# Updating SUDEP: Prevention

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SUDEP prevention

BIG CHALLENGE

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# Treatments for the prevention of Sudden Unexpected Death in Epilepsy (SUDEP) (Review)

Maguire MJ, Jackson CF, Marson AG, Nevitt SJ

- early versus delayed pre-surgical evaluation for lesional epilepsy
- educational programmes
- seizure-monitoring devices
- safety pillows
- nocturnal supervision
- SSRIs
- opiate antagonists
- adenosine antagonists

Maguire MJ, Jackson CF, Marson AG, Nevitt SJ.
Treatments for the prevention of SUDEP.
Cochrane Database of Systematic Reviews 2020, Issue 4. Art. No.: CD011792.

# Preventative strategies for SUDEP

Stop SZ

Detect Cardiorespiratory distress

SZ detecting devices

Prevent airway obstruction

Reduce central hypoventilation

# Preventative strategies for SUDEP

# Effective seizure control

- Appropriate AED
- Timely presurgical evaluation
- Surgery in candidates meeting the surgical criteria

# Appropriate AED

- A meta-analysis of adult patients with refractory[1]:
  - add-on AED vs placebo → ↓7x of SUDEP (0.9/1,000 vs 6.9/1000 pt-years)
- Drug compliance and adherence
- Lifestyle modification to avoid SZ triggering factors:
  - sleep deprivation, stress and excess alcohol intake
- Educating them about care plans for SZ clusters
  - rescue medicine
  - home management of SZs


1. Lancet Neurol. 2011;10:961–88
2. Canadian Journal of Neurological Sciences DOI:10.1017/cjn.2020.221

# Epilepsy surgery

- Timely refer for presurgical evaluation
- Some studies → ↑risk of SUDEP in patients who have failed surgery.
- Patients failing temporal lobe surgery → epileptogenic zone involving extratemporal regions → control cardiorespiratory functions → ↑risk of SUDEP post surgery

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-Canadian Journal of Neurological Sciences DOI:10.1017/cjn.2020.221

# Misconception Re; Epilepsy surgery

| Misconception | Fact |
|---|---|
| Many drugs need to be tried. | After failing 2 AEDs, the chance of SZ remission is very low. |
| Multiple or diffuse lesions on MRI C/I surgery. | The EZ may involve only 1 lesion |
| Bilateral EEG spikes C/I surgery | Bilateral interictal spikes are common in people w/ unilat SZ onset |
| Surgery is not possible if eloquent cortex is involved | Risks and benefits can be evaluated on a case-by-case basis. |
| If there is an existing memory deficit, surgery will worsen it. | Poor memory may improve after surgery. |
| Chronic psychosis C/I surgery. | These individuals may benefit from stopping or reducing SZ. |
| IQ<70 C/I surgery | These individuals may benefit from stopping or reducing SZ. |

Adapted from Vakharia et al. Ann Neurol 2018;83:676-90

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# Seizure-monitoring devices

- Seizure-monitoring devices
  - bed sensors
  - fall alarms
  - tracking devices
- These systems alert caregivers or parents to potential seizure activity, which in turn may prevent SUDEP.

