Seizure: European Journal of Epilepsy 71 (2019) 295–303

Contents lists available at ScienceDirect

Seizure: European Journal of Epilepsy

journal homepage: www.elsevier.com/locate/seizure

Estimating the cost of status epilepticus admissions in the United States of America using ICD-10 codes

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ARTICLE INFO

Keywords:
Cost
Economic evaluation of health policy
Health services research
Hospital admission
Status epilepticus

ABSTRACT

Purpose: Estimate the cost of status epilepticus (SE) admissions in the USA using claim databases based on ICD-10 codes.
Method: Descriptive retrospective study using national estimates for the year 2016 from the KID's Inpatient Database (KID) for pediatric patients and from the National Inpatient Sample (NIS) for adults. These databases are comprehensive collections of all-payer, encounter-level hospital care data in the United States of America.
Results: From a population of 6,106,405 pediatric admissions there were 580 admissions related to SE. From a population of 29,274,158 adult admissions there were 1,405 admissions related to SE. The median (p25–p75) cost of pediatric admissions related to SE was $8,749 ($4,875–$19,067) in 2016 USA dollars [$9,295 ($5,180–$20,258) in inflation-adjusted 2019 USA dollars], and for adult admissions related to SE it was $14,678 ($7,203–$28,388) in 2016 USA dollars [$15,595 ($7,653–$30,161) in inflation-adjusted 2019 USA dollars]. Transforming to 2019 USA dollars, the values from the current study are consistent with prior estimates in the literature from the KID and NIS databases with a progressive increase, except for the cost of super-refractory SE in children that has increased disproportionately.
Conclusions: This study estimates that the cost of admissions related to SE in the USA is approximately $9,000 in children and $15,000 in adults and shows that the cost estimates have not markedly changed with the advent of ICD-10.

1. Introduction

There are approximately 17–23/100,000 status epilepticus (SE) episodes per year in pediatric patients and approximately 4–15/100,000 SE episodes per year in adults [1,2]. SE is a condition with a mortality of approximately 2–5% in children and 13–19% in adults, even higher when SE is refractory or super-refractory [3]. Therefore, SE generally requires hospital management and close monitoring, frequently in the intensive care unit (ICU). The cost of caring for SE is substantial, but there is limited literature on cost associated with SE. Costs associated with SE markedly increase once SE becomes refractory or super-refractory [4–6]. Estimations on the cost of SE are largely based on claims data which is at least 4 years old [4–9]. Further, the change from ICD-9 to ICD-10 in the USA may have modified the coding of SE and, therefore, the estimations on cost of SE. The original ICD-10 coding system has provided more granularity in the study of SE from claims data than ICD-9 coding [6], and the USA implementation of ICD-10 coding system has further modified the coding for SE [10]. Hence, coding changes may modify the cost of SE as estimated from claims data. Unfortunately, there are no estimations on the cost of SE in the USA based on ICD-10 codes [4,5,7]. The purpose of this study was to provide a more recent estimate of the cost of SE in the USA and to evaluate whether the use of ICD-10 has modified the cost estimates.

2. Patients and methods

2.1. Protocol approvals, registrations, and patient consent

This study was performed using the Kids' Inpatient Database (KID) and National Inpatient Sample (NIS), publicly available databases from

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https://doi.org/10.1016/j.seizure.2019.09.001
Received 14 June 2019; Received in revised form 30 August 2019; Accepted 3 September 2019

the Health Care Cost and Utilization Project (HCUP) maintained by the Agency for Healthcare Research and Quality (AHRQ) [11]. The Institutional Review Board at Boston Children's Hospital deemed this study non-human subjects research as these data derive from de-identified publicly available datasets (IRB-A00023607-3).

2.2. Study design

This is a retrospective descriptive study evaluating the cost of admissions related to SE in the KID and NIS databases for the year 2016. HCUP is the largest all-payer encounter-level hospital care data in the USA. The KID database contains data for pediatric admissions, defined in this database as admissions where the patient was 20 year-old or younger at admission [12]. The NIS database contains data from all inpatients [13]. As the KID database provides more granularity in admissions of patients during the first 20 years of life, we included all admissions of patients in the KID database, and, to avoid overlap, we used only those admissions from the NIS database in which the patient was older than 20 years at admission. Both the KID and NIS databases are generated through a stratified sampling strategy that extracts data which includes all relevant strata in the US population [12,13]. For the year 2016, the KID database consisted of a sample of more than 3 million pediatric admissions representing a population of more than 6 million pediatric admissions [12]. For the year 2016, the NIS database consisted of a sample of more than 5 million discharges representing a population of more than 29 million admissions [13].

2.3. Population of interest

We included all admissions related to SE. Admissions having SE were identified using the USA version of the 10th revision of the International Classification of Diseases (ICD-10) codes. We defined SE with the codes G40.301 and G40.311 ("Generalized idiopathic epilepsy and epileptic syndromes, with status epilepticus") from the ICD-10 version, considered equivalent to "345.3 Grand mal status" from the ICD-9 version by the American Academy of Neurology [10]. Mechanical ventilation was identified using the ICD-10 procedural codes 5A1935Z (less than 24 hours), 5A1945Z (24–96 hours), and 5A1955Z (more than 96 hours) [14]. We excluded admissions with no information on age, sex, length of stay, mortality, and cost.

2.4. Classification of admissions related to status epilepticus

Adapting prior models for identification of SE based on ICD codes [5,6] to the USA version of ICD-10 codes, we divided admissions related to SE into: 1) non-refractory SE if the patient was not mechanically ventilated, 2) refractory SE if the patient was mechanically ventilated for less than 96 hours, and 3) super-refractory SE if the patient was mechanically ventilated for at least 96 hours. SE is considered refractory or super-refractory based on the response to the administered treatments. Treatment information is not available in the KID and NIS databases, hence the classification of SE was based on the surrogate variables of mechanical ventilation and its duration.

