



Mind the Gap: SUDEP in the United States

Socioeconomic Disparities in SUDEP in the US

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Objective: To determine the impact of socioeconomic status (SES) on sudden unexpected death in epilepsy (SUDEP) rates. **Methods:** We queried all decedents presented for medicolegal investigation at 3 medical examiner offices across the country (New York City, Maryland, San Diego County) in 2009 to 2010 and 2014 to 2015. We identified all decedents for whom epilepsy/seizure was listed as cause/contributor to death or comorbid condition on the death certificate. We then reviewed all available reports. Decedents determined to have SUDEP were included for analysis. We used median income in the ZIP code of residence as a surrogate for SES. For each region, zip code regions were ranked by median household income and divided into quartiles based on total population for 2 time periods. Region-, age-, and income-adjusted epilepsy prevalence were estimated in each zip code. Sudden unexpected death in epilepsy rates in the highest and lowest SES quartiles were evaluated to determine disparity. Examined SUDEP rates in 2 time periods were also compared. **Results:** There were 159 and 43 SUDEP cases in the lowest and highest SES quartiles. Medical examiner–investigated SUDEP rate ratio between the lowest and highest SES quartiles was 2.6 (95% CI: 1.7-4.1, $P < .0001$) in 2009 to 2010 and 3.3 (95% CI: 1.9-6.0, $P < .0001$) in 2014 to 2015. There was a significant decline in overall SUDEP rate between the 2 study periods (36% decrease, 95% CI: 22%-48%, $P < .0001$). **Conclusion:** Medical examiner–investigated SUDEP incidence was significantly higher in people with the lowest SES compared to the highest SES. The difference persisted over a 5-year period despite decreased overall SUDEP rates.

Commentary

Multiple population-based studies have reported an increased risk of premature mortality among people with epilepsy compared to the general population.^{1,2} In the Centers for Disease Control and Prevention Wide-ranging Online Data for Epidemiologic Research (wonder.cdc.gov), epilepsy was listed as the underlying cause of death for about 54% of all deaths with any mention of epilepsy in 2015 and 43% of such deaths in 2014.³ Among deaths attributable to seizures, important causes include sudden unexpected death in epilepsy (SUDEP), status epilepticus, physical injuries, and drowning. Many of these causes of death are potentially preventable. Compliance with antiseizure medications and maintenance of seizure precautions decrease the likelihood of status epilepticus and accidental injuries, respectively. However, how to effectively prevent SUDEP is not well understood mainly because its mechanisms remain largely unknown.

Sudden unexpected death in epilepsy affects approximately 1 in 1000 people with epilepsy, and its incidence is even higher in patients with medically refractory seizures. The main known risk factor for SUDEP is the presence and frequency of generalized tonic-clonic seizures (GTCs).⁴ People with 3 or more

GTCs per year have a 15-fold increased risk of SUDEP. The findings of a retrospective study on the incidence and mechanisms of cardiorespiratory arrests in epilepsy monitoring units, suggested that SUDEP primarily follows an early postictal, centrally mediated, severe alteration of respiratory, and cardiac function induced by GTCs.⁵ Improved control of an individual's GTCs should result in a reduced risk of SUDEP. In a retrospective examination of a surgical epilepsy population, the SUDEP rates were 1.9 versus 4.6 (per 1000 patient years) in surgical patients and the comparison group of patients treated medically, respectively.⁶ Hence, not being free of GTCs, not adding an antiseizure medication when the seizures are not well controlled and decreased access to epilepsy surgery appear to place patients at an increased risk of SUDEP. Seizure control is directly affected by access to medical care. Patients with epilepsy and lower socioeconomic status (SES) experience barriers to health care access which can account for the higher risk of all-cause mortality among people with epilepsy living in zip codes with lower median income.⁷

