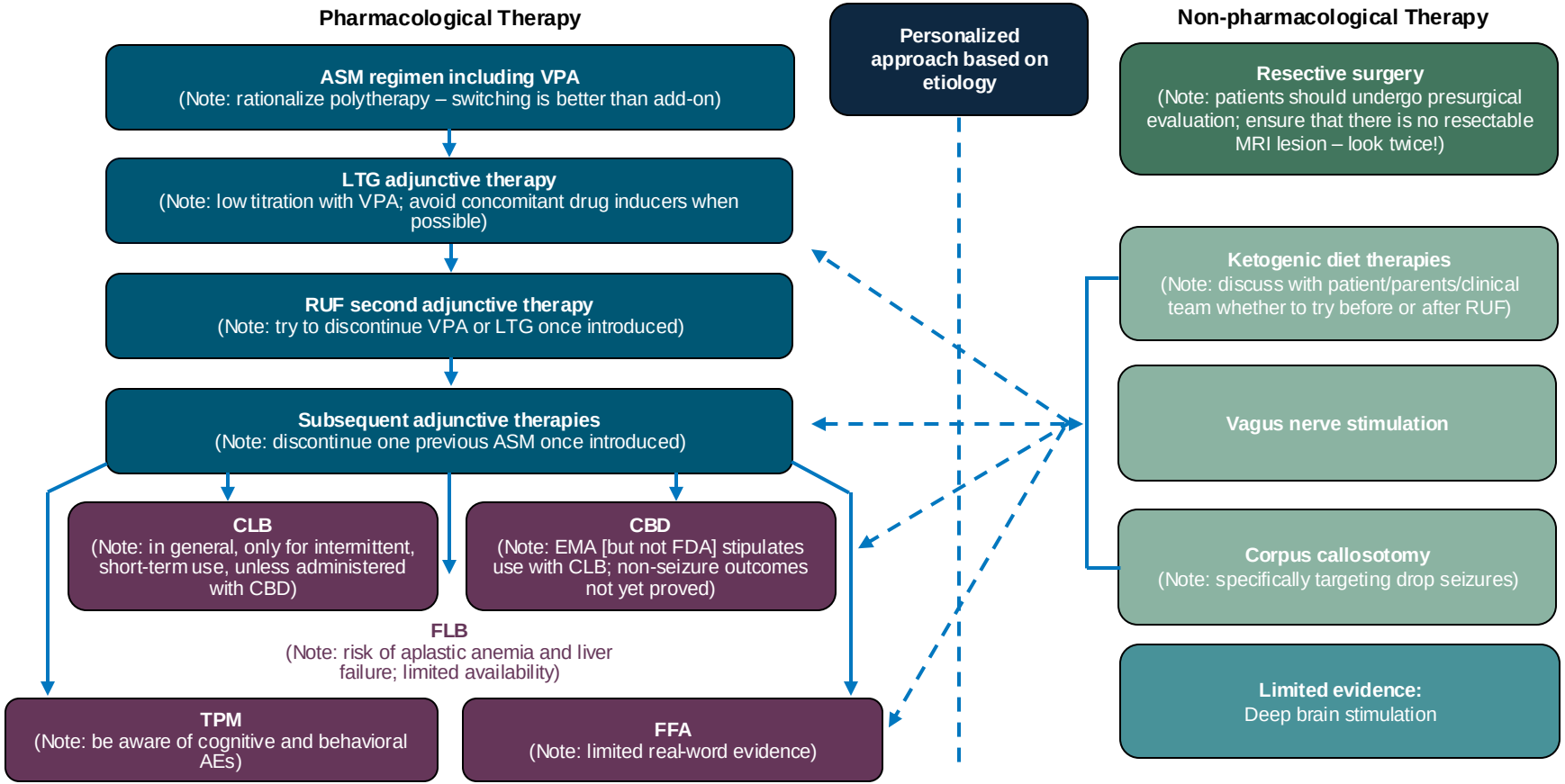
Safety and Tolerability of ASMs for LGS*

