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## Long-term survival following in-hospital cardiac arrest: A matched cohort study<sup>☆</sup>

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### Abstract

**Background**—Each year, 200,000 patients undergo an in-hospital cardiac arrest (IHCA), with approximately 15–20% surviving to discharge. Little is known, however, about the long-term prognosis of these patients after discharge. Previous efforts to describe out-of-hospital survival of IHCA patients have been limited by small sample sizes and narrow patient populations

**Methods**—A single institution matched cohort study was undertaken to describe mortality following IHCA. Patients surviving to discharge following an IHCA between 2008 and 2010 were matched on age, sex, race and hospital admission criteria with non-IHCA hospital controls and follow-up between 9 and 45 months. Kaplan–Meier curves and Cox PH models assessed differences in survival.

**Results**—Of the 1262 IHCAs, 20% survived to hospital discharge. Of those discharged, survival at 1 year post-discharge was 59% for IHCA patients and 82% for controls ( $p < 0.0001$ ). Hazard ratios (IHCA vs. controls) for mortality were greatest within the 90 days following discharge (HR = 2.90,  $p < 0.0001$ ) and decreased linearly thereafter, with those surviving to one year post-discharge having an HR for mortality below 1.0. Survival after discharge varied amongst IHCA survivors. When grouped by discharge destination, out of hospital survival varied; in fact, IHCA patients discharged home without services demonstrated no survival difference compared to their non-IHCA controls (HR 1.10,  $p = 0.72$ ). IHCA patients discharged to long-term hospital care or

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hospice, however, had a significantly higher mortality compared to matched controls (HR 3.91 and 20.3, respectively;  $p < 0.0001$ ).

**Conclusion**—Among IHCA patients who survive to hospital discharge, the highest risk of death is within the first 90 days after discharge. Additionally, IHCA survivors overall have increased long-term mortality vs. controls. Survival rates were varied widely with different discharge destinations, and those discharged to home, skilled nursing facilities or to rehabilitation services had survival rates no different than controls. Thus, increased mortality was primarily driven by patients discharged to long-term care or hospice.

## Keywords

Cardiopulmonary resuscitation; Outcome studies; Heart arrest; Survival

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## Introduction

Each year in the United States, an estimated 200,000 patients experience an in-hospital cardiac arrest (IHCA).<sup>1</sup> For these patients, prognosis is poor, with probability of surviving to discharge estimated at only 15–20%.<sup>2</sup> This rate reflects steady improvements with time—among the 374 hospitals participating in the “Get With The Guidelines-Resuscitation” registry, survival to discharge increased from 13.7% in 2000 to 20.7% in 2009.<sup>3</sup> Because inhospital mortality is a crucial metric along which hospitals are evaluated, several studies have examined survival-to-discharge following IHCA.<sup>1,2,3</sup> Little is known, however, about the long-term prognosis of IHCA patients who survive to discharge. Previous efforts to describe out-of-hospital survival in this patient population have been limited by small sample sizes<sup>4</sup> and narrow patient populations.<sup>5</sup> Survival to discharge has been reported to range between 21.9–34% for IHCA patients in the United States,<sup>6–8</sup> however, very little is known about these patients’ survival following hospital discharge. Here, we aim to estimate long-term survival of IHCA patients following hospital discharge, and determine whether variation in this outcome can be explained by indicators evaluable prior to hospital discharge.

## Methods

### Patient population, exposure criteria, and death determination

The Emory University Institution Review Board, also acting as the ethical review board, approved this research (IRB #00050806; Atlanta, GA). The Emory Office of Quality and Risk (EOQR) collects and reviews data on all IHCAs that occur at either Emory University Hospital (579 hospital beds) or Emory University Hospital Midtown (511 hospital beds), which are both tertiary care facilities located in Atlanta, Georgia. The EOQR manually enters each IHCA into an electronic databank based on a physical form that is filled out during the code. All IHCAs are captured including those that occur during diagnostic procedures, inside the operating room, or in monitored units. The EOQR provided clinical and demographic data were obtained for all patients that had an IHCA while admitted from 2008 to 2010. To construct a non-IHCA control group for matching, we collected clinical and demographic data for all patients who presented to the same two hospitals between June

1, 2007 and May 31, 2011 and did not experience an IHCA. Death status and date, if applicable, were retrieved from the United States Social Security Death Index (SSDI) for all patients on November 14, 2011.

