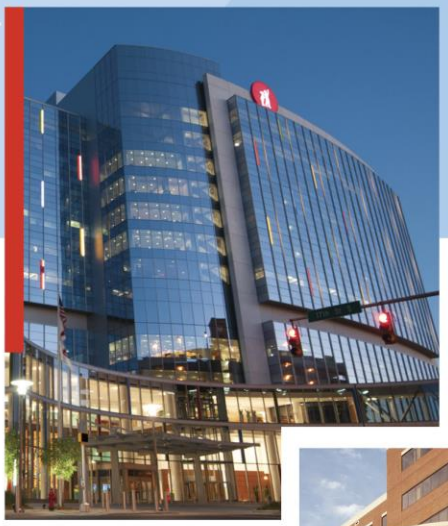


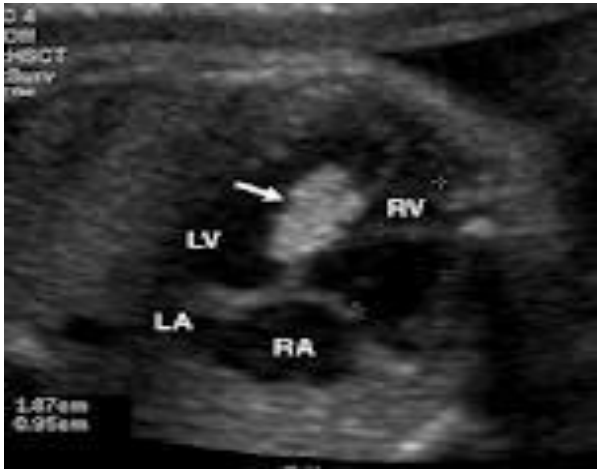
Infantile Spasms in the Age of COVID-19 & Telemedicine

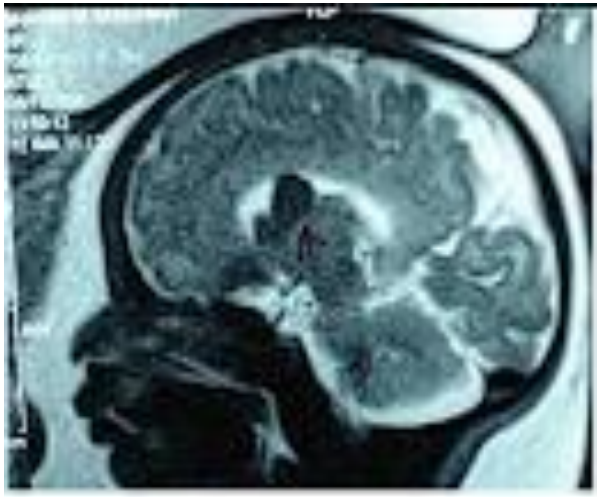
Martina Bebin M.D., M.P.A.

