

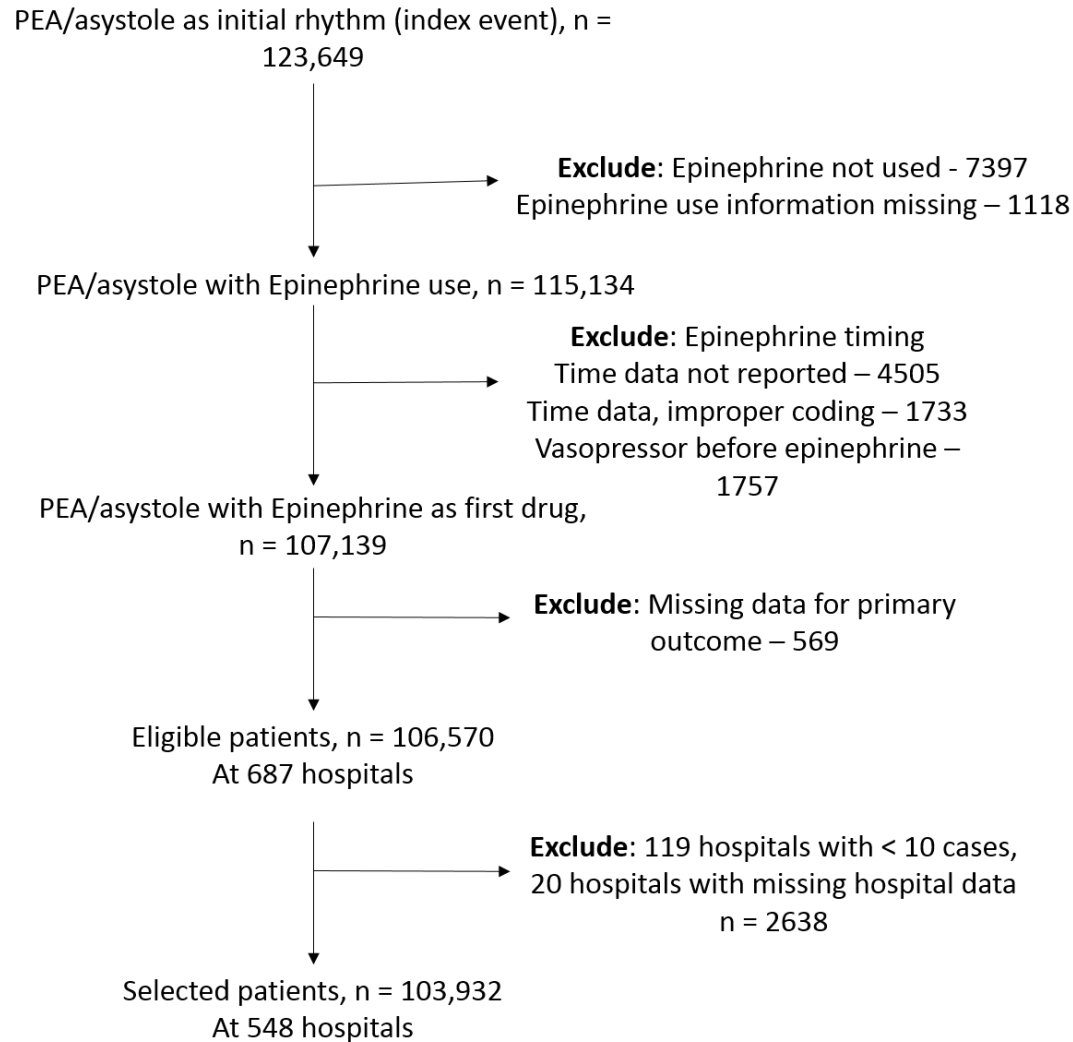
SUPPLEMENTAL MATERIAL

Hospital Variation in Time to Epinephrine for Non-Shockable In-Hospital Cardiac Arrest

