

Predictors of Survival From Out-of-Hospital Cardiac Arrest

A Systematic Review and Meta-Analysis

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Background—Prior studies have identified key predictors of out-of-hospital cardiac arrest (OHCA), but differences exist in the magnitude of these findings. In this meta-analysis, we evaluated the strength of associations between OHCA and key factors (event witnessed by a bystander or emergency medical services [EMS], provision of bystander cardiopulmonary resuscitation [CPR], initial cardiac rhythm, or the return of spontaneous circulation). We also examined trends in OHCA survival over time.

Methods and Results—An electronic search of PubMed, EMBASE, Web of Science, CINAHL, Cochrane DSR, DARE, ACP Journal Club, and CCTR was conducted (January 1, 1950 to August 21, 2008) for studies reporting OHCA of presumed cardiac etiology in adults. Data were extracted from 79 studies involving 142 740 patients. The pooled survival rate to hospital admission was 23.8% (95% CI, 21.1 to 26.6) and to hospital discharge was 7.6% (95% CI, 6.7 to 8.4). Stratified by baseline rates, survival to hospital discharge was more likely among those: witnessed by a bystander (6.4% to 13.5%), witnessed by EMS (4.9% to 18.2%), who received bystander CPR (3.9% to 16.1%), were found in ventricular fibrillation/ventricular tachycardia (14.8% to 23.0%), or achieved return of spontaneous circulation (15.5% to 33.6%). Although 53% (95% CI, 45.0% to 59.9%) of events were witnessed by a bystander, only 32% (95% CI, 26.7% to 37.8%) received bystander CPR. The number needed to treat to save 1 life ranged from 16 to 23 for EMS-witnessed arrests, 17 to 71 for bystander-witnessed, and 24 to 36 for those receiving bystander CPR, depending on baseline survival rates. The aggregate survival rate of OHCA (7.6%) has not significantly changed in almost 3 decades.

Conclusions—Overall survival from OHCA has been stable for almost 30 years, as have the strong associations between key predictors and survival. Because most OHCA events are witnessed, efforts to improve survival should focus on prompt delivery of interventions of known effectiveness by those who witness the event. (*Circ Cardiovasc Qual Outcomes*. 2010;3:63-81.)

Key Words: heart arrest ■ death, sudden ■ emergency medical services

In the United States, more than 166 000 patients experience an out-of-hospital cardiac arrest (OHCA) annually.¹ Approximately 60% are treated by emergency medical services.¹ Published rates of OHCA survival to hospital discharge range from 0.3% in Detroit² to 20.4% in Slovenia.³ Among cities reporting data, the median rate of survival to hospital discharge is 6.4%.⁴

Previous meta-analyses of cardiac arrest research have focused on the use of new or emerging therapies (ie, impedance threshold device,⁵ active compression-decompression cardiopulmonary resuscitation,⁶ hypothermia,⁷ emergency intubation⁸), new medications (ie, vasopressin,^{9–11} epinephrine,^{11,12} time to first medication administration¹³), and the use of automated external defibrillators by bystanders^{14–16} and emergency medical technicians.^{4,17} However, no group has conducted a systematic review to assess, with precision, the associations between key clinical factors and survival, and examine temporal trends in OHCA survival through the decades.

Two resuscitation rules^{18,19} for emergency medical services (EMS) personnel have recently been shown to accurately predict which OHCA patients warrant rapid transport to the hospital for further care. These rules use 5 clinical criteria to predict survival from OHCA: arrest witnessed by a bystander, arrest witnessed by EMS, provision of bystander CPR, shockable cardiac rhythm, and return of spontaneous circulation (ROSC) in the field. Recently, 3 independent teams of researchers have validated these decision rules with a misclassification rate of 0.1%.^{20–22} Despite these findings, the variability of survival by each clinical criterion has not been systematically evaluated across populations. Accordingly, we analyzed 30 years of data on OHCA in a systematic review and meta-analysis, taking into account potential sources of variation such as type of EMS system, baseline survival rates in the region, and location. We also analyzed temporal trends

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in OHCA survival over this time frame to determine whether knowledge of OHCA pathophysiology and treatment is being effectively translated into improvements in outcome.