## Statistical analysis

**Matching methodology**—For each IHCA patient surviving to discharge, we matched up to three non-IHCA hospital controls on demographics and admission characteristics. Matching demographics included race (White, Black, Hispanic or other), gender (male, female), and age ( $\pm 2$  years). Hospital admission criteria for matching were admission source, level of admission urgency, and admitting specialty, including all major subspecialties (Table 1 and Table S1). IHCA patients for whom no matches could be identified were excluded from analysis. Matching was performed first, without viewing outcomes,<sup>9</sup> and was performed within the “Coarsened Exact Matching” package of the R statistical and programming environment.<sup>10</sup> Coarseness bins were set to zero to obtain an exact match for all matching criteria except age, for which the bins were set to match within 2 years while minimizing the distance between cases and controls.<sup>11</sup>

**Statistical methodology**—The primary outcome was time to death. Crude outcomes estimates for overall survival (OS) at 1 and 3 years in the IHCA and control non-IHCA patient cohorts were obtained and using Kaplan–Meier curves. Differences were assessed using the Log-rank test with confidence bands (95%) computed based on the Greenwood variance<sup>12</sup> and lower limits modified based on Peto,<sup>13</sup> to better reflect uncertainty proportional to the degree of censoring.

Cox proportional hazards regression models<sup>14</sup> were used to assess survival differences over time between IHCA and non-IHCA control patients. Models included IHCA status as the only predictor and the matched design was accounted for using a frailty term including a unique identifier for each matched cluster.<sup>15</sup> Proportional hazards assumptions were assessed for all models by regressing the scaled Schoenfeld residuals against the log-time.<sup>16</sup> No violations were noted. The hazard ratio (HR) and 95% confidence intervals for mortality for IHCA patients versus non-IHCA matched controls were calculated from the maximum-likelihood estimates for IHCA in the proportional hazards regression model. Sub-analyses to calculate HR's during discrete observation windows following discharge were conditional on survival until at least the first day of the observation window.

In secondary analyses, survival comparisons between IHCA patients and their controls were stratified by discharge disposition and categorized into one of four distinct strata: (1) home without health services; (2) home with health services, skilled nursing, rehabilitation, intermediate care facility or short-term hospital stay; (3) long-term hospital care and; (4) hospice care. We performed two separate sets of secondary analyses. First, we stratified data by discharge status of the IHCA patients, while retaining each of the respective matched controls—allowing for discordance in discharge disposition between IHCA patients and their controls. Thus, the hazard ratios for these analyses reflect survival of IHCA patients given a specific discharge disposition benchmarked against the “average” non-IHCA matched

hospital control and HR's largely reflect early pre-discharge effects of IHCA (which dictate discharge disposition) on long-term survival.

Secondly, we stratified by discharge location but included only IHCA patients and their matched controls concordant on discharge disposition, thus effectively including discharge disposition as a post-hoc matching criteria. By removing discharge-discordant clusters, short-term effects of IHCA sufficient to alter discharge disposition are removed and the hazard ratios described for each discharge stratum best reflect only the long-term effects of IHCA. Survival differences and calculation of hazards ratios in these secondary analyses were performed using similar Kaplan–Meier curves and Cox proportional hazards frailty models as those described for the primary outcomes.

## Results

Between January 1, 2008 and December 31, 2010, among 145,054 hospital admissions, 1,262 individual patients experienced an IHCA, with 253 (20.0%) surviving to hospital discharge (Fig. 1), a rate similar to previous estimates of survival-to-discharge following IHCA.<sup>5</sup> Of the 253 survivors, 238 (94%) were successfully matched to at least one non-IHCA hospital control with 196 (82%), 28 (12%), and 14 (6%) matched to 3, 2, and one controls, respectively. The 15 IHCA patients for whom a match could not be identified were excluded from analysis. Among the 238 survivors, 51% were male, 52% were black, and the mean age was 61 ( $\pm 14.3$ ; Table 1). There were no differences in the IHCA patients versus controls for any of the matching criteria (Table 1). IHCA patients surviving to discharge spent, on average, significantly more time in the hospital than their non-IHCA counterparts (mean 26.1 days versus 7.6 days, respectively;  $p < 0.001$ ) with, on average, 7 days spent as in-patients in the IHCA group prior to cardiac arrest.

Overall survival at one year following discharge for IHCA patients was 59% (95% confidence interval: 53–66%), versus 82% (79–85%) for controls ( $p < 0.0001$ ; Fig. 2a). Similarly, overall survival at three years for IHCA patients was 52% (42–60%), versus 69% (64–73%) for controls ( $p < 0.0001$ ; Fig. 2a).

