

ESETT ELIGIBILITY OVERVIEW

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Eligibility

- Age
- Convulsive Status
- Benzos
- Not excluded

Eligibility

- Age
 - 2 years to < 18 years (Pediatric)
 - 18 years to 65 years (Adult)
 - > 65 years (Geriatric)

Eligibility

- Convulsive status
 - Generalized tonic clonic
 - May have started focally, then generalized
 - May have been generalized but patient remains unconscious and exhibiting focal convulsions (i.e. motor activity)
 - Unresponsive to pain (no pseudoseizures please)
 - At least 5 minutes in total duration

Eligibility

- Benzos

- Adequate dose

- Diazepam
 - Lorazepam
 - Midazolam

- Within last 5-30 minutes

- At least 5 minutes ago
 - Not more than 30 minutes ago

- Prehospital meds count (including home meds)

| | Adult (≥ 40 kg) | Child (< 40 kg) |
|-----------|-----------------------|--|
| Diazepam | 10 mg | 0.3 mg/kg IV |
| Lorazepam | 4 mg | 0.1 mg/kg |
| Midazolam | 10 mg | 0.3 mg/kg IM 0.2 mg/kg IV |

Eligibility Summary

- The 5:30 rule
 - At least 5 minutes of convulsive activity
 - Last benzos at least 5 minutes ago
 - Last benzos not more than 30 minutes ago

Eligibility

- Excluded

- Known pregnancy
- Prisoner
- Patient opted out of study
- Already treated with a second line agent
- Already sedated/paralyzed/intubated
- Acute traumatic brain injury
- Post cardiac arrest/anoxic seizures
- Known metabolic disorder
- Known liver disease
- Known severe renal disease
- Hypoglycemia (<50) or hyperglycemia (> 400)
- Known allergy to FOS, LEV, VPA

Ethics/regulatory considerations

Efficacy confounders

These diseases are different

Drug toxicity/metabolism

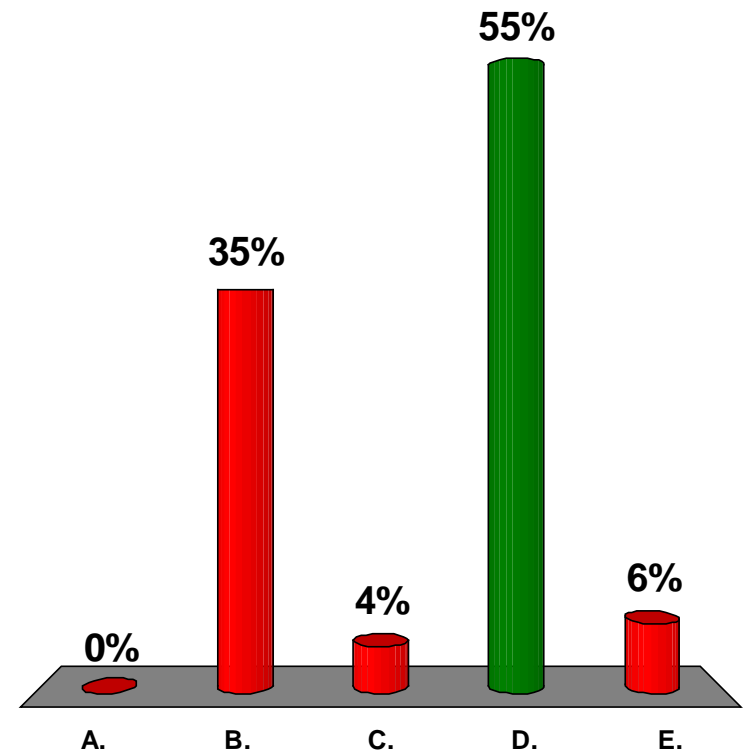
Treatment is glucose management



Let's Review: Vignette # 1

A 2 y.o. male began seizing at home (generalized TC). Parents gave Diastat 10 mg rectally and EMS gave 2 mg of midazolam (Versed) IM. He has not woken yet and on ED arrival he has rhythmic twitching of the left hand and forearm. With regard to his eligibility,