Study	Treatment	Any AE, Active/Placebo	Dropouts for Any Reason, Active/ Placebo	Dropouts Due to AE, Active/ Placebo	Serious AEs, Active/Placebo	Most Common AEs
Ohtsuka et al	Rufinamide	27/21	4/1	4/1	1/1	Somnolence, pyrexia, decreased appetite, vomiting, status epilepticus
Glauser et al	Rufinamide	60/52	10/5	9/1	2/2	Somnolence, vomiting, pyrexia, diarrhea
Thiele et al	Pharmaceutical CBD	74/79	14/1	8/1	20/4	Diarrhea, somnolence, pyrexia, decreased appetite, vomiting
Devinsky et al	Pharmaceutical CBD	133/55	11/2	7/1	26/7	Somnolence, decreased appetite, diarrhea, URTI, vomiting, pyrexia, nasopharyngitis, status epilepticus
Sachdeo et al	Topiramate	NA	1/0	NA	11/5	Somnolence, anorexia, nervousness, behavioral problems, fatigue, dizziness, weight loss
Ng et al	Clobazam	142/40	42/18	29/12	14/2	Somnolence, pyrexia, lethargy, drooling, constipation
Motte et al	Lamotrigine	NA	3/7	3/7	3/0	Pharyngitis, fever, infection
Felbamate Study Group	Felbamate	NA	1/1	NA	8/3	URTI, anorexia, vomiting, somnolence, injury, fever, insomnia, nervousness, headache, fatigue, purpura, abnormal gait, ataxia
Knupp et al	Fenfluramine	78 (0.2 mg/kg) 90 (0.7 mg/kg) / 75	--	--	4 (0.2 mg/kg) 11 (0.7 mg/kg) / 5	Decreased appetite, somnolence, fatigue

*All agents on this slide are FDA-approved for the treatment of LGS.
AE = adverse effect; URTI = upper respiratory tract infection.
Zhang L, et al. *Dev Med Child Neurol.* 2022;64(3):305-313. Knupp KG, et al. *JAMA Neurol.* 2022;79(6):554-564.

CME OUTFITTERS

Multimodal Approach to Therapy



All agents and procedures on this slide are FDA approved for use in patients with LGS

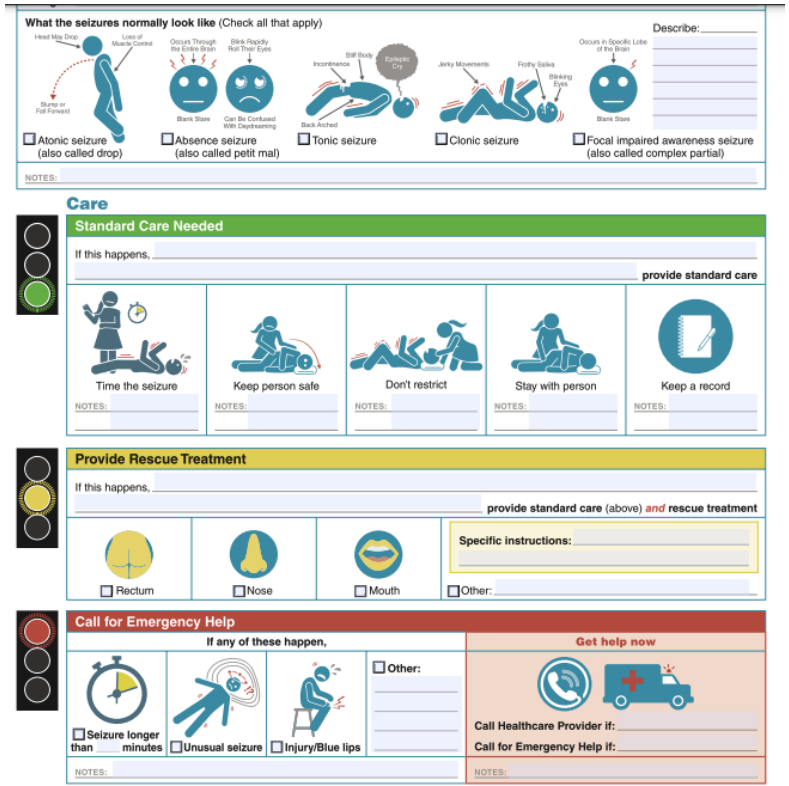
CLB = clobazam; EMA = European Medicines Agency; FLB = felbamate; MRI = magnetic resonance imaging; RUF = rufinamide; TPM = topiramate; VPA = sodium valproate.