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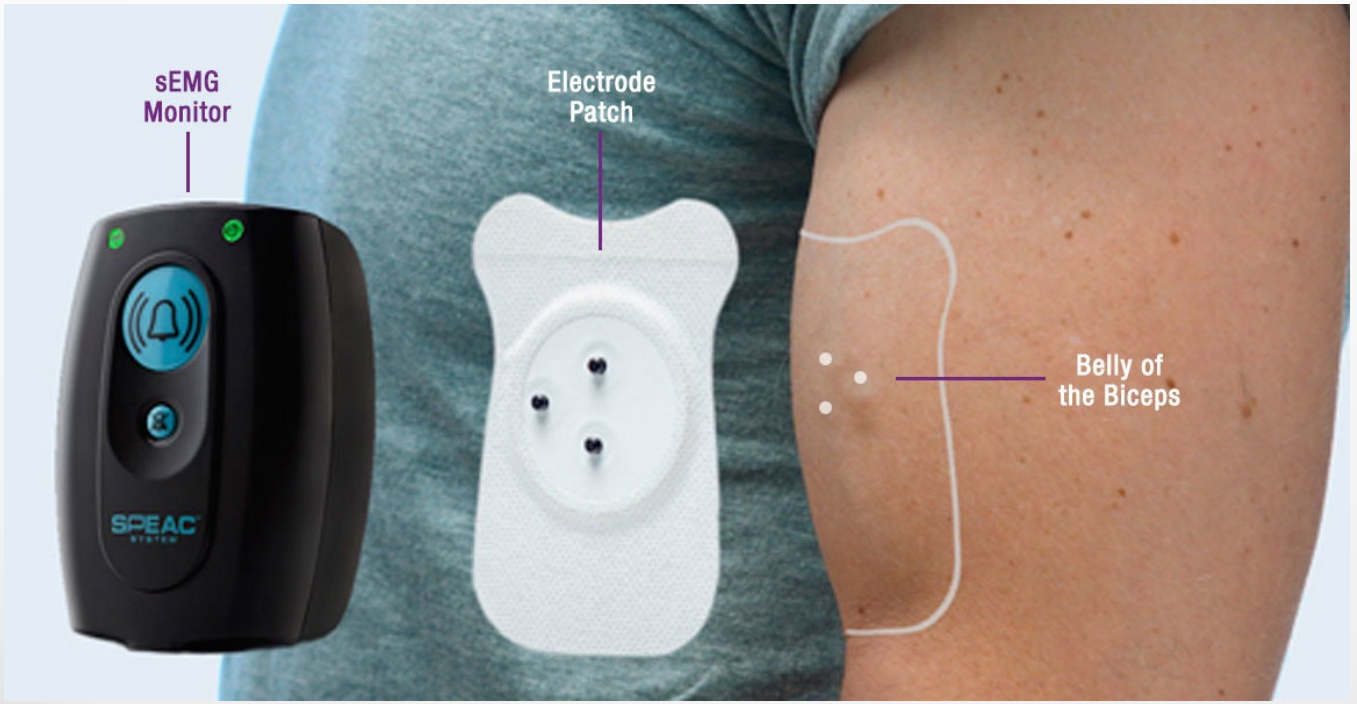
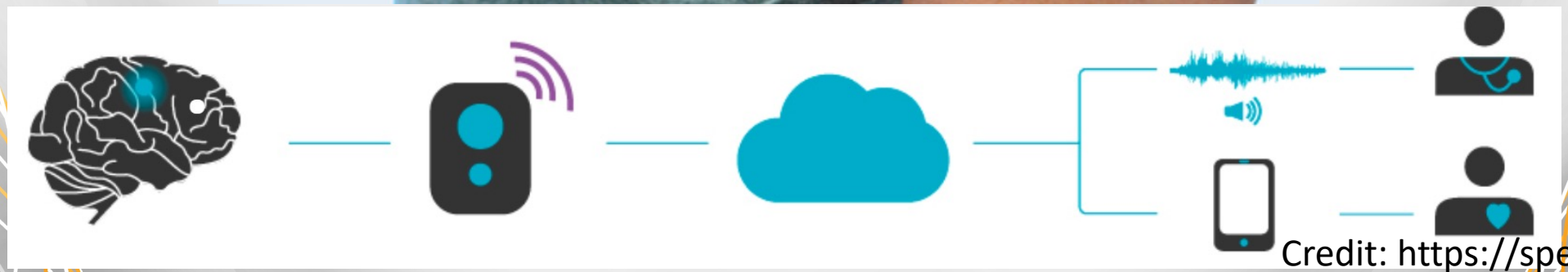
The FDA has approved an mHealth wearable for people living with epilepsy that's designed to detect convulsive seizures and immediately notify care team members.



