

Sudden Unexpected Death in Epilepsy (SUDEP): 10 Misconceptions

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Misconception 1: SUDEP is RARE

- Premature mortality: 11x odds ratio (Fazel et al, 2013)
- Childhood onset
 - In childhood, most die from underlying disorder
 - Peds 40 year followup: 55% died from epilepsy (Sillanpaa & Shinnar, 2010)
 - SUDEP (35%)seizure/status – 45%, Drowning 10%
- Sudden death >27x in people with epilepsy (Holst et al, Epilepsia, 2013)
- Odds ratio of death in epilepsy patients (Fazel et al, 2013):
 - Natural causes 15.5x (mainly SUDEP and Status)

Misconception 2: SUDEP = Seizure/Epilepsy Related-Mortality

Deaths directly due to epilepsy

Sudden unexpected death in epilepsy

Status epilepticus

Drowning

Motor vehicle accidents

Falls, burns, and other seizure-related accidents

Deaths due to acute symptomatic seizures⁵⁹

With or without status epilepticus, occurring within 1 week of stroke, traumatic brain injury, anoxic encephalopathy, or intracranial surgery

First identification of subdural hematoma or CNS infection

Active phase of multiple sclerosis or other autoimmune disorders

Deaths indirectly due to epilepsy

Aspiration pneumonia

Suicide

Cardiovascular disease that may be exacerbated or caused by antiseizure drugs

Deaths due to underlying neurologic disease

Brain tumor

Stroke

Metabolic/genetic and neurodegenerative diseases

Misconception 2: SUDEP = Seizure/Epilepsy Related-Mortality

- Low SES groups: young adults die ~17 years prematurely (Kaiboriboon et al, 2013)
 - This excludes bronchopneumonia (RR 7.2), suicide (RR>3x), etc (Cockerall et al, Lancet 1994)
- Odds ratio of death in epilepsy patients (Fazel et al, 2013):
 - External causes 3.6x; 75% have psychiatric comorbidity
 - Suicide 3.5 – 5 x
 - Vehicular 1.4x
 - Drug poisoning 5.1x
 - Fall 8.5x
 - Drowning 7.7x
 - Assault 2.8x