Auvin S, et al. *Epilepsia Open.* 2024;10(1):85-106.

CME OUTFITTERS

Seizure Action Plan

- Should be provided to all patients/caregivers with LGS
- Provides information on what to do in emergency situations
- Reduces time to action during seizures is reduced



Lennox-Gastaut Foundation. 2024. https://www.lgsfoundation.org/create-a-seizure-action-plan/.

CME OUTFITTERS

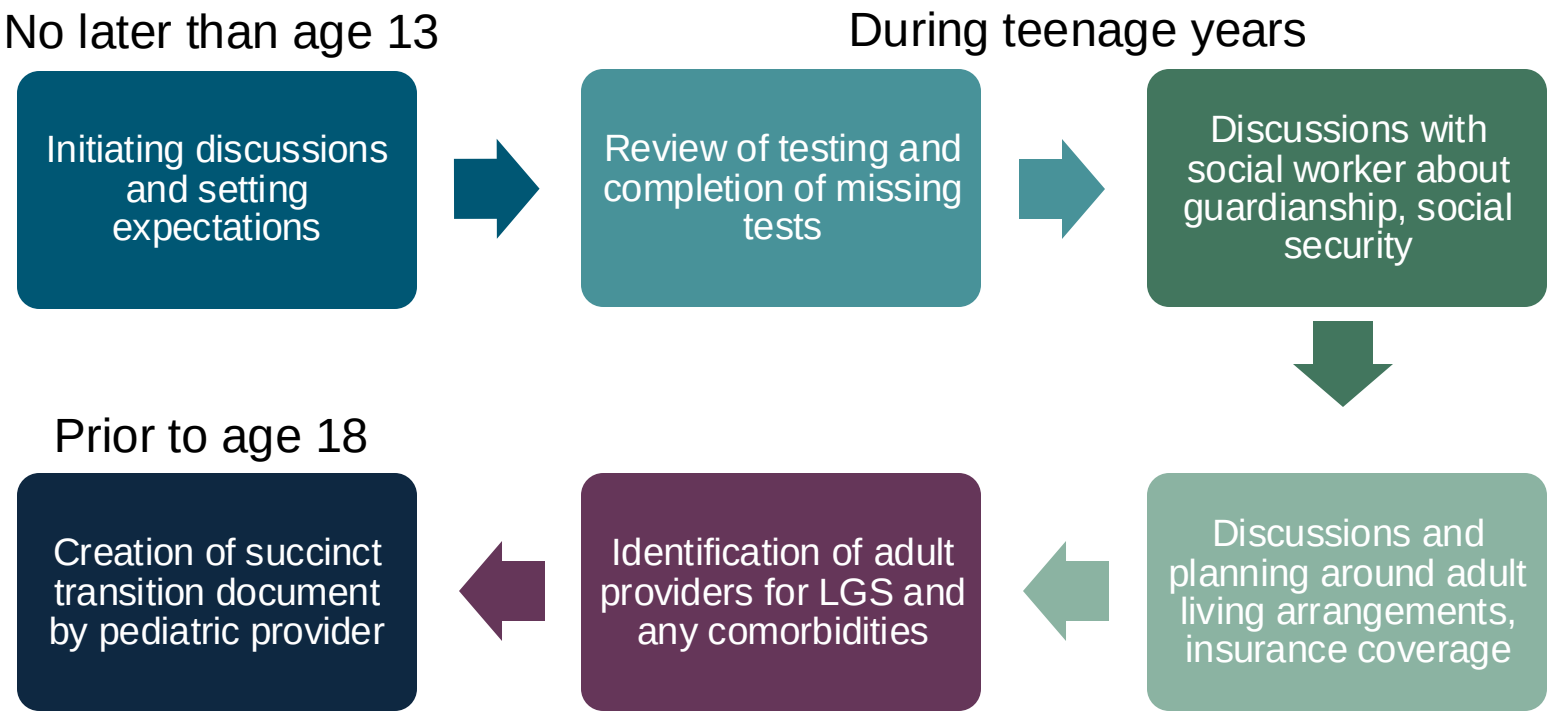
Transition From Pediatric to Adult Care

- Transition from pediatric to adult care can be difficult for both the patient and the caregiver
- Failure to plan for transition may limit access to specialty care and newer treatments and result in poor management of comorbid conditions
- Many new challenges exist when patients with LGS reach adulthood, including issues of guardianship, medical insurance, and long-term care