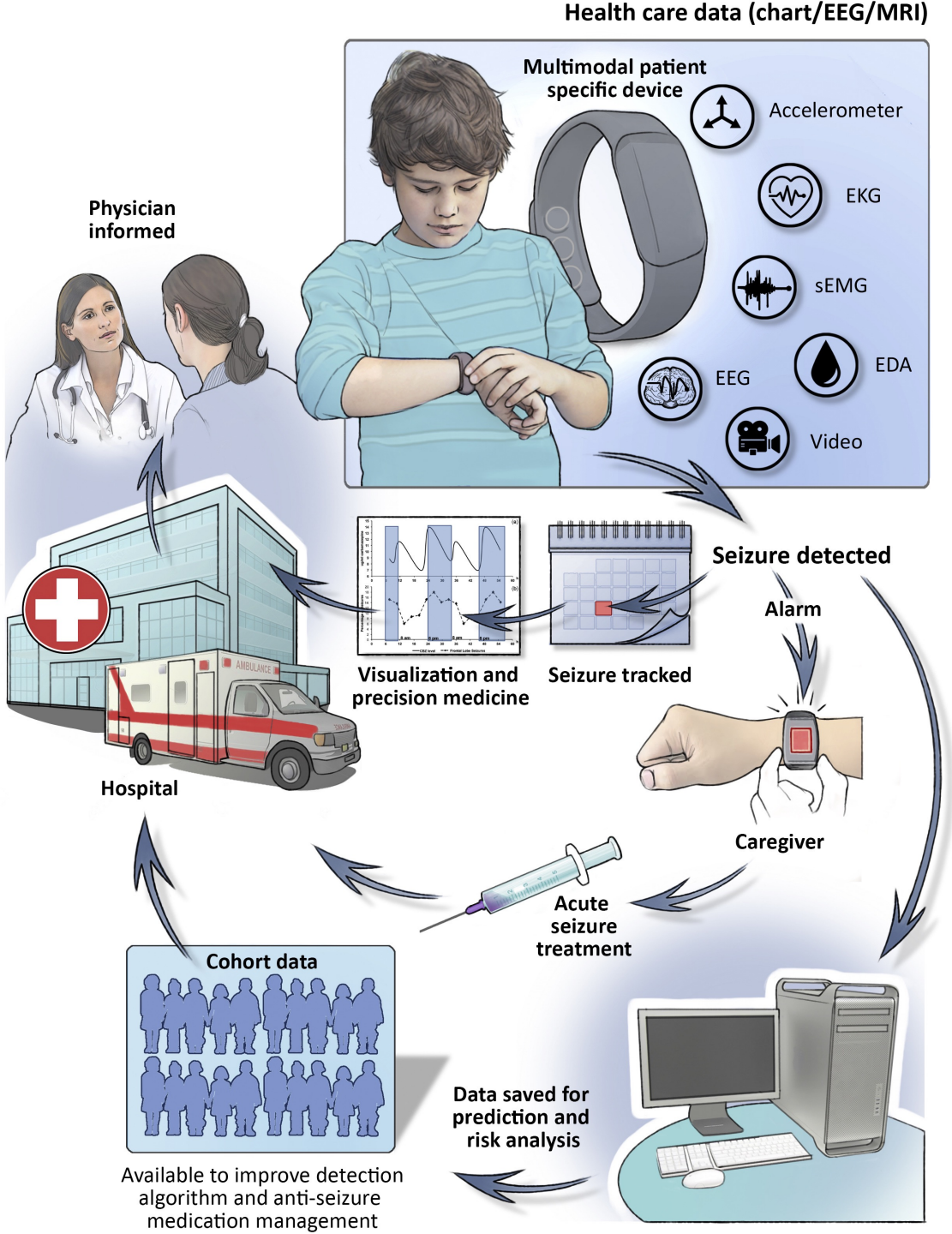
Credit: https://mhealthintelligence.com/
https://www.hcplive.com/

# Seizure-monitoring device



Credit: https://speacsystem.com


Health care data (chart/EEG/MRI)
Multimodal patient specific device
Accelerometer
EKG
sEMG
EDA
EEG
Video
Physician informed
Seizure detected
Alarm
Visualization and precision medicine
Seizure tracked
Hospital
Caregiver
Acute seizure treatment
Cohort data
Data saved for prediction and risk analysis
Available to improve detection algorithm and anti-seizure medication management

# Bed sensor


BED
AIRlert™
BED
PRESSURE MAT
Air-operated bed sensor
Position under Mattress
www.pressuremat.com
Frequency Prec
FREQUENCY PRECISION
airlert
Convulsion Sensor
Wireless Call System
Sensitivity
Bed Mat
Extra Sensor
Fp

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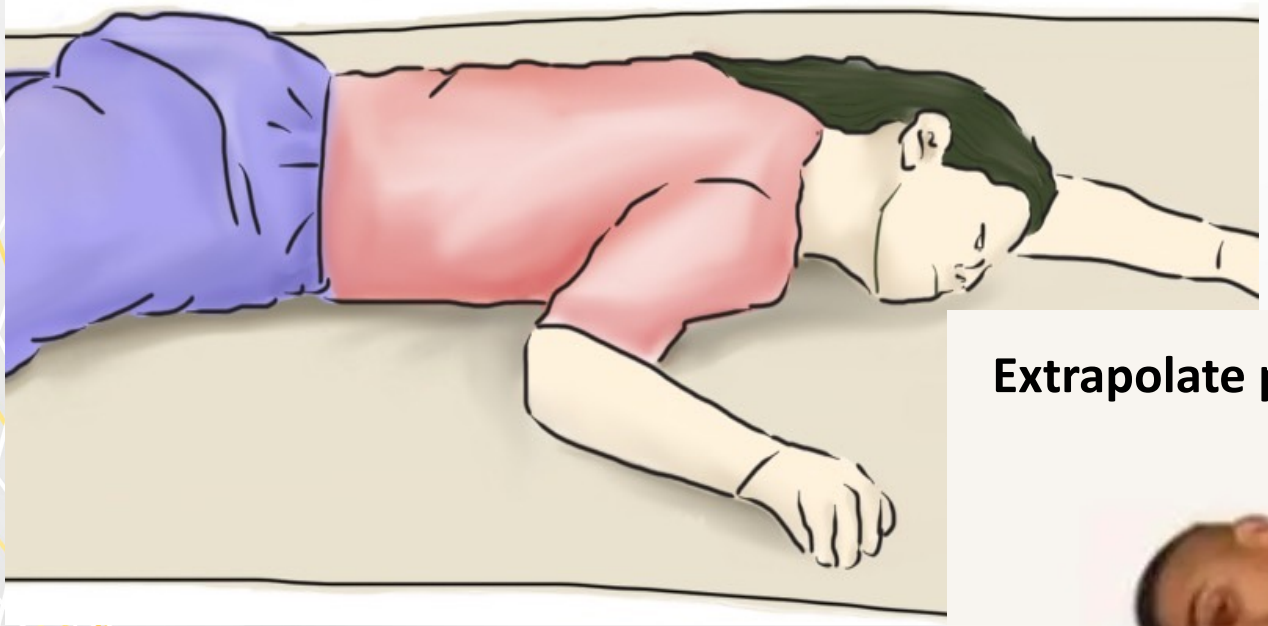
# Prone position