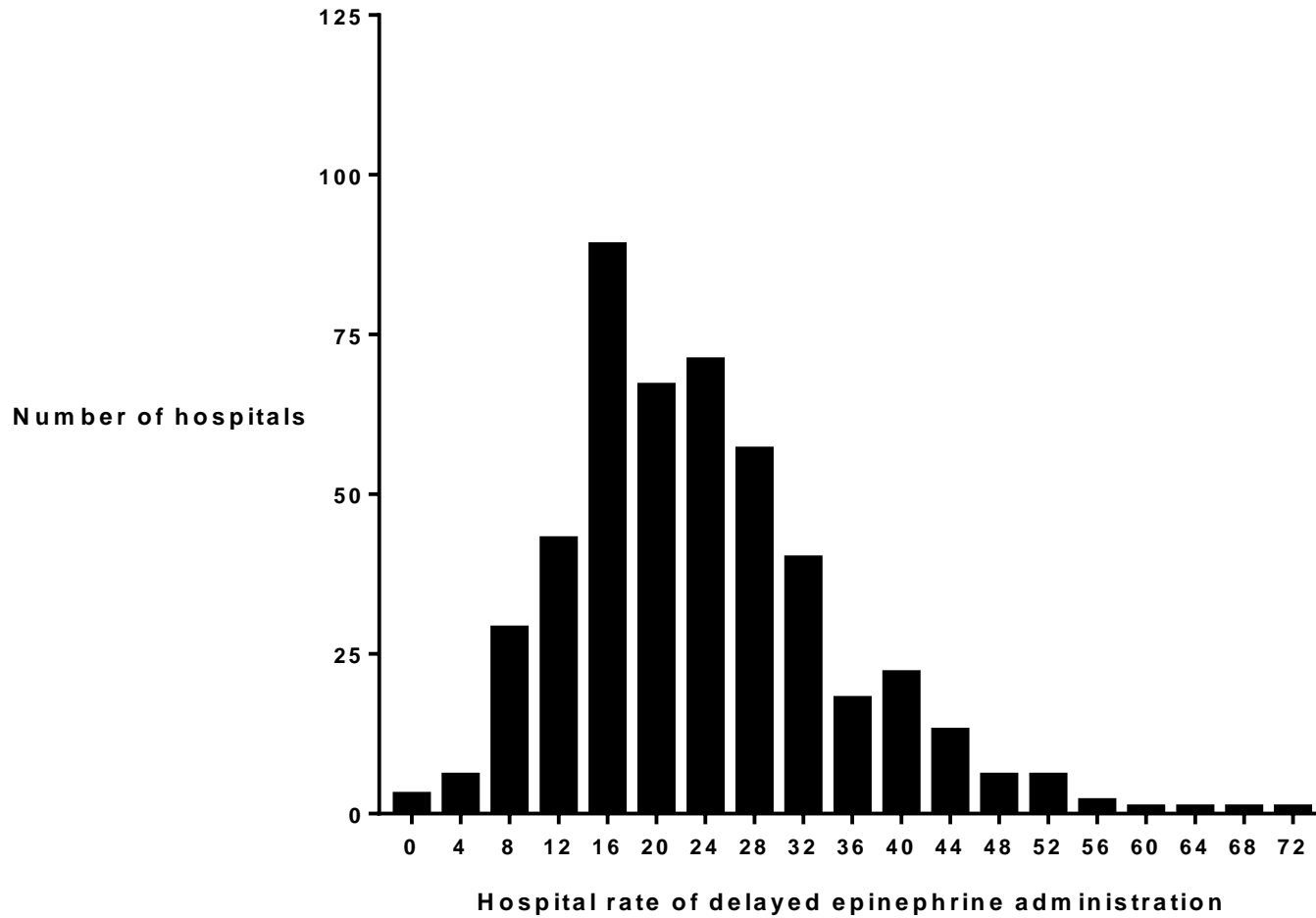
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for the American Heart Association's Get With The Guidelines-Resuscitation Investigators

