

Introduction

- Status epilepticus (SE) is associated with poor outcomes, high costs, and considerable healthcare resource utilization^{1,2}
- Nearly 30% of patients with SE fail to respond to first-line and second-line anti-epileptic drugs (AEDs) and are classified as refractory SE (RSE)³⁻⁵
- We lack a full understanding of how the burden of illness associated with hospitalization for SE changes with increasing severity of disease^{1,2}

Objectives

- To examine the clinical and economic burden of illness associated with SE of varying severity

Methods

- Patients of all ages with SE were identified using International Classification of Diseases, Tenth Revision, Clinical Modification (ICD-10) diagnosis codes explicitly specifying "with SE" from the 2016-2018 Premier Healthcare Database
- SE patients were required to have an inpatient admission and a complete episode of care (i.e., no outpatient visits or transfers in or out of the facility)
- Three SE patient cohorts were defined using medications as a marker of increasing severity:
 - Cohort 1 (mild severity) received ≤ 1 IV AED and did not receive an IV anesthetic for 3rd-line SE treatment
 - Cohort 2 (moderate severity) received >1 IV AED and did not receive an IV anesthetic for 3rd-line SE treatment
 - Cohort 3 (high severity) received ≥ 1 IV AED and required an IV anesthetic for 3rd-line SE treatment (defined as IV anesthetic and an ICU stay)
- Based on extensive use of benzodiazepines by emergency medical services, first-line benzodiazepine use was assumed for all patients and was not used for selection due to potential missingness in the chargemaster data⁶
 - Midazolam use on the same day or after the 1st IV AED was assumed as anesthetic
- Comparisons across SE severity cohorts were assessed in pairwise comparisons using a bootstrap-based analysis of variance for parametric data, Kruskal-Wallis tests for nonparametric data, and chi-square tests for categorical data

Results

Table 1. Baseline characteristics of patients with status epilepticus

Characteristic	Low Severity	Moderate Severity	High Severity	All
Visits, n (%)	14,694 (33.4%)	10,140 (23.1%)	19,154 (43.5%)	43,988 (100%)
Female, n (%)	7,342 (50.0%) [†]	5,068 (50.0%) [†]	8,727 (45.6%)*, #	21,137 (48.1%)
Age, mean (bootstrap 95% CI)	45.5 (45.1, 46.0) ^{#, †}	52.2 (51.7, 52.7)*	52.0 (51.7, 52.3)*	49.9 (49.7, 50.1)
Race, n (%)				
White	9,292 (63.2%)	5,973 (58.9%)	11,670 (60.9%)	26,935 (61.2%)
Black	3,204 (21.8%)	2,758 (27.2%)	4,760 (24.9%)	10,722 (24.4%)
Other	1,853 (12.6%)	1,197 (11.8%)	2,264 (11.8%)	5,314 (12.1%)
Unknown	345 (2.3%)	212 (2.1%)	460 (2.4%)	1017 (2.3%)
Ethnicity, n (%)				
Hispanic	1,153 (7.8%)	793 (7.8%)	1,510 (7.9%)	3,456 (7.9%)
Non-Hispanic	10,084 (68.6)	7,240 (71.4%)	13,800 (72.0%)	31,124 (71%)
Unknown	3,457 (23.5%)	2,107 (20.8%)	3,844 (20.1%)	9,408 (21%)

[†]p<0.01 versus low severity; *p<0.01 versus moderate severity; #p<0.01 versus high severity; CI = confidence interval.

Figure 2. Discharge disposition in patients with increasing disease severity.

