

ORIGINAL RESEARCH

Shortening Ambulance Response Time Increases Survival in Out-of-Hospital Cardiac Arrest

Johan Holmén , MD, PhD; Johan Herlitz, MD, PhD; Sven-Erik Ricksten, MD, PhD; Anneli Strömsöe, RN, PhD; Eva Hagberg, MD; Christer Axelsson, RN, PhD; Araz Rawshani, MD, PhD

BACKGROUND: The ambulance response time in out-of-hospital cardiac arrest (OHCA) has doubled over the past 30 years in Sweden. At the same time, the chances of surviving an OHCA have increased substantially. A correct understanding of the effect of ambulance response time on the outcome after OHCA is fundamental for further advancement in cardiac arrest care.

METHODS AND RESULTS: We used data from the SRCR (Swedish Registry of Cardiopulmonary Resuscitation) to determine the effect of ambulance response time on 30-day survival after OHCA. We included 20 420 cases of OHCA occurring in Sweden between 2008 and 2017. Survival to 30 days was our primary outcome. Stratification and multiple logistic regression were used to control for confounding variables. In a model adjusted for age, sex, calendar year, and place of collapse, survival to 30 days is presented for 4 different groups of emergency medical services (EMS)-crew response time: 0 to 6 minutes, 7 to 9 minutes, 10 to 15 minutes, and >15 minutes. Survival to 30 days after a witnessed OHCA decreased as ambulance response time increased. For EMS response times of >10 minutes, the overall survival among those receiving cardiopulmonary resuscitation before EMS arrival was slightly higher than survival for the sub-group of patients treated with compressions-only cardiopulmonary resuscitation.

CONCLUSIONS: Survival to 30 days after a witnessed OHCA decreases as ambulance response times increase. This correlation was seen independently of initial rhythm and whether cardiopulmonary resuscitation was performed before EMS-crew arrival. Shortening EMS response times is likely to be a fast and effective way of increasing survival in OHCA.

Key Words: cardiac arrest ■ cardiopulmonary resuscitation ■ out-of-hospital ■ response time

The chances of surviving an out-of-hospital cardiac arrest (OHCA) in Sweden have improved dramatically over the years, from 3.6% in 1990 to 11.6% in 2018.¹ A follow-up of neurologic outcomes during the past 10 years shows that 90% of the survivors either have a good cerebral performance or a moderate disability with sufficient function for independent activities of daily life.¹

Important factors behind this welcome development include more frequent bystander interventions, more effective in-hospital treatment, and an increasing proportion of ambulance crew-witnessed cases.^{1,2}

Meanwhile, the median ambulance response time in OHCA has doubled over the years, from 5 to 6 minutes in the early 1990s to 11 minutes in 2017.¹ This is an unfortunate combination of factors, as it could potentially lead to the conclusion that minimizing ambulance response times is less important in reducing mortality rates from cardiac arrest. Sweden had more than 6000 cardiac arrest victims in 2018, where cardiopulmonary resuscitation (CPR) was initiated. Effective measures to further increase survival and improve neurologic outcomes after OHCA are challenging and resource-intensive.

Correspondence to Johan Holmén, MD, PhD, Department of Anesthesiology and Intensive Care, Queen Silvia's Children's Hospital, Sahlgrenska University Hospital, Rondvägen 10, 416 50 Gothenburg, Sweden. E-mail: johan.holmen@vgregion.se

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CLINICAL PERSPECTIVE

What is New?

- We report decreasing survival as ambulance response time increases in witnessed out-of-hospital cardiac arrest. This association was independent of both initial rhythm and whether bystander-initiated cardiopulmonary resuscitation (CPR) was performed or not.
- Bystander-initiated CPR was associated with an increased survival only if the emergency medical services crew arrived on scene within 15 minutes from dispatch, in out-of-hospital cardiac arrest cases with a presumed cardiac cause.
- The association between emergency medical services response time and survival was observed for all ages, including 0 to 1 and 1 to 16 years, specifically.

What Are the Clinical Implications?

- Bystander-initiated CPR has proven to be an important factor in increasing the chances of survival in out-of-hospital cardiac arrest, and short emergency medical services response times are critical to maintain the benefit from bystander-initiated CPR.
- CPR with compressions only is gaining ground on behalf of bystander-CPR with rescue breaths; in this scenario, emergency medical services response time equals time from dispatch to CPR with ensured ventilation, and this highlights the importance of future emergency medical services response time.
- Our observations suggest substantially improved chances of survival by reducing ambulance response time in witnessed out-of-hospital cardiac arrest.

Nonstandard Abbreviations and Acronyms

CPC	cerebral performance categories
OHCA	out-of-hospital cardiac arrest
PEA	pulseless electrical activity
pVT	pulseless ventricular tachycardia
SRCR	Swedish Registry of Cardiopulmonary Resuscitation

Ambulance response time is commonly used as an important indicator when assessing the quality of emergency medical services (EMS) systems. Although shortening EMS response times is an appealing approach that is likely to be beneficial for selected medical emergencies, evidence is scarce.

A correct understanding of the impact of ambulance response time is fundamental. In the context of an increase in both survival rates and in the EMS response time, this question is crucial when it comes to directing future efforts to combat death from cardiac arrest.

We hypothesize that shorter ambulance response times in OHCA has a positive effect on the chances of survival. Our primary aim was to determine the effect of ambulance response time on 30-day survival after OHCA. Secondly, we describe the association between response time and the usefulness of CPR before EMS arrival (bystander CPR).

METHODS

Requests to access the data that support the findings of this study should be made through the SRCR internal website at <https://shlr.registercentrum.se>.

Study Design

This is an observational study based on data from the SRCR (Swedish Registry of Cardiopulmonary Resuscitation) during a 10-year period. The SRCR, initiated in 1990, is a national quality register collecting Utstein-style data from all (100%) Swedish EMS organizations. There is a national web-based procedure for OHCA registration, independent of the different medical records that are used throughout the country. The criterion for inclusion is every attempt at CPR and/or defibrillation, and the routine registration of these events is well known to all EMS personnel in Sweden. The registration of patient and cardiac arrest characteristics is performed by 1 of the EMS crews involved, normally the first crew on the scene.

OHCA cases in which CPR has been initiated before the arrival of an EMS crew are included in the SRCR if resuscitation attempts are continued by EMS personnel or if the patient has already regained spontaneous circulation on EMS arrival. In some cases of bystander-initiated CPR the arriving EMS crew faces a patient with definitive signs of death and resuscitation attempts are discontinued. These patients are not included in the register.

The unconscious patient is unable to give informed consent and this requirement was waived. Obtaining an informed consent from a legal surrogate would delay resuscitation attempts and was considered unethical.

A validation of the SRCR³ has shown that 75% of the cases were reported prospectively and the remainder were detected retrospectively. In 2017, n=5781 OHCA cases were reported to the register. An incidence of 57 OHCA/100 000 person-years supports our estimation that the coverage of the

SRCR is good. The SRCR has been described in more detail elsewhere.^{1,4,5}

Setting and Population

In 2017, the population of Sweden was 10.1 million,⁶ covering an area of approximately 450 000 km². This means a population density of 22 people/km², compared with, for example, Germany's 231 people/km² or the Netherlands' 411 people/km². Most Swedes live in urban areas, and the northern parts of the country are more sparsely populated than the southern parts. Normally, a cardiac arrest dispatch center activates 2 EMS units, enabling advanced life support both on the scene and during transport. National resuscitation guidelines are in conformity with guidelines from the European Resuscitation Council and each EMS unit carries at least 1 registered nurse. Some regions have physician-staffed units, but the involvement of a prehospital physician is not customary.

Selection and Outcome

We investigated the time period from 2008 to 2017, making 48 325 patients eligible for inclusion. For pediatric cases, registration is not validated separately and relatively few cases were reported during the study period. After exclusion of infants assessed by the EMS crews as caused by sudden infant death syndrome, 1.4% (n=284) of included patients who experienced OHCA were children.

For EMS response time to correspond to the actual time spent from cardiac arrest to EMS arrival, all unwitnessed cases were excluded. All exclusion criteria are specified in Figure 1.

Short-term survival was reported as survival to 30 days, according to the Utstein style consensus reporting guidelines from 2015.⁷

Statistical Analysis

Multiple logistic regression was used to study the association between ambulance response time and the dependent variable of survival to 30 days. The model was adjusted for the following 4 covariates: age, sex, calendar year, and place of OHCA.

By assessing physiologic plausibility and previous studies of this subject, a direct acyclic graph (Figure S1) was constructed in an attempt to identify potential confounding factors. Calendar year, place of OHCA, age, sex, initial rhythm, and time to CPR and defibrillation were all regarded as possible factors associated with both 30-day survival and EMS response time. All 7 of these variables have previously been shown to be associated with survival to 30 days in witnessed OHCA in our population.⁵

Sub-group analyses were performed for the first recorded rhythm (Figures 2C, 2D) and for whether or not

CPR was initiated before EMS arrival (Figures 2E, 2F). Apart from the cases defibrillated by bystanders, the time to defibrillation can be regarded as a proxy for response time and no adjustment was made for time to defibrillation. Prehospital interventions were regarded as a link in the causal chain and were not adjusted for in the model. Hospital interventions were regarded as possible confounders, but no such data were available for analysis.

For the pediatric model, adjustments were made for sex, calendar year, and place of arrest.

Using the predicted probability of survival in each EMS response time interval (0–6 minutes, 7–9 minutes, 10–15 minutes, >15 minutes), we calculated the number of individuals expected to survive an OHCA nationally. We noted a non-linear association between EMS response time and survival, and we therefore used restricted cubic splines (with 4 knots) to capture this non-linear association.

Finally, we performed a logistic regression adjusted for all available covariates and accounted for their odd ratios (OR) in a forest plot.

We imputed missing data using the Multivariate Imputation by Chained Equation algorithm. We imputed a single complete data set, and this was done separately for patients with shockable and non-shockable rhythm. The imputed data were used for regression modelling. We did not use imputation for survival, initial rhythm, or defibrillation.

All analyses were performed using R.

RESULTS

Patient and cardiac arrest characteristics are presented in Table 1. In a model adjusted for age, sex, calendar year, and place of collapse, survival to 30 days is presented for 4 different groups of EMS crew response time (Figure 2, Figure S2). In the overall group, survival was 19.5% when the EMS crew arrived within 0 to 6 minutes, as compared with 9.4% if the crew arrived after 10 minutes or more (Figure 2A).

