Sleep Apnea is Associated With High Mortality Risk in Children With Severe Epilepsies: An Observational Analysis From Large Scale US Claims Data

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*At the time when the current study was conducted.

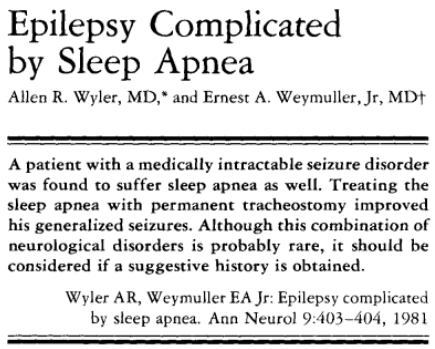
Sleep Apnea and Mortality in Administrative Claims Data

- Patients with uncontrolled epilepsy experience an increased risk of premature mortality,[1] a reduced quality of life,[2] and various comorbidities, including sleep disturbances such as sleep apnea[3]
- Obstructive sleep apnea in patients with uncontrolled epilepsy is correlated with increased seizures, which can be ameliorated through interventions such as positive airway pressure therapy[4]
- The link between sleep apnea and mortality in individuals with uncontrolled epilepsy has not been studied at scale

Objective

- This real-world study used administrative claims data to describe the excess mortality risk of sleep apnea in patients with uncontrolled epilepsy

A case by Wyler and Weymuller in 1981 described the improvement of refractory generalized seizures after treatment of sleep apnea[5]



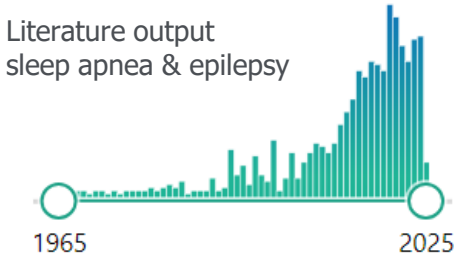
Epilepsy Complicated by Sleep Apnea

Allen R. Wyler, MD,* and Ernest A. Weymuller, Jr, MD†

A patient with a medically intractable seizure disorder was found to suffer sleep apnea as well. Treating the sleep apnea with permanent tracheostomy improved his generalized seizures. Although this combination of neurological disorders is probably rare, it should be considered if a suggestive history is obtained.

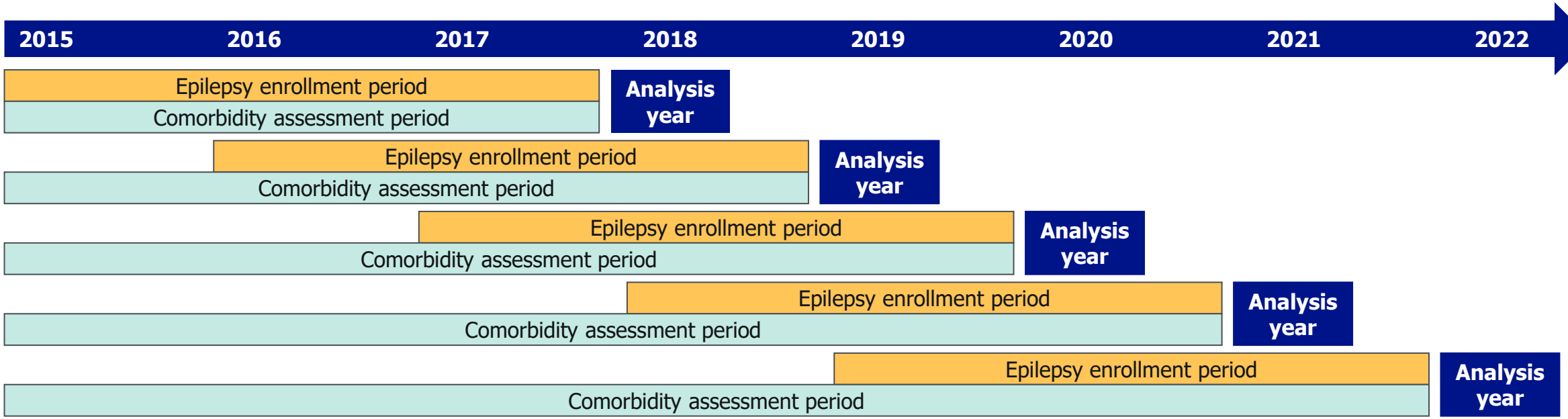
Wyler AR, Weymuller EA Jr: Epilepsy complicated by sleep apnea. Ann Neurol 9:403–404, 1981