TS Alliance Webinar April 24th, 2020

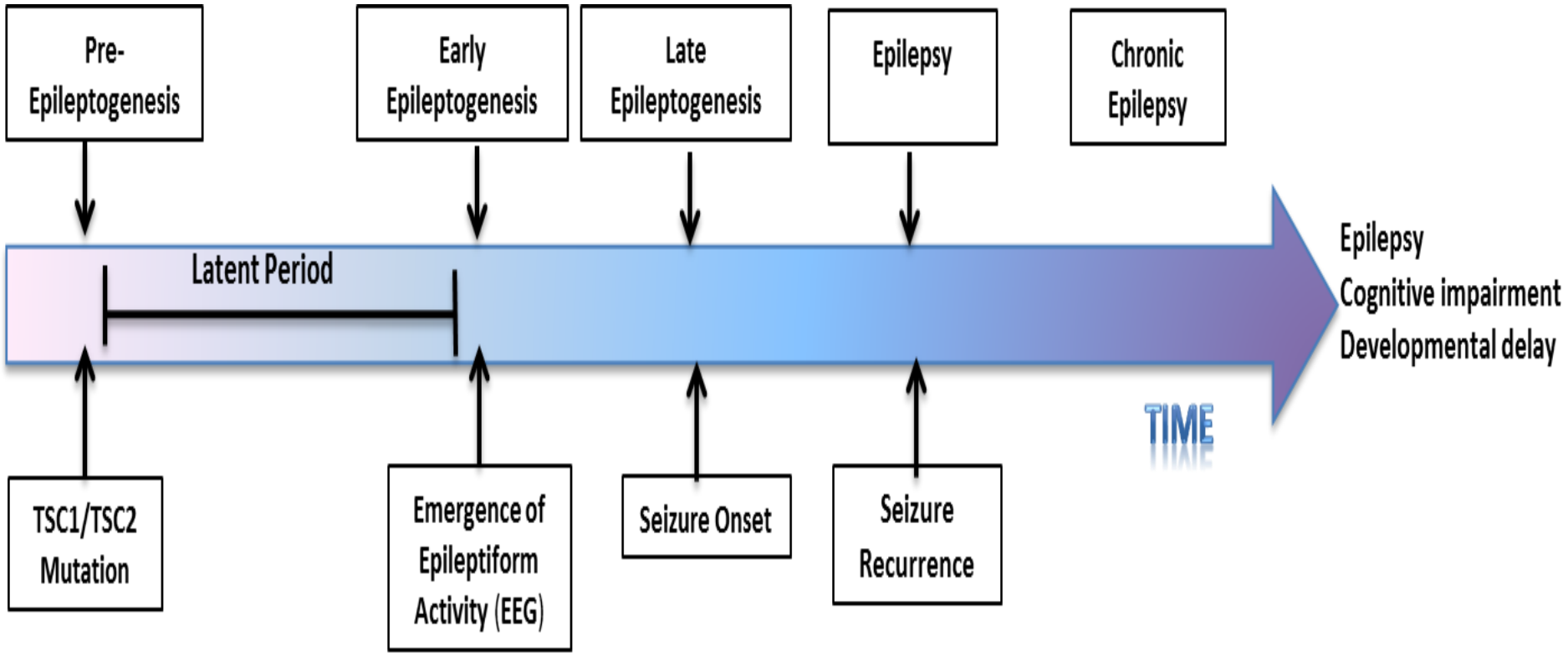
Feasibility for Prevention Trials

- Ability to Dx TSC prenatally
  - Heart-Cardiac Rhabdomyoma-47% of infants also have cardiac dysrhythmias
    - 80% fetuses and infants with TSC have cardiac rhabdomyomas
    - Brain-cortical tubers, subependymal nodules on prenatal brain MRI (60-70% positive exams)
- Early Diagnosis and referral to neurologist
- Education of parents and care givers on seizure recognition
- EEG at the time of TSC diagnosis