A decrease in survival with increasing EMS response time was seen, regardless of the initial heart rhythm (Figures 2C, 2D). The same observation was made regardless of whether or not CPR was performed before EMS arrival (Figures 2E, 2F), for the time intervals of 0 to 6 minutes, 7 to 9 minutes, and 10 to 15 minutes, but not for OHCA cases where the EMS crew arrived more than 15 minutes after the collapse. Figure 2C presents the adjusted survival in the sub-group presenting with a shockable rhythm, for whom survival dropped from 44% to 25% when the EMS response time increased from 0 to 6 minutes to 10 to 15 minutes. Similarly, in the sub-groups of patients with a non-shockable rhythm (Figure 2D) and those with and without bystander CPR

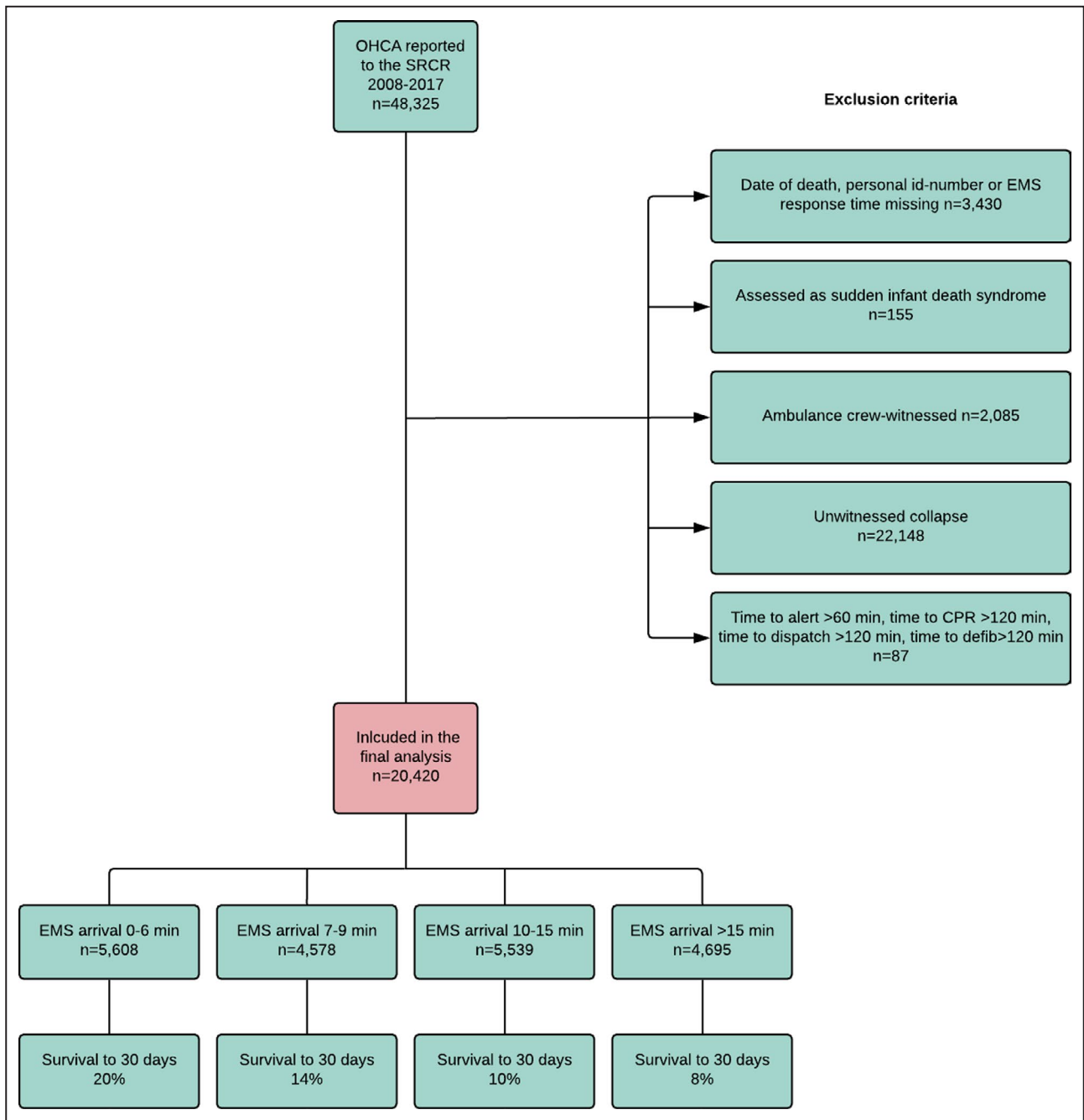


Figure 1. Inclusion of patients who experienced OHCA and unadjusted survival to 30 days. CPR indicates cardiopulmonary resuscitation; EMS, emergency medical services; OHCA, out-of-hospital cardiac arrest; and SRCR, The Swedish register of cardiopulmonary resuscitation.

(Figures 2E, 2F), we note a more than 2-fold difference in survival.

Figure 3 presents the non-linear association between EMS response time and survival, stratified by

cause of cardiac arrest and whether CPR was initiated before EMS arrival.

The probability of survival was lower in patients assessed (by the EMS crew) as having a non-cardiac

Figure 2. The association between EMS response time (“Delay”) and survival to 30 days for all patients (a, n=20 420), among patients receiving compressions-only CPR before EMS arrival (b, n=2762), among patients found in a shockable rhythm (c, n=5970) and a non-shockable rhythm (d, n=14 450), and among patients receiving CPR before EMS arrival (e, n=13 047) and patients not receiving CPR before EMS arrival (f, n=5775).

Model predictors were age, sex, place of cardiac arrest, calendar year, and EMS response time. All numbers in the figures are percentages, with whiskers representing a 95% CI.

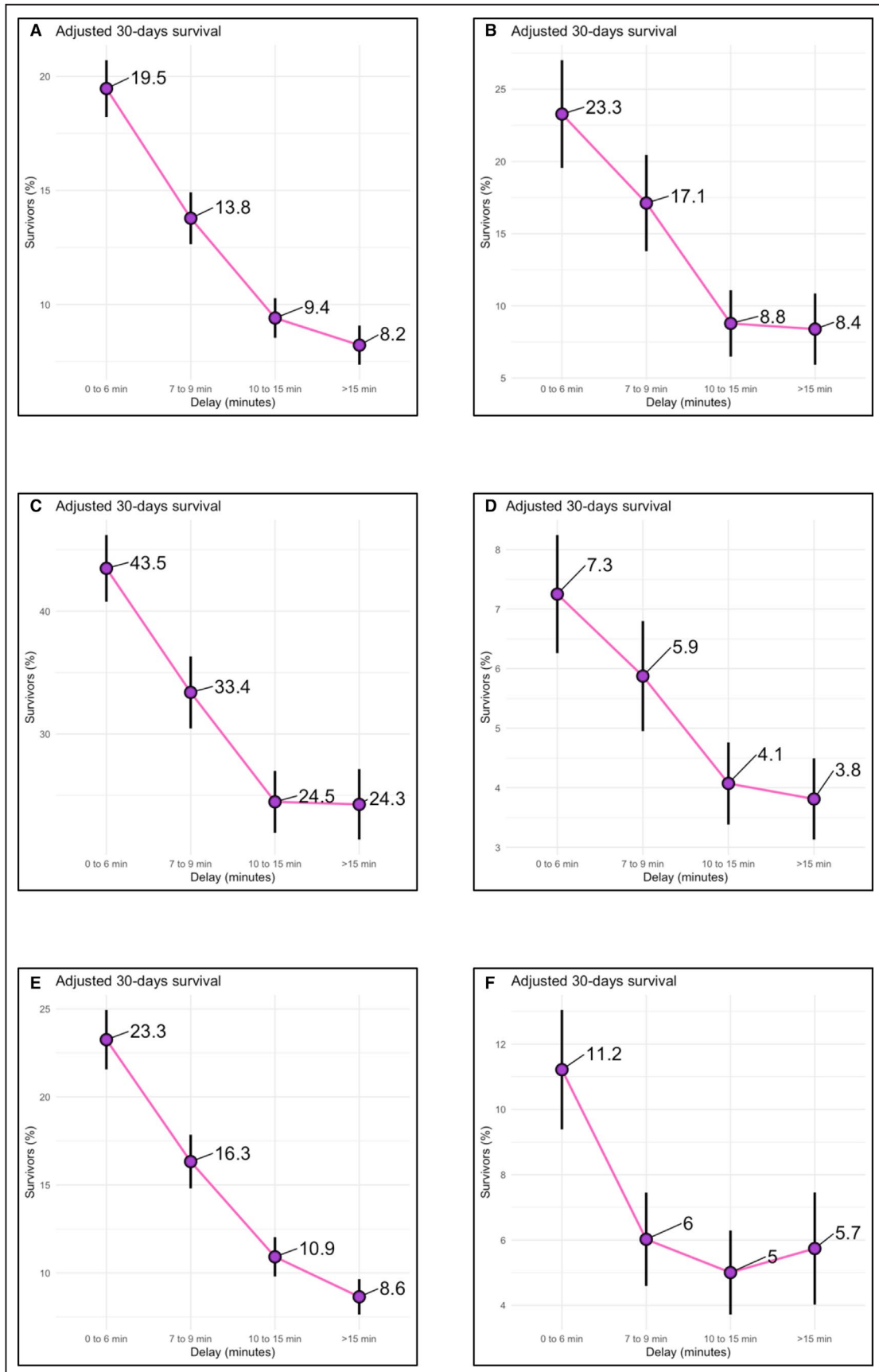


Table 1. Patient and Cardiac Arrest Characteristics Stratified by EMS Response Time

EMS Response Time	0–6 min	7–9 min	10–15 min	>15 min
	(n=5608)	(n=4578)	(n=5539)	(n=4695)
Age				
Y, median (IQR)	73 (62-82)	72 (62-82)	72 (62-81)	72 (63-81)
Missing	180 (3.2%)	146 (3.2%)	201 (3.6%)	153 (3.3%)
Sex				
Men	3946 (70.4%)	3073 (67.1%)	3825 (69.1%)	3230 (68.8%)
Women	1657 (29.5%)	1502 (32.8%)	1712 (30.9%)	1461 (31.1%)
Missing	5 (0.1%)	3 (0.1%)	2 (0.0%)	4 (0.1%)
Place of collapse				
Home	3054 (54.5%)	3038 (66.4%)	3903 (70.5%)	3311 (70.5%)
Public place	1608 (28.7%)	831 (18.2%)	877 (15.8%)	753 (16.0%)
Other place	563 (10.0%)	435 (9.5%)	461 (8.3%)	396 (8.4%)
Missing	383 (6.8%)	274 (6.0%)	298 (5.4%)	235 (5.0%)
CPR before EMS arrival				
Bystander CPR	3157 (56.3%)	2636 (57.6%)	3689 (66.6%)	3565 (75.9%)
No bystander CPR	2010 (35.8%)	1534 (33.5%)	1439 (26.0%)	792 (16.9%)
Missing	441 (7.9%)	408 (8.9%)	411 (7.4%)	338 (7.2%)
Type of CPR before EMS arrival				
Compressions only	735 (23.3%)	680 (25.8%)	763 (20.7%)	584 (16.4%)
Compressions and ventilation	478 (15.1%)	412 (15.6%)	580 (15.7%)	634 (17.8%)
Ventilation	18 (0.57%)	10 (0.38%)	8 (0.22%)	13 (0.36%)
Missing	1926 (61.0%)	1534 (58.2%)	2338 (63.4%)	2334 (65.5%)
Initial rhythm				
Asystole/PEA	3312 (59.1%)	3055 (66.7%)	3864 (69.8%)	3530 (75.2%)
VF/pVT	2088 (37.2%)	1369 (29.9%)	1507 (27.2%)	1006 (21.4%)
Missing	208 (3.7%)	154 (3.4%)	168 (3.0%)	159 (3.4%)
Time to alarm				
2 (1-4)	2 (1-5)	2 (1-5)	2 (1-5)	
1109 (19.8%)	1102 (24.1%)	1626 (29.4%)	1658 (35.3%)	
Time to CPR				
Min, median (IQR)	3 (0-7)	4 (1-10)	4 (1-11)	3 (0-11)
Missing	650 (11.6%)	545 (11.9%)	667 (12.0%)	733 (15.6%)
Time to defibrillation				
Min, median (IQR)	10 (8-15)	14 (11-20)	19 (15-25)	25 (17-34)
Missing	3041 (54.2%)	2708 (59.2%)	3334 (60.2%)	3171 (67.5%)
Time to EMS dispatch				
Min, median (IQR)	1 (0-1)	1 (0-1)	1 (0-1)	1 (0-1)
Missing	769 (13.7%)	571 (12.5%)	702 (12.7%)	611 (13.0%)
Time to EMS arrival				
Min, mean (SD)	4.64 (1.36)	7.92 (0.814)	12.3 (1.72)	26.3 (13.6)
Min, median (IQR)	5 (4-6)	8 (7-9)	12 (11-14)	21 (18-26)
Defibrillation				
Proportion defibrillated	50.0 %	44.0%	43.7%	36.5%
Missing	394 (7.0%)	286 (6.2%)	310 (5.6%)	245 (5.2%)

