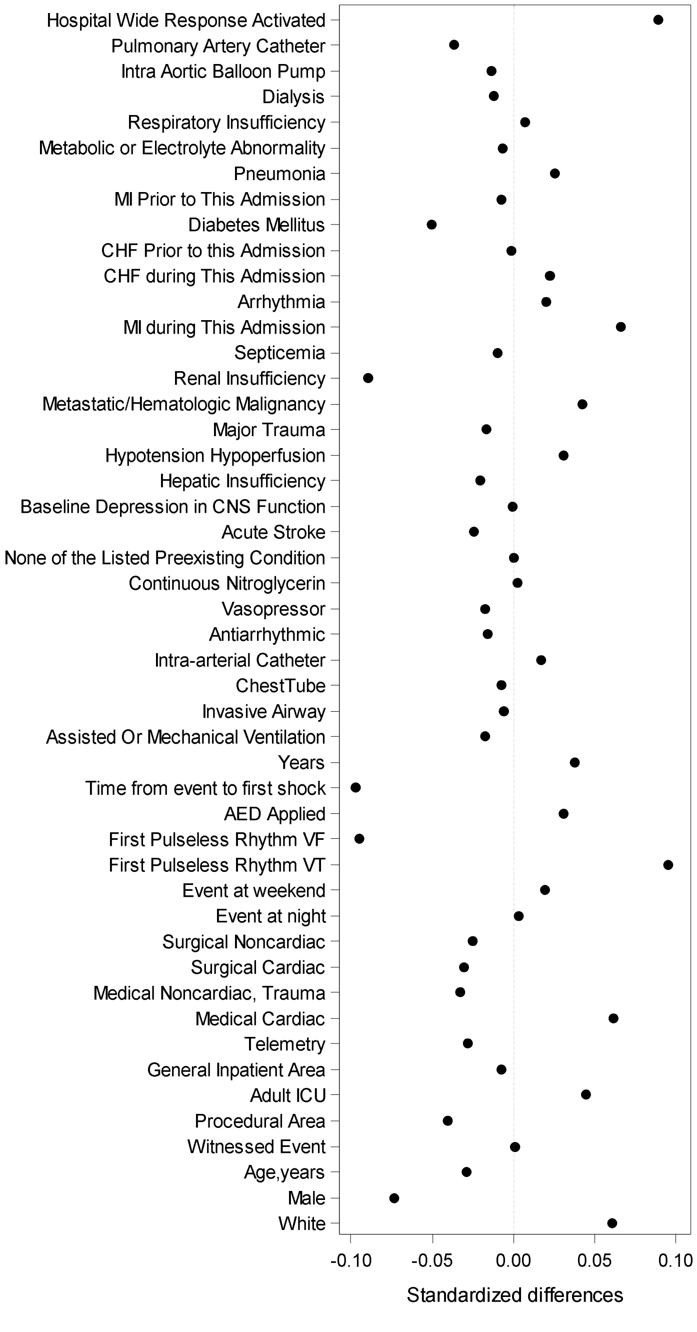
Appendix: Supplementary material [posted as supplied by author]

Figure A. Standardized differences for patients with known versus unknown defibrillation time intervals



All absolute standardized differences were under 10%. The maximum difference was in time from CPA event to first shock (9.69%). The next largest differences were in initial cardiac arrest rhythm (9.5%). Most of the absolute differences were under 5%.

Propensity Modeling Analysis

We estimated the propensity to have a longer time interval between the first two defibrillation attempts using a binary logistic regression model. We used a non-parsimonious model that included 39 patient level covariates and a random effect for hospitals. The covariates included were: patient demographics (sex, race, age); patient pre-existing conditions (heart failure this admission, previous heart failure, myocardial infarction this admission, previous myocardial infarction, arrhythmia, hypotension, respiratory insufficiency, hepatic insufficiency, metabolic or electrolyte abnormality, diabetes mellitus, baseline depression in CNS function, acute stroke, pneumonia, septicemia, major trauma, metastatic cancer, renal insufficiency, none of the above); intervention already in place during defibrillation (assisted or mechanical ventilation, invasive airway device, chest tube, monitoring with an arterial line, vasodilator drugs, intravenous vasopressor medication, dialysis, intra-aortic balloon pump, pulmonary artery catheter); and characteristics of the arrest (illness category, initial cardiac arrest rhythm, event locations, witnessed, event time (day, night, weekend), hospital-wide response activated, assessed with AED), time from event to first shock, and calendar year. Due to variation across hospitals in the proportion of patients receiving defibrillation after longer time intervals, we compared 3 different propensity models for balancing covariates – a marginal model, fixed effect model, and random effect model.[20] The fixed effect model resulted in the best balance of all covariates and was selected for our analysis.