2.5. Variables

The main outcome variable was the cost of hospital admission. The KID and NIS databases contain data on total charges related to the admission [15]. These charges represent the amount that hospitals billed for services [15]. However, the real value of interest is the amount of resources that were spent during the admissions: the cost. The KID and NIS databases contain cost-to-charge ratio files that allow the conversion of charges into cost estimates [15]. Secondary outcomes in this analysis were length of stay and mortality. We described hospital characteristics, and demographic and clinical features. The specific definitions and categories of each variable can be found in the description of data elements for the KID [16] and the NIS [17] databases.

2.6. Sampling and weighting

The KID and NIS databases are samples designed to represent a larger population. Data is weighted to achieve nationally representative estimates [18]. For the KID database, discharge weights were calculated by stratifying the hospitals based on geographic region, urban/rural location, teaching status, bed size, ownership, and children's hospital, the same variables that were used for creating the sample [18]. For the NIS database, the weights were calculated by stratifying the NIS hospitals on census division, urban/rural location, teaching status, bed size, and ownership, the same variables that were used for creating the sample [18].

2.7. Adjustment for inflation

Costs refer to 2016 USA dollars. To evaluate how these costs would translate to 2019 USA dollars, we also calculated inflation-adjusted costs. We used the inflation statistics from the United States Department of Labor, Bureau of Labor Statistics [19]. In particular, we used the consumer price index (CPI), which is a measure of the average change over time in the prices paid by urban consumers for a market basket of consumer goods and services [20].

2.8. Statistical analysis

Analyses were performed using complex survey weights and procedures for obtaining appropriate national projections. We summarized hospital characteristics, demographics, and clinical characteristics with descriptive statistics, including median and 25^{th}-75^{th} percentiles (p_{25}-p_{75}) for continuous variables, and number and percentage for categorical variables. We stratified costs by relevant factors such as hospital size or disease severity. The individual observation in the NIS and KID databases is the individual hospital admission, not the individual patient. Some of the different admissions may belong to the same patient, but there is no variable in the databases to detect repeated patients. Hence, the assumption of independent observations may not hold and, strictly, statistical tests for independent data are not applicable, nor it is possible to manage non-independent observations in these databases. However, the proportion of repeated admissions from the same patient is likely small in KID and NIS, national databases derived from statewide databases. Consequently, the impact of strictly non-independent data on statistical tests is likely small. Statistical tests of significance may not be particularly informative in the NIS and KID databases because with a very large number of observations minor differences in effect size may reach statistical significance. For completeness, we have provided a linear regression to evaluate variables most associated with the cost of admission for SE.

2.9. Statistical software

Statistical analyses were performed with R: a language and environment for statistical computing, version 3.4.1 [21], RStudio [22], and the packages readr [23], gmodels [24], tidyverse [25], qdapRegex [26], and survey [27].

2.10. Data access

The NIS and KID databases are publicly available databases. The code for our analyses can be found at GitHub (https://github.com/IvanSanchezFernandez/costse2019) and at Zenodo (https://zenodo.org/badge/latestdoi/184500470).

Table 1
Demographic and clinical characteristics of the admission.

KID 2016 N = 6,106,405 (sample 3,040,080)

		Non-refractory SE N = 422	Refractory SE N = 116	Super-refractory SE N = 42	SE, all categories N = 580
HOSPITAL					
Bedsize	**Large**	271 (64.2%)	75 (64.7%)	#	373 (64.3%)
	Medium	111 (26.3%)	28 (24.1%)	#	150 (25.9%)
	Small	40 (9.5%)	13 (11.2%)	#	57 (9.8%)
Region	**Northeast**	101 (23.9%)	25 (21.4%)	#	139 (23.9%)
	Midwest	69 (16.3%)	18 (15.4%)	#	98 (16.9%)
	South	147 (34.8%)	39 (33.3%)	#	197 (33.9%)
	West	106 (25.1%)	35 (29.9%)	#	147 (25.3%)
ADMISSION					
Emergency department admission		240 (56.9%)	69 (59.5%)	22 (53.7%)	332 (57.2%)
SE developed during elective admission		52 (12.3%)	0 (0%)	#	54 (9.3%)
Admission during the weekend		102 (24.2%)	37 (31.9%)	14 (33.3%)	153 (26.4%)
DEMOGRAPHICS					
Race	**White**	184 (49.5%)	41 (39.8%)	17 (48.6%)	241 (47.4%)
	Non-white	188 (50.5%)	62 (60.2%)	18 (51.4%)	268 (52.7%)
Income	**Upper half**	189 (45.2%)	53 (46.5%)	22 (61.1%)	264 (46.5%)
	Lower half	229 (54.8%)	61 (53.5%)	14 (38.9%)	304 (53.5%)
Primary payer	**Private insurance**	161 (38.2%)	33 (28.5%)	15 (36.6%)	209 (36%)
	Medicare or Medicaid	232 (55%)	72 (62.1%)	21 (0.5%)	325 (56%)
	Other (self-pay, no charge, or other)	28 (6.6%)	#	#	44 (7.6%)
CLINICAL CHARACTERISTICS					
Age in years		6 (2-12)	5 (2-13.9)	5 (1-10.9)	6 (2-12)
Sex	**Male**	213 (50.5%)	62 (53.5%)	20 (47.6%)	295 (50.9%)
	Female	209 (49.5%)	54 (46.6%)	22 (52.4%)	285 (49.1%)
Disease severity	**Extreme or major**	184 (43.6%)	104 (89.7%)	42 (100%)	330 (56.9%)
	Moderate or minor	238 (56.4%)	12 (10.4%)	0 (0%)	250 (43.1%)
Mortality risk	**Extreme or major**	46 (10.9%)	#	#	194 (33.5%)
	Moderate or minor	376 (89.1%)	#	#	386 (66.6%)
CLINICAL OUTCOMES					
Length of stay		2 (1-4)	3 (2-6)	28 (10.7-37.5)	3 (1-5)
Mortality		#	#	#	16 (2.8%)