CPR indicates cardiopulmonary resuscitation; EMS, emergency medical services; IQR, interquartile range; PEA, pulseless electrical activity; SD, standard deviation; VF, ventricular fibrillation; and pVT, pulseless ventricular tachycardia.

cause of the collapse. Overall, as well as in the sub-groups with and without cardiac cause, the drop in survival was most pronounced between 0 and 10 minutes. This was observed regardless of whether or not CPR was performed before EMS arrival.

Among patients on whom CPR was started before EMS arrival, some received compressions-only CPR. The association between EMS response time and survival to 30 days in this sub-group is shown in Figure 2B. Survival dropped from 23.3% to 8.8% when EMS response time increased from 0 to 6 minutes to 10 to 15 minutes in this sub-group.

In an attempt to illustrate the association in pediatric patients, we analyzed data for children aged 0 to 1 year and 1 to 16 years (Figure 4).

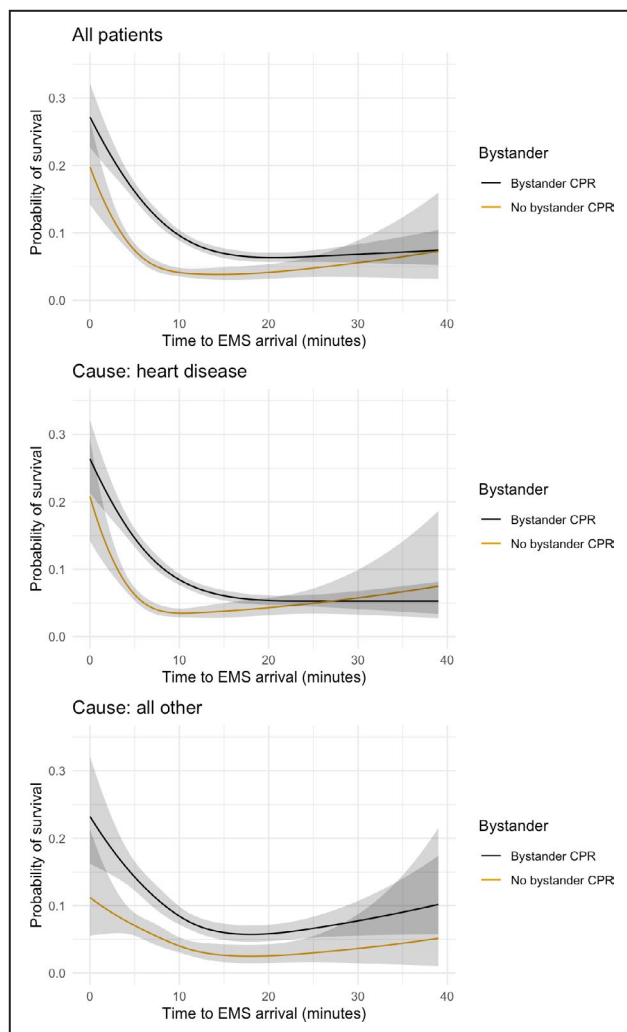


Figure 3. Adjusted survival to 30 days in relation to EMS response time for patients receiving CPR before EMS arrival and those that did not. Presented for all patients (top), those assessed by the EMS crew as having a cardiac cause (middle), and a non-cardiac cause (bottom), respectively. CPR indicates cardiopulmonary resuscitation; and EMS, emergency medical services.

The overall neurologic outcome was measured by a cerebral performance category score (CPC), which is presented in Figure 5.

The unadjusted analysis is in conformity with the adjusted results (Figures S3-S10). A fully adjusted model is presented in Figure S11.

A prediction of the effect of different EMS response times was made, based on patients who experienced OHCA reported to the SRCR in 2018 (Figure 6). The total number of survivors of OHCA nationally was predicted to be $n=504$, with an EMS response time greater than, or equal to, 15 minutes. Reducing EMS response times to 10 to 15 minutes would result in $n=577$ survivors, and the model predicted $n=1194$ survivors with a response time of 0 to 6 minutes.

DISCUSSION

We have explored the association between EMS response time and survival to 30 days after an OHCA, and we can confirm a clear correlation. Our findings, together with previous work,^{8–13} indicate that shortening ambulance response times will reduce mortality from OHCA.

Despite increasing ambulance response times since 1990, the time from collapse to defibrillation has remained essentially unchanged. This is because several other instances in the community now contribute to the defibrillation of patients who experienced OHCA. Apart from bystander defibrillation, several firefighters and police officers carry a defibrillator and can perform semi-automatic defibrillation. This means that the increasing ambulance response time has not ended up delaying defibrillation at the population level. Again, this could contribute to the false conclusion that ambulance response time is a less important factor for patients experiencing cardiac arrest. Among patients in Sweden presenting with a shockable rhythm, only about 1 out of 4 is defibrillated before EMS arrival.¹ In our investigation, the proportion of patients found in a shockable rhythm decreases with increasing EMS response time (Table 1).

When assessing the increasing EMS response time and its effect on survival after OHCA, the time from collapse to dispatch at the dispatch center (the first link in the chain of survival) must be considered. The time from collapse to the first registration of an event at the dispatch center is registered in the SRCR. The median time from collapse to registered emergency call was 5 minutes in 1990 and 2 minutes in 2018.¹ This means that the 5-minute increase in EMS response time from 1990 to 2018 has been partly compensated for by a 3-minute decrease in time from collapse to emergency call. Together with

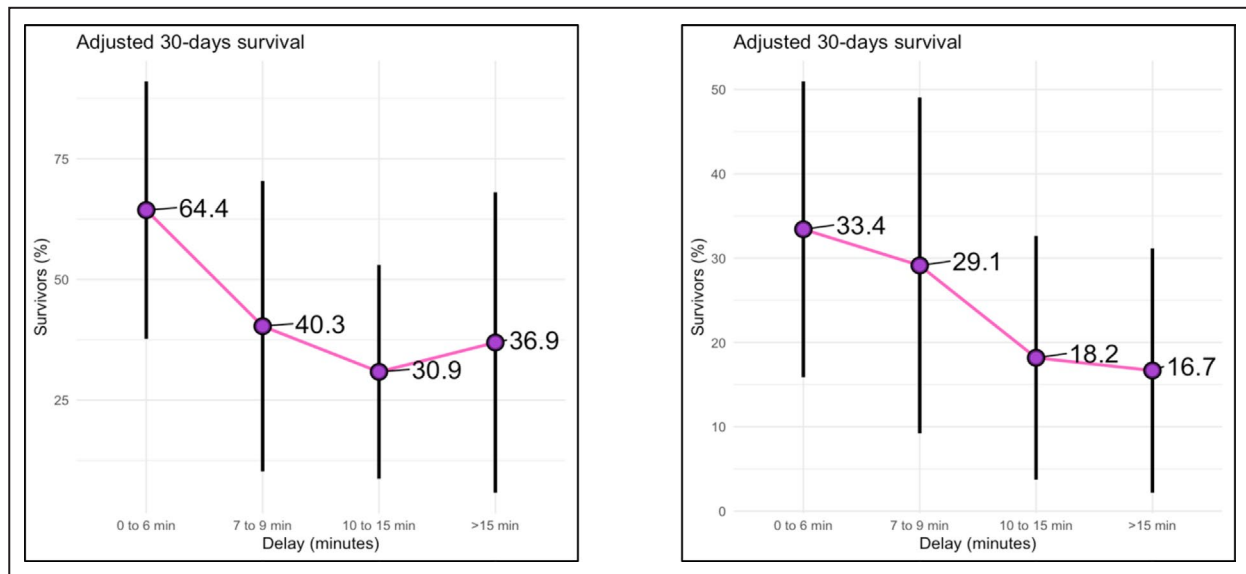


Figure 4. Association between survival to 30 days and emergency medical services response time in pediatric cases, aged 0-1 year (left, n=84) and 1-16 years (right, n=200). EMS indicates emergency medical services.

more frequent bystander interventions, an increasing proportion of EMS crew-witnessed cases, and more effective hospital interventions, this is likely to explain why survival after OHCA has improved, despite the heavy increase in EMS response time. We conclude that lives can be saved after an OHCA by shortening the time from collapse to EMS crew arrival.

CPR Before EMS Arrival

An increasing number of patients who experienced OHCA are treated with CPR before the ambulance arrives. Bystander CPR has been shown to more than double the chances of survival.¹⁴

In patients who experienced OHCA receiving CPR before EMS arrival, survival to 30 days increased with decreasing response time (Figure 2E). This was also the case for patients not receiving CPR before EMS arrival, if the response time was 15 minutes or less (Figure 2f) but not for a response time over 15 minutes. In cases where EMS crews decided to initiate CPR even when they arrived as much as 15 minutes or more after collapse, it is possible that the patient did not suffer complete circulatory arrest during the entire delay. It is also reasonable to believe that, in some OHCA cases with EMS arrival of >15 minutes, the patient was assessed by the crew as beyond resuscitation and CPR was not initiated and the patient was consequently not included in our study. This selective mechanism is one possible explanation of the slight increase in survival seen in OHCA cases in which CPR was not initiated before EMS arrival and the EMS response time was >15 minutes (Figure 2f).