From the propensity score model, we calculated the stabilized inverse probability weight. Balance in the patient covariates was evaluated using standardized differences of the covariates between the long and short defibrillation interval groups (Figure B). After weighting, the standardized differences were much smaller. The maximum standardized difference after weighting was 7%, with the majority under 2.5%, much smaller than the commonly accepted adequate balance of 10% for absolute standardized difference.[21] The outcome model included the main effect for the defibrillation time interval, weighted by the stabilized inverse probability weight. The sandwich estimator of the variance was used in estimating the standard error of the estimated main effect, to account for clustering of patients within hospitals and for modified Poisson estimation of relative risk.

We conducted a survival analysis of time from in-hospital cardiac arrest to death, censored at discharge or 30 days (whichever came first). In this analysis, 120 patients were missing values for the time of the censoring event (death or discharge) and were excluded from the analysis. The adjusted Kaplan-Meier curves weighted on the inverse probability of treatment weights (IPTW) of the propensity score are shown below (Figure C; log-rank P=0.17). Using a Cox model with IPTW, we observed a hazard ratio of 1.07 (95% Confidence Interval 0.98, 1.17; P=0.17).

Figure B. Standardized differences of patient-level covariates before and after propensity weighting

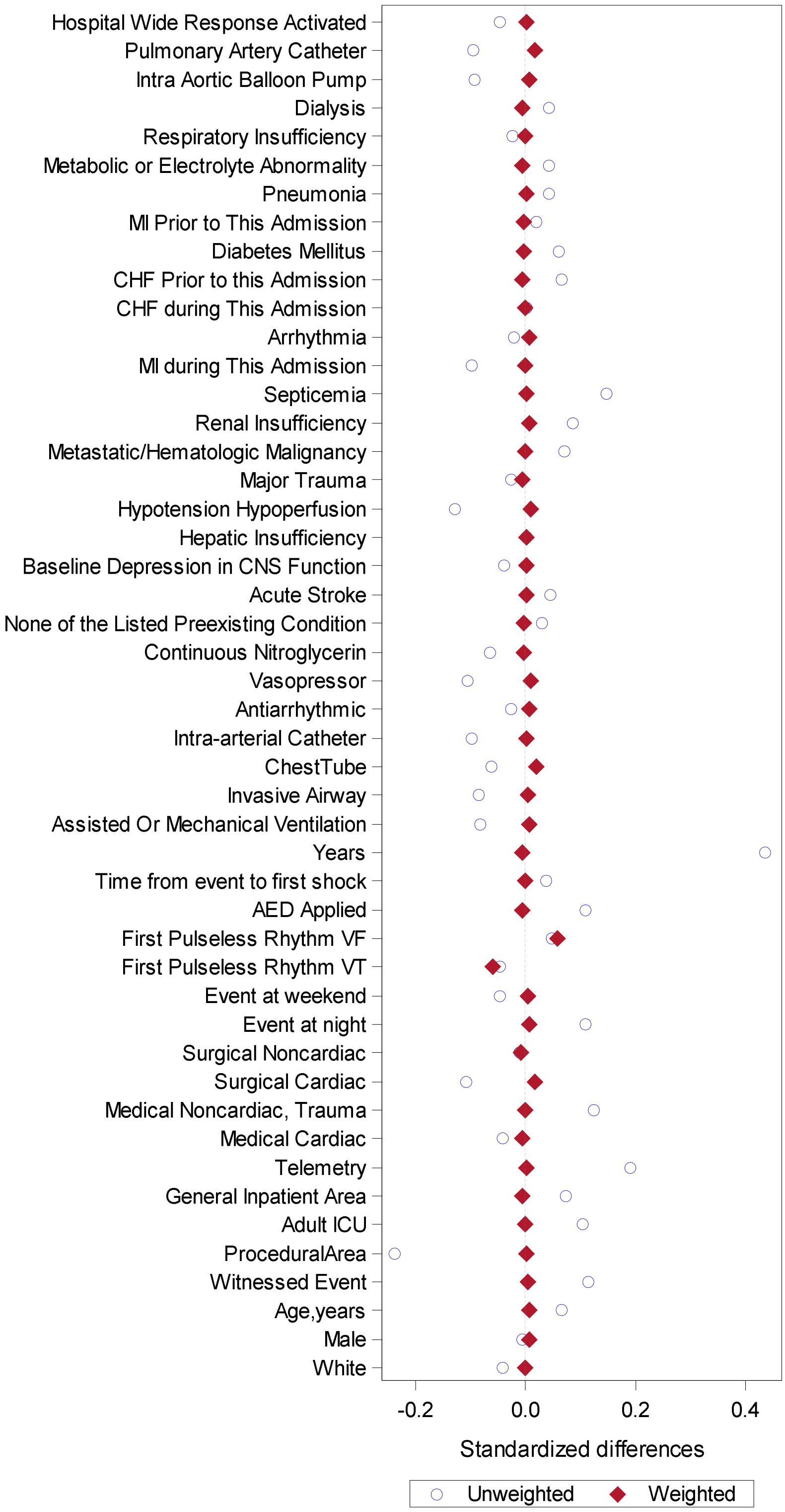


Figure C. Temporal Trends in Defibrillation Intervals Categorized by Minute

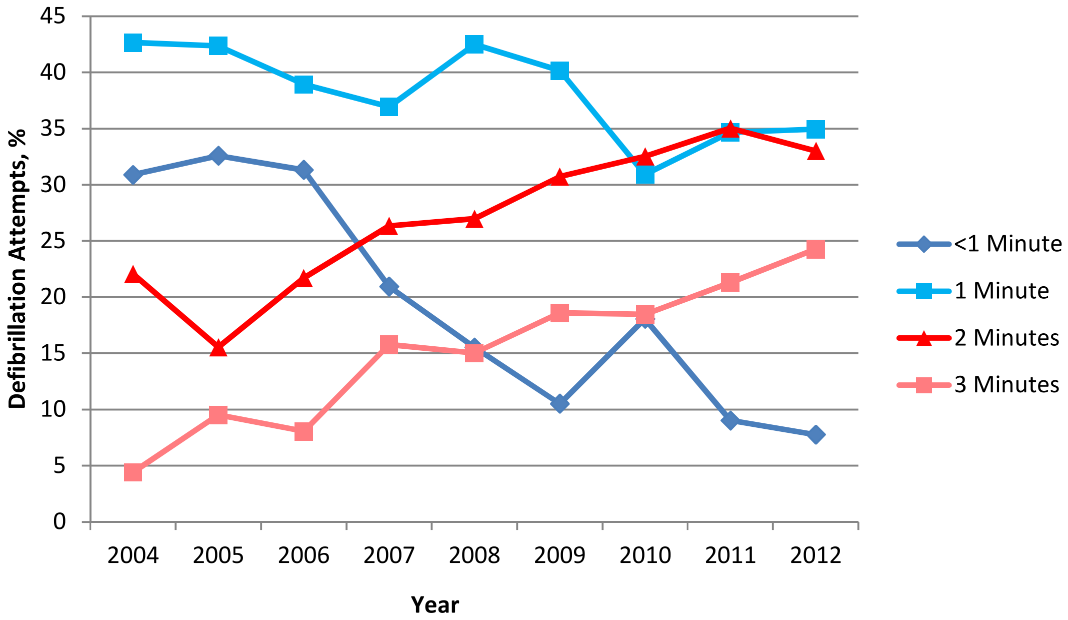


Figure D. Proportion of Patients Excluded Over Time

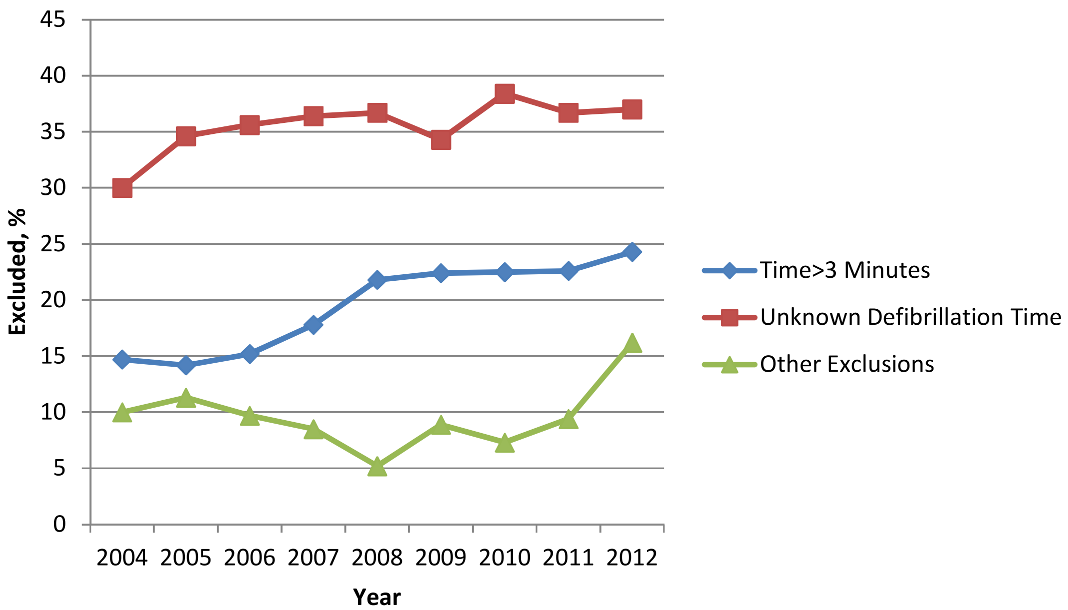
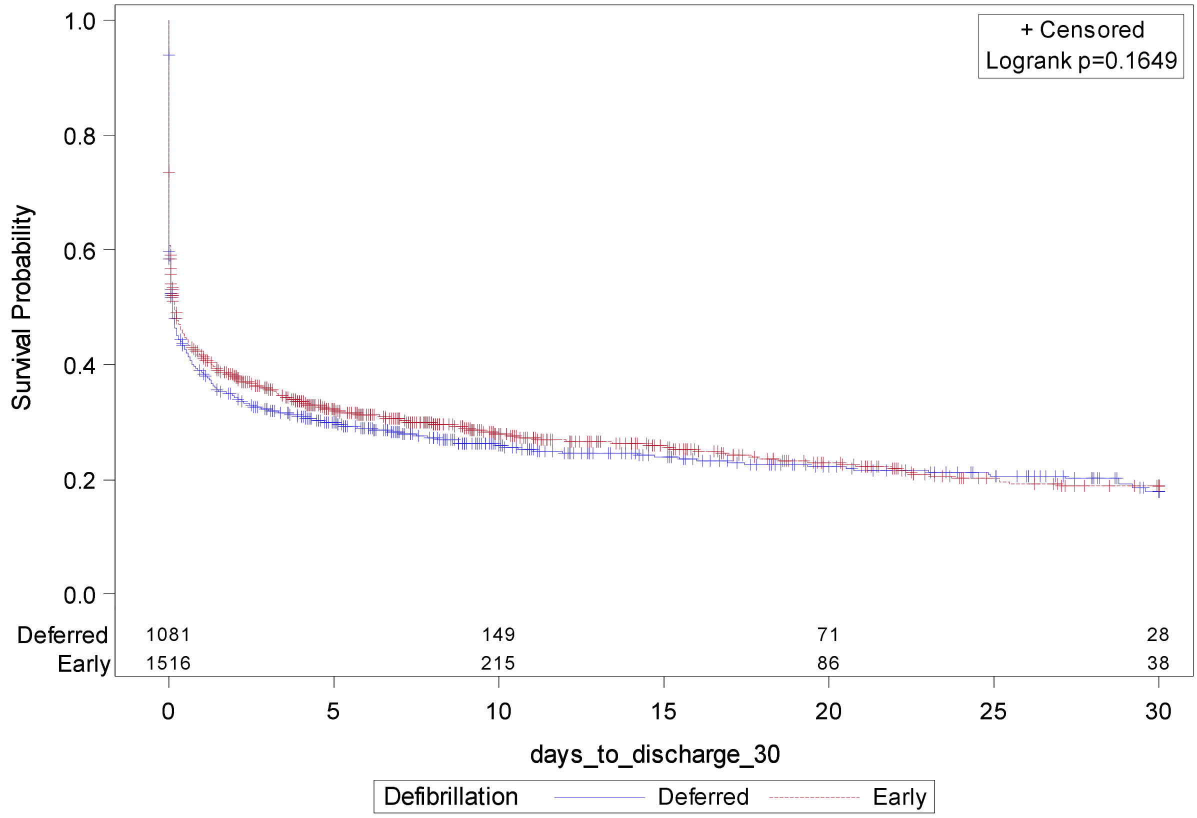