**SUDEP cases are more often found in prone position.**

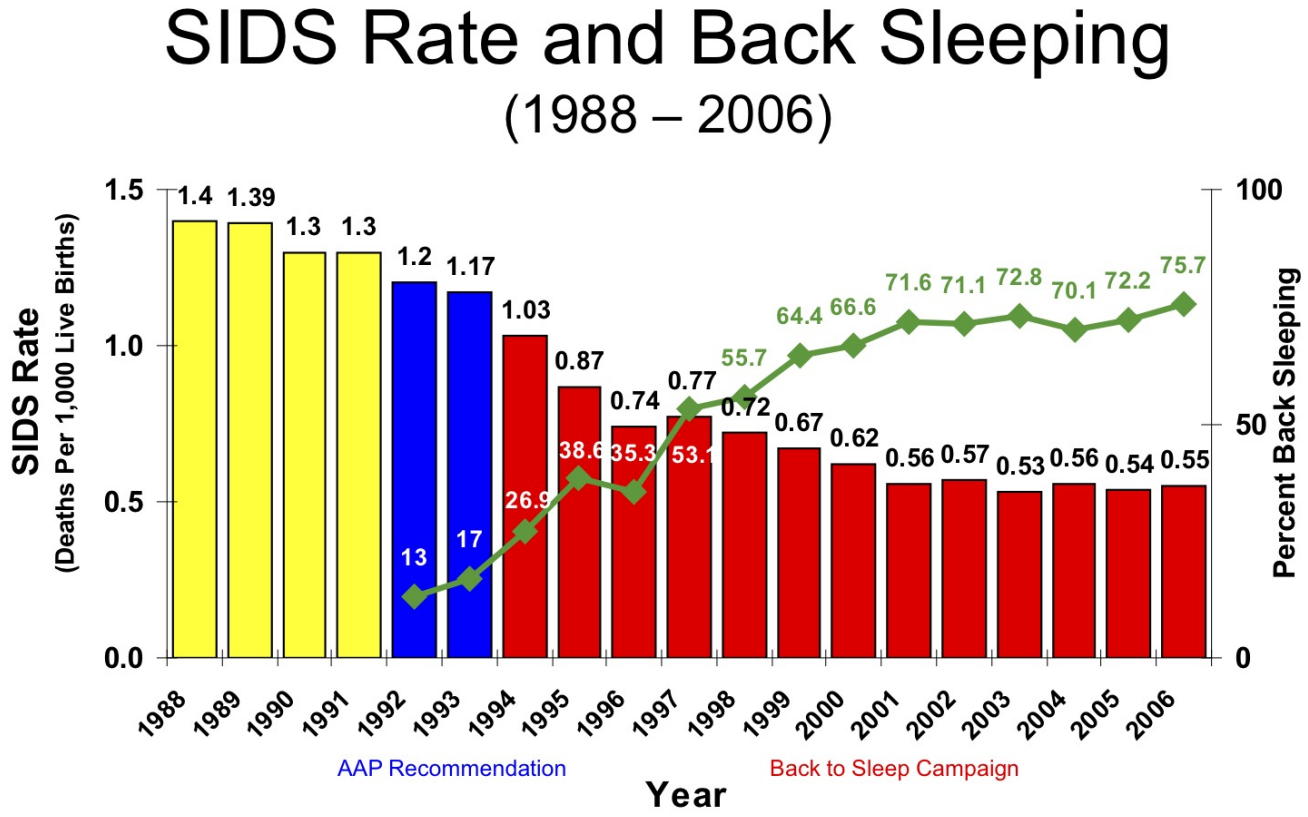


possible mechanism suggested is that turning to prone position during a GTCS followed by post-ictal apnea → obstructive apnea.

**Extrapolate prone position may lead to SUDEP (no evidence)**

- Retrospective study reported → 71% of people who died of SUDEP were in the prone position (Kloster 1999).