Our data indicate that CPR before the arrival of EMS only has a significant effect on survival if an EMS crew

arrives on the scene within the first 15 minutes after dispatch, among patients where the cause is assumed to be heart disease (Figure 3). After this, the CIs overlapped when comparing victims who did and did not receive CPR before EMS arrival. This agrees with previous findings.⁹

Compressions Only

Compressions only is the recommended method for both untrained bystanders and bystanders unwilling to perform mouth-to-mouth inflations. This most likely contributes to the fact that CPR interventions before EMS arrival are increasing.¹⁵ It also highlights the question of EMS response time, since the effect of prolonged CPR without rescue breaths is unknown.

Several observational studies have concluded that compressions only are equivalent to chest compressions in combination with rescue breaths in adult patients.¹⁶⁻¹⁹ In dispatcher-assisted CPR, compressions only is the method recommended for adult patients, according to both the International Liaison Committee on Resuscitation⁷ and the European Resuscitation Council.²⁰

Based on the fact that rescue breaths may be beneficial for OHCA of asphyxial origin, for children, and for prolonged resuscitation, the ERC recommends all providers who are “trained and able” to perform compressions together with rescue breaths.²⁰ Animal models indicate that compressions-only may be as effective as the combination of compressions and ventilation for the first minutes of a non-asphyxial cardiac arrest.^{21,22} On the other hand, both arterial and cerebral oxygenation have been shown to be higher in pigs resuscitated with a combination of

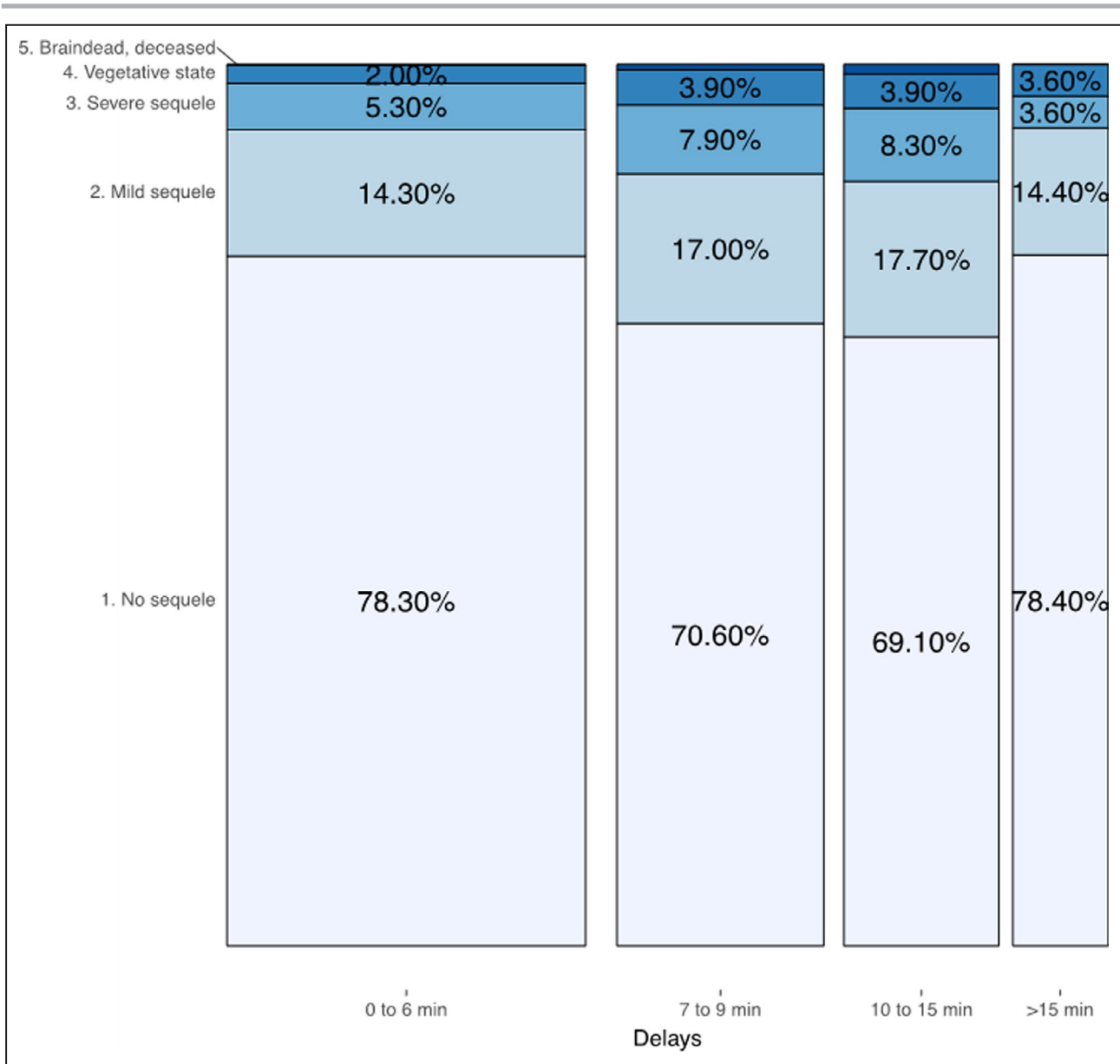


Figure 5. CPC score in relation to emergency medical services response time (n=2263). CPC indicates cerebral performance categories; and EMS, emergency medical services.

compressions and rescue breaths, compared with compressions only.²³

With an increasing spread of compressions-only CPR, the EMS response time affects the time to rescue breaths for many patients. A previous Swedish study found no association with compressions-only CPR and survival to 30 days when the EMS response time was 10–14 minutes.¹⁵

Our material reveals a similar 30-day survival rate when comparing patients receiving compressions-only CPR with all patients receiving CPR before EMS arrival, if the response time is 0 to 6 minutes or 7 to 9 minutes (Figure 2b and Figure 2e). When the EMS response time was >10 minutes, the overall survival among those receiving CPR before EMS arrival was slightly higher than survival for the sub-group of patients treated with

compressions-only CPR (10.9% versus 8.8% for response time 10 to 15 minutes, 8.6% versus 8.4% for response time >15 minutes, Figure 2B and 2E).

It is possible that a short EMS response time in OHCA will be even more beneficial in a future with more frequent compressions-only CPR. The close monitoring of the effect of EMS response time on survival and neurologic outcome is crucial.

Pediatric OHCA

The primary pathogenesis in pediatric cardiac arrest is a respiratory event.²⁴ Shockable rhythms are far less frequent compared with an adult population.^{25,26} These facts support the idea that EMS response times could

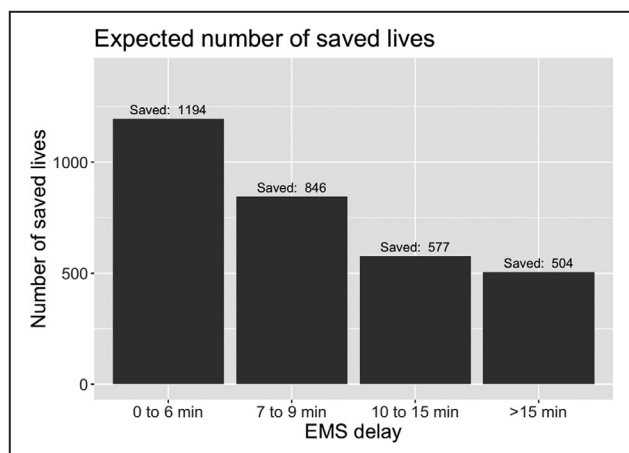


Figure 6. Predicted survival to 30 days, based on patients who experienced out-of-hospital cardiac arrest reported to the Swedish Registry of Cardiopulmonary Resuscitation in 2018 (n=6135).

EMS indicates emergency medical services.

have an even greater impact on survival in pediatric cases. Although we could confirm the association between EMS response times and survival to 30 days in both infants (0–1 years) and children aged 1 to 16 years (Figure 4), the number of pediatric cases was small and the CIs were wide. The material does not allow a comparison with the adult population, but our data support the importance of shortening EMS response time in pediatric patients who experienced OHCA.

Neurologic Outcome

Crude data on neurologic outcomes, presented as CPC-score values (Figure 5), show that the vast majority of survivors have no, or relatively mild, sequelae. About 90% of the survivors were assessed as CPC 1 or 2, and the proportions were similar in the 4 groups of EMS response time. We note that our results do not indicate a correlation between EMS response time and CPC outcome (Figure 5). The amount of missing data is considerable, and it is possible that the cognitive status of the survivors introduces a selection that is behind the similar distribution of CPC scores in all groups of EMS response time.

Shortening Response Times

Ambulance response time has been found to be an independent predictor of both defibrillation, survival, and favorable neurologic outcome after OHCA.^{11,12,27,28} Shorter response times are likely to be beneficial in major trauma,^{29,30} but there are conflicting results.³¹ In other emergencies, little is known about the importance of EMS response time.^{32–34} There is a great need for further knowledge on the importance of ambulance response time in different medical emergencies.

It is unknown whether increasing EMS response times are a global phenomenon. In informal discussions

with colleagues from different parts of the world, increasing EMS response times appear to be a common problem, but there is an obvious lack of reporting on the issue. To our knowledge, there is no national compilation of ambulance density in Sweden.

The bottom line is making the most of the resources allocated to patient care. Increasing the number of ambulances is the most straightforward way to cut the time from collapse to EMS-crew arrival. This option has to be considered next to investing in technically advanced interventions, such as prehospital endovascular aortic occlusion,³⁵ prehospital mechanical circulation,^{36,37} and drone-delivered defibrillators.³⁸

Based on patients who experienced OHCA reported in 2018, our model predicted that an EMS response time of 0–6 minutes would result in n=1194 survivors of OHCA (Figure 6). The actual number of survivors in 2018 was n=609, with a median response time of 11 minutes.¹ However, these predictions are speculative and based on all the patients who experienced OHCA reported to the SRCR in 2018, regardless of witnessed status, as we were aiming to obtain an overall figure of the potential number of lives saved.

The association between EMS response time and 30-day survival is affected by many factors and extrapolation to other populations must be done with caution. However, international consensus guidelines in cardiac arrest management are well established³⁹ and widely spread. Due to the similarities in OHCA management, applying our results to the US populations could still be of interest. Approximately 350 000 cardiac arrests occur in the United States each year⁴⁰ and the mean ambulance response time was around 8.5 minutes in 2014.⁴¹ Our model estimates 48 300 survivors from 350 000 out-of-hospital cardiac arrests, if the ambulance response time is 8.5 minutes. Reducing the 8.5 minutes to 6 minutes or less would result in 68 250 survivors, according to our model.

The overall effect of a higher density of ambulances is likely not to be restricted to patients who experienced OHCA. We already know that patients who suffer an OHCA in the presence of an EMS crew have a higher chance of survival than bystander-witnessed cases.⁴² Shortening the EMS response time is not only likely to increase the proportion of EMS-witnessed OHCA cases, it also has the potential to prevent the actual occurrence of a cardiac arrest. An estimation of the potential benefits of an increased density of ambulances for patients with other medical emergencies, as well as possible positive effects on the working conditions of EMS crews, is warranted.