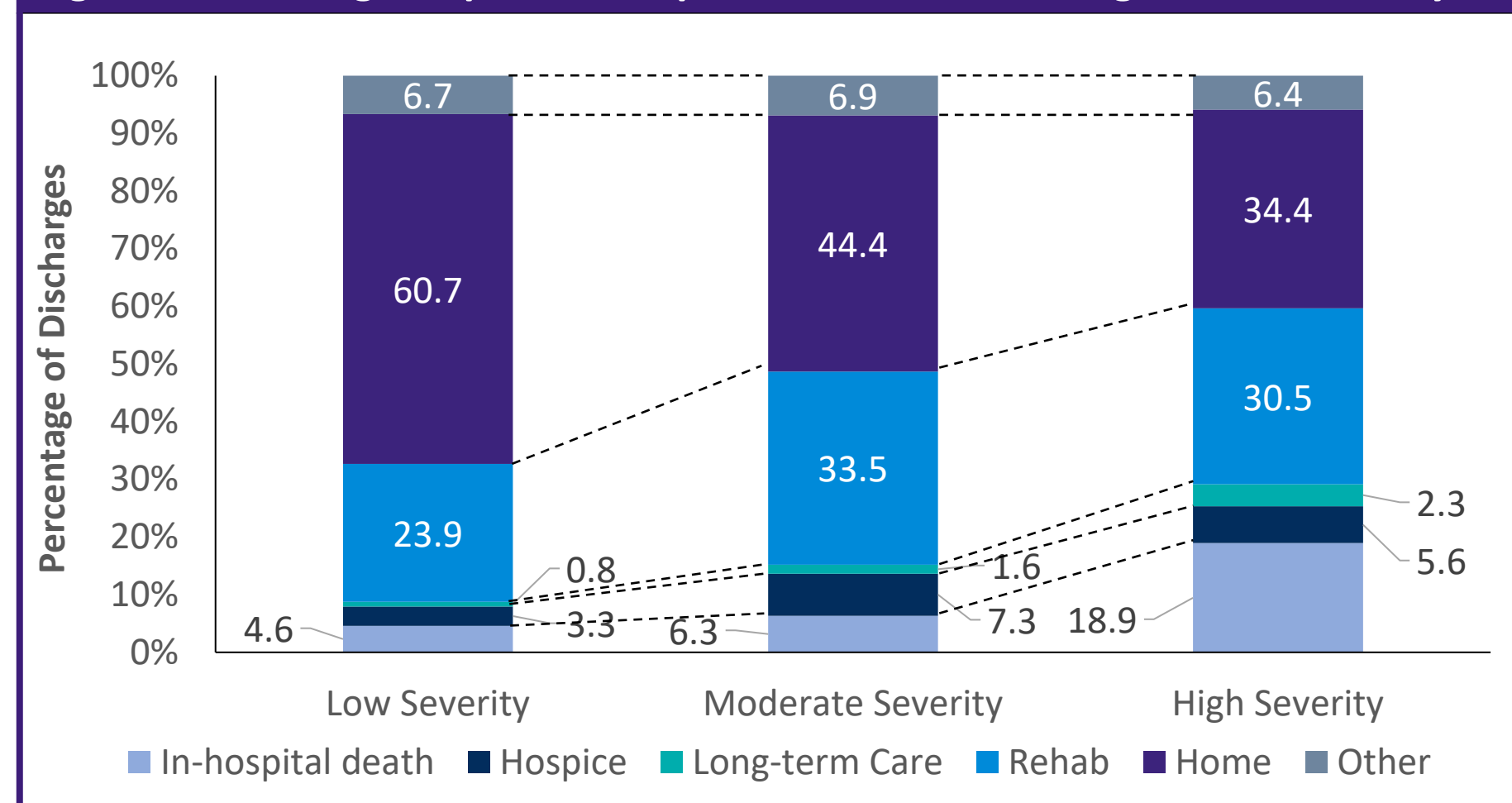
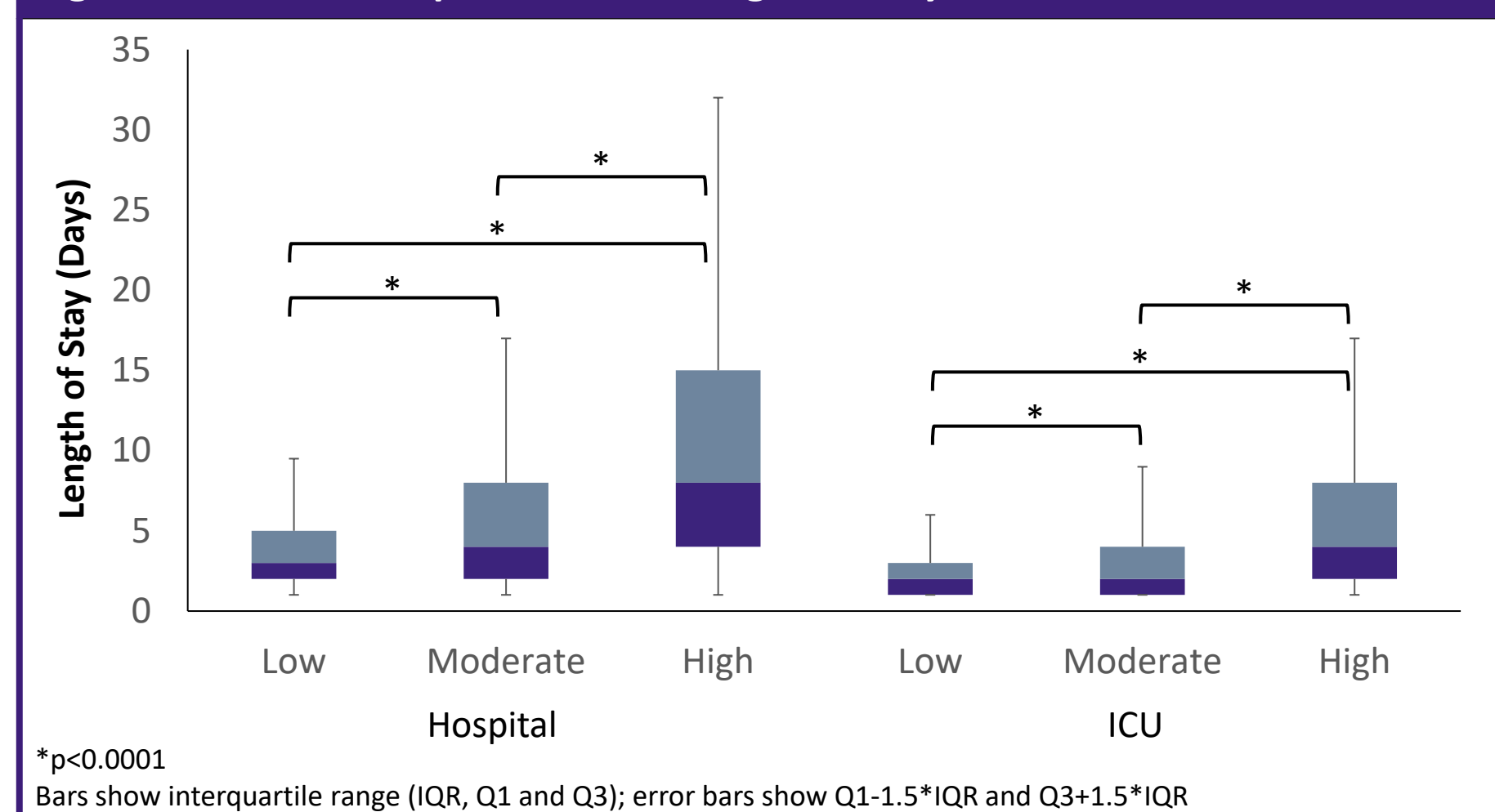