- Proper preparation beginning early in care can smooth the process and make successful transition more likely

Camfield PR, et al. *Epilepsia.* 2011;52(s5):21-27.

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Timeline of Transition Planning

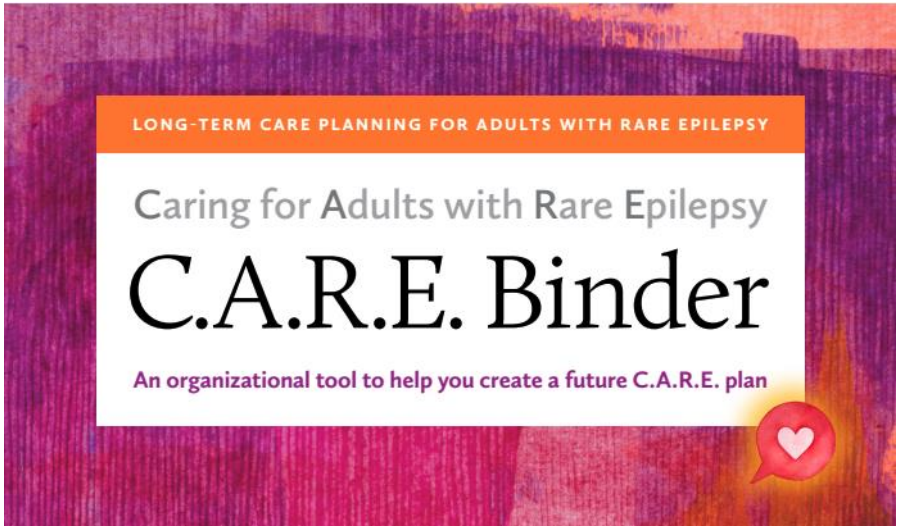


Child Neurology Foundation. 2020. https://www.childneurologyfoundation.org/wp-content/uploads/2020/10/TransInfoGraphicTools_2020-updates.pdf.

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Resource for Transition: C.A.R.E. Binder

- The C.A.R.E. Guide is a resource designed to help families in planning long-term care for LGS
- Includes:
  - Essential factors to consider during the transition process
  - Necessary preparations for adult care
  - Available support services and resources