Misconception 3: SUDEP Affects Drug-resistant Adult Patients

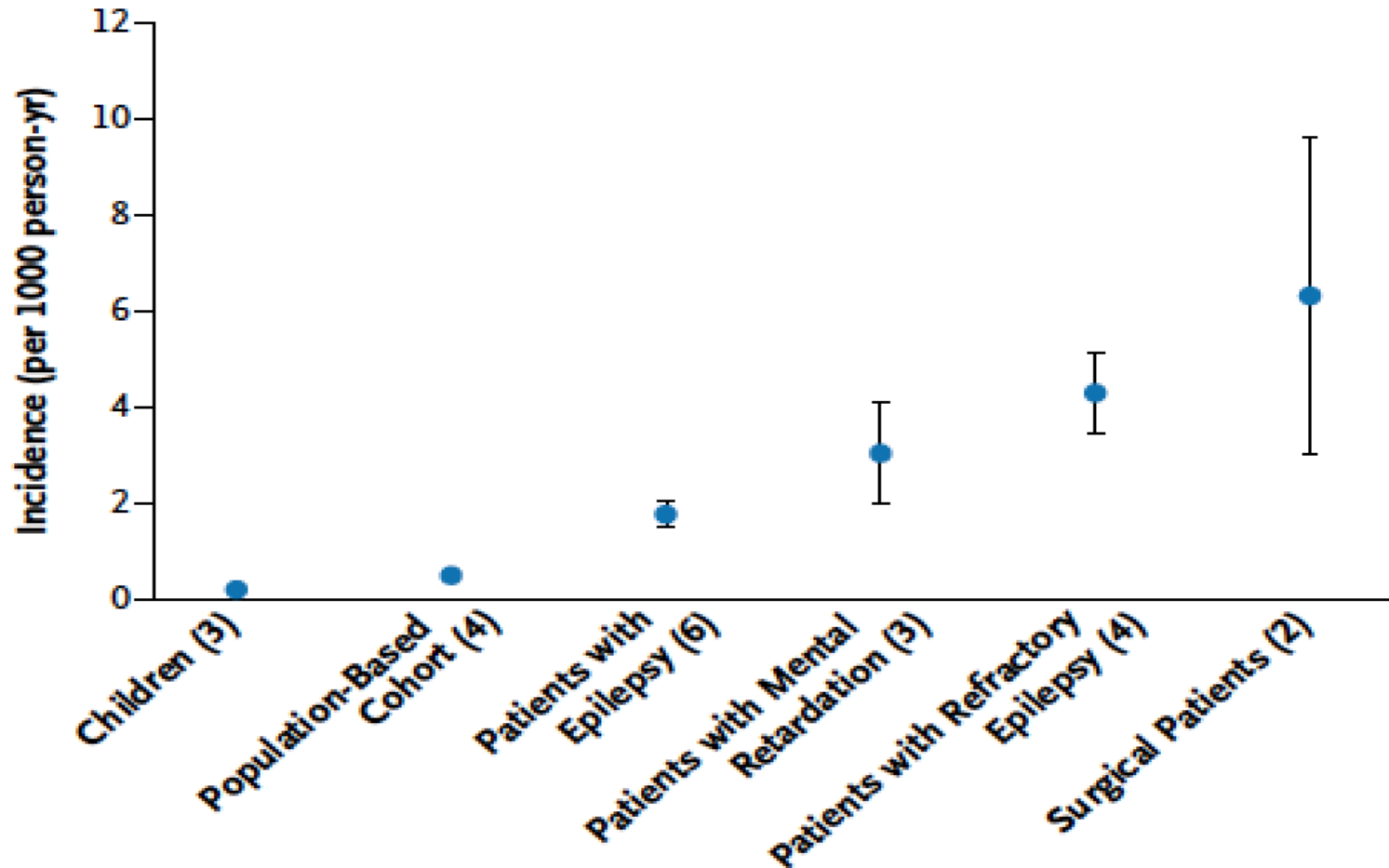


Figure 1. Incidence of Sudden, Unexpected Death in Epilepsy According to Population Type.

Rare in Kids?

- Sweden – all deaths in 2008
 - 99 SUDEPs (49 def, 19 prob)
 - SUDEP: 5.2% of deaths; 36% among 0-15 years
 - Definite/probable SUDEP: 1.2/1000 person-years:
M 1.41 > F 0.96
 - <16: 1.11; 16-50: 1.13; >50 1.29
- Ontario – 2014-15
 - Pediatric SUDEP 1.17 per 10000

Sveinsson et al, Neurology 2017; Keller et al, Neurology 2018

Benign Epilepsy with Centro-Temporal Spikes (BECTS)?

- 3 children, ages 9-13, diagnosed with BECTS among 189 NASR cases.
- 2 definite, 1 probable SUDEP.
- Independent confirmation of BECTS diagnosis
- No patients on antiseizure drugs: either physician recommendation or mutual physician-parental decision.
- All died in bed during sleep.
- Cases spanned BECTS severity spectrum