Overall mortality in IHCA patients was increased versus their matched controls, with a hazard ratio (HR) associated with IHCA of 2.35 (1.79–3.08;  $p < 0.0001$ ; Fig. 2b). The HR of mortality in IHCA patients versus controls was greatest shortly following discharge, and this increase was confined to the first year following discharge (Fig. 2b). Over the first 90 days following discharge, the HR for mortality for the IHCA group versus controls was 2.90 (1.96–4.25;  $p < 0.0001$ ); for days 90–365, the HR was 2.19 (1.18–4.06;  $p = 0.013$ ) (Fig. 2b). Once surviving beyond one year, the hazard of mortality was no different between groups, readily observable by the flat-tening of the survival curve in the IHCA group after one year. We observed HRs of 0.81 (0.33–1.96;  $p = 0.64$ ) for year 2 post-discharge and 1.29 (0.28–5.93;  $p = 0.74$ ) for years 3 and beyond (Fig. 2b).

IHCA cases were next grouped by discharge destination and compared to their initial matched controls (i.e. allowing for discordance in discharge disposition between the IHCA cases and their controls). This comparison provides information on survival for an IHCA

survivor with a given disposition, relative to the average similar, matched, non-IHCA patient with unknown disposition. In contrast to the above results, IHCA patients discharged directly home without health services did not demonstrate increased mortality compared to their non-IHCA controls [HR: 1.10 (0.64–1.92);  $p = 0.72$ ; Fig. 3a and Supp. Fig S1]. However, patients discharged to home-with-services, skilled nursing, rehabilitation, intermediate care facility or short-term hospital had a slightly elevated but statistically significant risk of mortality compared to their matched controls [HR 1.85 (1.17–2.94);  $p = 0.009$ ; Fig. 3b, Fig. S1b]. Further, IHCA patients discharged to long-term hospital care or hospice had a much higher mortality versus their initially matched controls [HR 3.91 (2.33–7.01) and 20.3 (4.74–90.63), respectively;  $p < 0.0001$ ; Fig. 3c and d and Fig. S1c and d].

Finally, survival was evaluated in IHCA survivors, again grouped by discharge destination, but only cases and controls concordant on discharge disposition were assessed. This comparison provides a more explicit measure of the importance of IHCA on long-term survival. In this analysis, IHCA patients discharged home without health services again demonstrated no statistically significant difference in overall survival relative to control patients also discharged home without health services [HR 1.60 (0.85–3.02);  $p = 0.142$ ; Fig. 4a and b]. Similarly, IHCA patients discharged to home-with-services, skilled nursing, rehabilitation, intermediate care facility or to short-term hospital stay demonstrated no difference in survival following discharge compared to non-IHCA controls with the same discharge dispositions [HR 1.31 (0.66–2.59);  $p = 0.45$ ; Fig. 4c and d]. Although no statistically significant differences were noted over the entire follow-up period, examination of the Kaplan-Meier curves (Fig. 4a and c) and HR's (Fig. 4b and d) show increased trends in mortality among IHCA cases during the first year, and in particular the first 90 days following discharge, and a relative reduction in mortality for those IHCA cases surviving to one year, compared with their controls.

## Discussion

Among 1262 IHCA patients identified over a 3-year period between January 2008 and December 2010, 253 (20%) survived to hospital discharge, a rate that is in agreement with previous investigations demonstrating survival rates following IHCA between 7% and 26%.<sup>17–19</sup> A previous study conducted at the Emory Veteran's Administration Medical Center (VAMC) demonstrated an out-of-hospital survival rate of 68% at one year for discharged IHCA patients.<sup>5</sup> Interestingly, in that study, survival did not drop below 60% until 2 years following discharge, twice as long as the duration it took to reach a 60% survival rate in IHCA patients following discharge in the current study. The VAMC study, however, had a considerably lower survival-to-hospital discharge of 6.6% (vs. 20% in our cohort), which might suggest that patients surviving to discharge in the VAMC study had a positively skewed baseline fitness level resulting in improved survival following discharge. The VAMC report was also limited by a homogenous VA patient population<sup>20</sup> and a considerably smaller patient sample size of 732 total IHCA patients, with fewer than 50 patients surviving to discharge.

Hazards analysis demonstrated that, overall, IHCA patients surviving to discharge had poor survival following hospital discharge, with only 59% and 52% surviving to one and 3 years

post discharge, respectively. Comparison with demographic- and admission-matched non-IHCA hospital controls demonstrated that hazards of mortality associated with IHCA are elevated within the first year post-discharge, in particular within the first 90 days. Those patients surviving for at least one year had hazards of survival no different than their matched non-IHCA controls.