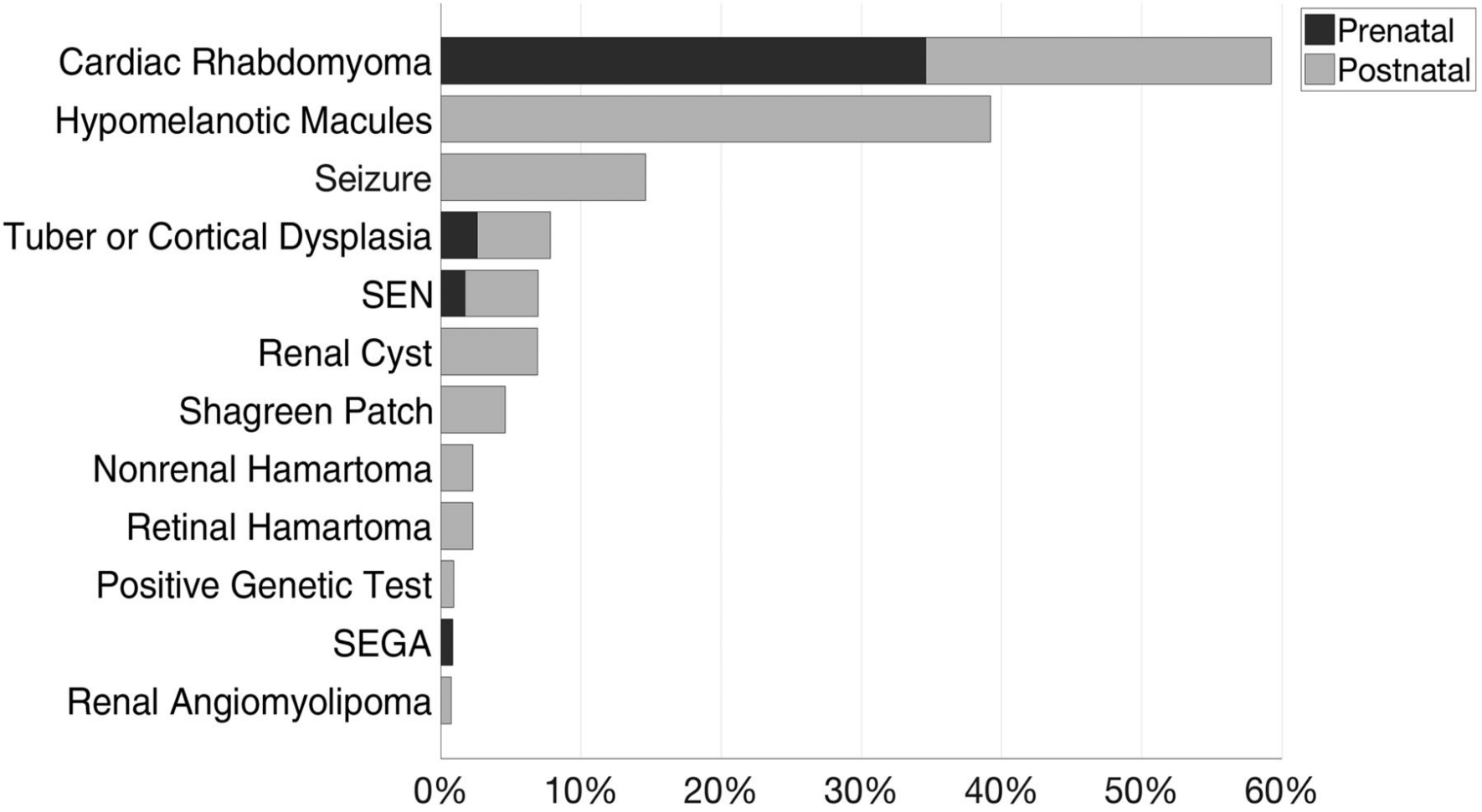




How Do Seizures Develop in TSC?



Prevalence of TSC features at initial