WHAT IS KNOWN

- Two resuscitation rules for emergency medical services (EMS) personnel have recently been shown to accurately predict which out-of-hospital cardiac arrest (OHCA) patients warrant rapid transport to the hospital for further care. These rules use 5 clinical criteria to predict survival from OHCA-arrest witnessed by a bystander, arrest witnessed by EMS, provision of bystander cardiopulmonary resuscitation (CPR), shockable cardiac rhythm, and return of spontaneous circulation (ROSC) in the field. Recently, 3 independent teams of researchers validated these decision rules with a misclassification rate of 0.1%.
- However, no group has conducted a systematic review to assess, with precision, the associations between these 5 key clinical factors and survival, and examine temporal trends in OHCA survival through the decades.

WHAT THE STUDY ADDS

- This meta-analysis brings together 30 years of research, involving more than 142 000 patients. Our findings conclusively affirm the value of bystander CPR, the critical importance of “shockable” rhythms, and the predictive value of ROSC in the prehospital setting.
- Forty percent of patients with OHCA are found with ventricular fibrillation/ventricular tachycardia, yet only 22% achieve ROSC. This group may be a priority population for future efforts to improve ROSC and survival to hospital discharge.
- The magnitude of effect sizes for the 5 clinical factors, such as provision of bystander CPR and an initial rhythm of ventricular fibrillation/ventricular tachycardia, are higher in communities that have low baseline survival rates. This suggests that efforts such as targeted CPR training to increase bystander CPR rates will have their greatest effect in communities with low baseline rates of survival.
- Survival from OHCA has not significantly improved in almost 3 decades, despite enormous efforts in research spending and the development of novel drugs and devices. The aggregate survival rate, recorded across various populations, is between 6.7% and 8.4%.

Methods

Data Sources and Searches

A systematic review of the literature was conducted to identify studies that evaluated 5 key factors known to be associated with survival: (1) arrest witnessed by a bystander, (2) arrest witnessed by an EMS provider, (3) provision of bystander cardiopulmonary resuscitation (CPR) before EMS arrival, (4) presenting rhythm (determined by EMS personnel to be ventricular fibrillation/ventric-

ular tachycardia [VF/VT] or asystole), and (5) patient response to prehospital emergency cardiac care with ROSC in the field.

All studies published between January 1, 1950 through August 21, 2008 were considered. The following electronic databases were searched with the assistance of an experienced health services librarian, using a Boolean Search Strategy: PubMed, EMBASE, Web of Science, CINAHL, and all EBM Reviews (includes Cochrane DSR, DARE, ACP Journal Club, and CCTR). The root search was “Heart Arrest”[MeSH] AND (“Cardiopulmonary Resuscitation” [MeSH] OR “Resuscitation Orders”[MeSH]) AND (English[lang] AND (“adolescent”[MeSH Terms] OR “adult”[MeSH Terms:noexp] OR (“middle aged”[MeSH Terms] OR “aged”[MeSH Terms]))). We then added the keywords “Witnessed or Bystander” to the root search with “AND ((witness* OR unwitnessed OR bystander* OR observer* OR observed)) AND (“Survival”[MeSH] OR “Mortality”[MeSH] OR “mortality”[Subheading] OR “Survival Rate”[MeSH])” or “Defibrillator or ROSC” with “AND (“Survival”[MeSH] OR “Mortality”[MeSH] OR “mortality”[Subheading] OR “Survival Rate”[MeSH]) AND (“Electric Countershock”[MeSH] OR ROSC OR defibrillation OR “Arrhythmias, Cardiac”[MeSH]).” The majority of articles we reviewed were retrieved from PubMed (353 of 909 articles). Only reports published in English were included.

In addition to these automated searchers, we conducted a hand search of bibliographies of key articles^{4,23–26} and abstracts presented at major scientific conferences in 2006 to 2008. We also contacted 2 national cardiac arrest experts to identify any relevant but unpublished studies.

