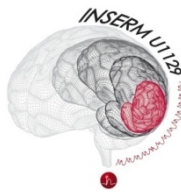


# Extrapolation for antiepileptic drugs (AED) in pediatrics

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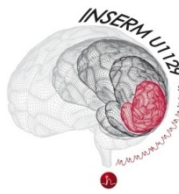
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# Need for AED development in pediatric epilepsies

- 30% of pediatric epilepsies still pharmacoresistant
- 50% of them with cognitive/behavior impact
- 90% of them with schooling/social impact
- Pharmacoresistance more frequent in infants
- Early treatment may prevent pharmacoresistance
- Need for monotherapy (2 new AEDs approved before 6y compared to 7 in adults)

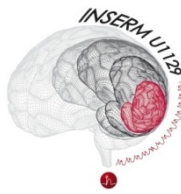
# Main pediatric epilepsy conditions



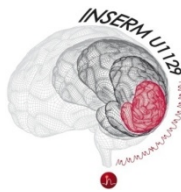
Epilepsy type	Age of onset	Frequency	Prognosis	Seizure types	New AEDs approved
<b>Focal Epilepsies</b> - BECTS* - <b>other E with POS</b>	2-10y Any	Frequent Frequent	Good <b>+ Severe</b>	Simple POS POS	1 5 ( <b>1 under 2y</b> )
<b>Idiopathic generalised epilepsies (IGE)</b> - Childhood absence E - Grand mal	2-10y Adolesc.	Frequent ± Frequent	± Good ± Good	Absences GTCS***	2 2
<b>Epileptic encephalopathies</b> - West syndrome - Dravet syndrome - <b>Lennox-Gastaut synd</b> - Myoclonic-astatic E - CSWS** - Rasmussen disease	Infant Infant 2-10y 2-10y 2-10y 2-10y	Rare Rare Rare Rare Rare Rare	<b>Severe</b> <b>Severe</b> <b>Severe</b> <b>Severe</b> <b>Severe</b> <b>Severe</b>	Infantile spasms GTCS/myoclonia Tonic/absences GTCS/myoclonia POS/myoclonia POS/myoclonia	<b>1</b> <b>1</b> 4 <b>0</b> <b>0</b> <b>0</b>
<b>Neonatal seizures</b>	Neonate	Frequent	<b>Severe</b>	any	<b>0</b> (except VGB)

\* Benign E with centro-temporal spikes, \*\* Continuous slow waves during sleep, \*\*\* Generalised tonic-clonic seizures

# Conditions with possible extrapolation



- **Efficacy:** when epilepsy type is similar in adults and children (no additional pediatric RCT needed)
  - Epilepsy with POS, over 2y, as adjunctive therapy
  - Epilepsy with POS (no BECTS), over 2y, as monotherapy
  - Lennox-Gastaut syndrome, as adjunctive therapy
  - *[Idiopathic generalised epilepsy, as adj.&monotherapy]*
- **PK/optimal dose:** modelling/simulating from adult trials (provided the maturational factors are known)
  - Any pediatric epilepsy
  - Any age (including neonates=modeling from older ages)
  - Adjunctive and monotherapy



# Conditions without possible extrapolation

- **Efficacy:** when epilepsy type is different in adults and children or does not exist in adults
  - Epilepsy with POS, under 2y
  - All epileptic encephalopathies other than Lennox-Gastaut syndrome
  - Neonates
- **PK/optimal dose:** when modeling from adults/older pediatric ages is not possible because the maturational profile of the drug of interest is not known
- **Safety**