presentation



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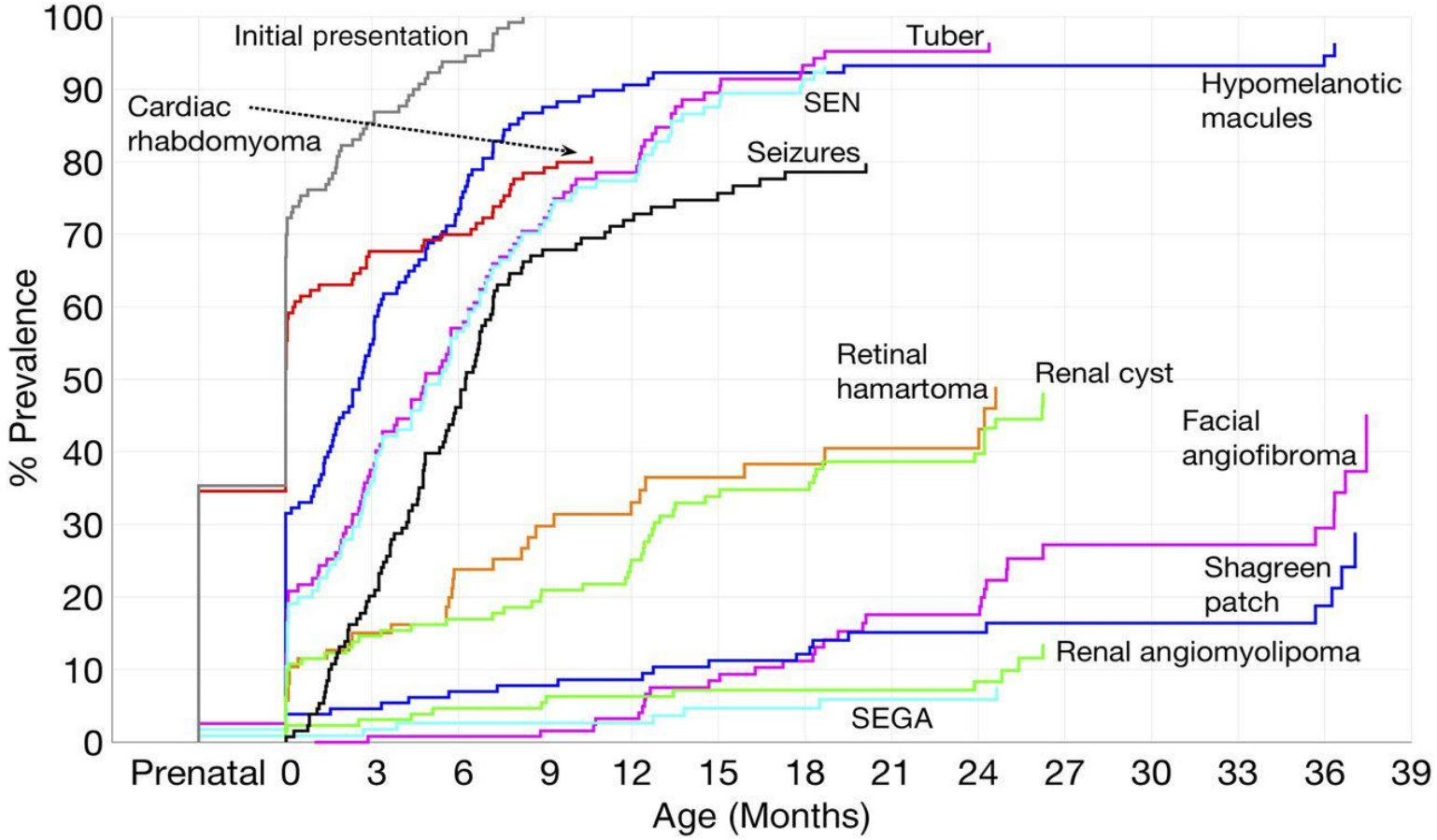