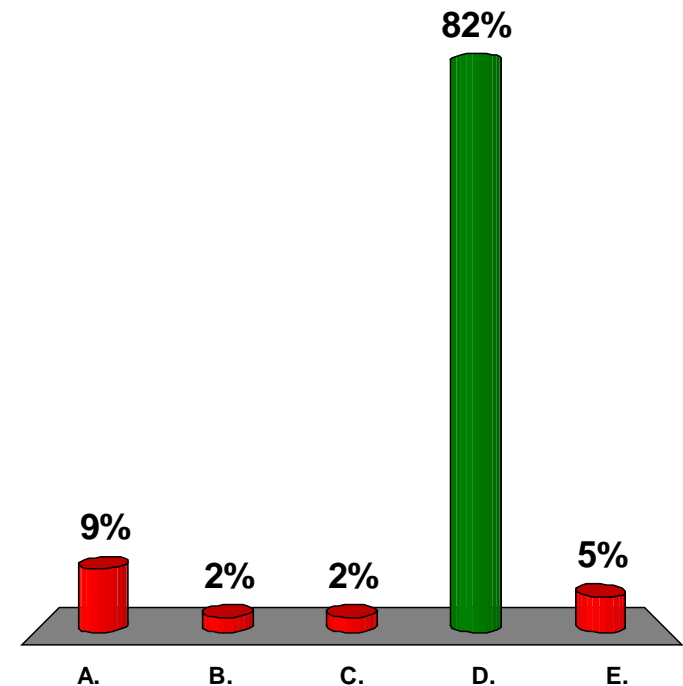
- A. He is not eligible because he is too young
- B. He is not eligible because he did not receive enough benzodiazepines
- C. He is not eligible because he is not in status
- D. He is eligible for enrollment and should be randomized
- E. He is not eligible because his seizures are focal only



Let's Review: Vignette # 2

A 2 y.o. male began seizing at home earlier in the day. Parents gave Diastat 10 mg rectally and EMS gave 2 mg of midazolam (Versed) IM en route. He has been seizure-free in the ED for one hour. He starts to have generalized TC seizures. With regard to his eligibility,

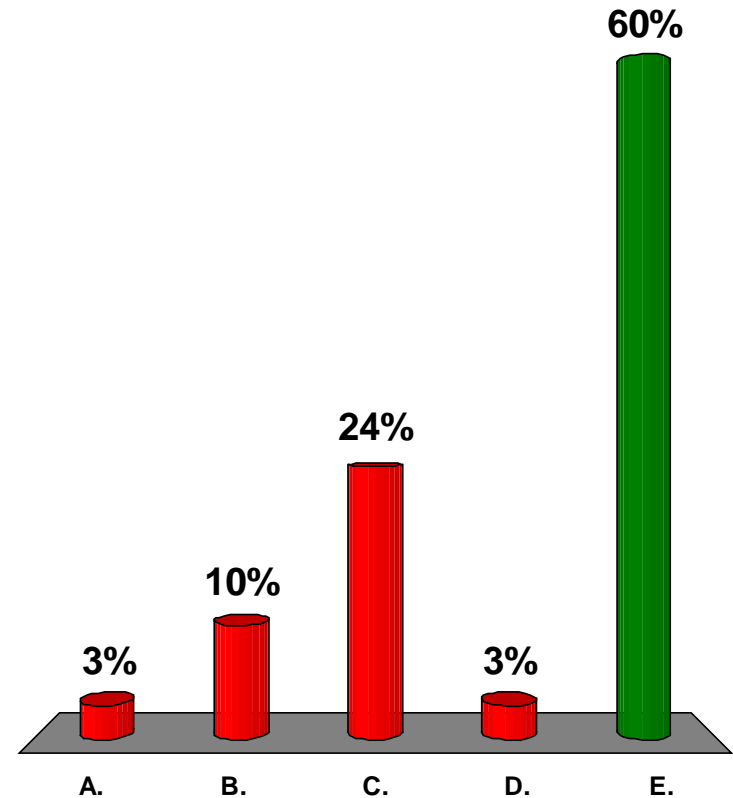
- A. He is not eligible until he seizes for at least 5 minutes
- B. He is not eligible because he did not receive enough benzodiazepines
- C. He is not eligible because his benzodiazepines were too long ago
- D. A & C
- E. B & C



Let's Review: Vignette # 3

A 2 y.o. male began seizing at home earlier in the day. Parents gave Diastat 10 mg rectally at 5 minutes. No additional meds given in ambulance. He arrives at the ED actively convulsing 40 minutes after seizure onset.