CONCLUSIONS

Survival to 30 days after a witnessed OHCA decreases as ambulance response times increase. This

correlation was seen independently of initial rhythm and whether CPR was performed before EMS-crew arrival.

LIMITATIONS

It is possible that hospital interventions, such as percutaneous coronary interventions and therapeutic hypothermia, are not equally distributed in the different categories of EMS response time and may thereby confound our results. We have no reason to believe that this potential bias would affect our analysis other than marginally.

The study period from 2008 to 2017 covers 3 different periods of CPR guidelines. This introduces another possible confounder in our investigation, since the use of the different guidelines is not necessarily equally distributed between the different groups of response time.

Neurologic outcome, measured as CPC, had a remarkably high degree of missing data, and selection bias is to be expected since it is reasonable to believe that follow-up is more often successful in patients with a less impaired cerebral performance. Furthermore, our study was not designed to address the effect of EMS response time on CPC score.

When analyzing compressions-only CPR, the amount of missing data was considerable and no direct comparison between compressions-only CPR and conventional CPR was possible.

ARTICLE INFORMATION

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Affiliations

From the Department of Anesthesiology and Intensive Care, Queen Silvia's Children's Hospital, Gothenburg, Sweden (J.H.); Department of Prehospital and Emergency Care, Sahlgrenska University Hospital, Gothenburg, Sweden (J.H.); Centre for Prehospital Research, Faculty of Caring Science, Work Life and Social Welfare, University of Borås, Borås, Sweden (J.H., C.A.); Department of Anesthesiology and Intensive Care Medicine, Sahlgrenska Academy, University of Gothenburg, Sahlgrenska University Hospital, Gothenburg, Sweden (S.-E.R., E.H., A.R.); School of Education, Health and Social Studies, Dalarna University, Falun, Sweden (A.S.); Centre for Clinical Research Dalarna, Uppsala University, Uppsala, Sweden (A.S.); and Department of Prehospital Care, Region of Dalarna, Falun, Sweden (A.S.).

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Disclosures

None.

Supplementary Material

Figures S1–S11

REFERENCES

1. Rawshani A, Herlitz J. The Swedish Register of Cardiopulmonary Resuscitation, annual report 2019. <https://hlrr.se/#sammanfattning>. Accessed March 14, 2020.
2. Hollenberg J, Herlitz J, Lindqvist J, Riva G, Bohm K, Rosenqvist M, Svensson L. Improved survival after out-of-hospital cardiac arrest is associated with an increase in proportion of emergency crew-witnessed cases and bystander cardiopulmonary resuscitation. *Circulation*. 2008;118:389–396.
3. Stromsoe A, Svensson L, Axelsson AB, Goransson K, Todorova L, Herlitz J. Validity of reported data in the Swedish cardiac arrest register in selected parts in Sweden. *Resuscitation*. 2013;84:952–956.
4. Strömsöe A, Svensson L, Axelsson ÅB, Claesson A, Göransson KE, Nordberg P, Herlitz J. Improved outcome in Sweden after out-of-hospital cardiac arrest and possible association with improvements in every link in the chain of survival. *Eur Heart J*. 2014;36:863–871.
5. Holmén J, Hollenberg J, Claesson A, Herrera MJ, Azeli Y, Herlitz J, Axelsson C. Survival in ventricular fibrillation with emphasis on the number of defibrillations in relation to other factors at resuscitation. *Resuscitation*. 2017;113:33–38.
6. Statistics Sweden 2017. <https://scb.se/en/About-us/about-the-website-and-terms-of-use/>. Accessed 14 March 2020.
7. Travers AH, Perkins GD, Berg RA, Castren M, Considine J, Escalante R, Gazmuri RJ, Koster RW, Lim SH, Nation KJ, et al. Part 3: adult basic life support and automated external defibrillation: 2015 international consensus on cardiopulmonary resuscitation and emergency cardiovascular care science with treatment recommendations. *Circulation*. 2015;132:S51–S83.
8. Bürger A, Wnent J, Bohn A, Jantzen T, Brenner S, Lefering R, Seewald S, Gräsner JT, Fischer M. The effect of ambulance response time on survival following out-of-hospital cardiac arrest-an analysis from the German resuscitation registry einfluss der hilfsfrist auf das überleben nach plötzlichem herz-kreislauf-stillstand: analyse aus dem deutschen reanimationsregister. *Deutsches Arzteblatt International*. 2018;115:541–548.
9. Rajan MS, Wissenberg AM, Folke MF, Hansen KS, Gerds HT, Kragholm HK, Hansen HC, Karlsson HL, Lippert HF, Køber HL, et al. Association of bystander cardiopulmonary resuscitation and survival according to ambulance response times after out-of-hospital cardiac arrest. *Circulation*. 2016;134:2095–2104.
10. Goto Y, Funada A, Goto Y. Relationship between emergency medical services response time and bystander intervention in patients with out-of-hospital cardiac arrest. *J Am Heart Assoc*. 2018;7:e007568. DOI: 10.1161/JAHA.117.007568.
11. Pell JP, Sirel JM, Marsden AK, Ford I, Cobbe SM. Effect of reducing ambulance response times on deaths from out of hospital cardiac arrest: Cohort study. *BMJ*. 2001;322:1385–1388.
12. Park GJ, Song KJ, Shin SD, Lee KW, Ahn KO, Lee EJ, Hong KJ, Ro YS. Timely bystander CPR improves outcomes despite longer ems times. *Am J Emerg Med*. 2017;35:1049–1055.
13. O'Keefe C, Nicholl J, Turner J, Goodacre S. Role of ambulance response times in the survival of patients with out-of-hospital cardiac arrest. *Emerg Med J*. 2011;28:703–706.
14. Hasselqvist-Ax I, Riva G, Herlitz J, Rosenqvist M, Hollenberg J, Nordberg P, Ringh M, Jonsson M, Axelsson C, Lindqvist J, et al. Early cardiopulmonary resuscitation in out-of-hospital cardiac arrest. *N Engl J Med*. 2015;372:2307–2315.
15. Riva G, Ringh M, Jonsson M, Svensson L, Herlitz J, Claesson A, Djarv T, Nordberg P, Forsberg S, Rubertsson S, et al. Survival in out-of-hospital cardiac arrest after standard cardiopulmonary resuscitation or chest compressions only before arrival of emergency medical services: nationwide study during three guideline periods. *Circulation*. 2019;139(23):2600–2609.
16. The SOS-KANTO study group. Cardiopulmonary resuscitation by bystanders with chest compression only (sos-kanto): an observational study. *Lancet* 2007;369:920–926.
17. Bohm K, Rosenqvist M, Herlitz J, Hollenberg J, Svensson L. Survival is similar after standard treatment and chest compression only in out-of-hospital bystander cardiopulmonary resuscitation. *Circulation*. 2007;116:2908–2912.
18. Olasveengen TM, Wik L, Steen PA. Standard basic life support vs. continuous chest compressions only in out-of-hospital cardiac arrest. *Acta Anaesthesiol Scand*. 2008;52:914–919.
19. Bobrow BJ, Spaite DW, Berg RA, Stolz U, Sanders AB, Kern KB, Vadeboncoeur TF, Clark LL, Gallagher JV, Stapczynski JS, et al. Chest compression-only CPR by lay rescuers and survival from out-of-hospital cardiac arrest. *JAMA*. 2010;304:1447–1454.
20. Perkins GD, Handley AJ, Koster RW, Castren M, Smyth MA, Olasveengen T, Monsieurs KG, Raffay V, Gräsner JT, Wenzel V,

- et al. European resuscitation council guidelines for resuscitation 2015: Section 2. Adult basic life support and automated external defibrillation. *Resuscitation*. 2015;95:81–99.
21. Chandra NC, Gruben KG, Tsitlik JE, Brower R, Guerci AD, Halperin HH, Weisfeldt ML, Permutt S. Observations of ventilation during resuscitation in a canine model. *Circulation*. 1994;90:3070–3075.
 22. Kern KB, Hilwig RW, Berg RA, Sanders AB, Ewy GA. Importance of continuous chest compressions during cardiopulmonary resuscitation: Improved outcome during a simulated single lay-rescuer scenario. *Circulation*. 2002;105:645–649.
 23. Dorph E, Wik L, Stromme TA, Eriksen M, Steen PA. Oxygen delivery and return of spontaneous circulation with ventilation: compression ratio 2:30 versus chest compressions only CPR in pigs. *Resuscitation*. 2004;60:309–318.
 24. Meert KL, Telford R, Holubkov R, Stomine BS, Christensen JR, Dean JM, Moler FW. Pediatric out-of-hospital cardiac arrest characteristics and their association with survival and neurobehavioral outcome. *Pediatr Crit Care Med*. 2016;17:e543–e550.
 25. Donoghue AJ, Nadkarni V, Berg RA, Osmond MH, Wells G, Nesbitt L, Stiell IG. CanAm pediatric cardiac arrest I. Out-of-hospital pediatric cardiac arrest: an epidemiologic review and assessment of current knowledge. *Ann Emerg Med*. 2005;46:512–522.
 26. Goto Y, Funada A, Goto Y. Duration of prehospital cardiopulmonary resuscitation and favorable neurological outcomes for pediatric out-of-hospital cardiac arrests. *Circulation*. 2016;134:2046–2059.
 27. Gold LS, Fahrenbruch CE, Rea TD, Eisenberg MS. The relationship between time to arrival of emergency medical services (ems) and survival from out-of-hospital ventricular fibrillation cardiac arrest. *Resuscitation*. 2010;81:622–625.
 28. Lee DW, Moon HJ, Heo NH. Association between ambulance response time and neurologic outcome in patients with cardiac arrest. *Am J Emerg Med*. 2019;37:1999–2003.
 29. Feero S, Hedges JR, Simmons E, Irwin L. Does out-of-hospital ems time affect trauma survival? *Am J Emerg Med*. 1995;13:133–135.
 30. Gonzalez RP, Cummings GR, Phelan HA, Mulekar MS, Rodning CB. Does increased emergency medical services prehospital time affect patient mortality in rural motor vehicle crashes? A statewide analysis. *Am J Surg*. 2009;197:30–34.
 31. Blanchard IE, Doig CJ, Hagel BE, Anton AR, Zygun DA, Kortbeek JB, Powell DG, Williamson TS, Fick GH, Innes GD. Emergency medical services response time and mortality in an urban setting. *Prehosp Emerg Care*. 2012;16:142–151.
 32. Blackwell TH, Kaufman JS. Response time effectiveness: Comparison of response time and survival in an urban emergency medical services system. *Acad Emerg Med*. 2002;9:288–295.
 33. Weiss S, Fullerton L, Oglesbee S, Duerden B, Froman P. Does ambulance response time influence patient condition among patients with specific medical and trauma emergencies? *South Med J*. 2013;106:230–235.
 34. Wilde ET. Do emergency medical system response times matter for health outcomes? *Health Econ*. 2013;22:790–806.
 35. Brede JR, Lafrenz T, Klepstad P, Skjærseth EA, Nordseth T, Søvik E, Krüger AJ. Feasibility of pre-hospital resuscitative endovascular balloon occlusion of the aorta in non-traumatic out-of-hospital cardiac arrest. *J Am Heart Assoc*. 2019;8:e014394. DOI: 10.1161/JAHA.119.014394.
 36. Kilner T, Stanton BL, Mazur SM. Prehospital extracorporeal cardiopulmonary resuscitation for out-of-hospital cardiac arrest: a retrospective eligibility study. *Emergency medicine Australasia: EMA*. 2019;31:1007.
 37. Lamhaut L, Hutin A, Puymirat E, Jouan J, Raphalen J-H, Jouffroy R, Jaffry M, Dagrón C, An K, Dumas F, et al. A pre-hospital extracorporeal cardio pulmonary resuscitation (ECP) strategy for treatment of refractory out hospital cardiac arrest: an observational study and propensity analysis. *Resuscitation*. 2017;117:109–117.
 38. Boutillier JJ, Brooks CS, Janmohamed EA, Byers PA, Buick JJ, Zhan YC, Schoellig YA, Cheskes YS, Morrison YL, Chan YTC. Optimizing a drone network to deliver automated external defibrillators. *Circulation*. 2017;135:2454–2465.
 39. Neumar RW, Perkins GD. Future vision for ilcor and its role in the global resuscitation community. *Circulation*. 2018;138:1085–1087.
 40. Benjamin Emelia J, Virani Salim S, Callaway Clifton W, Chamberlain Alanna M, Chang Alexander R, Cheng S, Chiuve Stephanie E, Cushman M, Delling Francesca N, Deo R, et al. Heart disease and stroke statistics—2018 update: a report from the American heart association. *Circulation*. 2018;137:e67–e492.
 41. Hsia RY, Huang D, Mann NC, Colwell C, Mercer MP, Dai M, Niedzwiecki MJ. A us national study of the association between income and ambulance response time in cardiac arrest. *JAMA Netw Open*. 2018;1:e185202.
 42. Axelsson C, Claesson A, Engdahl J, Herlitz J, Hollenberg J, Lindqvist J, Rosenqvist M, Svensson L. Outcome after out-of-hospital cardiac arrest witnessed by ems: changes over time and factors of importance for outcome in Sweden. *Resuscitation*. 2012;83:1253–1258.