There are 1000+ papers describing the **link between sleep apnea and epilepsy**



1. Kaiboriboon K, et al. *Epilepsia*. 2014;55(11):1781-8. 2. Foster E, et al. *Epilepsia*. 2019 Dec;60(12):2466-2476. 3. Malow BA. *Epilepsia*. 2007;48(suppl 9):36-8. 4. Pornsriniyom D, et al. *Epilepsy Behav*. 2014;37:270-5. 5. Wyler AR, Weymuller EA Jr. *Ann Neurol*. 1981 Apr;9(4):403-4.

Patients With Uncontrolled Epilepsy in the Komodo US Database



Primary objective: mortality rate in patients with uncontrolled epilepsy with and without a sleep apnea claim

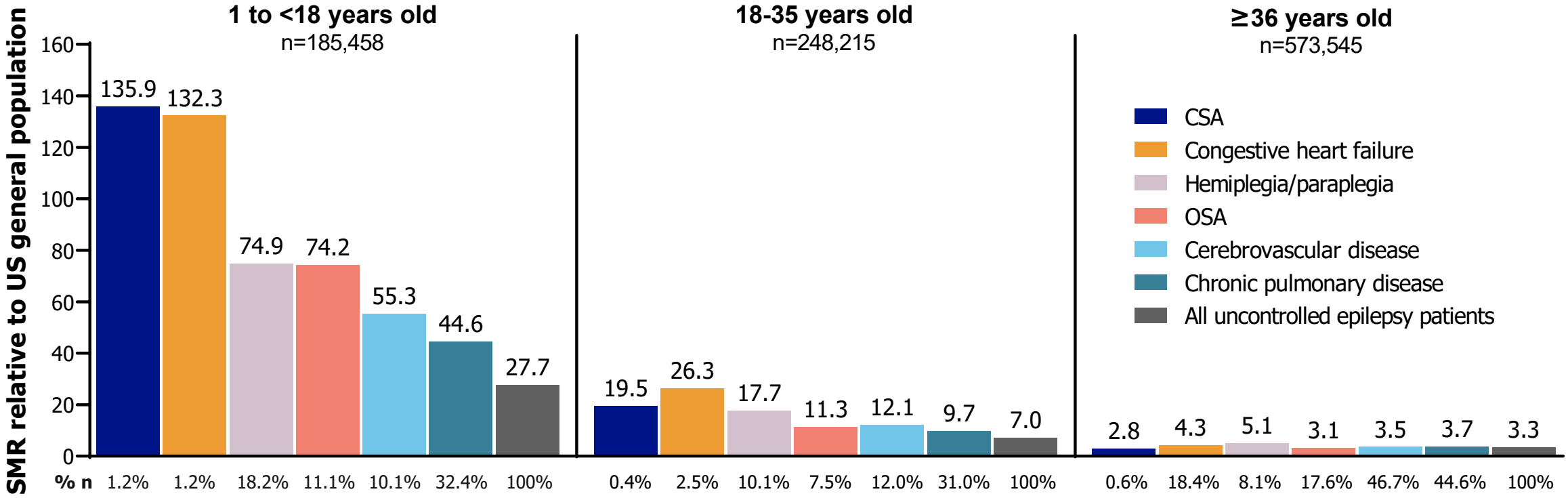
Secondary objective: SMR for uncontrolled epilepsy patients with and without a sleep apnea claim

- Uncontrolled epilepsy was defined as any ICD-10 code related to ER visit, hospital admission, status epilepticus, or GTC seizures
- Comorbidities of interest during the assessment period were selected using the Charlson Comorbidity Index
- The Komodo US database houses claims data for 325 million patients and 42 billion medical and pharmacy claims, beginning in 2015

ER, emergency room; GTC, generalized tonic-clonic; ICD-10, International Classification of Diseases, 10th revision; SMR, standardized mortality ratio.