# “Back-to-sleep” campaign (safe-to-sleep)

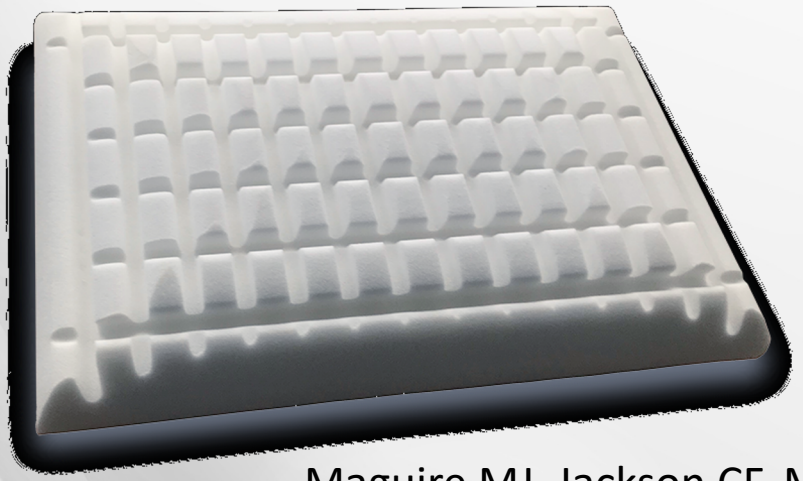



SIDS Rate Source: CDC, National Center for Health Statistics,
Sleep Position Data: NICHD, National Infant Sleep Position Study.



Credit: http://www.nichd.nih.gov/sids

# Safety (anti-suffocation) pillows

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# Nocturnal supervision

- Nocturnal supervision would allow turning of the person from a prone to a recovery position, reducing the risk of respiratory distress and reducing central hypoventilation.
- One case-control study found that nocturnal supervision was protective against SUDEP (Langan 2005).

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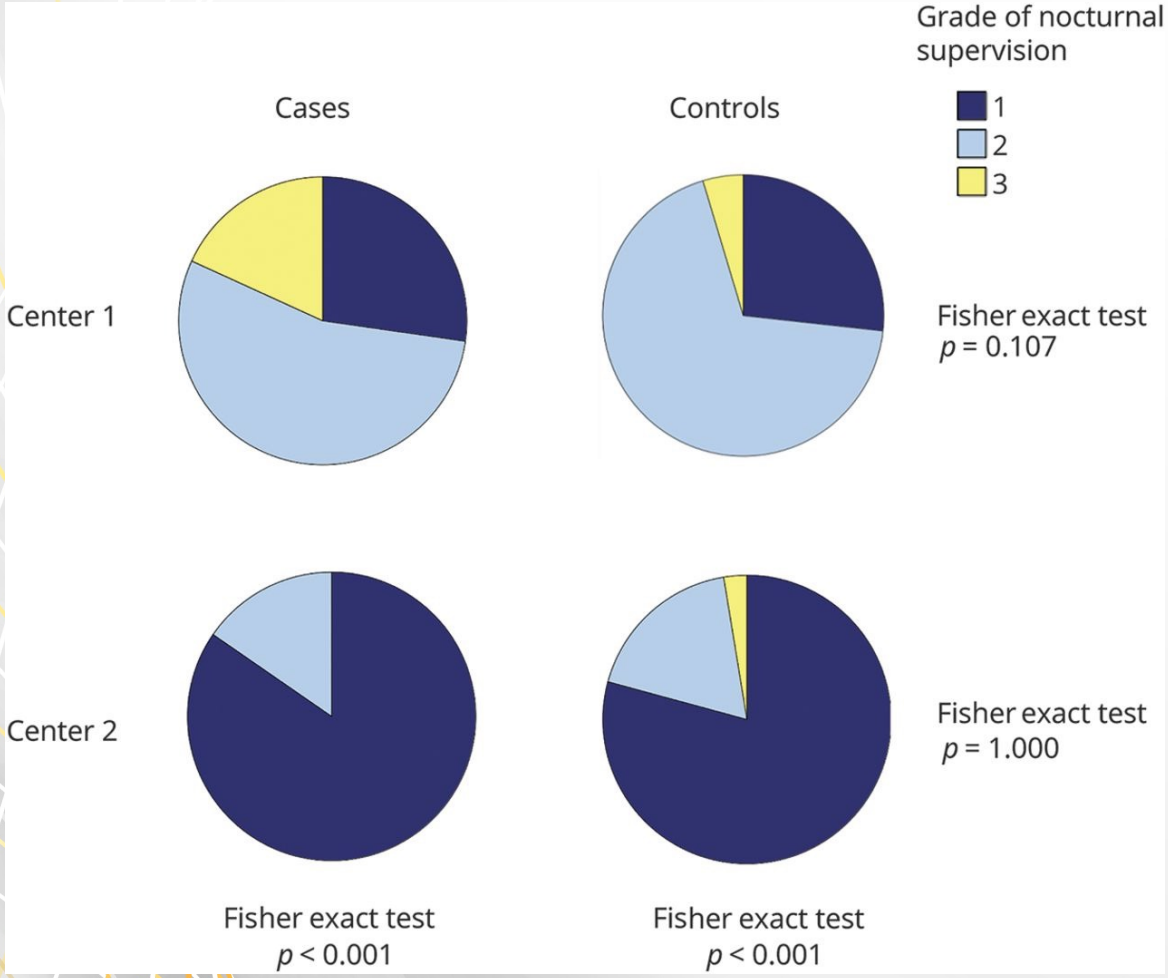
# Nocturnal supervision