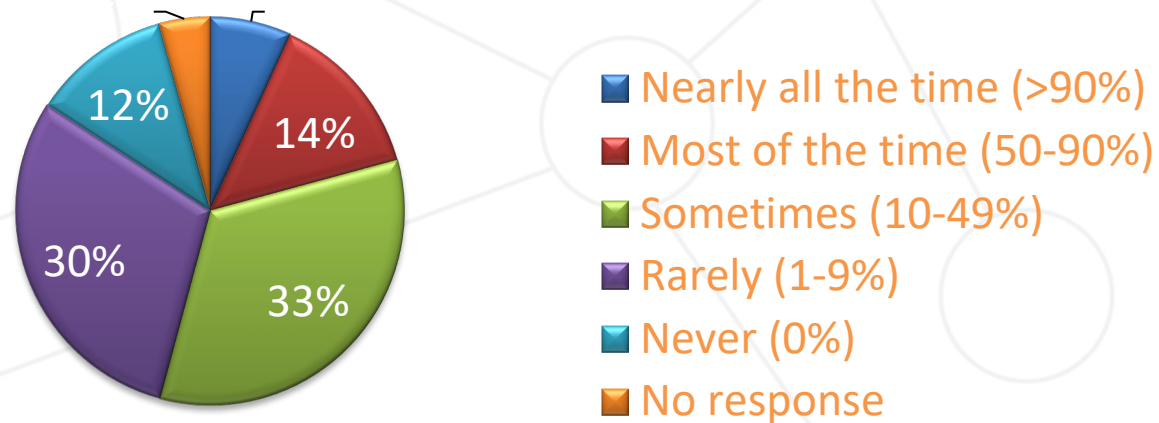
Doumlele et al, JAMA Neurology 2017

Misconception 4: Neurologists Learn & Talk About It

- 169 U.S. & 171 Latin American, EU. Asian. African neurology residents surveyed
- Know risk factors: 67% non-US vs. 61% US
- Understand prevention: ~60%
- ~50% rarely or never counseled patients
- <45% of U.S. and international trainees were educated about SUDEP

Misconception 4: Neurologists Learn & Talk About It

12% never do; 21% talk about it >50% of the time



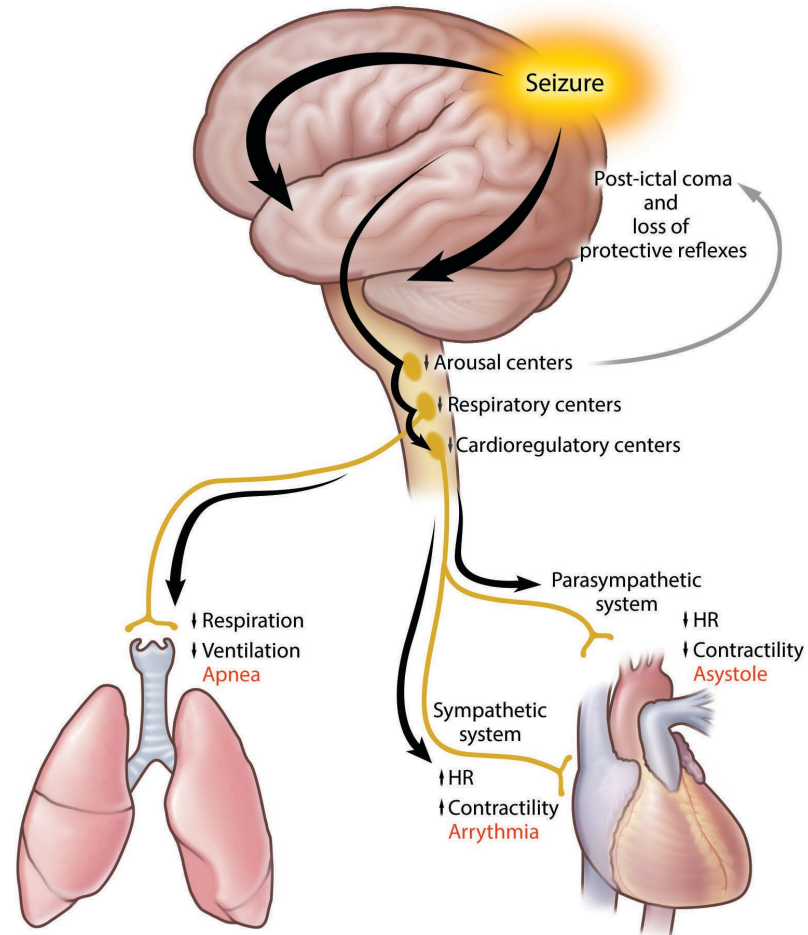
Freidman, et al., 2014

2017 NASR Series of 138 SUDEPs: 18% of Next-of-kin told about SUDEP Louik et al, 2017

Misconception 5: SUDEP

Mechanisms Are Understood

- Terminal convulsive seizure in sleep → death
- Genetics?
- Environment?