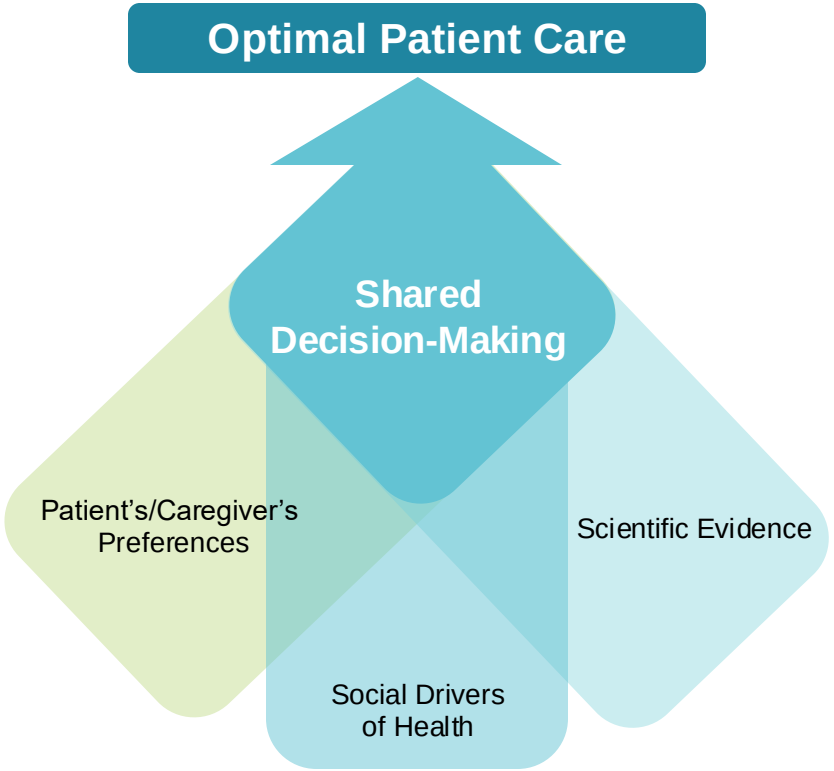
https://www.lgsfoundation.org/adult-care-binder/

Lennox-Gastaut Syndrome Foundation. 2025. https://www.lgsfoundation.org/adult-care-binder/.

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Shared Decision-Making in LGS

- Shared decision-making in LGS is done predominantly with the caregiver
- Follow SHARE model:
  - **S**eek caregiver's participation
  - **H**elp caregiver explore and compare treatment options
  - **A**ssess caregiver's values and preferences
  - **R**each a decision with the caregiver
  - **E**valuate the caregiver's decision

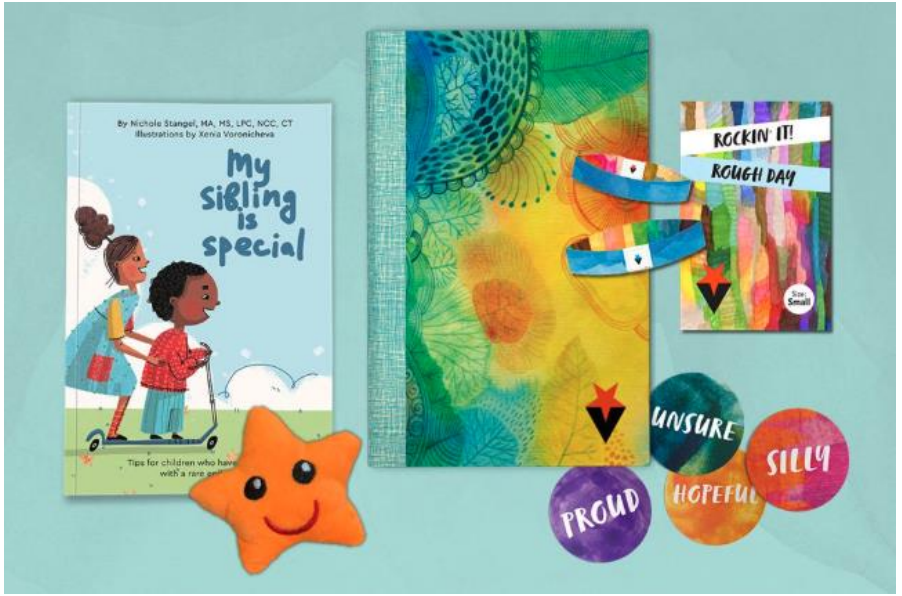


AHRQ. 2020. https://www.ahrq.gov/health-literacy/professional-training/shared-decision/tools/factsheet.html.
Turkson-Ocran RAN, et al. *J Am Heart Assoc.* 2021;10:e018183.