SMRs for Select Comorbidities in Patients With Uncontrolled Epilepsy by Age Category

- Overall, 2,355,410 patient-years were captured from 968,993 unique patients with uncontrolled epilepsy
- 6571 (0.7%) patients had central sleep apnea, 136,118 (14.0%) had other sleep apnea, and 826,304 (85.3%) reported no sleep apnea



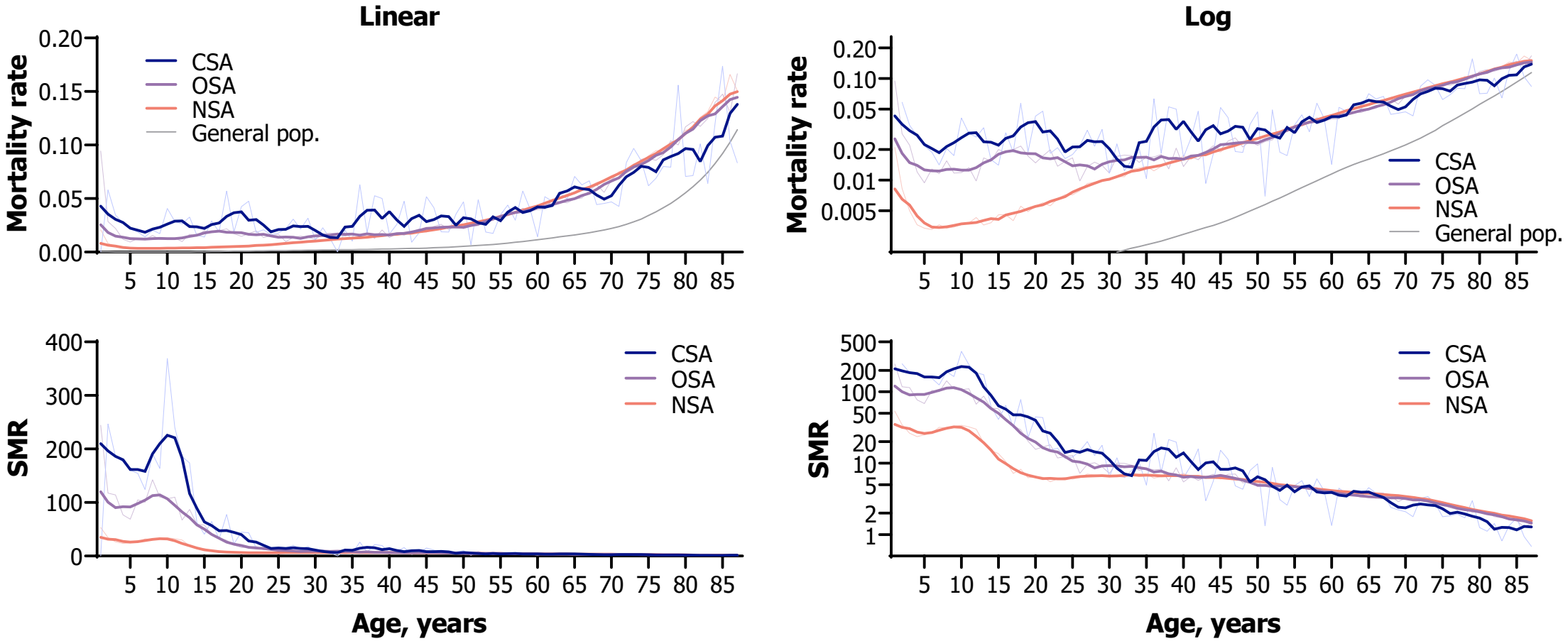
SMR data are not mutually exclusive. Patients may have multiple comorbidities.
Some patients were observed in multiple age groups; age totals may not match precisely.
CSA, central sleep apnea; OSA, other sleep apnea; PY, patient years; SMR, standardized mortality ratio.