Friedman et al, JCI 2013

Misconception 6: SUDEP Is a Single Entity

- 2/3 in sleep but NOT ALL
- Most follow seizures, usually convulsive; some have been recorded without a preceding Sz
- Some drug-resistant patients survive 100's of convulsive Sz
- Some people die after their first or second Sz
- Laryngospasm likely a rare cause

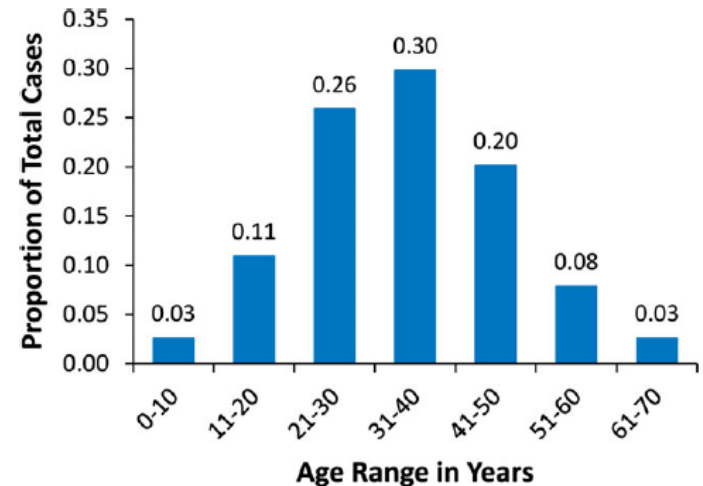
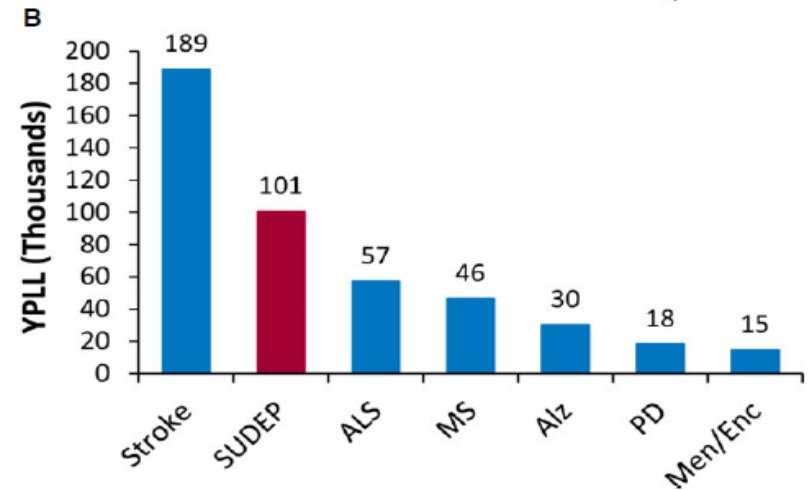
Misconception 7: SUDEP Epidemiology is Well Defined

Among Neuro Disorders:
SUDEP – 2nd leading cause of years of potential life lost (YPLL)

Epilepsy-related mortality is #1 cause of YPLL
(Accident, drowning, suicide)

Estimated annual U.S. SUDEPs — 2,750

An underestimate - cases not accounted for (elderly, children with progressive disorders, alcohol or drugs)