These results differ from a previous 5-year study of 1571 IHCA at a hospital group in London that demonstrated a mortality rate that remained elevated for at least 2 years relative to an age- and sex-matched control group drawn from the general population in the UK.<sup>21</sup> Our study improves upon this examination by comparing IHCA survivors against non-IHCA hospital controls, rather than a general non-hospitalized population, and by matching not only on age and sex, but also on specific hospitalization admission criteria.

As a secondary analysis in our study, we aimed to understand if long-term prognosis could be determined by early patient status, which we proxied using the location for patient discharge and the post-discharge serviced prescribed (discharge disposition). As expected, we observed significant variation in survival among IHCA patients when grouped by discharge disposition. Importantly, although overall survival following discharge was poor among IHCA patients, those discharged directly to their homes without medical services experienced similar survival to their original non-IHCA matched controls. IHCA patients that were discharged to skilled nursing facilities, rehab, or home with health services had a slightly elevated hazard of mortality relative to their initially matched controls. When comparisons were limited to IHCA patients versus matched controls concordant on discharge dispositions, there were no significant difference in overall survival between the two groups. We note however that this study was powered for the primary analysis, and may not have been sufficiently powered to detect mortality differences of less than 10% in the stratified analyses. Indeed, while not meeting statistical significance, we did observe trends of increased mortality among the IHCA cases in each discharge group during the first 90 days following discharge, as shown in Fig. 4. Interestingly however, these trends disappear among those surviving to one year. Taken together, these findings suggest that the long-term effects of IHCA on overall survival may be driven primarily by the early effects of IHCA on the surviving patient. These effects are borne out prior to hospital discharge, and thus influence discharge disposition. Indeed, the presence of IHCA in our data is highly influential in discharge disposition—patients with dispositions other than home without health services had significantly increased odds of having had an IHCA prior to discharge as compared to those discharged to home without health services. In particular, those discharged to long-term hospital care and hospice had substantially increased odds of IHCA prior to discharge (OR: 18.2 and 4.17;  $p < 0.00001$  for both).

Thus, we find that long-term patient prognosis following an IHCA can be much more accurately assessed than has been previously realized, utilizing only discharge disposition as a simple predictor of patient status prior to hospital discharge. In other words, the consequences of IHCA are not universal amongst IHCA patients, and the severity of the effects, in terms of long-term survival, can be predicted soon following IHCA, prior to patient discharge.

Our out-of-hospital survival data was obtained through a combination of methods including hospital records and utilization of the SSDI Master File (DMF). This file was accessed on November 14th, 2011. In 2012, the Social Security administration restricted access to the death master file, and even expunged some records in a re-interpretation of a 1983 law amidst concerns about privacy. The restriction of the DMF increases the value of the information presented here, as obtaining out-of-hospital survival for a study group and their matched controls would now be more challenging.

Our study is limited in that it is a single institution analysis of the long-term survival following IHCA. However, a previous analysis (unpublished) comparing long-term survival following IHCA in our institution versus a 10% sample of the US Medicare data demonstrated nearly identical overall long-term survival between our IHCA patients and those within the US Medicare database. Thus, it is probable that our post-discharge survival data from 2 busy, urban, tertiary-care academic hospitals may be a good representation of overall survival in the US population as a whole.

## Limitations

The study is limited by a regional sample patient population limited to those hospitalized in a single tertiary academic hospital system in the southeastern United States. Although our investigation includes a large population of IHCA survivors, results may not be fully applicable to distinct patient populations. Additionally, for 15 (6%) of patients that had an IHCA, adequate matched controls were not available. Given our stringent matching process on multiple demographic and admissions criteria, a 6% unmatched rate was not unexpected. Further, the removal of these 15 IHCA patients is unlikely to have any qualitative or quantitatively important effects on our overall results and conclusions as this group demonstrated no important nor statistically significant differences from the included 238 IHCA patients on any matching criteria including: race, gender, age, admission type and discharge disposition. As well, overall survival and time-to-death too were not different between excluded and included IHCA patients. Additionally, given the available data, it was not possible to match on unknown or unrecorded covariates that could be predictive of survival, such as the overall or global health status of the individual prior to arrest. Future prospective studies might consider capturing this type of hospital information in similar survival studies. Finally, utilization of the SSDI, can, on occasion, have incomplete or out of date information regarding mortality, which, if significant, could impact on our results. Our search for vital status was complemented by a review of clinical records and patient families were contacted in cases where patients were suspected to be deceased.