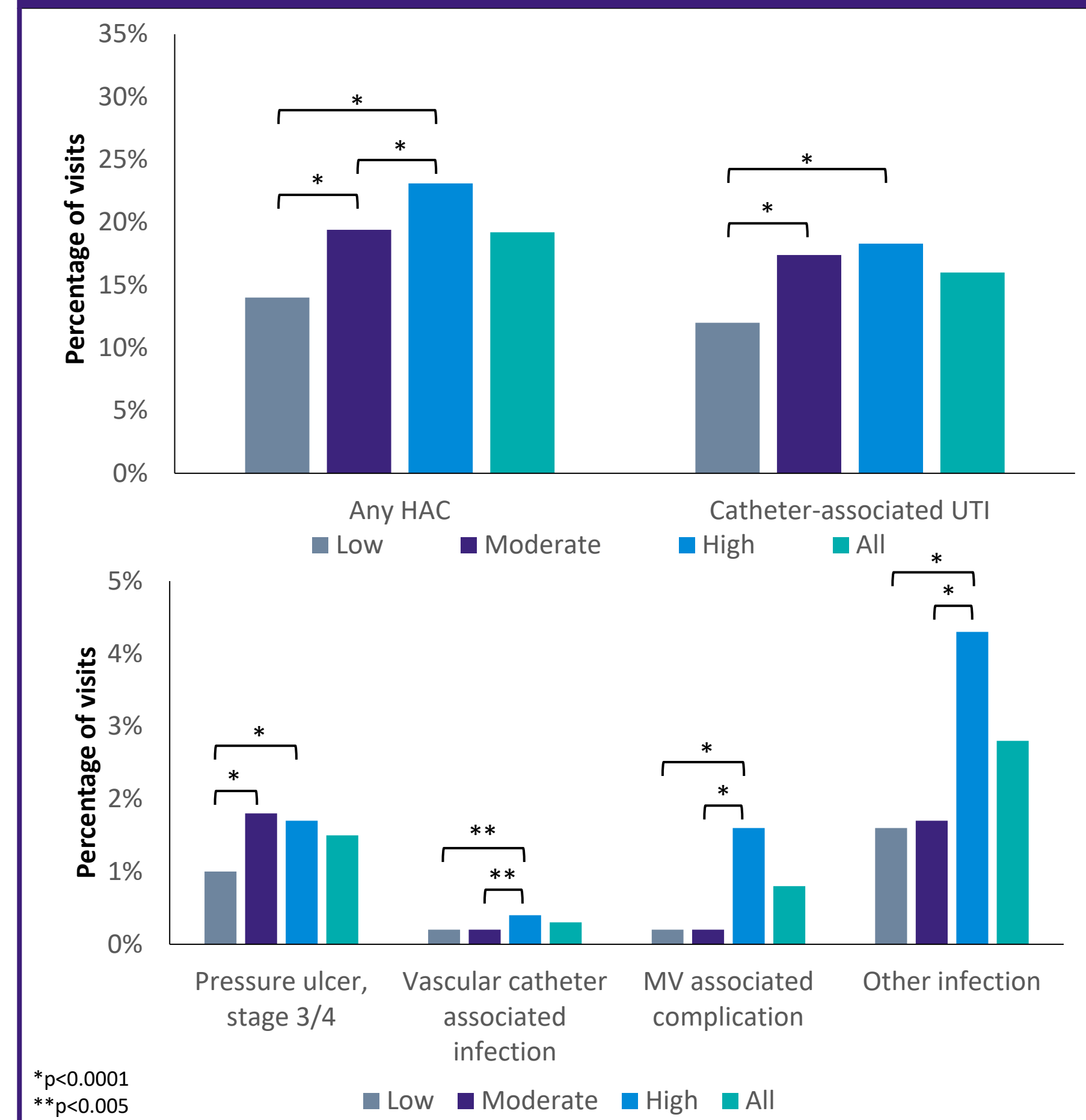