Misconception 8: SUDEP Can Always be Prevented

SUDEP can occur in medical setting or ICU with attentive medical care

Misconception 9: SUDEP Cannot be Prevented



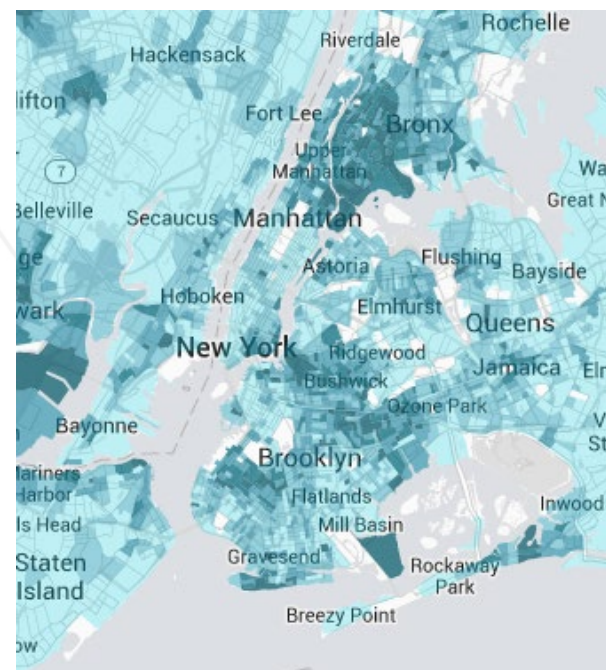
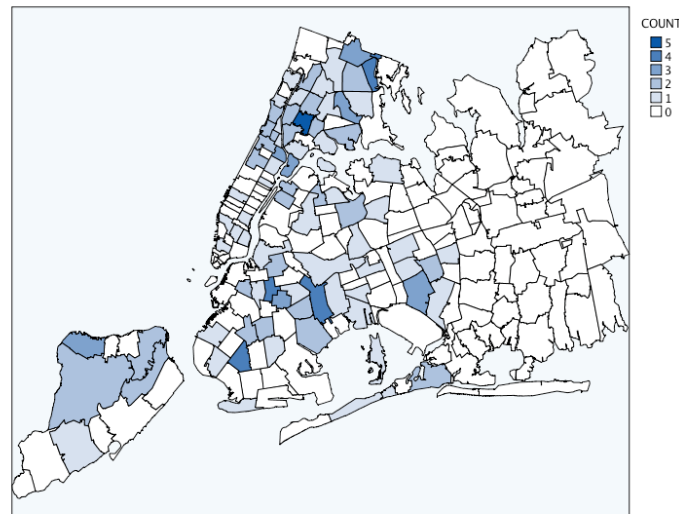
- Seat belts: Tell A Teenager:
 - 1/3.5 million person trips kills → NO change in behavior
 - Over 50 years, 1% chance of death; 33% of disabling accident → CHANGES behavior
- SUDEP: young adult
 - Well controlled epilepsy: SUDEP risk - 1% per decade
 - Drug-resistant epilepsy; SUDEP risk - 5% per decad