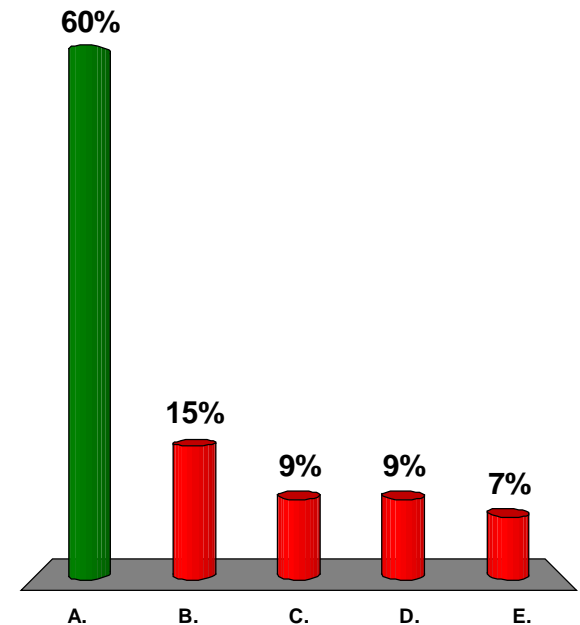
- A. He is eligible because continues to have seizures despite diazepam and should be randomized.
- B. He is not eligible because he only received rectal diazepam and needs to receive a dose of IV or IM benzodiazepenes before being eligible
- C. He is not eligible because his benzodiazepines were too long ago
- D. He is not eligible because he is too young
- E. B & C