NIS 2016 N = 29,274,158 (sample 5,854,836)

		Non-refractory SE N = 710	Refractory SE N = 530	Super-refractory SE N = 165	SE, all categories N = 1,405
HOSPITAL					
Bedsize	**Large**	415 (58.5%)	340 (64.2%)	105 (63.6%)	860 (61.2%)
	Medium	155 (21.8%)	130 (24.5%)	30 (18.2%)	315 (22.4%)
	Small	140 (19.7%)	60 (11.3%)	30 (18.2%)	230 (16.4%)
Region	**Northeast**	190 (26.8%)	125 (23.6%)	40 (24.2%)	355 (25.3%)
	Midwest	130 (18.3%)	90 (17%)	20 (12.1%)	240 (17.1%)
	South	225 (31.7%)	215 (40.6%)	50 (30.3%)	490 (34.9%)
	West	165 (23.2%)	100 (18.9%)	55 (33.3%)	320 (22.8%)
ADMISSION					
Emergency department admission		525 (73.9%)	410 (77.4%)	95 (57.6%)	1,030 (73.3%)
SE developed during elective admission		75 (10.7%)	20 (3.8%)	#	100 (7.2%)
Admission during the weekend		180 (25.4%)	160 (30.2%)	35 (21.2%)	375 (26.7%)
DEMOGRAPHICS					
Race	**White**	410 (59%)	335 (68.4%)	85 (51.5%)	830 (61.5%)
	Non-white	285 (41%)	155 (31.6%)	80 (48.5%)	520 (38.5%)
Income	**Upper half**	320 (45.4%)	210 (40.4%)	55 (35.5%)	585 (42.4%)
	Lower half	385 (54.6%)	310 (59.6%)	100 (64.5%)	795 (57.6%)
Primary payer	**Private insurance**	160 (22.5%)	125 (23.6%)	15 (9.1%)	300 (21.4%)
	Medicare or Medicaid	520 (73.2%)	360 (67.9%)	145 (87.9%)	1,025 (73%)
	Other (self-pay, no charge, or other)	30 (4.2%)	#	#	80 (5.7%)
CLINICAL CHARACTERISTICS					
Age in years		54 (37-65.5)	54 (34.5-63.5)	60 (50.3-73)	55 (37-66)
Sex	**Male**	365 (51.4%)	335 (63.2%)	85 (51.5%)	785 (55.9%)
	Female	345 (48.6%)	195 (36.8%)	80 (48.5%)	620 (44.1%)
Disease severity	**Extreme or major**	325 (45.8%)	490 (92.5%)	165 (100%)	980 (69.8%)
	Moderate or minor	385 (54.2%)	40 (7.6%)	0 (0%)	425 (30.3%)
Mortality risk	**Extreme or major**	240 (33.8%)	#	#	915 (65.1%)
	Moderate or minor	470 (66.2%)	#	#	490 (34.9%)
CLINICAL OUTCOMES					
Length of stay		4 (2-7)	5 (2-8.5)	18.5 (13-26)	5 (2-10)

(*continued on next page*)

Table 1 (*continued*)

NIS 2016 N = 29,274,158 (sample 5,854,836)				
	Non-refractory SE N = 710	Refractory SE N = 530	Super-refractory SE N = 165	SE, all categories N = 1,405
Mortality	20 (2.8%)	40 (7.6%)	65 (39.4%)	125 (8.9%)

Legend: KID: Kid's inpatient database. **NIS:** National inpatient sample. **SE:** Status epilepticus.
Some values may not add up to 100% depending on estimation rounding.
#This outcome cannot be reported because of the HCUP requirement to not report cells smaller than 11 individuals to preserve privacy and confidentiality.

3. Results

3.1. Demographic and clinical characteristics

From a population of 6,106,405 pediatric admissions there were 580 admissions related to SE. From a population of 29,274,158 adult admissions there were 1,405 admissions related to SE. That translates into approximately 9.5/100,000 pediatric hospital admissions related to SE and approximately 4.8/100,000 adult hospital admissions related to SE. The main hospital characteristics, demographic, and clinical features including length of stay and mortality are summarized in Table 1.

3.2. Cost of admissions related to SE

The median (p_{25}-p_{75}) cost of pediatric admissions related to SE was \$8,749 (\$4,875–\$19,067) in 2016 USA dollars [\$9,295 (\$5,180–\$20,258) in inflation-adjusted 2019 USA dollars], and for adult admissions related to SE it was \$14,678 (\$7,203–\$28,388) in 2016 USA dollars [\$15,595 (\$7,653–\$30,161) in inflation-adjusted 2019 USA dollars]. Costs were higher for super-refractory SE than for refractory SE and non-refractory SE both in the KID and NIS databases (Table 2). The most relevant variables associated with the cost of admission for SE based on a linear regression model are summarized in Table e-1 and Table e-2 in Supplementary materials. How cost of admission varies by variables of interest is presented in Table 3.

3.3. Comparison with prior literature

Transforming to 2019 USA dollars the values from the current study are consistent with prior estimations in the literature using the KID and NIS databases and also transforming to 2019 USA dollars [5]. This comparison also shows a steady increase in cost over time, except for the cost of super-refractory SE in children that has increased disproportionately (Figs. 1 and 2).