Study Selection

Two reviewers (C.S. and J.D.) evaluated each full text article and determined exclusions based on a priori criteria. This excluded any study which contained greater than 20% pediatric patients (age <18 years), a majority of events caused by a noncardiac etiology (trauma, drowning, electrocution, respiratory), cases of in-hospital arrest, survival through hospital discharge not reported, use of investigational interventions that were outside the standard of care at the time the study was conducted (eg, hypothermia), use of investigational devices (eg, abdominal compression device), and those that did not report any of the 5 variables of interest.

Using these criteria, the kappa for interrater reliability to be included in the study was 0.71. Disagreements were resolved by discussion. Three authors were contacted to clarify the dates of their study to ensure that we did not inadvertently double-count some patients,^{27,28} to obtain specific data on a sole survivor of OHCA,² to clarify certain aspects of a field termination protocol,²⁹ and to obtain more information on survivors.³⁰

Data Extraction and Quality Assessment

The 204 studies that met our preliminary selection criteria were further evaluated using the Newcastle Ottawa Scale for cohort studies. The Newcastle Ottawa Scale has been shown to be useful in rating the quality of observational studies in a standardized format.³¹ Ultimately, 79 of these 204 studies met an a priori aggregate measure of quality, based on clearly defined patient selection, assessment of exposures and outcome, comparability of groups, and adequacy of follow-up to hospital discharge. Reasons for exclusion included: failure to comparably report outcome data for survivors versus nonsurvivors for at least 1 of the 5 clinical factors of interest (n=84); reporting of duplicate cohorts from the same study (n=18), majority of patients with noncardiac etiologies (n=14), and in-hospital cardiac arrests (n=9).

The following variables were extracted from the 79 studies: number of arrests in the study, total survivors followed to hospital discharge, case attributable to a presumed cardiac etiology, mean age, arrest witnessed by bystander or EMS, provision of bystander CPR, initial rhythm (VF/VT or asystole), achievement of ROSC, and outcome to hospital discharge. Bystander CPR was defined as any attempt at CPR initiated by someone other than the EMS/first responder team regardless of whether the event was witnessed or not. The presenting rhythm was based on the paramedic’s assessment on scene. ROSC was recorded in any study that