Figure E. Adjusted Kaplan-Meier Curve



Summary of the Number of Censored and Uncensored Values					
Stratum	**Defibrillation**	**Total**	**Failed**	**Censored**	**Percent Censored**
1	**Deferred**	1087	820	267	24.56
2	**Early**	1526	1090	436	28.57
Total		2613	1910	703	26.9

Table A. Specification of covariates used in multivariate analyses

Variable	Definition	Model specification
Demographics		
Age	Age in years	Continuous (years)
Race	Self-reported	White, black, or other
Sex	Self-reported	Male or female
Pre-existing disorders		
Acute stroke	Documented diagnosis of an intracranial or intraventricular hemorrhage or thrombosis during this admission	Yes or no
Baseline depression in CNS	Evidence of a motor, cognitive, or functional baseline deficit (at time of system entry)	Yes or no
Hepatic insufficiency	Evidence of hepatic insufficiency within 24 hours up to the time of the event, defined by ANY of the following 1. Total bilirubin > 2 mg/dL and AST > 2x normal 2. Cirrhosis	Yes or no
Hypotension	Evidence of hypotension within 4 hours up to the time of the event, defined by ANY of the following 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	Yes or no
Major trauma	Evidence of multi-system injury or single system injury associated with shock or altered mental status (during this hospitalization)	Yes or no
Metastatic cancer	Any solid tissue malignancy with evidence of metastasis, or any blood borne malignancy	Yes or no
Renal insufficiency	Evidence of renal insufficiency prior to the event, defined by ANY of the following 1. Requiring ongoing dialysis or extra corporeal filtration therapies 2. Creatinine > 2 mg/dL within 24 hours up to the time of the event	Yes or no
Septicemia	Bloodstream infection where antibiotics have not yet been started or the infection is still being treated with antibiotics	Yes or no
Myocardial infarction this admission	Documented diagnosis of myocardial ischemia (acute coronary syndrome) or myocardial infarction during this admission	Yes or no
None	None of the above pre-existing conditions	Yes or no
Interventions in place at the time of arrest		

Assisted or mechanical ventilation	Including use of ventilation via invasive airway or non-invasive ventilation (CPAP or BiPAP)	Yes or no
Invasive airway device	Use of an endotracheal tube or tracheostomy tube	Yes or no
Chest tube	Use of a chest tube	Yes or no
Monitoring with an arterial line	Use of an arterial line for continuous monitoring	Yes or no
Antiarrhythmic drugs	Use of amiodarone, lidocaine, procainamide, or other antiarrhythmic agents ongoing at the time of the even	Yes or no
Vasopressor	Use of dobutamine, dopamine > 3 mcg/kg/min, epinephrine, norepinephrine, phenylephrine, other vasopressor agent ongoing at the time of the event	Yes or no
Vasodilators	Use of nitroglycerin ongoing at the time of the event	Yes or no
Arrest characteristics		
Illness category	Category of illness at time of admission	Medical-cardiac, medical-noncardiac, surgical-cardiac, surgical-noncardiac, obstetric, trauma, other
Witnessed arrest	Cardiac arrest event was witnessed	Yes or no
Event location	Location of patient in the hospital at the time of cardiac arrest	ICU, monitored unit [telemetry], non-monitored unit, procedural area, other
Time of cardiac arrest	Time of day when cardiac arrest occurred	daytime (7:00 AM–10:59 PM) night time (11:00 PM - 6:59 AM) weekend (11:00 PM Fri. - 6:59 AM Mon.)
Time to first defibrillation attempt	Time to first defibrillation shock in minutes	Continuous (minutes)
Time from admission to arrest	Time from admission to cardiac arrest in days	Continuous (days)
Calendar year	Year of cardiac arrest	Year