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Education and Resources for Patients and Caregivers

- Rare Epilepsy Network Resources https://www.rareepilepsynetwork.org/resources
- Lennox-Gastaut Foundation Financial Resource Toolkit https://www.lgsfoundation.org/financial-resource-toolkit/
- DEE-P Connections Toolkits for Parents and Siblings https://deepconnections.net/request-form-for-parent-or-sibling-kits/



Discussion:

What can nurses do to facilitate the care transition process?





SMART Goals

Specific, Measurable, Attainable, Relevant, Timely

- Monitor patients and caregivers for quality-of-life challenges, and address these challenges with resources and support when possible
- Evaluate children with a history of infantile epilepsies for LGS diagnostic criteria
- Provide all patients and caregivers with a detailed seizure action plan
- Prepare patients and caregivers for the transition from pediatric to adult care by initiating discussions early and following key milestones for successful transition

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QUESTIONS & ANSWERS



To submit a question, please go to the *Ask Question* tab at the bottom of the screen.

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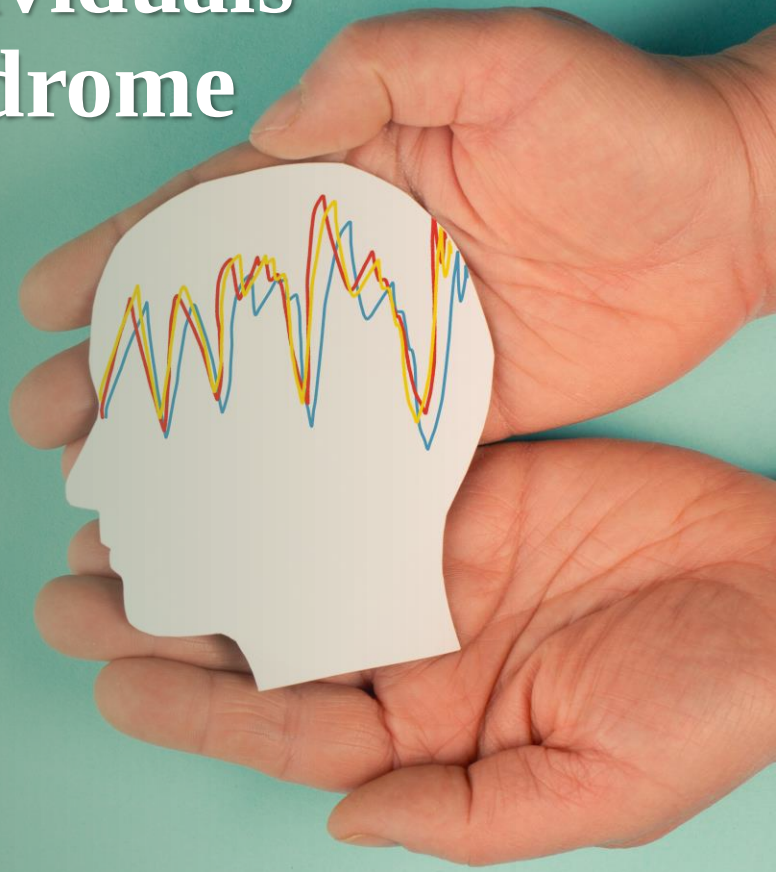
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In-Person

Livestream

The Life-long Care of Individuals with Lennox-Gastaut Syndrome

Strategies for Outcomes Optimization from Childhood Through Adulthood



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