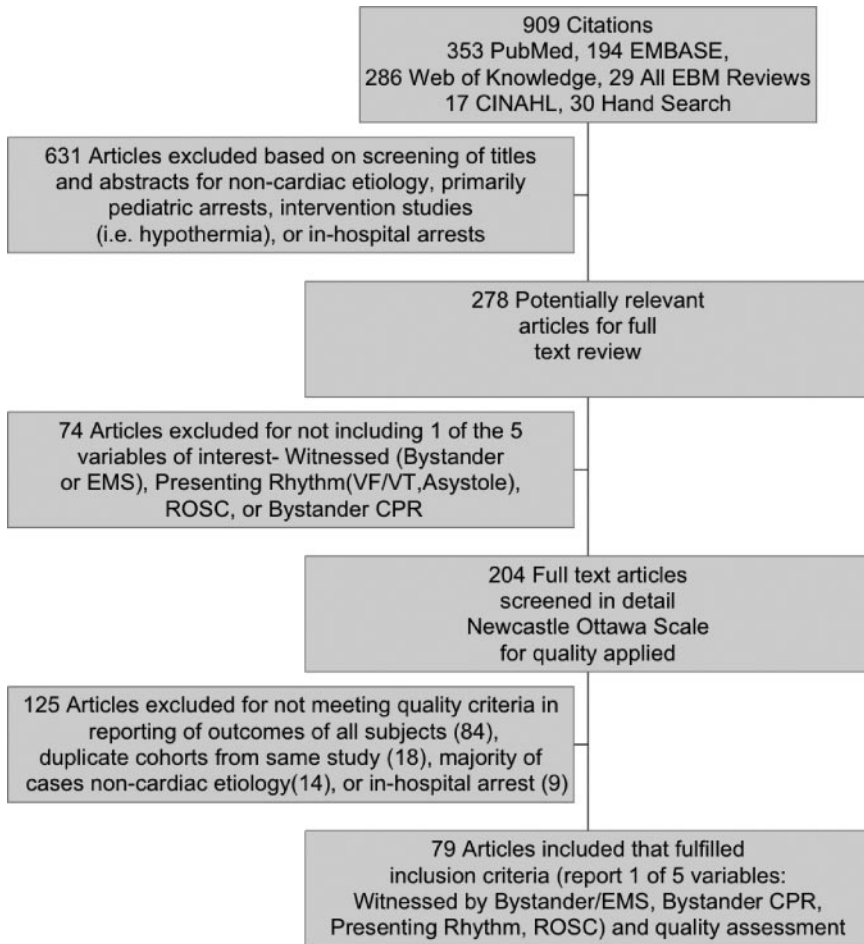


Figure 1. Flowchart of meta-analysis.

examined it as a predictor variable for survival to hospital discharge. Studies that used ROSC as an intermediate outcome were not included.

Data Synthesis and Analysis

The denominator for calculating rates of survival to hospital discharge in this meta-analysis was the number of adult patients with OHCA of presumed cardiac etiology for whom resuscitation was attempted in the prehospital setting. Crude (ie, unweighted) survival rates to hospital admission and to hospital discharge were calculated, as were pooled (ie, weighted) survival rates using the DerSimonian and Laird random-effects method.³² In addition, pooled odds ratios for survival to discharge were determined for each clinical criterion (eg, witnessed by bystander, witnessed by EMS, etc) using the random-effects model. Studies that were duplicates of the same patient cohort or involved only public-access defibrillation were not included. To evaluate heterogeneity, Cochran’s Q test and I², the degree of inconsistency among studies, were calculated. Begg’s test and a visual inspection of the funnel plot were conducted to evaluate publication bias. The number needed to treat was calculated for witnessed events and bystander CPR, based on pooled survival rates to hospital discharge. This represents the number of persons with OHCA in whom an intervention (eg, bystander CPR) would have to be used to save 1 life.

Meta-regression was used to explore the heterogeneity in odds ratios (dependent variable) across studies. A random-effects model was used with estimation of the between-study variance by the restricted maximum likelihood method. Independent variables considered for inclusion were type of EMS system, study design (retrospective versus prospective cohort), mean response interval, mean age, time of follow-up, inclusion of <20% pediatric patients, inclusion of any events of noncardiac etiology, dates of patient

inclusion, year of publication, physicians as part of the EMS out-of-hospital team, and baseline survival rates calculated as the survival rate of those OHCA patients without the variable of interest (eg, in the VF/VT meta-analysis, the survival rate for the patients in the sample who did not have a VF/VT arrest). Study location (international versus United States) was also evaluated, as many international EMS systems employ physicians in the prehospital setting and centralize operations.³³

Temporal trends in OHCA survival were anticipated because of emerging technologies^{7,34,35} and refinement of clinical guidelines.^{25,36,37} Therefore, a meta-regression was conducted by regressing time as the independent variable (ie, final year of patient enrollment in the study) on OHCA survival rates (dependent variable) with a random-effects model with adjustment for location (international versus United States), mean age of the patients, mean response time interval (minutes), and type of EMS service.

As a secondary analysis, the association between baseline survival and differences in survival rates were further evaluated. Weighted multivariate linear regression was performed using 2 outcomes: (1) survival difference between bystander witnessed and bystander unwitnessed events; and (2) survival difference between EMS witnessed and EMS unwitnessed events (n=25 studies). In addition, weighted linear regression was conducted using survival difference for patients in VF/VT versus asystole as the dependent variable (n=40 studies). Weights were generated using the DerSimonian and Laird random-effects model. If there were no survivors in a given study, the LaPlace estimate was used to calculate the weights.^{38,39}

All statistical tests were 2-sided, with α set at 0.05. STATA version 10.0 was used to conduct all analyses.