Slovic et al, Risk Analysis 1982; Tomson et al, 2008



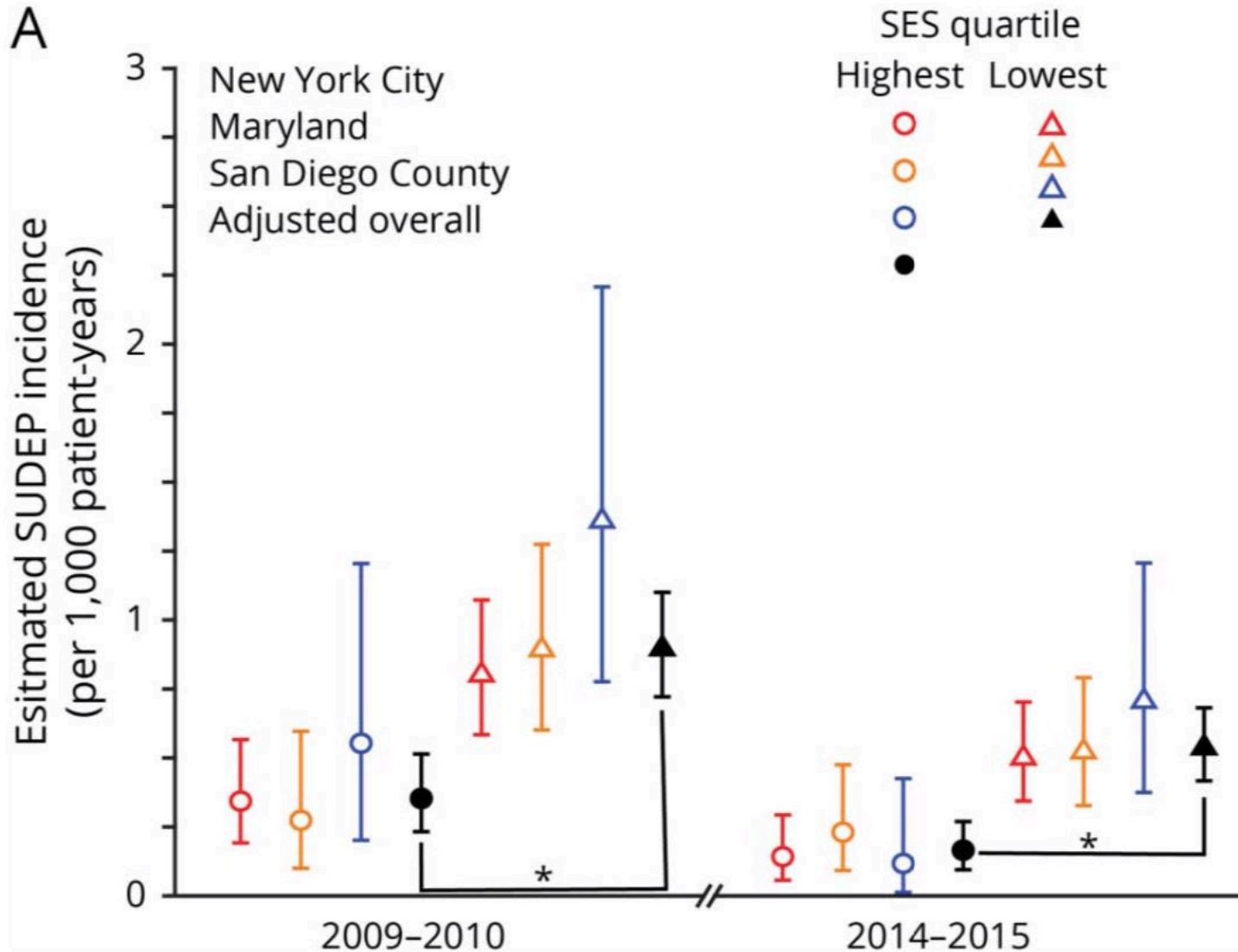
Who Dies from SUDEP?

- Ohio Medicaid – epilepsy prevalence 10x > general pop
Kaiboriboon et al, Neurology 2013
- NYC – ↑SUDEP → ↓SES zipcodes
(Friedman & Brown)
- 2013 NINDS: Disparities
 - \$40 million to ↓ stroke disparities
 - \$0 to ↓ epilepsy disparities
- ? National priorities
 - SIDS 1563/yr - \$>500 Million last 20 years
 - SUDEP > 3000/yr - <\$75 million last 20 years