Online-only Figures

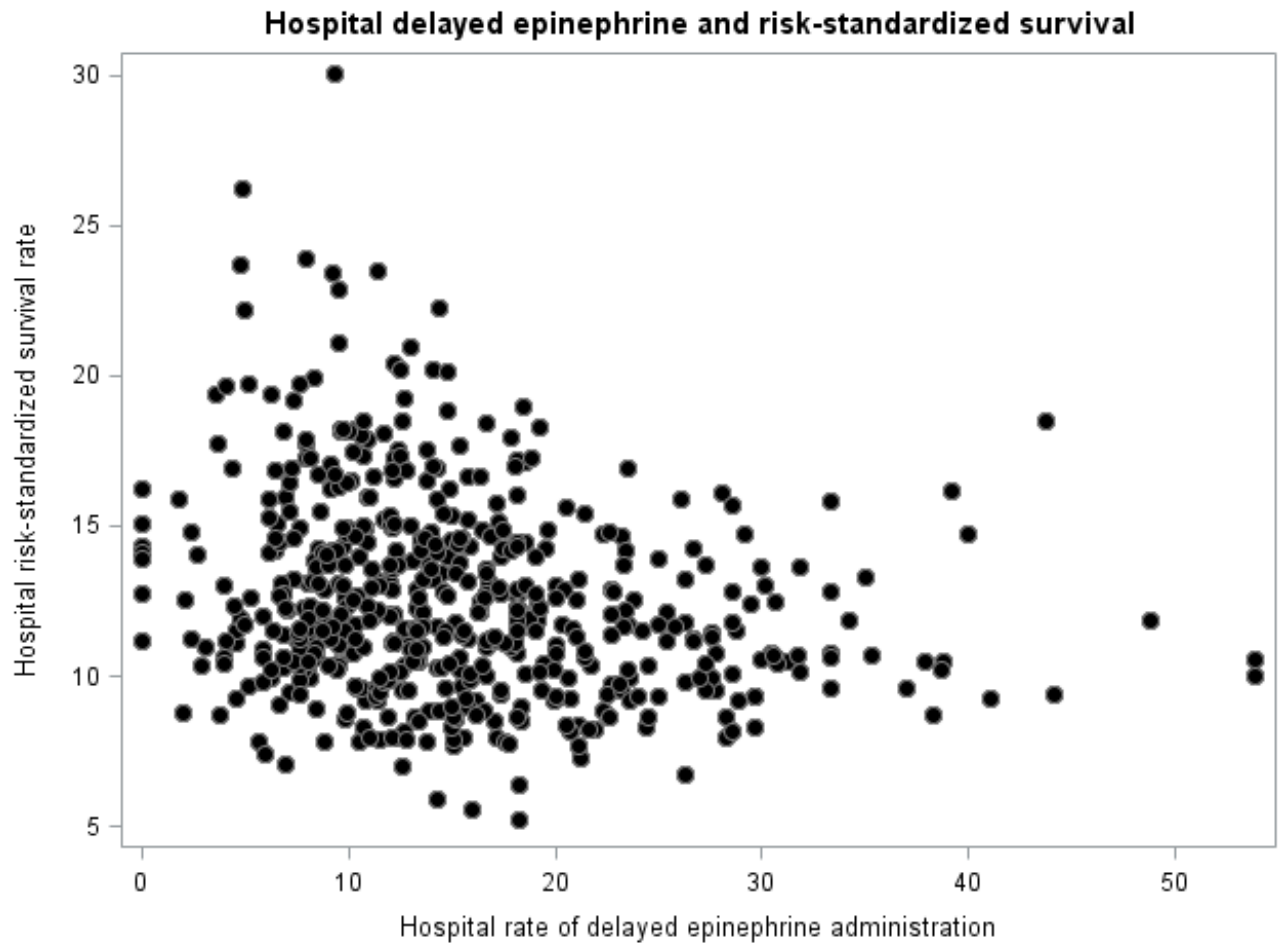
eFigure 1: Flowchart depicting selection of patients and hospitals.



eFigure 2: Non-ICU - Rate of delayed epinephrine administration (first dose > 5 minutes) in non-intensive care unit (non-ICU) patients - across 476 hospitals with at least 10 non-ICU non-shockable cardiac arrest cases. **Median Odds Ratio – 1.48 (95% C.I. 1.42, 1.54).**