1. no supervision
2. a listening device or a roommate or physical checks at least every 15 min
3. 2 of the following: a listening device, roommate, additional device (bed motion sensor/video monitoring), or physical checks every 15 min

## Conclusion

- Different levels of nocturnal supervision may account for some of the difference in incidence.

Neurology® 2018;00:e1-e11.
doi:10.1212/WNL.0000000000006356

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# SSRI

- Lower brainstem serotoninergic nuclei play an important role in the regulation of respiration.
- Serotonin neurons in the brainstem sense rising CO2 and low pH thereby stimulating breathing and arousal.

- The SSRI: fluoxetine → prevent apnea in these mice models.
- A clinical retrospective study: people with video telemetry and taking an SSRI → significantly less ictal/postictal hypoxia.
- ↓duration of hypoxemia and EEG suppression

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# Inhibitors of opiate and adenosine receptors

- may prevent SUDEP by reducing the severity of postictal EEG depression and brainstem dysfunction.
- Caffeine, an antagonist of adenosine receptors, is potentially proconvulsant.
- Naloxone, an opiate receptor antagonist, not a proconvulsant and thus may have a use in preventing SUDEP.
- SZ activity → massive release of endogenous opioids and adenosine which helps in seizure termination.
- But their excessive release can lead to post ictal apnea.