4. Discussion

Our study estimates the median cost of admissions related to SE in the USA at approximately \$9,000 for pediatric patients, and at approximately \$15,000 for adults. There is a marked increase in cost of admissions with increasing SE severity: the cost of an admission related to refractory SE is approximately double than that of an admission related to non-refractory SE, and the cost of an admission related to super-refractory SE is more than 5 times higher than the cost of an admission related to non-refractory SE.

Increase in health care costs in the USA is an urgent problem that may lead to access limitations [28,29]. Health care costs currently represent approximately one third of the median household income for families in the USA [29], and the projected increase is unsustainable, possibly leading to potential rationing, based on access, increased out-of-pocket cost, restricted service provision, or through extended wait times, in the near future [28–30]. Identifying clinical presentations where relatively inexpensive early interventions may prevent evolution towards a complicated and costly condition may be one of the more feasible cost-saving approaches in the short term; hence, resource prioritization towards high-value prevention or early intervention efforts may provide benefit. SE usually needs hospital admission and often includes management in the intensive care unit (ICU), one of the most resource-consuming settings in a hospital. The cost associated with managing SE is much higher than that associated with managing other forms of epilepsy. In a study of 96 adult German patients admitted during a 4-month period in 2008 with epilepsy (86 patients) or SE (10 patients), the median admission costs related to SE were markedly higher per patient per admission (€4,702) [assuming a 1 euro : 1.47 USA dollar conversion in 2008, which was the average 2008 exchange, this would be approximately \$8,243 in 2019 USA dollars] than those related to patients with newly-diagnosed epilepsy (€2,098) [assuming a 1 euro : 1.47 USA dollar conversion in 2008, which was the average 2008 exchange, this would be approximately \$3,678 in 2019 USA dollars], or with established epilepsy €2,098 [assuming a 1 euro : 1.47 USA dollar conversion in 2008, which was the average 2008 exchange, this would be approximately \$3,678 in 2019 USA dollars] [9]. However, estimates of the cost of SE are limited, and most recent data are

Table 2
Cost data (in 2016 US dollars, and estimation in 2019 US dollars).

KID 2016 N = 6,106,405 (sample 3,040,080)					
		Non-refractory SE N = 422	Refractory SE N = 116	Super-refractory SE N = 42	SE, all categories N = 580
Cost	Original data in 2016 USA dollars	6,625 (3,678-13,995)	13,286 (8,392-22,273)	139,790 (65,089-230,451)	8,749 (4,875-19,067)
	Estimation in 2019 USA dollars	7,039 (3,908-14,869)	14,116 (8,916-23,664)	148,520 (69,154-244,843)	9,295 (5,180-20,258)
NIS 2016 N = 29,274,158 (sample 5,854,836)					
		Non-refractory SE N = 710	Refractory SE N = 530	Super-refractory SE N = 165	SE, all categories N = 1,405
Cost	Original data in 2016 USA dollars	9,127 (5,715-17,209)	17,179 (9,671-28,298)	54,584 (39,139-78,273)	14,678 (7,203-28,388)
	Estimation in 2019 USA dollars	9,697 (6,072-18,284)	18,252 (10,275-30,065)	57,993 (41,583-83,161)	15,595 (7,653-30,161)

Legend: KID: Kid's Inpatient Database. **NIS:** National Inpatient Sample. **SE:** Status epilepticus. **USA:** United States of America.

Table 3
Cost data (in 2016 US dollars) stratified by relevant factors.

KID 2016 N = 6,106,405 (sample 3,040,080)

		Non-refractory SE N = 422	Refractory SE N = 116	Super-refractory SE N = 42	SE, all categories N = 580
STRATIFICATION					
Cost by hospital bedsize	**Large**	6,485 (3,692-14,576)	12,505 (8,098-19,426)	94,188 (50,111-179,629)	8,593 (4,816-18,730)
	Medium	6,692 (4,157-11,947)	21,444 (11,442-35,358)	162,195 (80,249-383,464)	8,879 (5,338-21,392)
	Small	7,036 (2,641-11,313)	11,176 (4,467-14,826)	103,685 (101,170-131,365)	8,728 (3,398-18,791)
Cost by emergency department admission	**Emergency department admission**	6,813 (3,965-12,982)	13,268 (9,357-21,751)	143,672 (65,748-191,682)	9,083 (5,483-18,352)
	No emergency department admission	6,067 (3,283-15,198)	12,789 (6,395-22,203)	106,950 (53,624-234,003)	7,551 (3,972-23,449)
SE developed during elective admission	**No**	6,588 (3,521-13,069)	13,286 (8,392-22,273)	143,791 (66,658-250,188)	8,831 (4,879-19,039)
	Yes	6,710 (4,567-17,593)	No admissions in this category	19,216 (18,336-43,168)	7,281 (4,680-18,498)
Cost by primary payer	**Private insurance**	7,652 (4,512-18,252)	18,868 (8,111-24,757)	77,934 (60,298-141,929)	10,293 (5,130-21,730)
	Medicare/Medicaid	6,151 (3,360-10,710)	12,141 (8,217-20,998)	169,592 (97,354-253,970)	7,777 (4,207-16,353)
	Other insurance (self-pay, no charge, or other)	7,912 (3,603-16,577)	12,686 (9,453-24,542)	54,715 (15,682-258,438)	11,828 (5,511-24,056)
Cost by sex	**Male**	6,633 (3,970-12,498)	12,826 (8,283-22,829)	106,155 (61,962-198,264)	8,277 (5,024-18,645)
	Female	6,544 (3,367-15,530)	14,151 (8,787-21,053)	139,828 (68,862-263,398)	9,147 (4,458-19,894)
Cost by disease severity	**Extreme or major**	9,348 (5,555-20,902)	14,412 (9,102-22,829)	No admissions in this category	13,876 (6,684-32,356)
	Moderate or minor	5,573 (3,015-9,410)	8,494 (7,242-13,671)	139,790 (65,089-230,451)	5,651 (3,086-9,558)
Cost by mortality risk	**Extreme or major**	19,170 (10,183-75,868)	13,616 (8,345-21,674)	139,790 (64,444-208,647)	18,974 (9,818-58,921)
	Moderate or minor	6,128 (3,475-10,984)	11,335 (6,082-21,337)	106,199 (106,199-256,707)	6,209 (3,493-11,278)