Supplemental Material

Figure S1. Direct acyclic graph presenting possible factors affecting survival in OHCA.

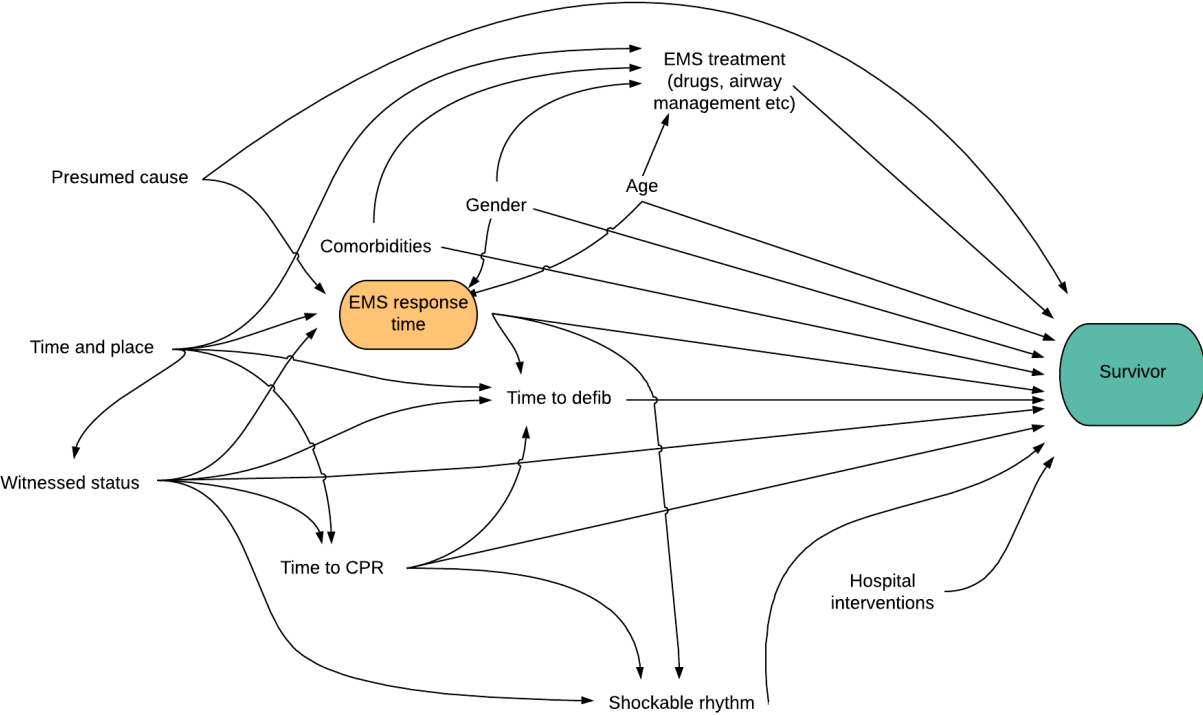


Figure S2. The association between EMS response time and 30-day survival, stratified by three periods of calendar year.

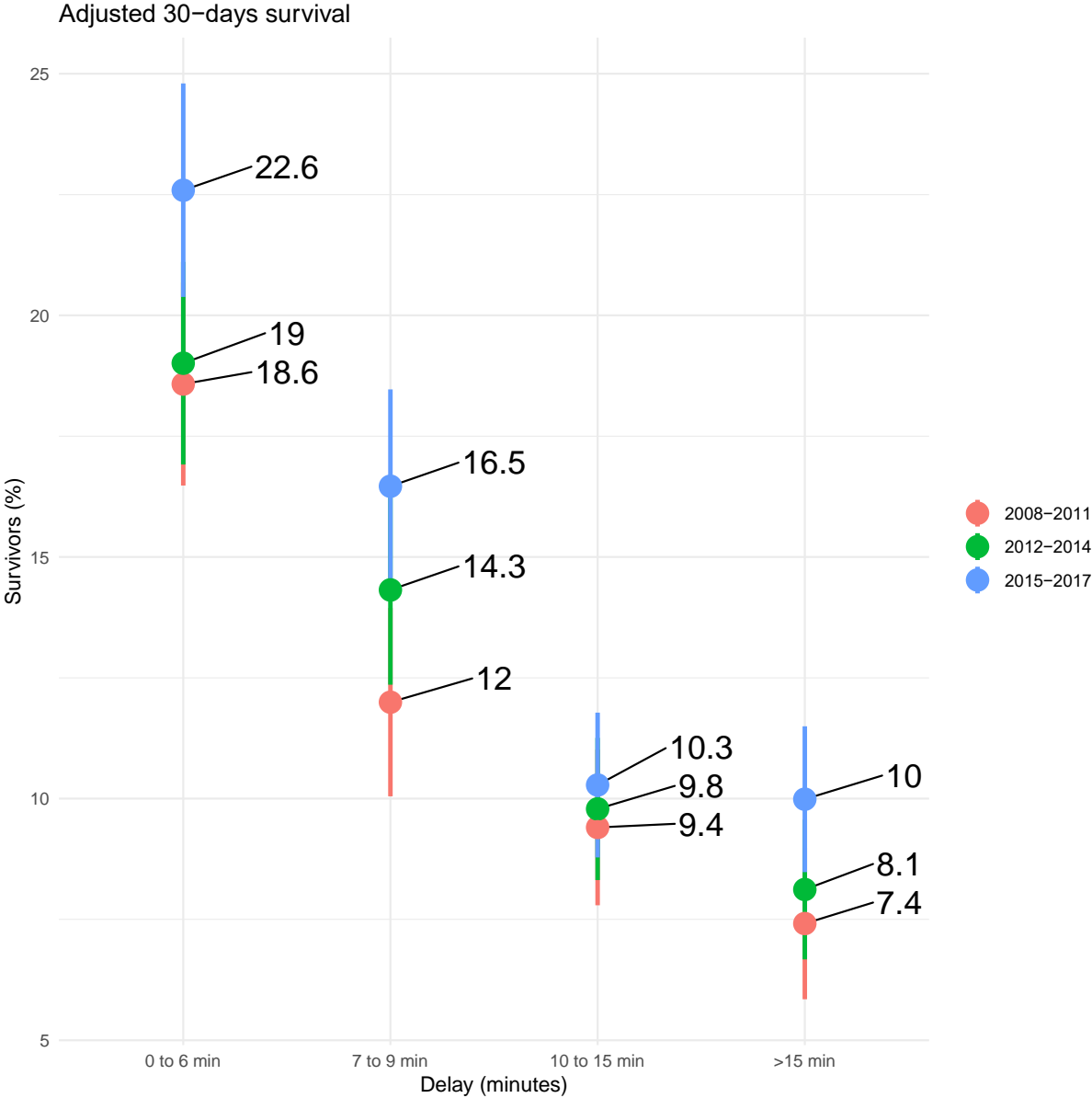


Figure S3. The association of EMS response time and survival to 30 days for all patients, adjusted and unadjusted values.

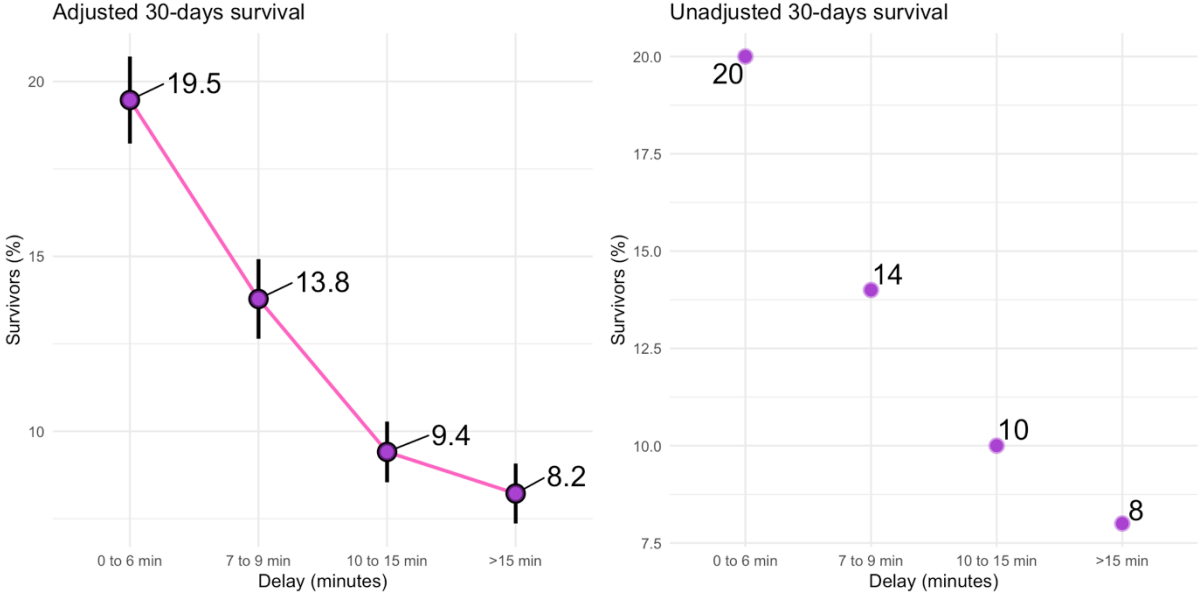


Figure S4. The association of EMS response time and survival to 30 days among patients receiving compressions-only CPR before EMS arrival.