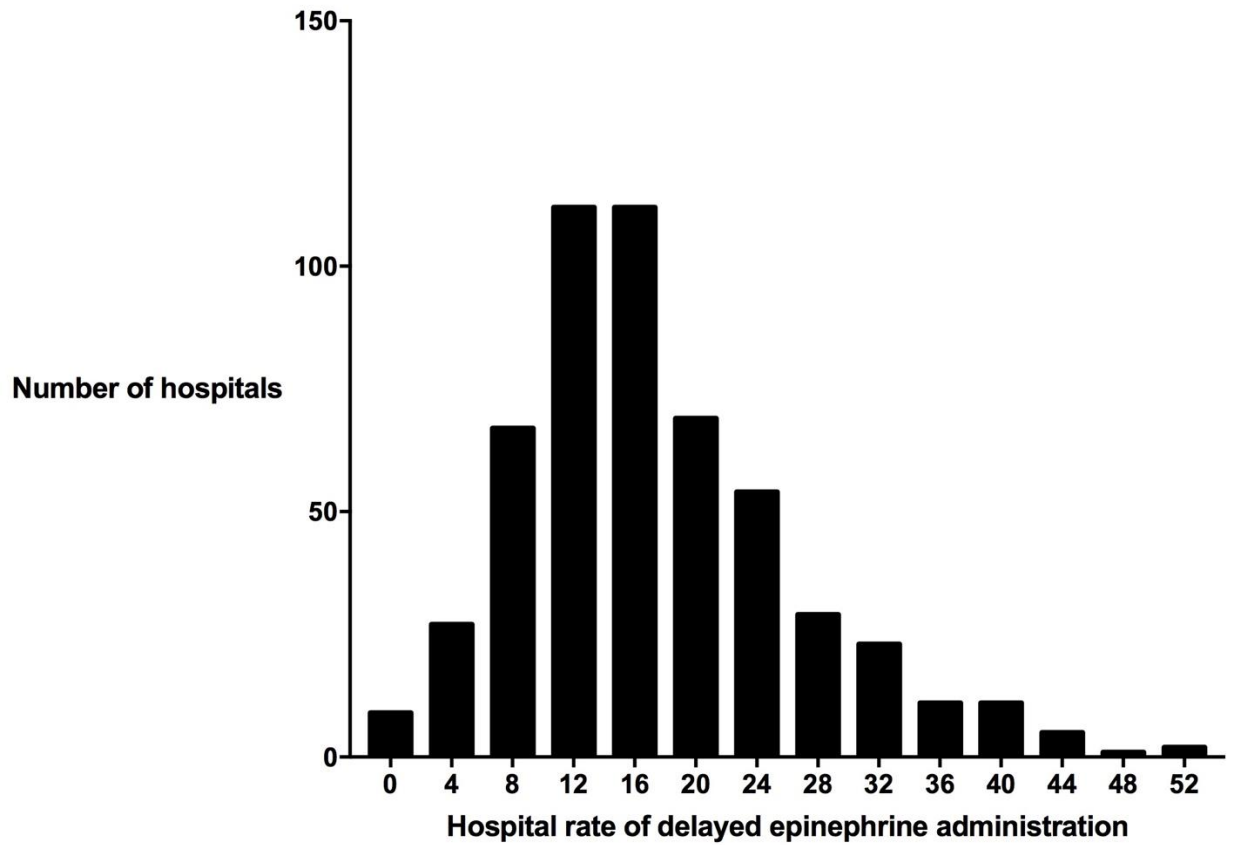


eFigure 3: Non-ICU - Association between hospital rate of delayed epinephrine administration in non-ICU non-shockable cardiac arrests and its cardiac arrest survival (*correlation coefficient -0.19, P-value <.0001*), and across hospital quartiles of delayed epinephrine use.