NIS 2016 N = 29,274,158 (sample 5,854,836)

		Non-refractory SE N = 710	Refractory SE N = 530	Super-refractory SE N = 165	SE, all categories N = 1,405
STRATIFICATION					
Cost by hospital bedsize	**Large**	9,854 (5,834-16,687)	18,073 (12,695-28,475)	54,584 (37,668-78,273)	16,213 (7,796-31,903)
	Medium	7,612 (5,377-17,738)	11,862 (8,687-17,918)	46,907 (33,610-59,061)	10,869 (6,908-24,874)
	Small	8,510 (5,782-16,105)	14,195 (6,570-31,665)	57,019 (30,242-77,243)	11,675 (6,412-26,116)
Cost by emergency department admission	**Emergency department admission**	8,473 (5,613-16,367)	15,675 (8,853-25,841)	50,482 (34,846-71,564)	12,752 (6,736-24,945)
	No emergency department admission	11,497 (6,010-21,165)	20,166 (12,825-30,424)	55,099 (45,662-80,945)	18,938 (9,879-36,053)
Status epilepticus developed during elective admission	**No**	8,611 (5,613-16,890)	17,179 (9,671-27,995)	54,068 (38,639-73,855)	14,744 (7,097-28,791)
	Yes	10,973 (8,511-20,325)	16,325 (8,555-29,426)	#	12,914 (8,911-26,815)
Cost by primary payer	**Private insurance**	11,188 (6,311-17,382)	16,752 (9,756-24,126)	46,112 (38,639-54,875)	14,951 (8,555-23,072)
	Medicare/Medicaid	8,454 (5,012-17,639)	16,953 (9,300-28,475)	56,059 (40,736-85,963)	14,361 (6,655-31,707)
	Other insurance (self-pay, no charge, or other)	7,521 (5,742-9,767)	15,999 (11,574-31,801)	Not enough admissions in this category to calculate percentiles	11,862 (8,493-19,577)
Cost by sex	**Male**	9,137 (5,797-19,633)	17,187 (11,247-29,272)	56,059 (40,736-67,644)	14,678 (8,098-28,388)
	Female	8,812 (5,613-15,056)	16,065 (7,841-25,303)	53,585 (35,829-90,562)	13,752 (6,269-27,958)
Cost by disease severity	**Extreme or major**	15,261 (8,519-26,107)	17,420 (9,999-28,298)	54,584 (39,139-78,273)	19,238 (10,553-36,726)
	Moderate or minor	6,293 (4,985-10,994)	9,560 (7,855-11,809)	#	7,036 (5,176-11,305)
Cost by mortality risk	**Extreme or major**	16,190 (8,713-26,815)	17,179 (9,783-28,121)	54,063 (38,116-75,328)	7,106 (4,994-13,315)
	Moderate or minor	7,001 (4,855-12,797)	7,855 (7,855-21,396)	55,099 (55,099-72,831)	19,339 (10,772-36,593)

Legend: KID: Kid's Inpatient Database. **NIS:** National Inpatient Sample. **SE:** Status epilepticus. **USA:** United States of America.