Regression Analysis Shows Other and Central Sleep Apnea are Strongly Associated With Mortality in Children With Uncontrolled Epilepsy

	1 to <18 years old		18 to <35 years old		≥36 years old	
	Odds ratio	***P* value**	**Odds ratio**	***P* value**	**Odds ratio**	***P* value**
Demographics						
Age[a]	0.9745	<0.0001	1.0519	<0.0001	1.0437	<0.0001
Male[b]	0.9459	n.s.	1.4978	<0.0001	1.2518	<0.0001
Race/ethnicity[c]						
Asian or Pacific Islander	0.5484	<0.001	0.5145	<0.0001	0.6504	<0.0001
Hispanic or Latino	0.6151	<0.0001	0.6046	<0.0001	0.6322	<0.0001
Black or African American	0.7621	<0.0001	1.0071	n.s.	0.9315	<0.0001
Unknown/Other	1.2374	<0.0001	1.1474	<0.001	1.0323	<0.05
Comorbidities						
Other sleep apnea	2.0738	<0.0001	1.2899	<0.0001	0.8120	<0.0001
Central sleep apnea	2.8463	<0.0001	1.5536	<0.01	0.7620	<0.0001
Cerebrovascular disease	1.2863	<0.0001	1.5240	<0.0001	1.3807	<0.0001
Chronic pulmonary disease	1.4365	<0.0001	1.3042	<0.0001	1.1716	<0.0001
Congestive heart failure	2.9360	<0.0001	3.1314	<0.0001	1.6877	<0.0001
Hemiplegia or paraplegia	3.1188	<0.0001	2.8156	<0.0001	1.5056	<0.0001
Peripheral vascular disease	2.5961	<0.0001	1.6073	<0.0001	1.2392	<0.0001

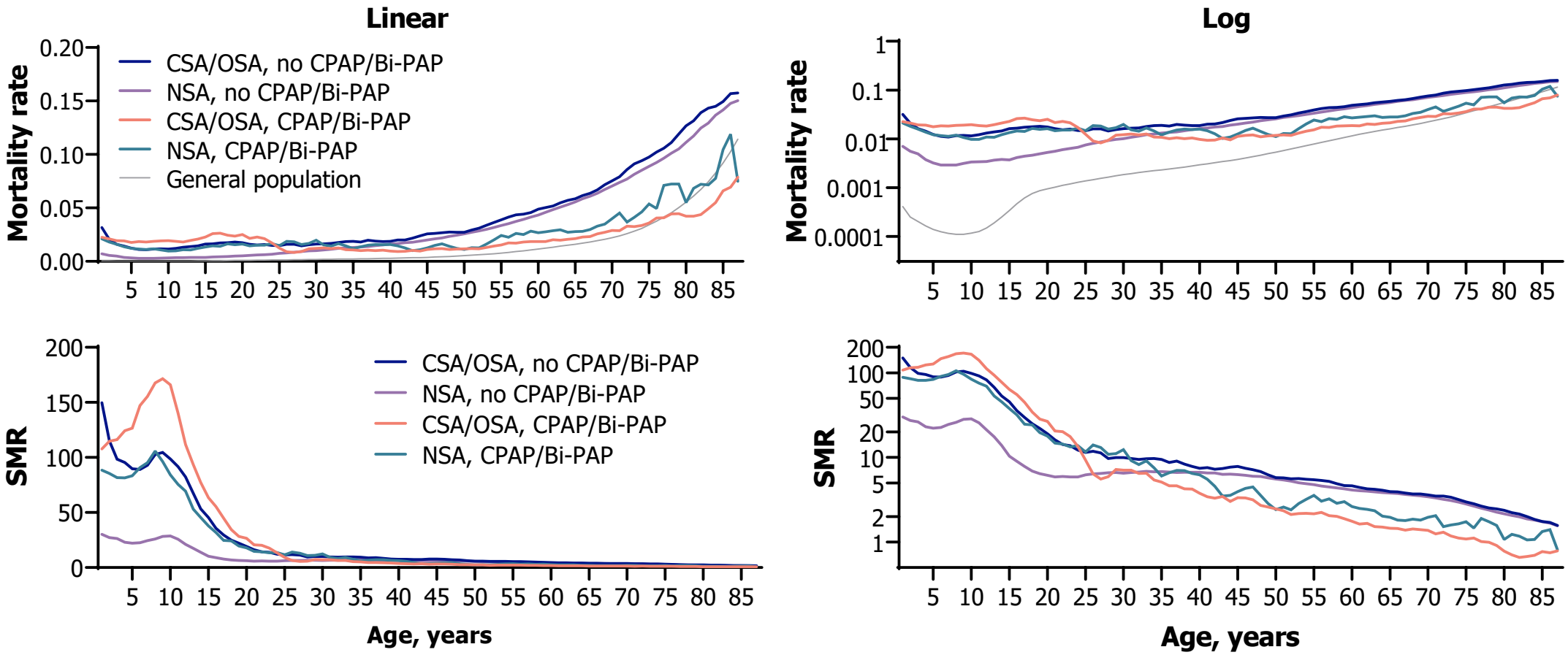
Intercept for each age cohort was 0.0036, 0.0013, and 0.0022, respectively.
[a] Odds ratio of each additional year of age.
[b] Odds ratio relative to female patients.
[c] Odds ratio relative to White patients.
n.s., not significant.