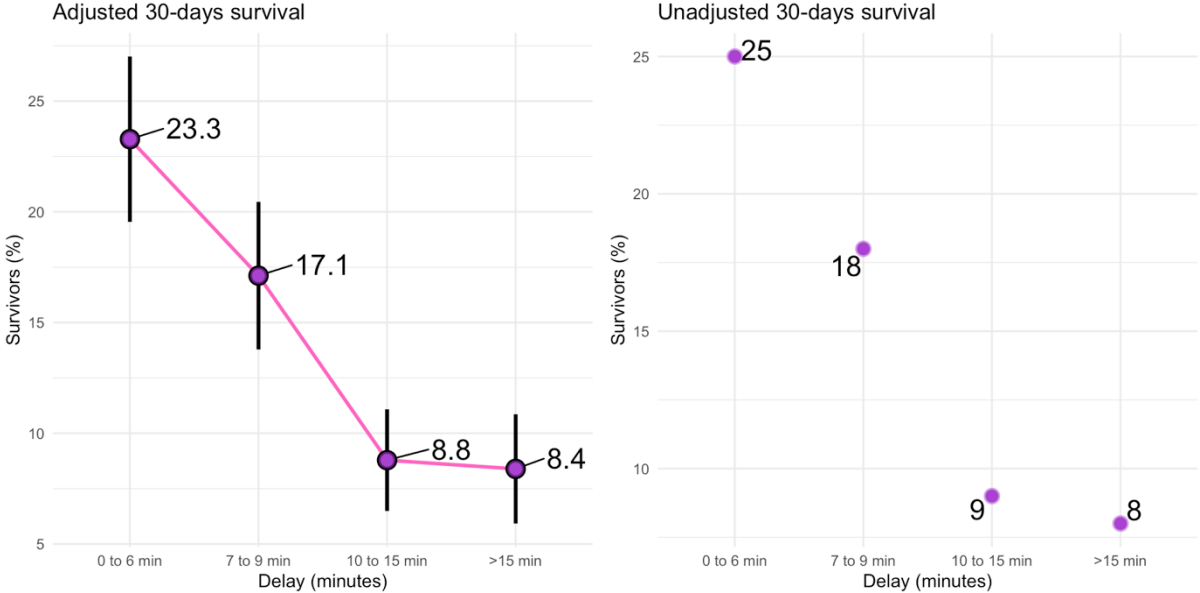


Figure S5. The association between EMS response time and survival to 30 days among patients found in a shockable rhythm, adjusted and unadjusted values.

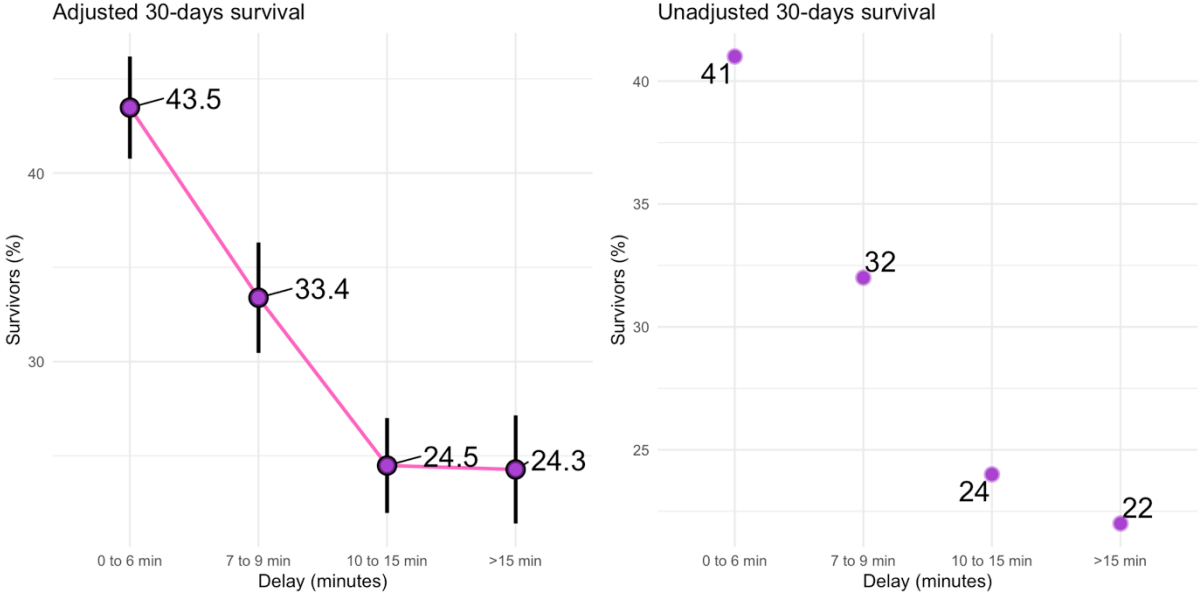


Figure S6. The association between EMS response time and survival to 30 days among patients found in a non-shockable rhythm, adjusted and unadjusted values.

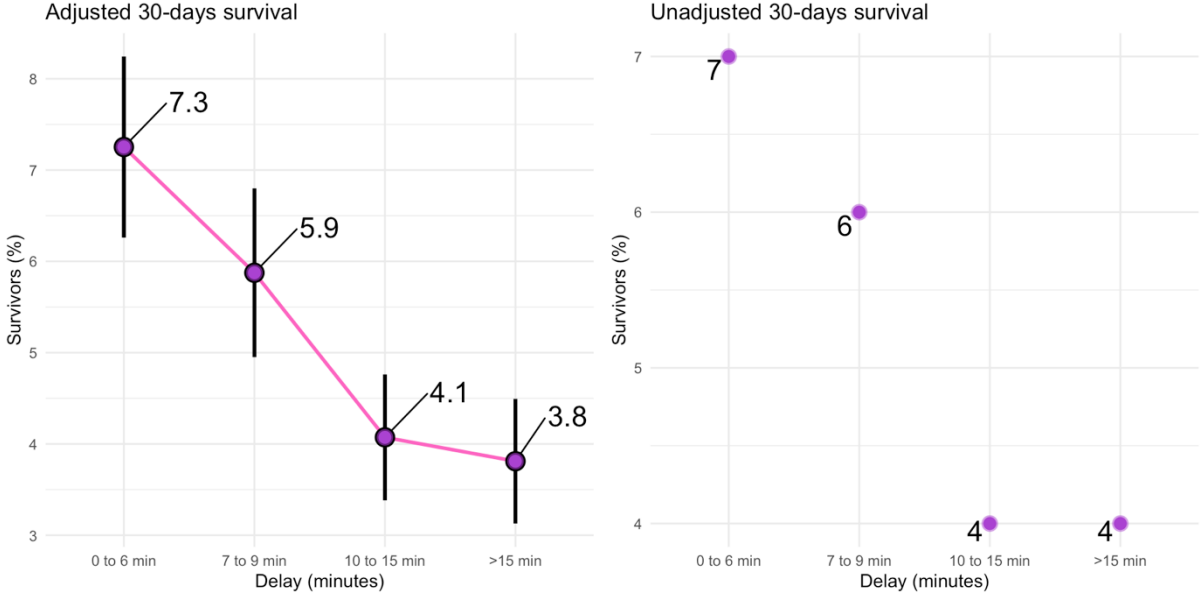


Figure S7. The association between EMS response time and survival to 30 days among patients receiving CPR before EMS arrival, adjusted and unadjusted values.

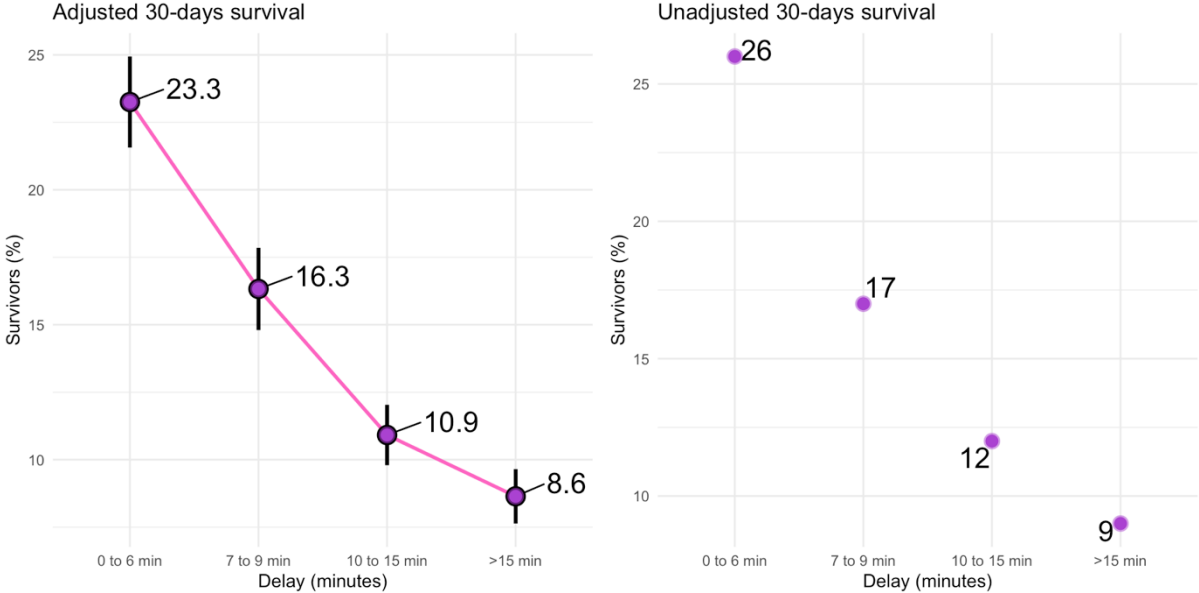


Figure S8. The association between EMS response time and survival to 30 days among patients not receiving CPR before EMS arrival, adjusted and unadjusted values.