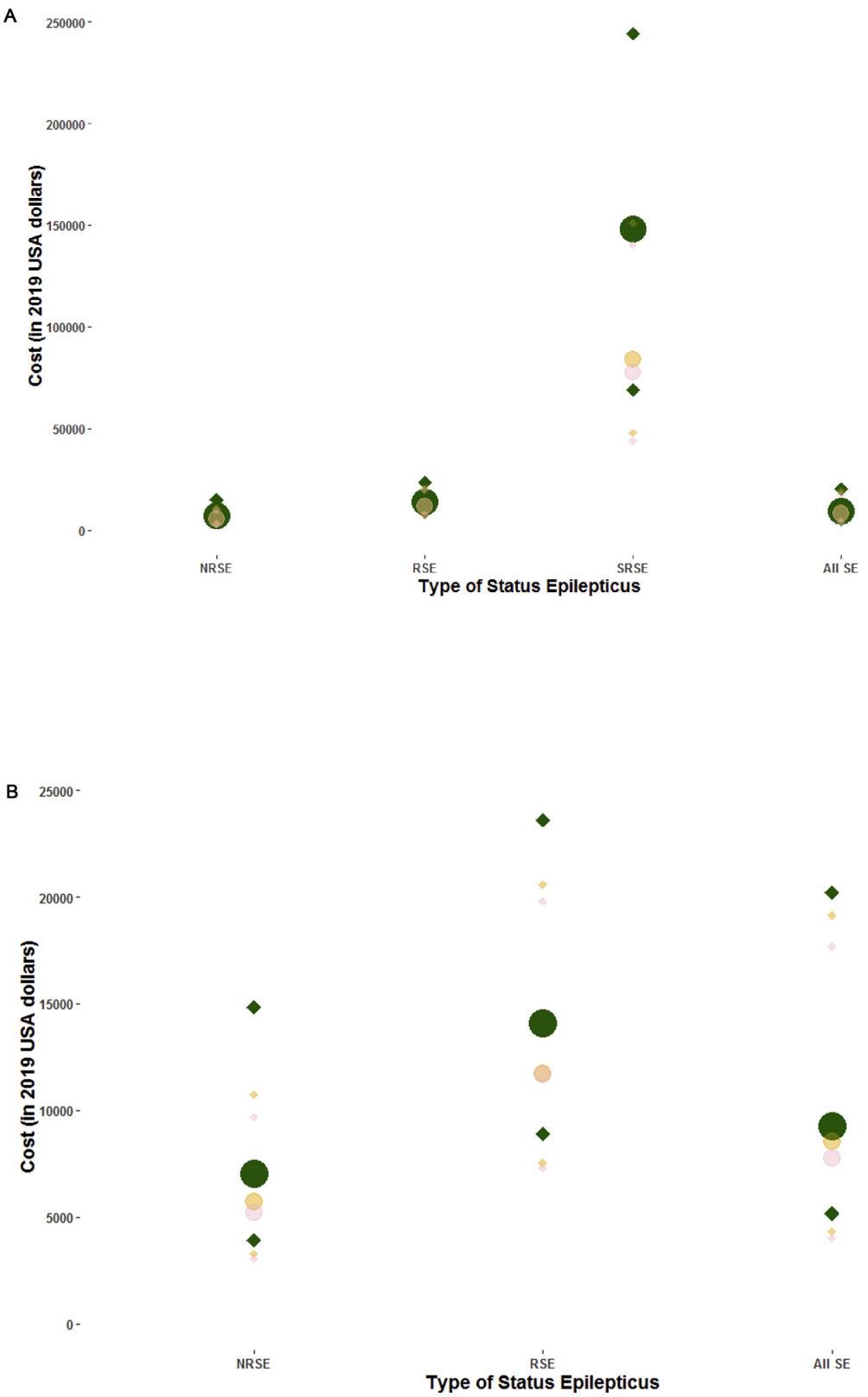

Fig. 1. Cost in 2019 USA dollars for pediatric admissions. Comparison of the estimates from KID2016 (green), KID2012 (orange), and KID2009 (pink). The circles represent the median values, the diamonds represent the 25th and 75th percentiles. A. Comparison of non-refractory status epilepticus (NRSE), refractory status epilepticus (RSE), super-refractory status epilepticus (SRSE), and all status epilepticus (All SE). B. As the cost of SRSE drives most of the y-axis, we provide the same graph without SRSE to better appreciate the differences in NRSE, RSE, and All SE. Colors may not be distinguishable in the print (black and white) version of the article.

more than 5 years old [4–79].

In the USA, there are very few studies evaluating the economic burden of SE, and these studies rely on ICD-9 codes [4,5,7]. In a study based on data from admissions for SE from July 1993 to June 1994 at the Medical College of Virginia, the median (p25–p75) inpatient reimbursement was $8,417 ($5,592–$21,155) [$14,492 ($9,628-$36,423) in 2019 USA dollars] [7]. Similar to our study, costs were lower for children (0–16 years of age): $6,140 ($3,423–$14,795) [$10,571 ($5,893–$25,473) in 2019 USA dollars] than for adults (17–45 years of age): $14,689 ($7,892–$26,604) [$25,290 ($13,588–$45,804) in 2019 USA dollars] [7]. Based on these data, it was estimated that the direct cost of SE admissions in the USA for SE