## Conclusion

This study demonstrates that, overall, the outlook for IHCA survivors-to-discharge is grim, particularly within the first 6 months post-discharge. However, we also find large variability in long-term prognosis and show that early in-hospital patient status prior to discharge (estimated by the type of planned discharge facility and scheduled post-discharge services to be rendered) can explain much of this variation. Although IHCA will likely affect the IHCA patients' discharge destination, once that location is determined, long-term mortality is

generally not different than a non-IHCA population discharged to a similar location or with similar prescribed services. In other words, the long-term consequences of IHCA are primarily driven by their short-term effects on patient status prior to hospital discharge. Given the generally very grim short- and long-term survival rates associated with IHCA, our findings are particularly important for those IHCA patients who are discharged to their home without further health services. This lowest-risk discharge group (and to a lesser degree those discharged to skilled nursing/home with services), have a long-term prognosis no different than their non-IHCA patient counterparts. This finding can serve to help inform clinician counseling of IHCA patients and patient-families, especially in regard to medical decision making as well as code status determination.

## Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

## Acknowledgments

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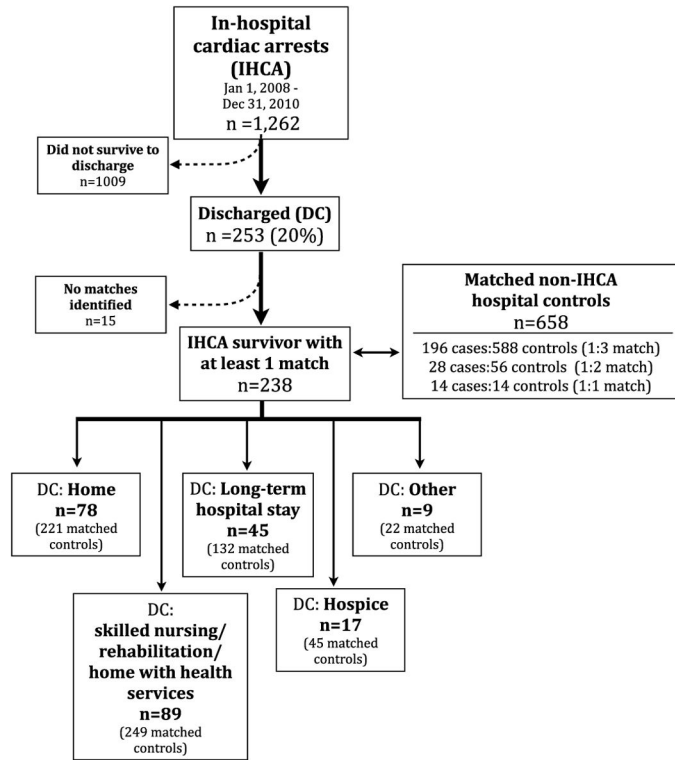
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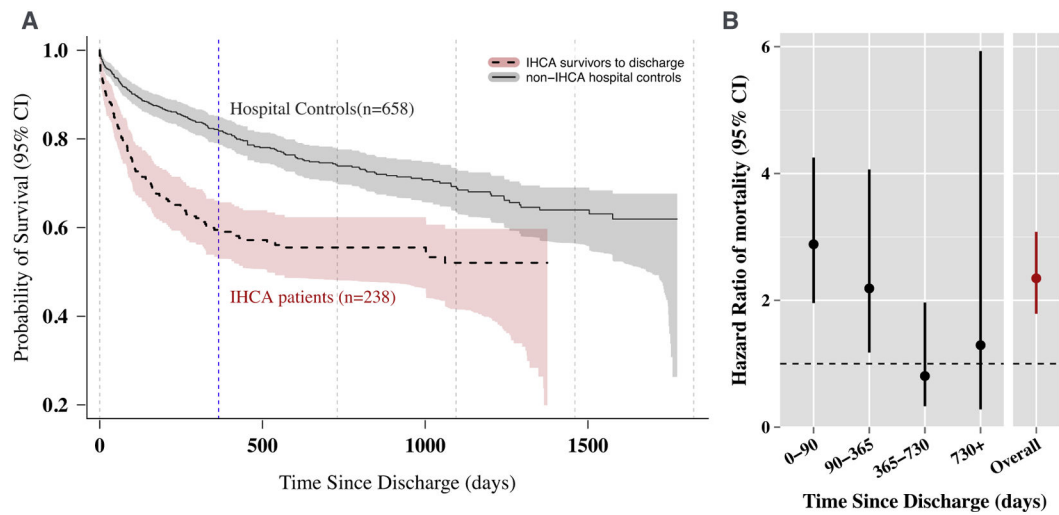
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## Appendix A. Supplementary data