Figure 3. Median hospital and ICU length of stay across the cohorts



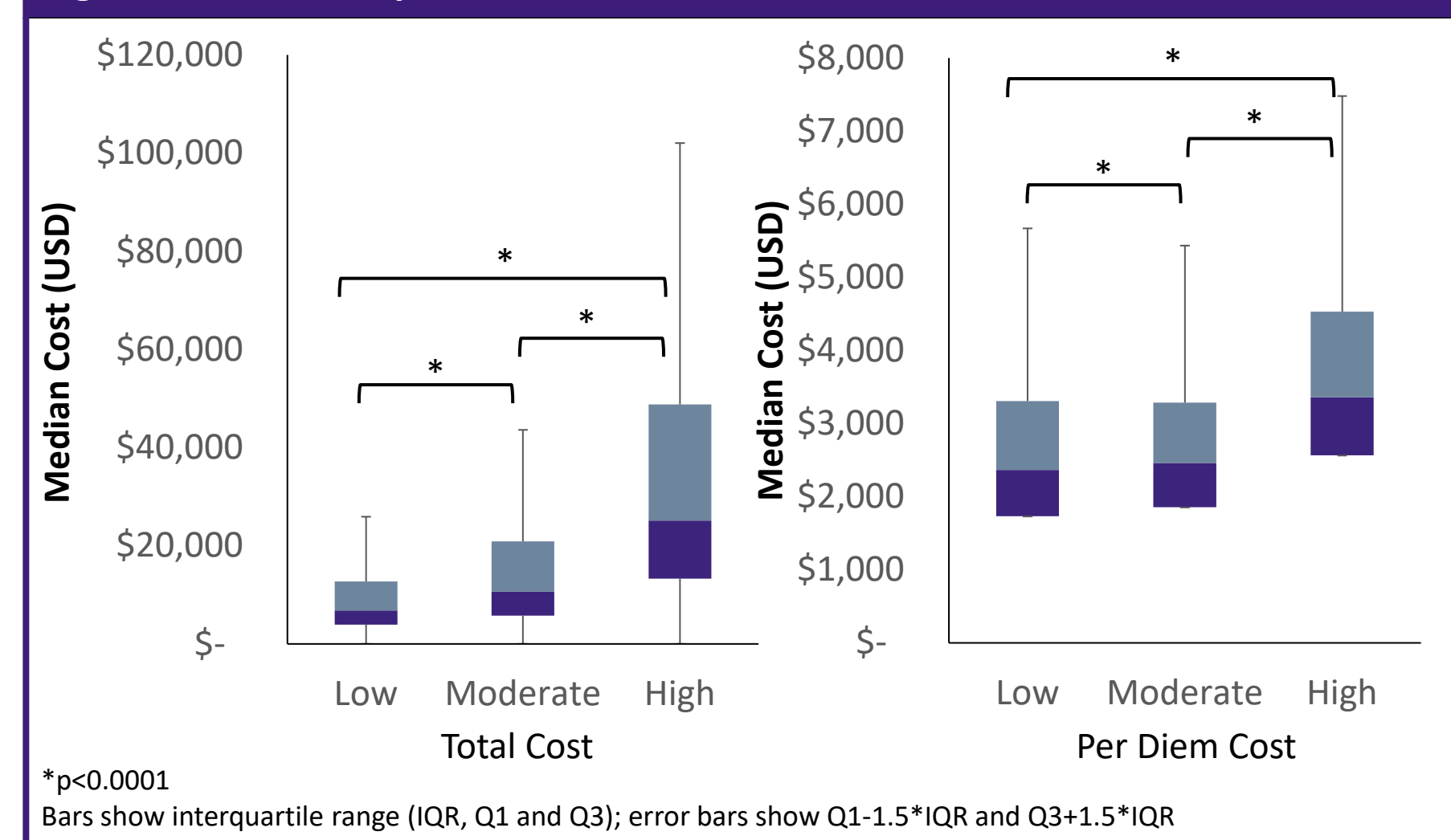
*p<0.0001
Bars show interquartile range (IQR, Q1 and Q3); error bars show Q1-1.5*IQR and Q3+1.5*IQR