Age of onset or recognition of the most prevalent TSC features in infants. Hypomelanotic macules, tubers, SENs, and cardiac rhabdomyomas are often seen before the onset of seizures, whereas other manifestations are more commonly first seen later in life.

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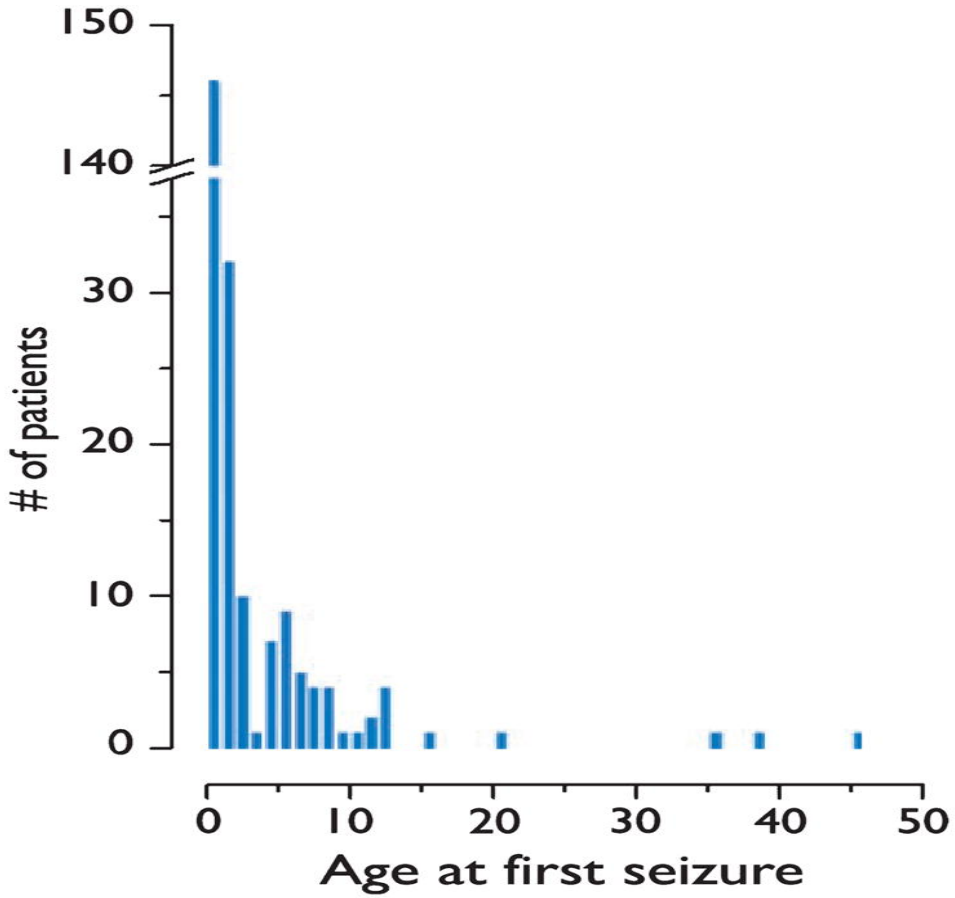
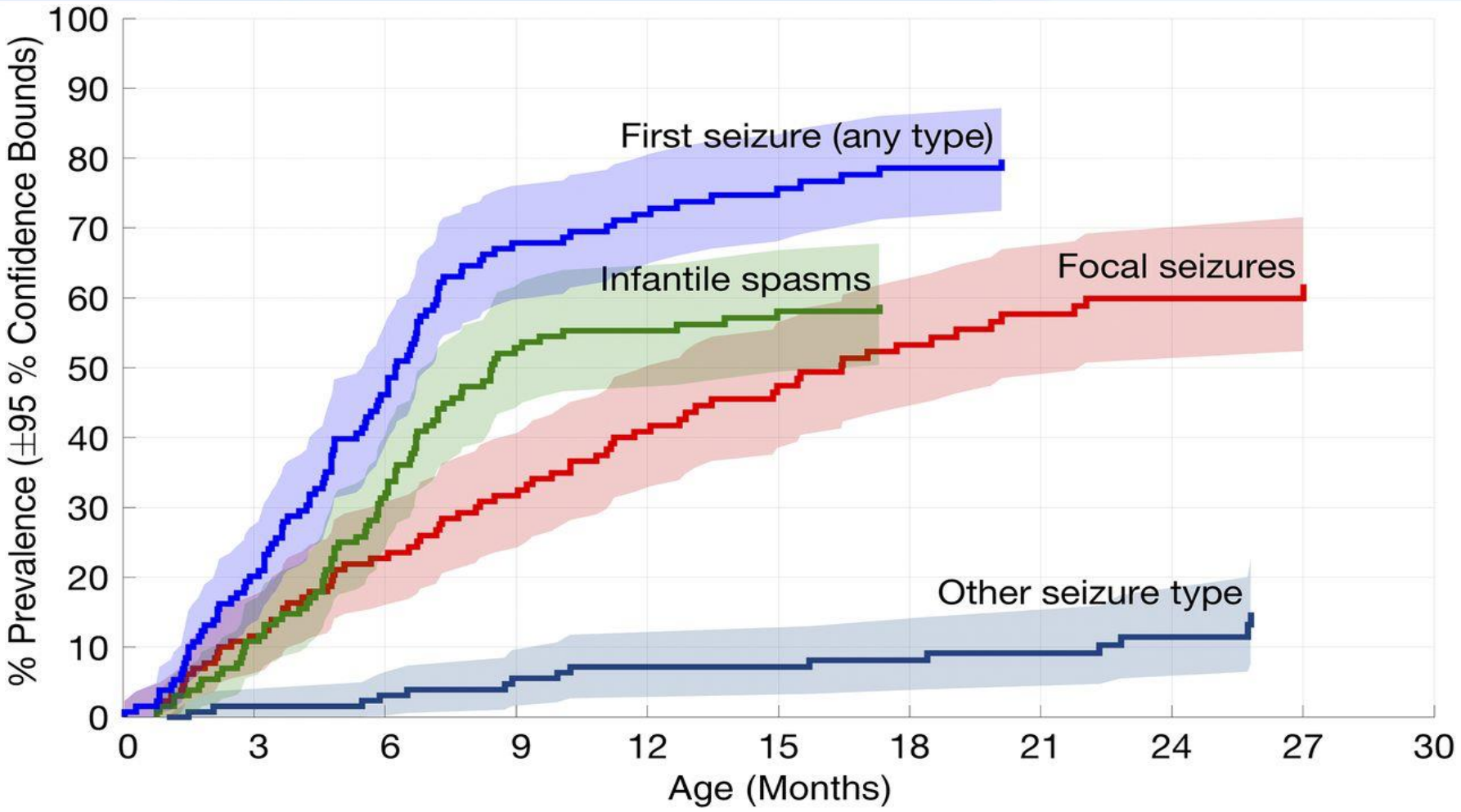
The Natural History of Epilepsy in TSC



Epilepsia. 2010 Jul; 51(7): 1236–1241.



Seizure onset prevalence in TSC by age and seizure type.

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TSC AND EPILEPSY

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- Seizures present in infancy as infantile spasms, partial seizures, or a combination of both.
  - Studies suggest a correlation between earlier seizure onset and worse cognitive outcome.
  - Outcomes studies have also suggested that the more severe and poorly controlled the epilepsy may contribute to developmental outcomes in children with TSC + ASD.
- Early studies suggest treatment of epileptic EEG abnormalities in TSC prior to seizure onset results in improved developmental outcomes and seizure control (Jozwiak et al. 2011).