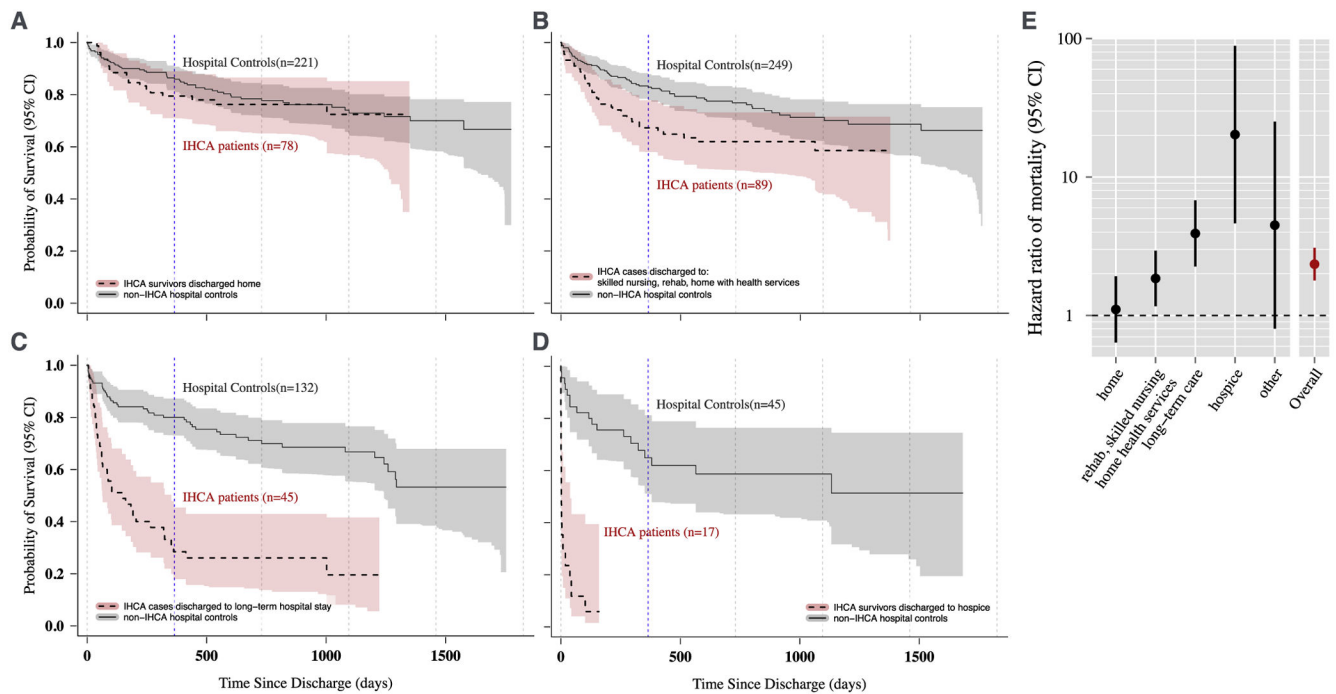
Supplementary data associated with this article can be found, in the online version, at <http://dx.doi.org/10.1016/j.resuscitation.2015.12.001>.