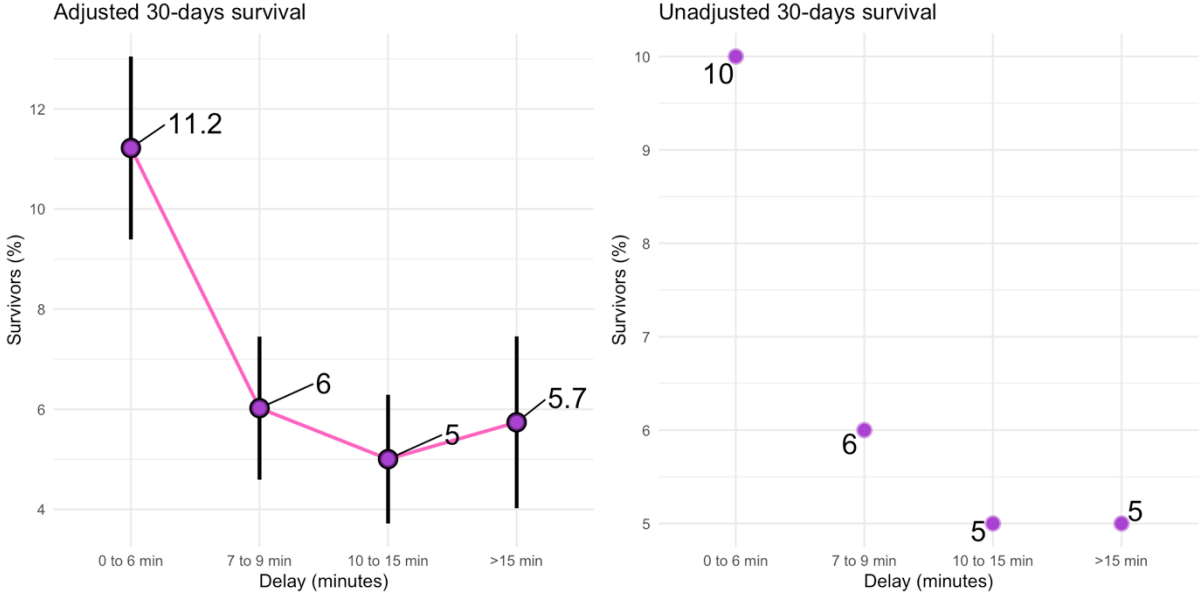


Figure S9. The association between EMS response time and survival to 30 days in pediatric cases (aged 0-1 year), adjusted and unadjusted values.

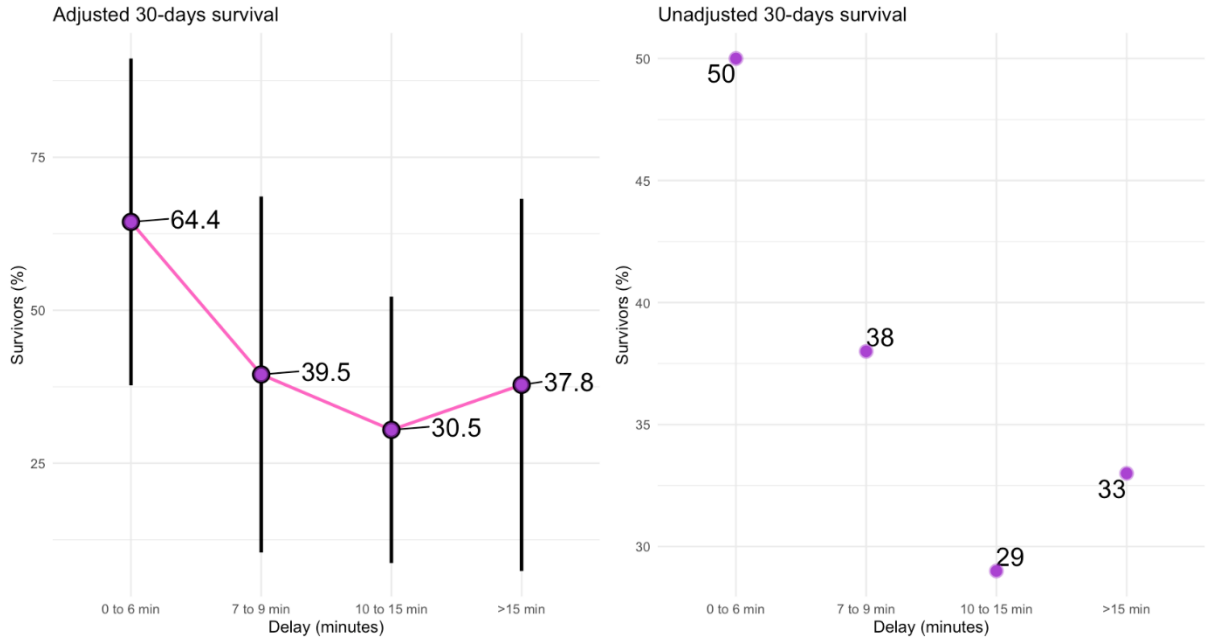


Figure S10. The association between EMS response time and survival to 30 days in pediatric cases (aged 1-16 year), adjusted and unadjusted values.

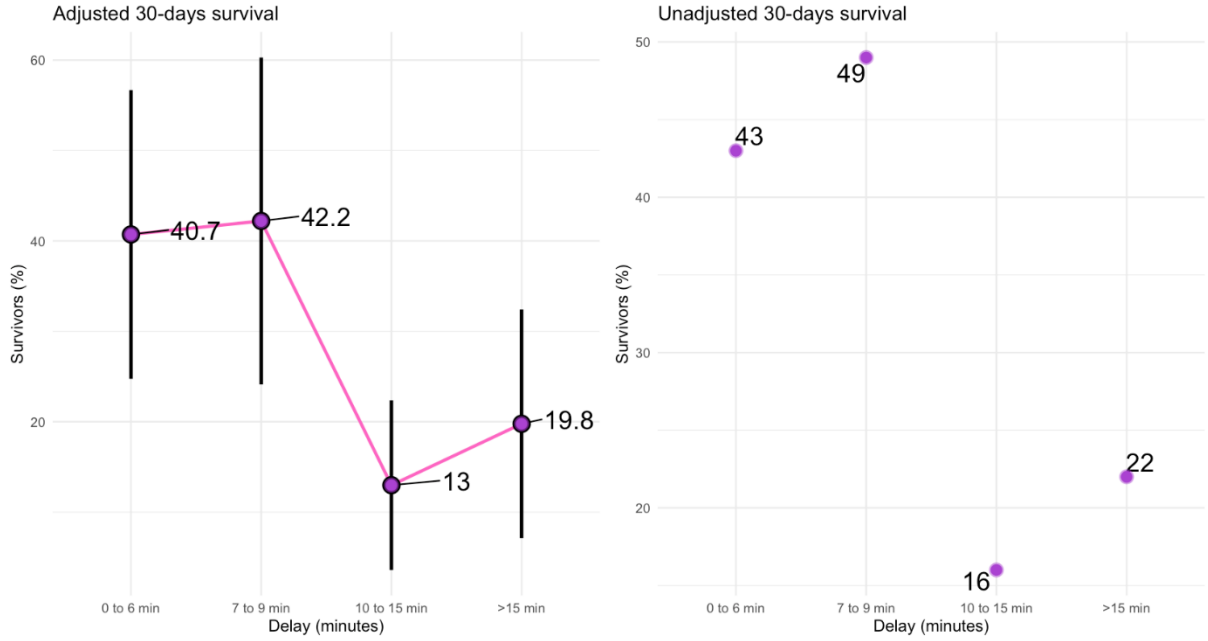
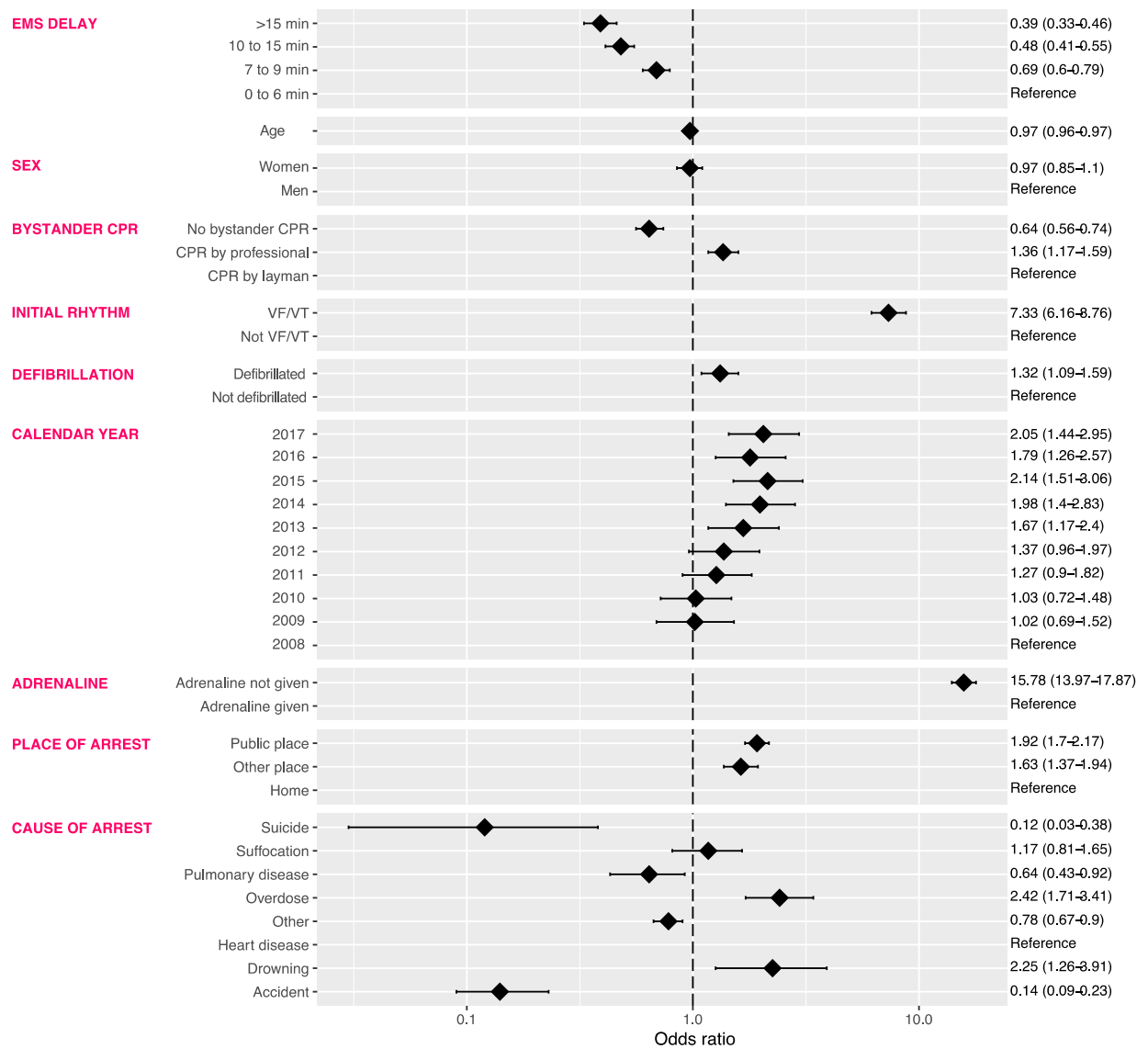


Figure S11. Fully adjusted logistic regression.



EMS indicates emergency medical services; CPR – cardiopulmonary resuscitation; VF – ventricular fibrillation; pVT – pulseless ventricular tachycardia. Odds ratios and their 95% CI are presented in the right column.