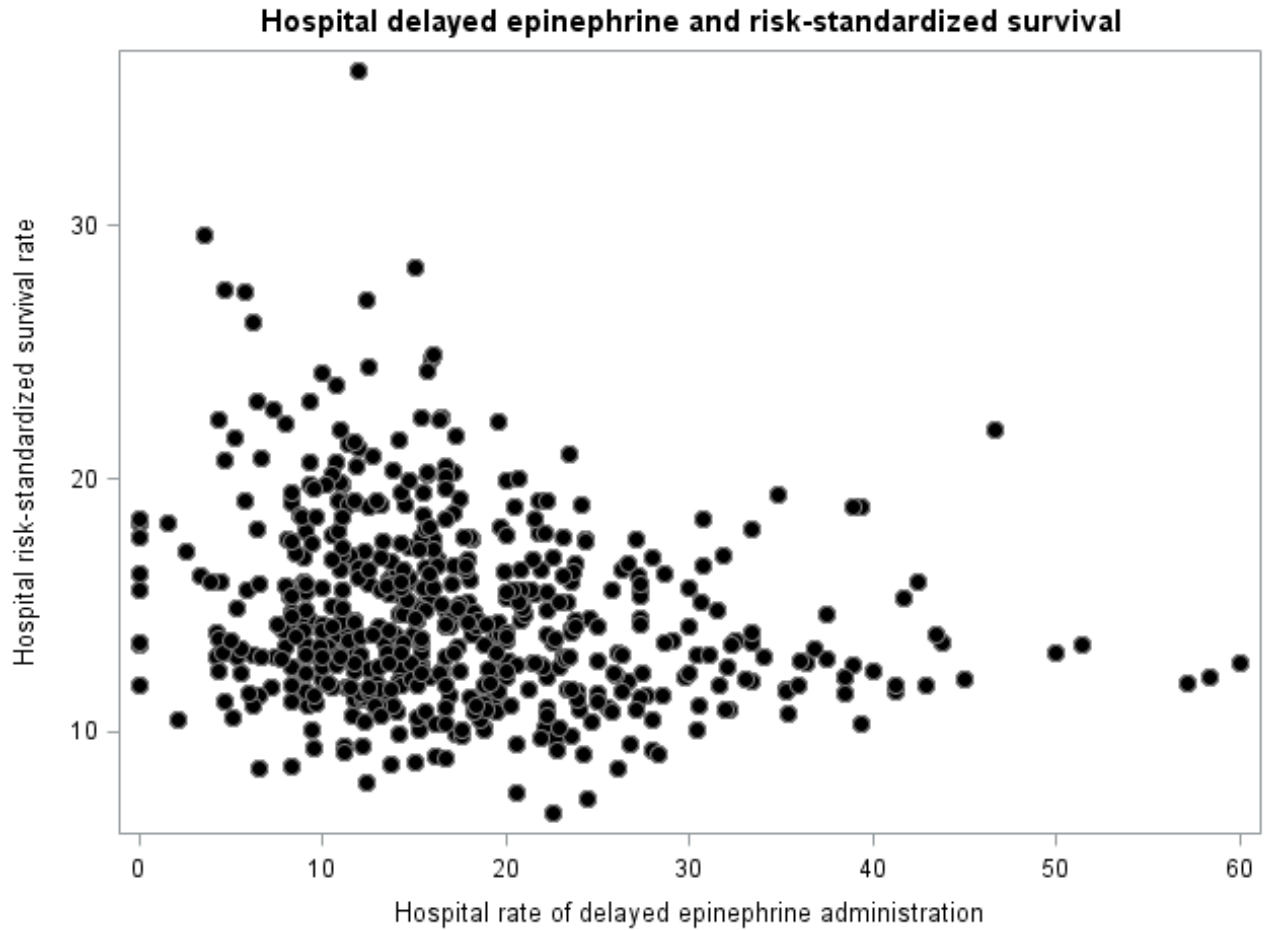


	Quartiles of delay				P-value (trend)
	Q1	Q2	Q3	Q4	
Median Hospital risk-standardized survival rate (Interquartile range)	13.3% (11.6% - 16.6%)	14.3% (11.7% - 16.9%)	13.0% (10.9% - 16.4%)	12.0% (10.4% - 14.1%)	<.0001

eFigure 4: Excluding patients receiving vasopressors - Rate of delayed epinephrine administration (first dose > 5 minutes) in patients not receiving vasopressors at the time of cardiac arrest- across 534 hospitals with at least 10 non-shockable cardiac arrest cases. **Median Odds Ratio – 1.51 (95% C.I.1.44, 1.57)**.



eFigure 5: Excluding patients receiving vasopressors - Association between hospital rate of delayed epinephrine administration in patients not receiving vasopressors with non-shockable cardiac arrests and its cardiac arrest survival (*correlation coefficient -0.22. P-value <.0001*) and across hospital quartiles of delayed epinephrine use.