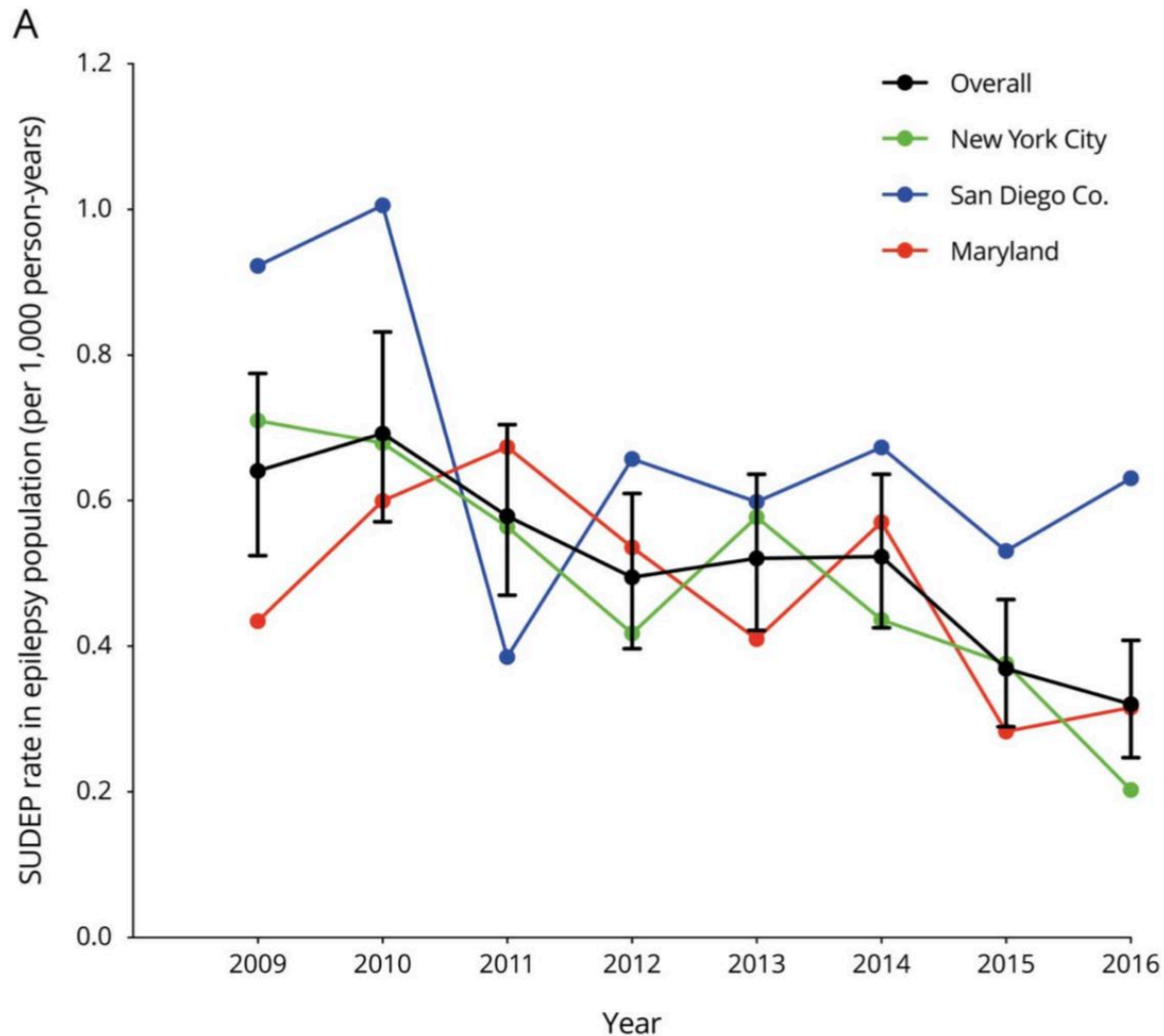
Who Dies from SUDEP?

Cihan et al, 2020



Is SUDEP Becoming Less Frequent?

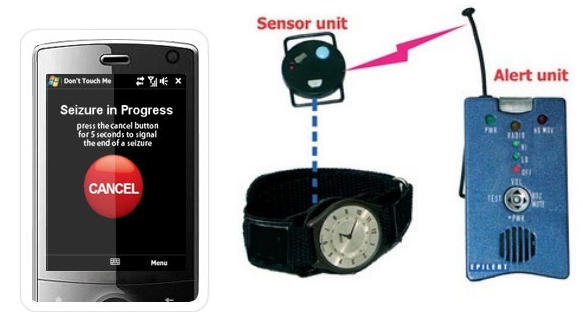
Cihan et al 2020



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Detecting Szs Can Save Lives – Probably!

- Alarms/Detectors
 - Supervision - ↓SUDEP risk (Nashef et al 1997)
 - Unproven in preventing SUDEP
 - Terminal cascade may progress
 - Some SUDEP witnessed in the hospital with immediate medical attention (Swinghammer et al, 2012)
- Anti-suffocation pillows
- Clinical trials difficult
 - Need surrogate end-points to evaluate intervention
 - Defining surrogate endpoints require prospective evaluation of high risk patients



Misconception 10:

Families Can't Make A Difference

Parents and Families have Led the Charge

Funding research

Pushing NIH to fund research

Inform other families

Educate doctors to educate patients

& parents

Educate Med Examiners to recognize

Create NASR, PAME