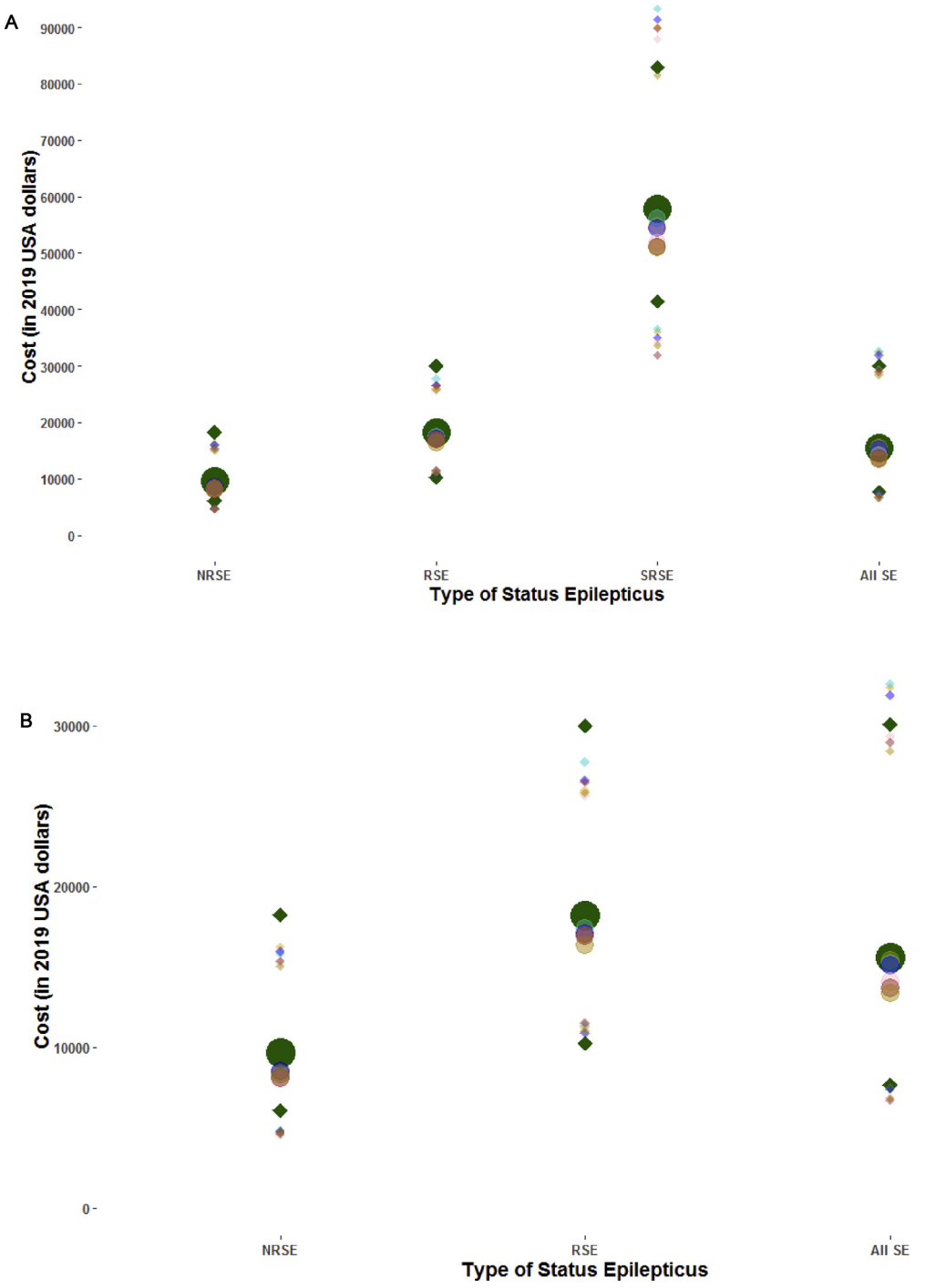

Fig. 2. Cost in 2019 USA dollars for adult admissions. Comparison of the estimations from NIS2016 (green), NIS2012 (orange), NIS2011 (turquoise), NIS2010 (blue), NIS2009 (pink), NIS2008 (brown), and NIS2007 (gold). The circles represent the median values, the diamonds represent the 25th and 75th percentiles. A. Comparison of non-refractory status epilepticus (NRSE), refractory status epilepticus (RSE), super-refractory status epilepticus (SRSE), and all status epilepticus (All SE). B. As the cost of SRSE drives most of the y-axis, we provide the same graph without SRSE to better appreciate the differences in NRSE, RSE, and All SE. Colors may not be distinguishable in the print (black and white) version of the article.

was approximately $4 billion per year [7]. A more recent estimate was based on the 2012 Premier Hospital Database with a total of 5,300,000 hospital discharges representing approximately 20% of all USA hospitalizations [4]. The median cost of admissions for super-refractory SE was estimated at $33,294 in 2012 USA dollars [$36,973 in 2019 USA dollars] [4], close to the range of $39,139–$78,273 in 2016 USA dollars estimated in our study. The higher costs in our study may be attributed to a requirement for classifying an episode as super-refractory SE of mechanical ventilation for at least 96 hours as opposed to at least 48 hours in other studies [4,6]. As in prior literature, we found that a major proportion of the cost associated with SE can be attributed to super-refractory SE. In a study using the Gesundheitsforen Leipzig research database, which contains data from approximately 4.1 million patients across Germany, the median cost for admissions was much higher for super-refractory SE (€32,706) [assuming a 1 euro : 1.39 USA dollar conversion in 2011, which was the average 2011 exchange, this would be approximately $51,961 in 2019 USA dollars] than for refractory SE (€4,581) [assuming a 1 euro : 1.39 USA dollar conversion in 2011, which was the average 2011 exchange, this would be approximately $7,279 in 2019 USA dollars] and non-refractory SE (€4,063) [assuming a 1 euro : 1.39 USA dollar conversion in 2011, which was the average 2011 exchange, this would be approximately $5,648 in 2019 USA dollars] [6]. In a similar study using the Arvato Health Analytics research database, which contains data from approximately 4 million patients in Germany, the median cost of admission for pediatric SE was €15,880 [assuming a 1 euro : 1.39 USA dollar conversion in 2011,

which was the average 2011 exchange, this would be approximately $25,229 in 2019 USA dollars], also much higher for super-refractory SE (€75,358 [assuming a 1 euro : 1.39 USA dollar conversion in 2011, which was the average 2011 exchange, this would be approximately $119,726 in 2019 USA dollars]), than for refractory SE (€13,864 [assuming a 1 euro : 1.39 USA dollar conversion in 2011, which was the average 2011 exchange, this would be approximately $22,027 in 2019 USA dollars]), and non-refractory SE (€4,119 [assuming a 1 euro : 1.39 USA dollar conversion in 2011, which was the average 2011 exchange, this would be approximately $6,544 in 2019 USA dollars]) [8]. A prior study based on the KID and NIS databases evaluated 186,013,640 admissions over 6 years (2007–2012), of which 184,500 admissions were related to SE [5], and estimated a median cost of admission related to SE around $7,000 in children and around $13,000 in adults [5]. The current study provides the most updated estimates of the cost of admissions associated with SE and also adds to the literature the first costs evaluated with the USA version of the ICD-10 coding system. The ICD-10 coding system provided by the World Health Organization has specific codes of SE and its subcategories under G41.: G41.0 as "grand mal status epilepticus", G41.1 as "petit mal status epilepticus", G41.2 as "complex partial status epilepticus", G41.8 as "other status epilepticus", and G41.9 as "status epilepticus, unspecified" [31]. In the original ICD-10 coding system all codes for focal epilepsies or unspecified epilepsies allow the designation of "with status epilepticus" to be used for history of SE, while patients with active SE are codified under G41. This system has allowed more granularity in the study of SE from claims data [6]. Unfortunately, the USA implementation of the ICD-10 coding system does not use codes under G41 and codifies SE under two codes according the American Academy of Neurology [10]: G40.301 as "Generalized idiopathic epilepsy and epileptic syndromes, not intractable, with status epilepticus" and G40.311 as "Generalized idiopathic epilepsy and epileptic syndromes, intractable, with status epilepticus" [10]. Codes for focal epilepsies and unspecified epilepsies with the designation of "with status epilepticus" are used for history of SE rather than for active SE [10]. Therefore, the USA implementation of the ICD-10 coding system might be more specific and less sensitive to the recognition of SE than in the more standard ICD-10 implementation. The estimated approximately 9.5/100,000 pediatric hospital admissions related to SE and approximately 4.8/100,000 adult hospital admissions related to SE in the current study is within the lower range of epidemiological studies in the literature [1,2], which is expected because all patients who had SE which resolved before hospital arrival or in the emergency room with no hospital admission are not captured in this database but are typically captured in population studies.