	Quartiles of delay				P-value (trend)
	Q1	Q2	Q3	Q4	
Median Hospital risk-standardized survival rate (Interquartile range)	14.6% (12.9%, 18.0%)	14.7% (12.3%, 17.2%)	14.4% (12.3%, 16.8%)	12.9% (11.6%, 15.1%)	<.0001

Online-only Tables

eTable 1: Description of variables included in the study.

Variable	Definition
Demographics	
Age	Age in years
Sex	Self-reported (male or female)
Race	Self-reported (white, black or other)
Cardiac arrest characteristics	
Initial cardiac arrest rhythm	First documented rhythm at the time of cardiac arrest (asystole or Pulseless Electrical Activity [PEA])
Hospital location	Location of patient in the hospital at the time of cardiac arrest (ICU, monitored unit [telemetry], or non-monitored unit)
Delayed chest compression	Initiation of chest compression >1 minute from the onset of cardiac arrest
Time of cardiac arrest	Time of day when cardiac arrest daytime (working hours [7:00 AM – 10:59] or nighttime [11:00 PM – 6:59 AM])
Weekend/Holiday arrest	Weekend [Saturday, Sunday] or National Holiday on day of cardiac arrest
Use of a hospital-wide cardiopulmonary arrest alert (“Code Blue”)	Use of a general hospital broadcast method for cardiac arrest notification (e.g., overhead pagers or audio alert)
Co-morbidities	
Diabetes mellitus	Documented diagnosis of Type I or Type II diabetes mellitus
Heart failure	Documented diagnosis of congestive heart failure prior to this admission
Acute Myocardial infarction	Documented diagnosis of myocardial ischemia (acute coronary syndrome) or myocardial infarction during this admission
Acute stroke	Documented diagnosis of an intracranial or intraventricular hemorrhage or thrombosis during this admission
Hypotension/Hypoperfusion	Evidence of hypotension within 4 hours up to the time of the event, defined by ANY of the following <ol style="list-style-type: none"> 1. SBP < 90 or MAP < 60 mmHg 2. Vasopressor or inotropic requirement after volume expansion (except for dopamine ≤ 3 mcg/kg/min) 3. Intra-aortic balloon pump
Hepatic insufficiency	Evidence of hepatic insufficiency within 24 hours up to the time of the event, defined by ANY of the following <ol style="list-style-type: none"> 1. Total bilirubin > 2 mg/dL and AST > 2x normal 2. Cirrhosis

Renal insufficiency	Evidence of renal insufficiency prior to the event, defined by ANY of the following 1. Requiring ongoing dialysis or extracorporeal filtration therapies 2. Creatinine > 2 mg/dL within 24 hours up to the time of the event
Metabolic or electrolyte abnormality	Evidence of metabolic/electrolyte abnormality within 4 hours up to the time of the event, defined by ANY of the following 1. Sodium < 125 or > 150 mEq/L 2. Potassium < 2.5 or > 6 mEq/L 3. Arterial pH < 7.3 or > 7.5 4. Lactate > 2.5 mmol/L 5. Blood glucose < 60 mg/dL
Septicemia	Bloodstream infection where antibiotics have not yet been started or the infection is still being treated with antibiotics
Major Trauma	Evidence of multi-system injury or single system injury associated with shock or altered mental status (during this hospitalization)
Metastatic or hematologic malignancy	Any solid tissue malignancy with evidence of metastasis, or any blood borne malignancy
Therapeutic interventions in place at the time of cardiac arrest	
Mechanical ventilation	Including use of ventilation via invasive airway or non-invasive ventilation (CPAP or BiPAP)
Intravenous vasopressors	Use of dobutamine, dopamine > 3 mcg/kg/min, epinephrine, norepinephrine, phenylephrine, other vasoactive agent ongoing at the time of the event
Dialysis	Use of hemodialysis, peritoneal dialysis, continuous arteriovenous or veno-venous hemofiltration/dialysis ongoing at time of the event
Hospital characteristics	(Source: American Hospital Association Data Year 2009)
Geographic location	Categorized as North Mid-Atlantic, South Atlantic (including Puerto Rico, North Central, South Central Mountain/Pacific based on the United States Census 2010
Hospital ownership	Categorized as for-profit, government, and not-profit
Hospital bed size	Categorized as less than 250, 250-499, and 500 or more
Number of cardiac ICU beds	Defined as cardiac ICU beds as percent of total beds, less than 2.5, 2.5-10, and 10 or more.
Teaching status	Categorized as major teaching (hospitals with a residency and a fellowship program), minor teaching (hospitals with a residency program but no fellowship program), and non-teaching (hospitals without a residency or fellowship program)