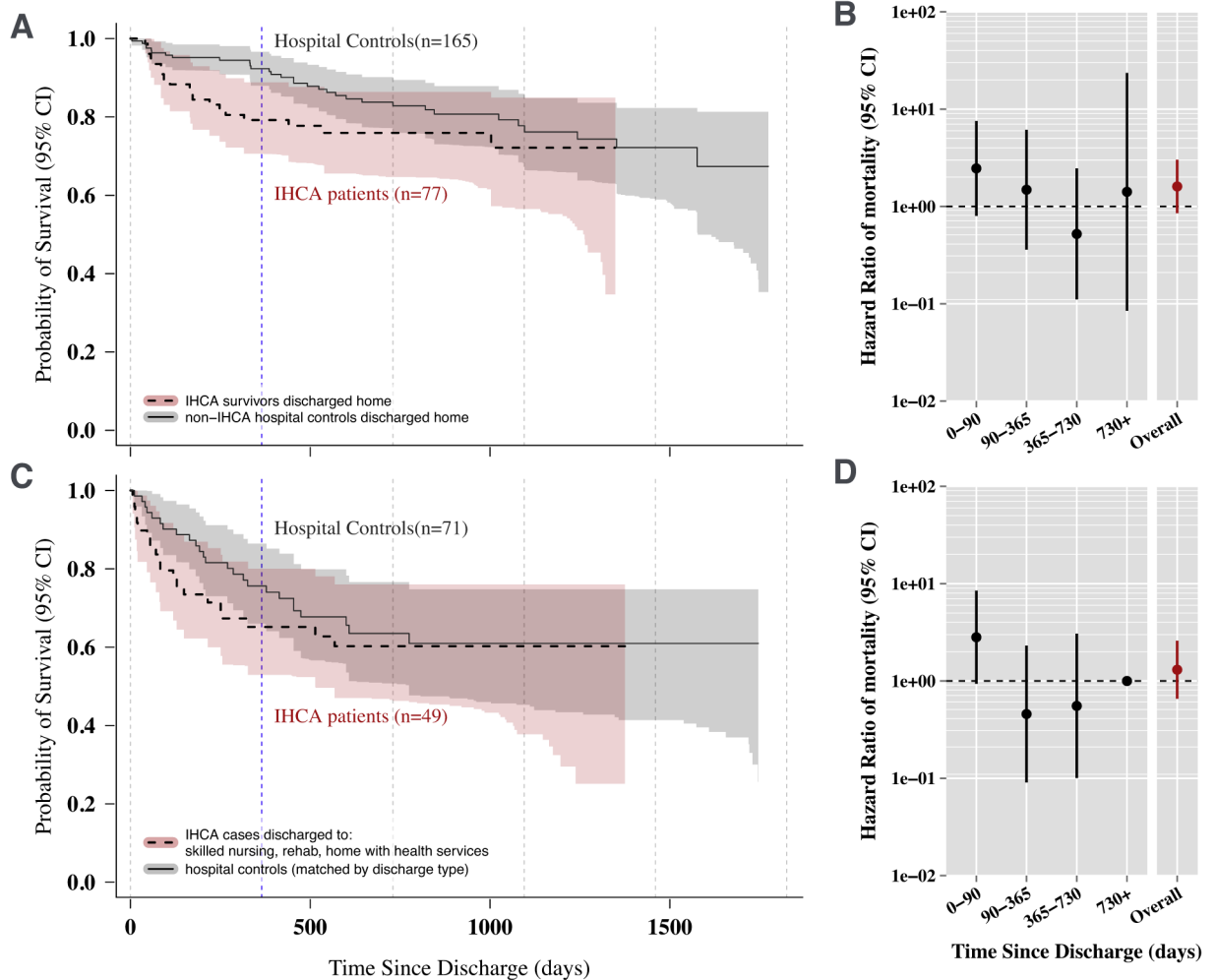
**Fig. 1.** Flow diagram for IHCA patients and matching controls.



**Fig. 2.** Survival and hazard ratios for mortality following hospital discharge among IHCA survivors versus matched hospital controls. (A) Kaplan–Meier curves for survival following discharge for IHCA patients surviving to discharge and matched non-IHCA hospital controls. Shaded regions represent 95% confidence bands for survival. (B) Hazard ratios for mortality of IHCA survivors versus matched non-IHCA controls during discrete observation windows following discharge, conditioned on survival to the start of each period of time. “Overall” indicates the hazard ratio for mortality over the entire follow-up period (shown in A). Hazard ratios with 95% confidence intervals not including the value 1 are statistically significant to an alpha of 0.05. Vertical lines represent 1-year intervals.

**Fig. 3.**

Survival and hazard ratios of mortality following discharge for IHCA survivors versus matched hospital controls: stratified by discharge disposition of IHCA patients. Kaplan–Meier survival curves were plotted for IHCA patients (broken lines) and their matched non-IHCA hospital controls (solid lines), stratified by IHCA patient discharge disposition: (A) home without health services; (B) home with health services, skilled nursing, rehabilitation, intermediate care facility or short-term hospital stay; (C) long-term hospital care and; (D) hospice care. Shaded regions indicate 95% confidence bands. (E) Cox proportional hazards ratios of mortality for IHCA patients versus non-IHCA matched controls for each of the pairs of curves plotted in (A–D) are shown. “Overall” is the combined hazard ratio for mortality for all patients and “other” includes 9 IHCA patients (and 22 controls), 6 who were transferred to cancer facilities and 3 who left against medical advice. 95% confidence intervals are shown surrounding the point estimate for the hazard ratio. Hazard ratios with 95% confidence intervals not including the value 1 are statistically significant to an alpha of 0.05. (Note log-scale on y-axis). Vertical lines represent 1-year intervals.