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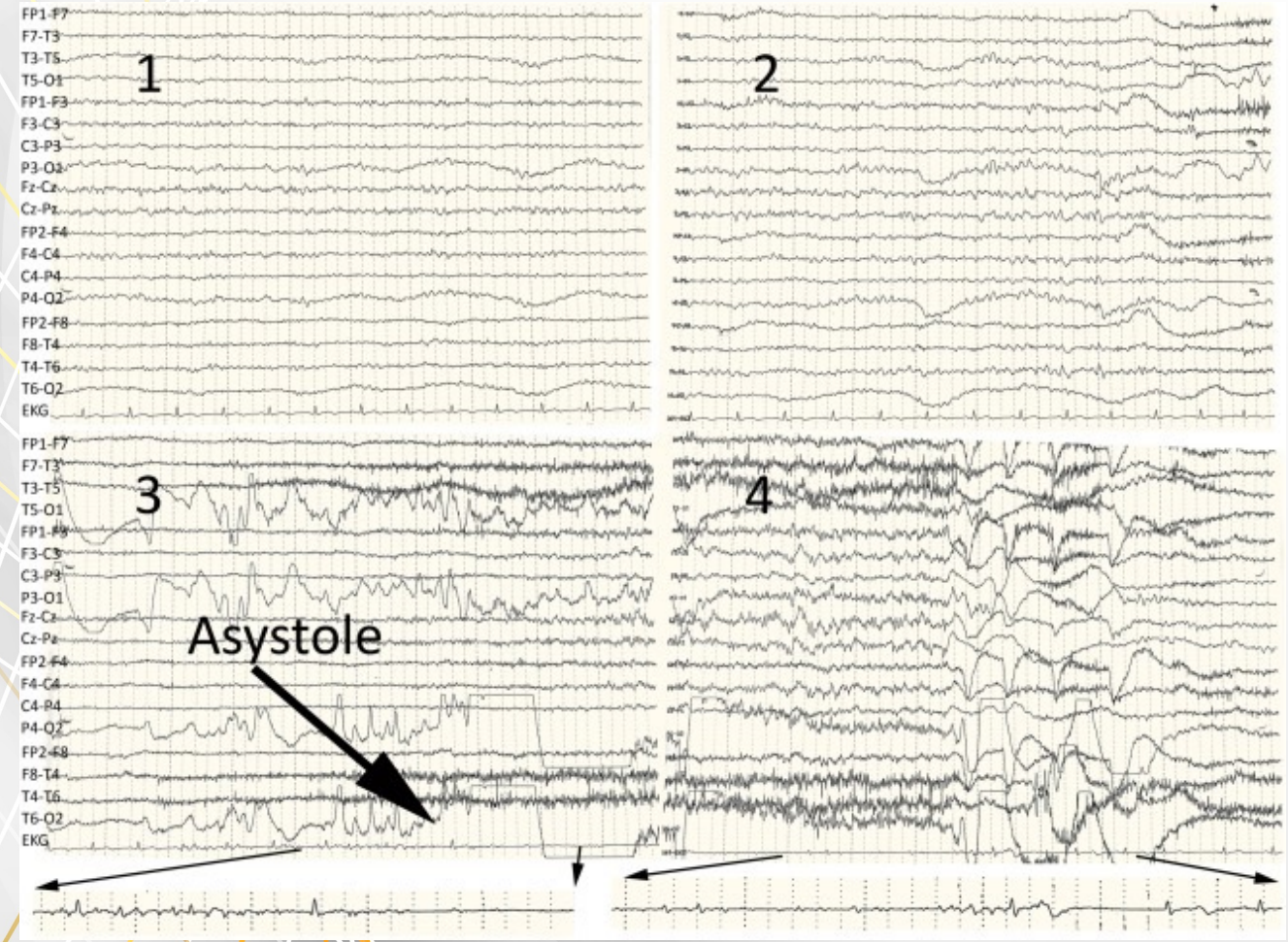
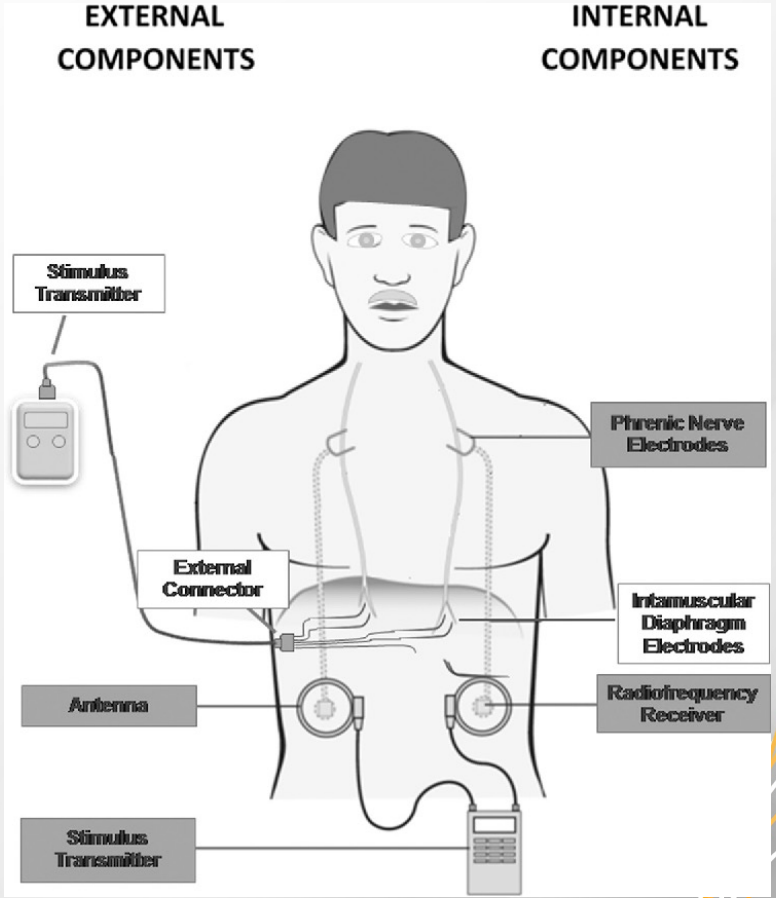
# Cardiac and Diaphragmatic pacing

- Cardiac pacing prevents brain hypoperfusion




- Respiratory failure which might require diaphragmatic pacing or phrenic nerve stimulation