Figure 4. Hospital-acquired conditions (HACs) across the SE cohorts



*p<0.0001
**p<0.005
Patients with high severity SE developed the largest proportion of hospital-acquired conditions overall, including higher rates of urinary tract infection (UTI), vascular catheter associated infection, miscellaneous infections, as well as complications associated with mechanical ventilation (MV)

Figure 5. Total and per diem costs associated with the SE cohorts.



*p<0.0001
Bars show interquartile range (IQR, Q1 and Q3); error bars show Q1-1.5*IQR and Q3+1.5*IQR
The greatest costs were observed in high severity patients [median \$25,105; mean (SD) \$41,858 (\$59,063)], which were significantly higher than either low [median \$6,812; mean (SD) \$11,532 (\$17,228)] or moderate [median \$10,592; mean (SD) \$18,328 (\$30,776)] severity patients
SD = standard deviation

Table 2. Anesthetic and AED use in patients with status epilepticus

Drug	Low Severity	Moderate Severity	High Severity	All
IV Anesthetics				
Propofol	1,705 (11.6%)	926 (9.1%)	16,373 (85.5%)	19,004 (43.2%)
Etomidate	498 (3.4%)	289 (2.9%)	7,602 (39.7%)	8,389 (19.1%)
Ketamine	156 (1.1%)	95 (0.9%)	1,239 (6.5%)	1,490 (3.4%)
Pentobarbital	5 (0.0%)	7 (0.1%)	326 (1.7%)	338 (0.8%)
IV AEDs				
Levetiracetam	7,085 (48.2%)	8,712 (85.9%)	16,851 (88.0%)	32,648 (74.2%)
Phenytoin	968 (6.6%)	5,567 (54.9%)	7,861 (41.0%)	14,396 (32.7%)
Fosphenytoin	383 (2.6%)	4,392 (43.3%)	6,549 (34.2%)	11,324 (25.7%)
Lacosamide	278 (1.9%)	3,317 (32.7%)	4,984 (26.0%)	8,579 (19.5%)
Valproate	491 (3.3%)	2,715 (26.8%)	4,117 (21.5%)	7,323 (16.6%)
Phenobarbital	281 (1.9%)	1,400 (13.8%)	2,294 (12.0%)	3,975 (9.0%)
Brivaracetam	5 (0.0%)	73 (0.7%)	103 (0.5%)	181 (0.4%)

- The mean number of IV AEDs used per patient increased from low [0.7 (0.64, 0.66)] to moderate [2.7 (2.72, 2.76)] to high [2.5 (2.46, 2.50)] severity SE
- On average, high severity patients received 1.4 (1.41, 1.43) IV anesthetics
- IV anesthetic use was permitted in the low and moderate severity groups if there was no ICU stay

Conclusions

- Among patients with SE, increasing severity of illness is associated with worse clinical outcomes, increased resource utilization, and higher costs
- High severity SE has an in-hospital mortality nearing 20%, median length of stay of 7 days, and median total hospital costs exceeding \$25,000
- Preventing the progression of patients to more severe forms of SE has the potential to reduce the clinical and economic burden of SE

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Disclosures

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