The article reviewed in this commentary examined the relationship between socioeconomic factors and SUDEP rates, a cause of death affected by seizure control.⁸ The authors queried





the database of all decedents who underwent medicolegal investigation at 3 medical examiner (ME) offices (New York City, San Diego County, and Maryland) for two 2-year periods, January 1, 2009, through December 31, 2010, and January 1, 2014, through December 31, 2015. All deaths in individuals for whom epilepsy or seizure was listed as a cause or contributor of death or comorbid condition were reviewed. The decedent's zip code of residence was used as a surrogate for community SES. Zip codes in each ME region were ranked by median household income. For each of the 2 time periods under review, the ranked zip codes were assigned to 4 groups of equal population based on estimates of zip-code population. Each decedent was then assigned a zip code–based SES quartile. Age-, region-, and income-adjusted epilepsy population estimates from each zip code were combined to determine the estimated epilepsy population for each SES quartile for each ME jurisdiction for the 2 time periods studied. The SUDEP rate per 1000 patient-years was determined for each 2-year period for each ME region and SES quartile area by dividing the number of definite or probable SUDEP cases (as defined by Nashef et al in 2012⁹) by the estimated number of individuals with epilepsy in each ME region and SES quartile group zip codes.


Including the 3 ME offices during the 2 periods, there were 84 293 cases, of which 555 decedents had epilepsy or seizure listed as a cause or contributor of death, or comorbid condition. After excluding residents with unknown or misassigned zip codes, and those with insufficient information, 389 of the remaining decedents were determined to be SUDEP cases. There were 159 SUDEP cases in the lowest SES quartile zip codes and 43 SUDEP cases in the highest SES quartile. There were no significant differences in decedent's demographic characteristics, circumstances of death, comorbid conditions, reported nonadherence to medications, or epilepsy etiology between the highest and lowest SES quartile zip codes. In the 3 geographic regions studied, the estimated epilepsy prevalence using the National Health Interview Survey was 0.95% in 2009 to 2010 and 1.14% in 2014 to 2015. The SUDEP rate ratio (RR) between the lowest and highest community SES quartile was 2.6 (95% CI: 1.7-4.1, $P < .0001$) in 2009 to 2010 and 3.3 (95% CI: 1.9-6.0, $P < .0001$) in 2014 to 2015. Zip code median household income (per US\$10 000) was an independent predictor of SUDEP (incident RR: 0.85, CI: 0.81-0.90, $P < .001$).

When the 2 study periods were compared, despite an increase in the number of total ME-investigated deaths in each of the ME offices, the investigated epilepsy deaths decreased significantly. Nevertheless, the rate of epilepsy-related death investigations by the ME was still significantly higher in the lowest SES quartile zip codes compared to the highest quartile in 2009 to 2010 (RR: 2.4, 95% CI: 1.7-3.6, $P < .0001$) and 2014 to 2015 (RR: 2.5, 95% CI: 1.6-3.9, $P < .0001$). The overall ME-investigated SUDEP rate was 0.67 per 1000 patient-years (95% CI: 0.59-0.77) in 2009 to 2010 and 0.43 per 1000 patient-years (95% CI: 0.37-0.50) in 2014 to 2015. There was a significant decline in the SUDEP

rate between the 2 time periods (36% reduction in rate, 95% CI: 22%-48%, $P < .0001$), but the socioeconomic disparities in SUDEP persisted.

It is important to note that estimates of prevalent epilepsy population were not adjusted for race, and that the nonwhite population was higher in the lowest income zip codes compared to the highest income zip codes. Epilepsy-related deaths in the black population are higher compared to white and Hispanic populations.³ Although the authors point out that the disparity in race distribution may reflect the income disparity in the general population, this could be a confounder and could explain at least in part the disparities found in this study. A possible source of error is the imprecise nature of determining household income for a particular zip code using US Census data. However, after performing probabilistic bias analysis to account for classification errors in attribution of community household income, the authors continued to found a positive association between low community SES and SUDEP rate.

This study provides robust evidence that while we have made some scientific progress in the prevention of premature mortality in epilepsy, this progress has not benefitted patients of lower SES as much as those of the upper SES. Epilepsy patients in the less advantaged communities are more than twice as likely to suffer SUDEP than their counterparts at the highest end of the socioeconomic spectrum. Further studies are needed in order to identify the mechanisms of these disparities and the solutions to close the gaps in epilepsy care. Disparities in epilepsy are significant, and this study should serve as a call to action.


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