4.1. Strengths and weaknesses

Studies based on claims data necessarily estimate the cost of admissions related to SE with a "cost-adjusted charges" approach to estimating cost [32]. This method consists of adjusting billed charges by the ratio of cost-to-charges [32]. As billing and cost-to-charge data are available from most hospitals, it leads to estimates from a large population and from a wide range of hospitals and admissions [32]. However, the method of cost-adjusted charges requires the assumption that charge is proportional to economic cost and does not account for direct costs of SE occurring in the ambulatory setting after discharge [32]. Estimates of cost of admissions related to SE are quite stable when compared with prior literature [5] and have not changed markedly with the implementation of ICD-10 coding. Our results are also consistent with literature from Europe showing a marked increase in costs when SE becomes super-refractory [6]. All these approaches based on "cost-adjusted charges" may require further refinement with more granular analyses using microcosting and activity-based cost allocation approaches [32]. These more resource-intensive methods estimate costs from the individual components of an admission [32]. Therefore, they can only be applied in smaller populations, but provide an additional degree of granularity that prior "cost-adjusted charges" methods are not able to achieve.

Secondary use of data collected primarily for administrative purposes faces the problem of validity. In particular, ICD coding might not reflect clinical information accurately, and hence is subject to information bias. Research on the validity of the clinical information contained in administrative data have shown mixed results, but tend to support a high level of validity, especially for SE and for mechanical ventilation [33,34]. In order to preserve patient privacy, administrative data do not allow an in-depth evaluation of clinically relevant nuances and only allows rough estimates.

We used a modification of the classification used in prior literature where the refractoriness of SE is identified based on the duration of mechanical ventilation [6]. We classified SE as superrefractory when the patient was intubated for at least 96 hours. This does not follow the prior literature which classified SE as superrefractory when the patient was intubated for at least 48 hours [6], but it is the best that we can do considering that our data do not have information on intubation for 48 hours.

The main outcome in this study is cost of admissions related to SE. Even if our inclusion and exclusion criteria undersampled or oversampled admissions related to SE, cost estimates should not be markedly affected by that. The present study cannot estimate other economical and clinical aspects of SE such as lost career opportunities due to neurological impairment or indirect costs for loss of working hours in patients and family members. Therefore, the total costs of SE may be even higher than the inpatient costs estimated in this study.

4.2. Conclusion

The current study estimates the median cost of admissions related to SE in the USA at approximately $9,000 for pediatric patients, and at approximately $15,000 for adults, with a marked increase in cost of admissions with increasing SE severity. The cost of admissions related to SE has not markedly changed using ICD-10 codes when compared with the estimates based on ICD-9 codes.

Tobias Loddenkemper serves on the Council of the American Clinical Neurophysiology Society, on the American Board of Clinical Neurophysiology, as founder and consortium PI of the pediatric status epilepticus research group (pSERG), as an Associate Editor for Wyllie's Treatment of Epilepsy 6th edition and 7th editions, and as a member of the NORSE Institute, PACS1 Foundation, and CCEMRC. He served as Associate Editor of Seizure, and severed on the Laboratory Accreditation Board for Long Term (Epilepsy and Intensive Care Unit) Monitoring in the past.

Declaration of Competing Interest

Iván Sánchez Fernández was funded for the study of epileptic encephalopathies by Fundación Alfonso Martín Escudero and is funded by the Epilepsy Research Fund.

Marta Amengual-Gual is funded by Fundación Alfonso Martín Escudero.

Cristina Barcia Aguilar is funded by Fundación Alfonso Martín Escudero.

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He is part of patent applications to detect and predict clinical outcomes, and to manage, diagnose, and treat neurological conditions,

epilepsy, and seizures. Dr. Loddenkemper is co-inventor of the TriVox Health technology, and Dr. Loddenkemper, and Boston Children's Hospital might receive financial benefits from this technology in the form of compensation in the future.

He received research support from the Epilepsy Research Fund, NIH, the Epilepsy Foundation of America, the Epilepsy Therapy Project, the Pediatric Epilepsy Research Foundation, and received research grants from Lundbeck, Eisai, Upsher-Smith, Mallinckrodt, Sunovion, Sage, Empatica, and Pfizer, including past device donations from various companies, including Empatica, SmartWatch, and Neuro-electrics.

In the past, he served as a consultant for Zogenix, Upsher Smith, Amzell, Engage, Elsevier, UCB, Grand Rounds, Advance Medical, and Sunovion.

He performs video electroencephalogram long-term and ICU monitoring, electroencephalograms, and other electrophysiological studies at Boston Children's Hospital and affiliated hospitals and bills for these procedures and he evaluates pediatric neurology patients and bills for clinical care.

He has received speaker honorariums from national societies including the AAN, AES and ACNS, and for grand rounds at various academic centers.

His wife, Dr. Karen Stannard, is a pediatric neurologist and she performs video electroencephalogram long-term and ICU monitoring, electroencephalograms, and other electrophysiological studies and bills for these procedures and she evaluates pediatric neurology patients and bills for clinical care.

Acknowledgement

This study was supported by the Epilepsy Research Fund.

Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:https://doi.org/10.1016/j.seizure.2019.09.001.

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