Mortality of Children With Sleep Apnea With Uncontrolled Epilepsy is Similar to That of a Middle-Aged Adult With Uncontrolled Epilepsy



Thick lines represent smoothed mortality rates and SMRs. Thin lines represent single-year mortality rates and SMRs. SMR for the United States general population equals 1.0.
CSA, central sleep apnea; NSA, no sleep apnea; OSA, other sleep apnea; pop, population; SMR, standardized mortality ratio.

Association of CPAP/Bi-PAP and Mortality in Patients With Central Sleep Apnea, Other Sleep Apnea, or No Sleep Apnea and Uncontrolled Epilepsy



Bi-PAP, bilevel positive airway pressure; CPAP, continuous positive airway pressure; CSA, central sleep apnea; NSA, no sleep apnea; OSA, other sleep apnea; SMR, standardized mortality ratio.

Limitations of the Current Study

- Comorbidities were identified using ICD-10 codes from claims data and were not confirmed clinically
- There was no control for confounding variables, such as socioeconomic status, treatment status, comorbidities, or congenital conditions

ICD-10, International Classification of Diseases, 10th revision.

Sleep Apnea in Children With Uncontrolled Epilepsy is Associated With High Mortality

Main Conclusions

- Pediatric and adult **patients with uncontrolled epilepsy** experience **increased mortality** relative to the US general population
- In children and young adults with uncontrolled epilepsy, **sleep apnea adds substantially to increased mortality risk**
- Low baseline mortality rates in younger populations makes risks associated with comorbidities in these groups especially pronounced, whereas in older patients age itself becomes the key driver of mortality risk
- **PAP therapy** is associated with better mortality outcomes in older patients but not in younger patients with uncontrolled epilepsy – warrants cautious interpretation

Implications of the work

- Identifying sleep apnea in patients with epilepsy can provide critical insights into their clinical condition, inform treatment plans, and aid in predicting patient outcomes[1]
- Young patients with uncontrolled epilepsy and sleep apnea comorbidities show elevated mortality risk
  - Suggests that a **vulnerable age group** has been identified and highlights the need to **raise awareness**
  - Further research is warranted to inform clinical practice

PAP, positive airway pressure.

1. Malow BA. *Epilepsia*. 2007;48(suppl 9):36-8.