Summary of EEG Characteristics and Statistical Analysis

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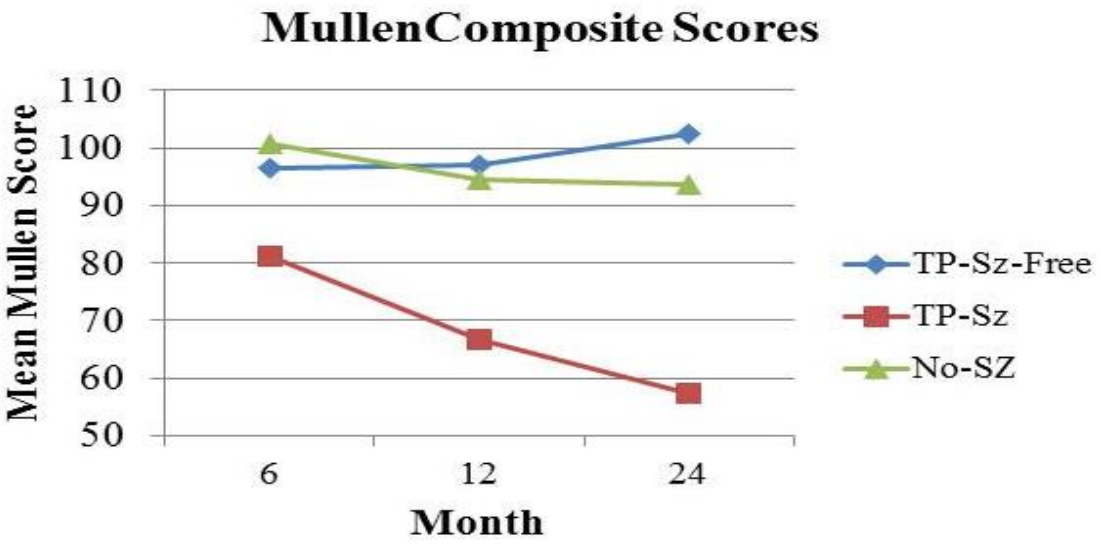
EEG Characteristics:		
Seventeen of 38 (45%) had epileptiform activity detected on EEG before onset of clinical seizures		
	Average (months)	Median (months)
Age at time of first epileptiform discharges	4.5 (S.D.=4)	4.0
Age at time of first clinical seizure	7.5 (S.D.=4.4)	6.0
Time interval between epileptiform discharges and seizure	3.6 (S.D.=3.4)	
Three of 38 (7%) had no epileptiform activity detected on EEG before the onset of clinical seizures		

Statistical Analysis Summary			
	Clinical seizure	No clinical seizure	
Epileptiform discharges	17	5	
No epileptiform discharges/Normal EEG	3	7	
Sensitivity (%)	Specificity (%)	Positive Predictive Value (%)	Negative Predictive Value (%)
85	58.3	77.3	70

Wu et al. Epilepsia Nov 5th, 2019 PMID:31691264

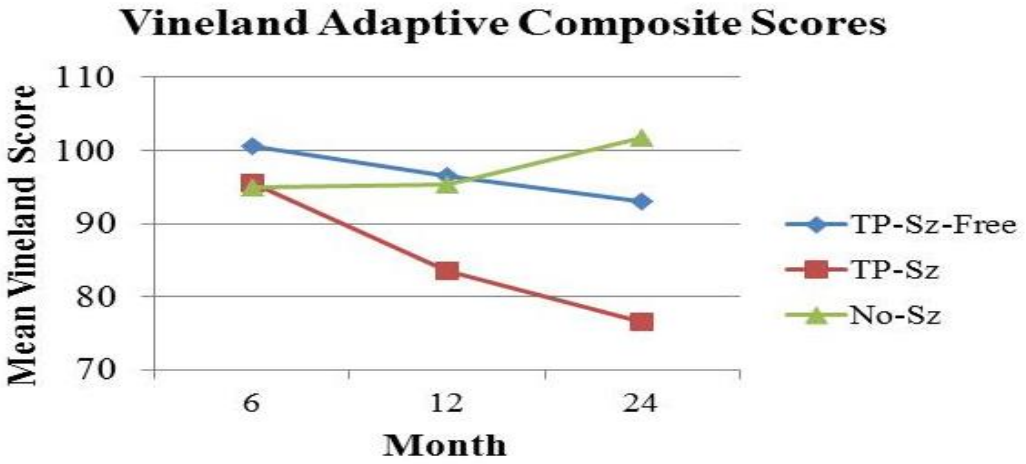
Mullen Scale of Early Learning Composite Scores