Abbreviations: AST, aspartate aminotransferase; BiPAP, bi-level positive airway pressure; CPAP, continuous positive airway pressure; ICU, intensive care unit; MAP, mean arterial pressure; PEA, pulseless electrical activity; SBP: systolic blood pressure

eTable 2: Hospital- and patient-level predictors of delayed epinephrine use in hierarchical model with hospital-level random effects and patient level fixed effects.

Characteristics	Odds ratio	Lower confidence limit	Upper confidence limit	P-Value
Hospital-level covariates				
Total hospital beds (compared to > 500 beds)				0.92
<250	0.97	0.80	1.19	
250-499	1.00	0.85	1.18	
Overall admissions (vs. >30,000)				0.0104
<10,000/year	1.10	0.87	1.39	
10,000 – 30,000	0.88	0.74	1.05	
Below median case volume (100 cases) vs. above	1.30	1.17	1.44	<.0001
Non-teaching vs. teaching hospital	1.01	0.91	1.13	0.84
CVICU to total beds (compared to >10%)				0.08
<2.5%	0.88	0.66	1.17	
2.5-10%	0.98	0.73	1.31	
Patient-level covariates				
Age categories (vs. >80 years)				0.021
<50 years	1.05	0.98	1.12	
50-59 years	1.03	0.96	1.10	
60-69 years	0.94	0.88	1.00	
70-79 years	0.99	0.93	1.05	
Sex	1.00	0.96	1.04	0.80
Initial rhythm, PEA vs. Asystole	1.12	1.08	1.17	<.0001
Delayed chest compression (>1 min)	2.66	2.52	2.81	<.0001
Monitored vs. non-monitored ward	0.50	0.48	0.53	<.0001
Acute stroke	1.05	0.95	1.16	0.31
Heart failure	1.07	1.02	1.13	0.0068
Diabetes	1.02	0.97	1.06	0.47
Hepatic insufficiency	0.93	0.86	1.01	0.07
Hypotension	0.91	0.86	0.96	0.0003
Major trauma	0.91	0.80	1.03	0.12
Metastatic malignancy	0.96	0.90	1.02	0.14
Fluid electrolyte disorder	0.97	0.92	1.03	0.33
Acute myocardial infarction	0.95	0.89	1.01	0.13
Renal insufficiency	1.02	0.98	1.07	0.37
Septicemia	0.83	0.79	0.88	<.0001
Mechanical ventilation	0.47	0.45	0.50	<.0001
Hemodialysis	1.00	0.88	1.13	0.95
Vasopressor use	0.69	0.65	0.74	<.0001

eTable 3: Sensitivity analysis for outcomes after redefining delayed epinephrine as 1st dose of epinephrine >3 minutes. Reported as medians and corresponding interquartile ranges (in parenthesis)

Hospital risk-standardized survival	Quartiles of delay				P-value (trend)
	Q1	Q2	Q3	Q4	
To discharge	13.5% (11.2% - 16.4%)	12.4% (10.7% - 14.6%)	11.9% (10.0% - 14.9%)	11.2% (9.8% - 12.7%)	<0.0001
With CPC 1 or 2	8.4% (5.0% - 12.1%)	8.2% (5.6% - 11.0%)	7.0% (5.0% - 10.9%)	6.7% (4.9% - 8.6%)	<0.0001

Q1-Q4: Hospital quartiles for proportion of patients with delayed epinephrine use, Q1 (least delay) through Q4 (most delay)

Abbreviations: CPC – cerebral performance score

Get With The Guidelines-Resuscitation Investigators

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