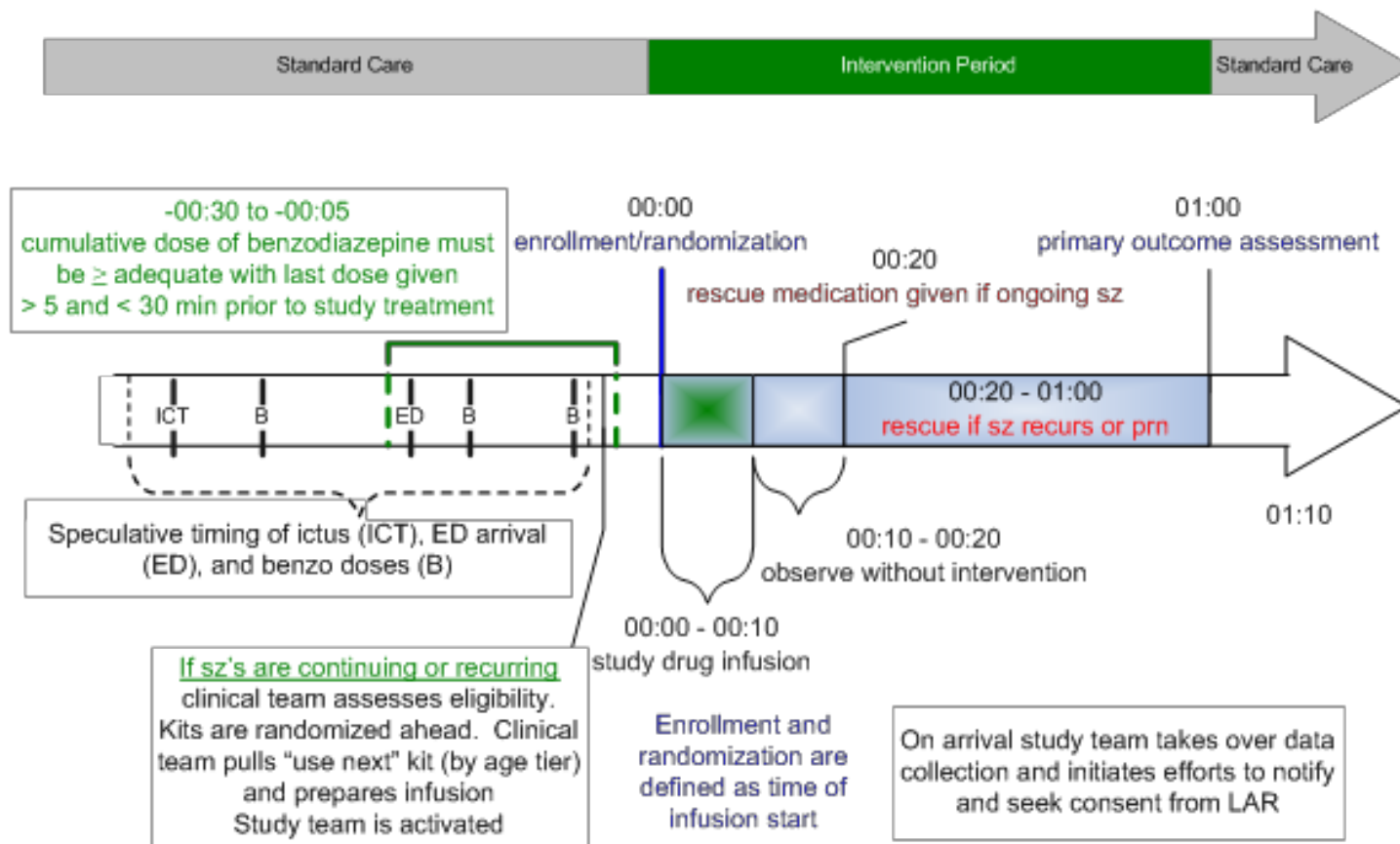
Let's Review: Vignette # 4

A 6 year old male with Lennox-Gastaut arrives in the ED with repeated brief convulsions with no recovery in between. Child is currently on Valproate, leviteracetam and clobazam. He is well known to ED staff with multiple visits, often in setting of intercurrent illness. Parents gave 10 mg rectal diazepam gel at home and he received 7.5 mg of midazolam IM in route. He is witnessed to still have brief 30-45 sec convulsions in ED without recovery in between.

- A. He is eligible because continues to have seizures despite diazepam and midazolam and should be randomized.
- B. He is not eligible because he is on valproate and leviteracetam
- C. He is not eligible because he is not in status
- D. He is not eligible because Lennox-Gastaut is not a localization related epilepsy
- E. B & C



Enrollment Overview



Enrollment

- Page the Study Team
- Use estimated weight if unknown (Broselow, etc)
- Open the **“Use Next” Box** for correct age group
- Start the **Protocol Assist Device**
- Use the **Dosing Chart** to draw up medication
- Second nurse confirm correct volume
- IV or IO route
- Use pump to deliver over 10 minutes
- Maintain usual care (monitoring, etc.)

**Dosing chart
will show this
side**

Dosing

| Subject Wt (kg) | Infusion Vol. (mL) | Infusion Rate (mL/min) over 10 min | FOS dose (mg) | LEV dose (mg) | VPA dose (mg) |
|-----------------|--------------------|------------------------------------|---------------|---------------|---------------|
| 7.5 | 9 | 0.9 | 150 | 450 | 300 |
| 10 | 12 | 1.2 | 200 | 600 | 400 |
| 12.5 | 15 | 1.5 | 250 | 750 | 500 |
| 15 | 18 | 1.8 | 300 | 900 | 600 |
| Etc. | | | | | |
| ≥75 | 90 | 9 | 1500 | 4500 | 3000 |

Enrollment and Dosing

Open study box
remove study drug



Estimate weight:
Use Broselow like
tape if necessary



| Wt. (kg) | Vol. |
|----------|------|
| 7.5 | 9 |
| 10 | 12 |
| 12.5 | 15 |
| 15 | 18 |
| 20 | 24 |
| 25 | 30 |
| 30 | 36 |
| 35 | 42 |
| 40 | 48 |
| 50 | 60 |
| 60 | 72 |
| 70 | 84 |
| 75 | 90 |
| >75 | 90 |



Connect to
patient IV
catheter



Dial
appropriate
volume in the
infusion
pump. Press
start

Enrollment

- T_0 = start of study drug infusion
- T_{10} : medication should be finished
- T_{20} : assess patient for ongoing status
 - Clinical status persists \rightarrow treatment failure \rightarrow treat with another agent, intubate, etc.
 - Clinical status stopped \rightarrow assess responsiveness and wait for patient to recover
- T_{60} : primary outcome determination

Continuous EEG

- If this is part of your hospital's usual care
- Secondary study

Vignettes for enrollment?

- IV falls out/infiltrates at T5 minutes
- Assist device fails
- Patient still in status at 20 minutes and study team has not arrived yet
- Cannot reach study team at all
- Patient becomes apneic at 10 minutes

Questions