Age (months)	TP-Sz-Free	TP-Sz	No-Sz
6	96.63 (19.73)	81.25 (18.23)	100.85 (21.64)
12	97.14 (25.96)	66.57 (13.23)	94.50 (12.82)
24	102.5 (18.09)	57.33 (6.83)	93.62 (25.60)

Wu et al. Epilepsia Nov 5th, 2019 PMID:31691264

Vineland Adaptive Composite Scores



Age (months)	TP-Sz-Free	TP-Sz	No-Sz
6	100.5 (12.00)	95.62 (18.10)	94.62 (13.02)
12	96.57 (17.10)	83.50 (24.48)	95.36 (8.15)
24	93.00 (11.22)	76.50 (13.93)	101.77 (8.89)

Wu et al. Epilepsia Nov 5th, 2019 PMID:31691264

PREVeNT Trial

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- Phase IIb clinical trial
- Enrollment Completed: April 2020
- Multicenter: 12 sites across the U.S.
- **Primary Study Objective**: Developmental Impact of early vs. delayed treatment with vigabatrin. Effect on development at 24 and 36 months

Secondary Objectives

- **Effectiveness of early versus delayed treatment with vigabatrin in clinical seizure prevention**
  - The outcome measure will be time to first clinical seizure following randomization
- **Determine the impact of early versus late treatment on subdomain scores of the Bayley-III, Vineland-II, Beery Visual Motor Integration (VMI), Peabody Picture Vocabulary Test (PPVT), and ADOS2 at 24 months and risk of autism spectrum disorders (ASD).**
  - exploratory analysis will be completed at 36 months to access changes observed at 24 months are consistent with those seen at 36 months and indicative of long-term outcome.
- **Confirm vigabatrin safety as a preventative treatment for clinical seizures in infants with TSC.**
- **Confirm of the feasibility of using EEG biomarkers to identify TSC infants at risk for developing epilepsy.**

NIH TSC Clinical Trial Sites

Preventing Epilepsy Using Vigabatrin In Infants With Tuberous Sclerosis Complex (PREVeNT trial)

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1. University of Alabama at Birmingham (UAB)
2. Boston Children's Hospital (BCH)
3. Cincinnati Children's Hospital Medical Center (CCHMC)
4. Mattel Children's Hospital (UCLA)
5. University of Texas at Houston (UTH)
6. Minnesota Epilepsy Group
7. Stanford University
8. Beaumont Hospital
9. Washington University in St. Louis
10. Children's National Medical Center
11. Children's Hospital of Philadelphia (CHOP)
12. Duke University Medical Center
13. Seattle Children's Hospital