**Fig. 4.** Survival and hazard ratios of mortality following hospital discharge for IHCA survivors and matched non-IHCA hospital controls with concordant discharge dispositions: stratified by discharge disposition. Kaplan–Meier survival curves were plotted for IHCA patients (broken lines) and their matched and discharge disposition concordant non-IHCA hospital controls (solid lines), stratified by discharge disposition: (A) home without health services; (C) home with health services, skilled nursing, rehabilitation, intermediate care facility or short-term hospital stay. Shaded regions indicate 95% confidence bands. In (B and D) Cox proportional hazards ratios of overall mortality and during discrete observation windows following discharge for IHCA patients versus discharge disposition-concordant non-IHCA matched controls are shown. “Overall” is the combined hazard ratio for mortality for the entire follow-period. 95% confidence intervals are shown surrounding the point estimate for the hazard ratios. Hazard ratios with 95% confidence intervals not including the value 1 are statistically significant to an alpha of 0.05. All intervals crossed 1 and thus none had statistically significant hazard ratios for mortality. (Note log-scale on y-axis). Vertical lines represent 1-year intervals.

Table 1

Characteristics of in-hospital cardiac arrest case patients and matched non-IHCA Hospital Controls.

	IHCA survivors by discharge destination <sup>d</sup>													
	IHCA Survivors to Discharge		Non-IHCA Hospital Controls		Home without services		Skilled Nursing, Home w/services, Rehab		Long-term stay hospital		Hospice		Other <sup>b</sup>	
	IHCA	Non-IHCA	IHCA	Non-IHCA	IHCA	Non-IHCA	IHCA	Non-IHCA	IHCA	Non-IHCA	IHCA	Non-IHCA	IHCA	Non-IHCA
Patients (n)	238	658	78	221	89	249	45	132	17	45	9	22		
Resuscitation	196 (82%)	588 (89%)	68	204	77	231	42	126	13	39	6	18		
1:1 match <sup>c</sup>	28 (12%)	56 (9%)	7	14	6	12	3	6	2	4	1	2		
1:1 match	14 (6%)	14 (2%)	3	3	6	6	0	0	2	2	2	2		
Male (%)	50.8	50.8	60.2	61.5	51.6	50.6	33.3	32.5	41.2	44.4	66.6	72.7		
Age, mean (SD) (p-value) <sup>e</sup>	61.1 (14.3)	61.7 (14.2)	58.6 (13.4)	59.3 (13.4)	61.5 (14.6)	61.8 (14.7)	66.1 (11.8)	66.2 (11.8)	62.6 (18.4)	63.7 (17.7)	51.8 (16.0)	50.6 (15.9)		
Race, n														
White	99 (42%)	274 (42%)	35	101	42	116	14	42	7	21	1	1		
Black	124 (52%)	344 (52%)	39	108	41	116	29	84	8	22	7	18		
Other	15 (6%)	40 (6%)	4	12	6	17	2	6	2	2	1	3		
Admit urgency (n)														
Elective	56	159	21	62	22	61	11	33	1	3	1	3		
Urgent	60	161	15	42	27	75	8	24	7	18	3	6		
Emergent	122	338	42	117	40	113	26	75	9	24	5	13		
Admit specialty (n) <sup>d</sup>														
Hospital medicine	60	175	16	47	24	70	12	36	5	15	3	9		
General surgery	20	56	3	8	8	22	6	18	2	6	1	2		
Medical subspecialty	83	168	33	95	28	74	12	34	7	17	3	7		
Surgical subspecialty	68	185	24	65	25	71	15	44	3	7	1	3		
Psychiatry	2	4	0	0	1	3	0	0	0	0	1	1		
Radiology	2	6	2	6	0	0	0	0	0	0	0	0		
Rehabilitation	3	9	0	0	3	9	0	0	0	0	0	0		

<sup>d</sup>Type of discharge facility each patient was discharged to following hospital stay was collected for all patients and categorized by acuity of care required in that facility.

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<sup>b</sup>This category included 6 IHCA cases transferred to cancer facilities and 3 IHCA cases who left against medical advice.

<sup>c</sup>Indicates the number of IHCA cases that were successfully matched to 3 controls. Similarly, 2:1 match and 1:1 match indicate numbers matched to 2 and 1 controls, respectively.

<sup>d</sup>See Supplementary Table S1 for complete table including all subspecialties.