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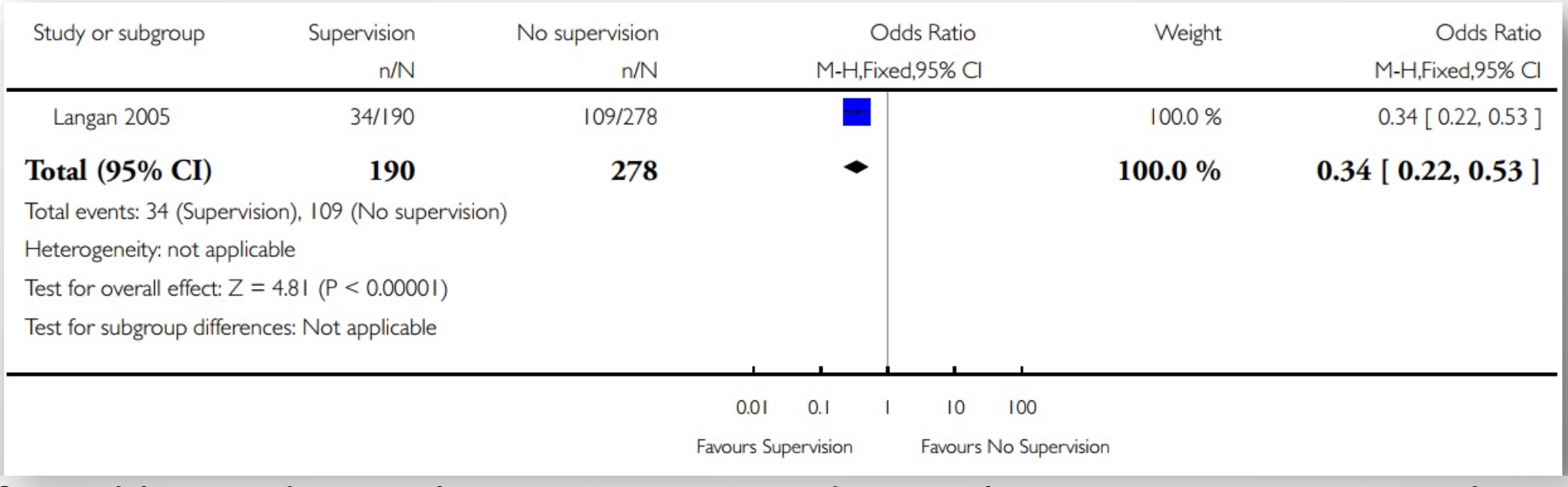


- We found limited, very low-certainty evidence that supervision at night prevents SUDEP.
- Further research is needed to identify if other treatments, such as seizure detection devices, safety pillows, and drug interventions working on serotonin, adenosine, and opiate levels in the brain are effective in preventing SUDEP in people with epilepsy

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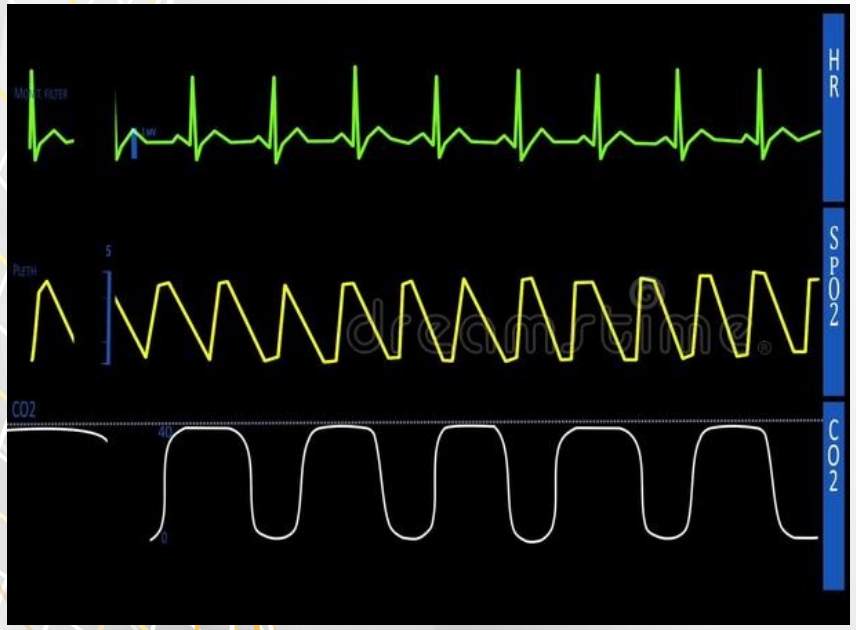
# Preventing SUDEP in epilepsy monitoring unit

- rapid withdrawal in promoting the seizures and associated cardiorespiratory arrest.




# Counselling

**Benefits:**

**Patient and caregivers should know about SUDEP**

**Risks:**

**may lead to panic and anxiety**

Epilepsy Behav. 2017 Feb;67:33-38. doi: 10.1016/j.yebeh.2016.12.001. Epub 2017 Jan 11.

# Sudden unexpected death in epilepsy (SUDEP) disclosure in pediatric epilepsy: An Italian survey on "to tell or not to tell"

Federica Galli [1], Aglaia Vignoli [2], Maria Paola Canevini [2], Gabriele Cerioli [3], Elena Vegni [2]

Affiliations + expand

PMID: 28088049 DOI: 10.1016/j.yebeh.2016.12.001

- 114 doctors completed the questionnaire
- 16.2% → should counsel to ALL patients
- 19.8% → should counsel to majority
- 52.3% → should counsel to minority
- 11.7% → should not counsel to any patients

In real practice only 1.8% counseled all their patients

# Potential modalities for preventing of SUDEP

- Identify patients at risk
  - Discuss with families
    - Early surgical refer
      - Appropriate AED Rx, stress on compliance, lifestyle
        - Train caregivers in home management of SZ
          - Nocturnal supervision
            - Safety pillows
              - Intranasal midazolam
                - Turning from prone to recovery position

-SZ monitoring devices – may be discussed