Seizures Types in TSC

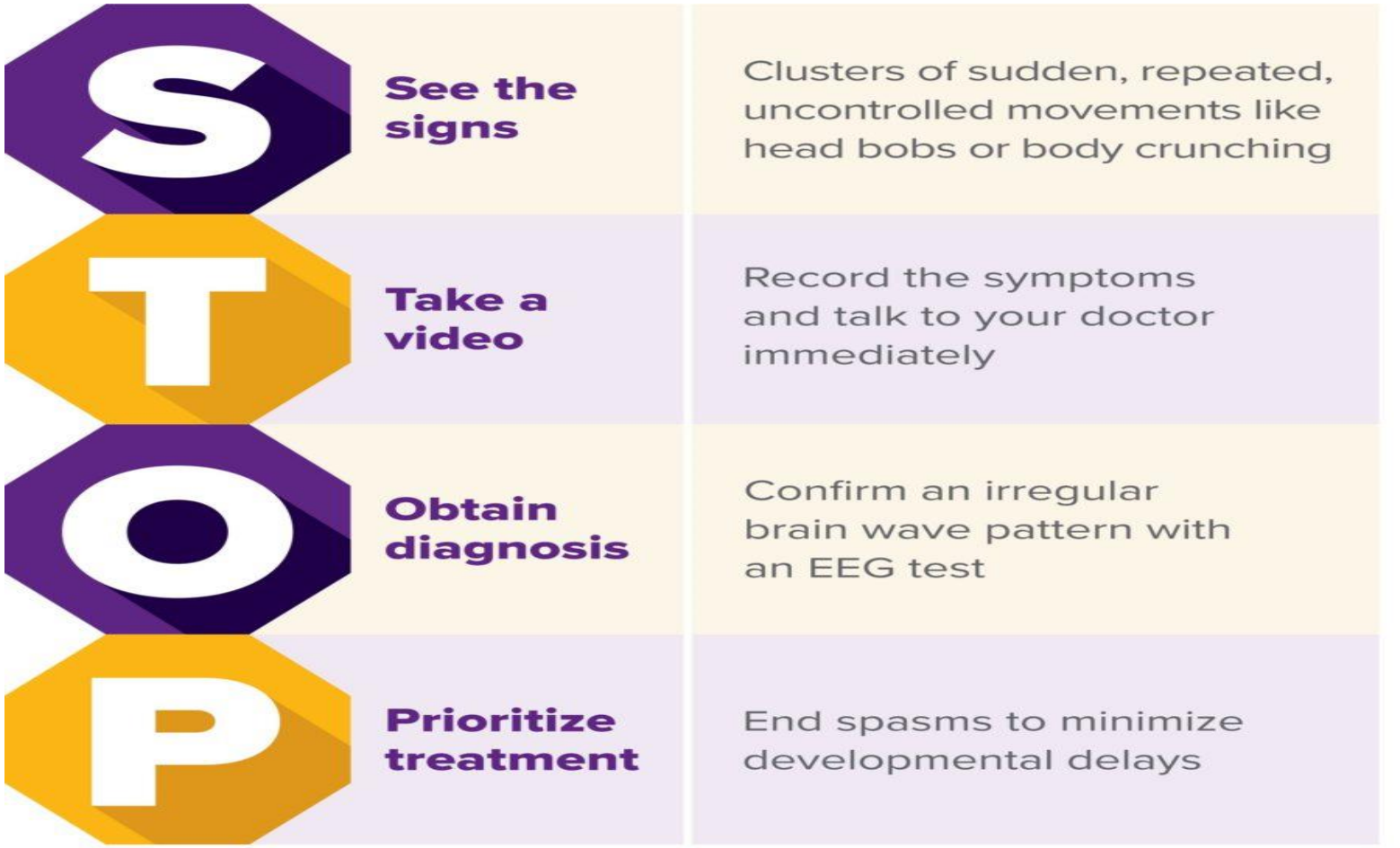
- Up to 85% of individuals with tuberous sclerosis complex (TSC) have epilepsy
  - Birth to 12 months- focal seizures, infantile spasms or a combination of both types
  - Febrile seizures and/or status epilepticus can occur
  - Untreated early-onset seizures are associated with an increased risk of autism and intellectual disability.
  - More than 60% of individuals with TSC and seizures do not achieve seizure control with standard treatment such as antiepileptic drugs, epilepsy surgery, ketogenic diet, and vagus nerve stimulation,
    - Compared to 30-40% of individuals with epilepsy who do not have TSC.

Recommendations for EEG

- Baseline EEG at the time of the TSC diagnosis even if there is no history of seizures
- Those with abnormal EEGs and symptoms associated with TAND should have a follow up 24 hour video EEG study to evaluate for subclinical/electrographic or subtle seizures
- Video EEG is helpful when the seizure semiology is unclear, unexplained changes in sleep pattern, behavior or cognitive or neurologic function.

Infantile Spasms Resources

- Infantile Spasms Action Network (ISAN)



Features if Infantile Spasms

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- They occur most often in the morning or after a nap, last from less than a few seconds to up to 10 seconds—and can occur in clusters of 2 to 100 at a time.
- Spasms, which are a type of seizure, involve sudden, uncontrolled movements, including:
  - Bending or bowing from the waist when sitting
  - Nodding or bobbing the head forward over and over
  - Stiffening the neck, trunk, arms, and legs, or extending them out
  - Bringing up the knees when lying down
  - Wrapping the arms across the body like the child is hugging themselves

Infantile Spasms Resources

- TS Alliance· IS video (http://www.youtube.com/watch?v=35wRjuvg9MI)
- NINDS: https://www.infantilespasms.org
- Infantile Spasms Awareness: https://infantilespasmsinfo.org
- American Epilepsy Society: http://www.aesnet.org
- Telemedicine
  - Check with your health insurance for specifics on coverage
    - During COVID-19 most are covering TM visits until 6/1/2020
  - Ask your PCP and Specialists if they offer TM visits
    - Go to quite place for TM visit
    - Weigh your child before the visit
    - Medication list and refills or PA needed

- **Questions**