Table 1. Articles Included in the Meta-Analysis

Author	Year	Location	Meta-Analysis Variable Reported	Study Design	EMS System	Age Mean, y	Response Time Mean, min
Wilson	1984	Durham, NC	CPR, VF/VT, Asys	Prospective cohort	BLS	*	6.5
Smith	1985	Sacramento, CA	VF/VT, Asys	Retrospective cohort	BLS+ALS	*	*
Aprahamian	1986	Milwaukee, WI	CPR, VF/VT, Asys	Retrospective cohort	BLS+ALS	65	6
Bachman	1986	Arrowhead Cty, MN	CPR	Prospective cohort	BLS+BLS-D+ALS	65.2	6.5
Bonnin	1989	Oakland County, MI	ROSC	Retrospective cohort	BLS+ALS	71	4.7
Becker	1991	Chicago, IL	Wit Bys, Wit EMS	Prospective cohort	ALS	67	8
Brisson	1992	Canada	Wit Bys, Wit EMS, CPR	Prospective cohort	BLS+BLS-D	68.1	7.7
Bonnin	1993	Houston, TX	CPR, ROSC	Prospective cohort	BLS+ALS	64.7	10.1
Kellermann	1993	Memphis, TN	Wit Bys, VF/VT, CPR, ROSC	Retrospective cohort	BLS+ALS	64	3.4
Pepe	1993	Houston, TX	Wit Bys, Wit EMS, VF/VT, Asys	Prospective cohort	BLS+ALS	65	5
Richless	1993	Allegheny, PA	VF/VT	Retrospective cohort	BLS+ALS	67.3	7.2
Tresch	1993	Milwaukee, WI	VF/VT	Retrospective cohort	BLS+ALS	78.5	*
Van der Hoeven	1993	Leiden, Netherlands	CPR, VF/VT, Asys	Retrospective cohort	BLS+ALS	61.7	4.89
Kass	1994	York/Adams, PA	Wit Bys, Wit EMS, VF/VT, Asys	Retrospective cohort	BLS+ALS	*	*
Lombardi	1994	NYC, NY	Wit Bys, Wit EMS, CPR	Prospective cohort	BLS-D+ALS	70†	9.9
Schneider	1994	Mainz, Germany	VF/VT, Asys	Prospective cohort	BLS+ALS-P	63.2	5†
Crone	1995	Auckland, New Zealand	Wit EMS, CPR, VF/VT, Asys	Prospective cohort	ALS	65	7
Hodgetts	1995	Salford, Australia	ROSC	Retrospective cohort	BLS-D+ALS	63	8†
Rainer	1995	Glasgow/Edinburgh, Scotland	VF/VT, Asys	Prospective cohort	BLS-D+ALS+ALS-P	63.5	6.5†
Giraud	1996	France	Wit Bys, Wit EMS, VF/VT, Asys	Prospective cohort	BLS-D+ALS-P	20% <14	14†
Killien	1996	San Juan Islands, WA	VF/VT, Asys	Retrospective cohort	BLS+ALS	66	4.5
Kuisma	1996	Helsinki, Finland	Wit Bystander	Prospective cohort	BLS-D+ALS+ALS-P	*	7
Adams	1997	Scotland	Wit Bys, Wit EMS	Retrospective cohort	BLS-D	*	*
Fischer	1997	Bonn, Germany	Wit Bys, Wit EMS, VF/VT, Asys	Retrospective cohort	BLS+ALS-P	54% >65	5.5
Kuisma	1997	Helsinki, Finland	VF/VT, Asystole, CPR	Prospective cohort	BLS-D+ALS+ALS-P	56.7	8.4
Mitchell	1997	Edinburgh, Scotland	Wit EMS	Prospective cohort	BLS-D+ALS	67	7.7
Stapczynski	1997	Kentucky	VF/VT, CPR	Retrospective cohort	BLS-D	66	7.38
Valenzuela	1997	King County, WA	VF/VT	Retrospective cohort	BLS+ALS	64	5.1
Valenzuela	1997	Tucson, AZ	VF/VT	Retrospective cohort	BLS+ALS	66	9.5
De Vreede	1998	Maastricht, Netherlands	VF/VT, CPR	Prospective cohort	ALS	60.3	5.9
Joyce	1998	Salt lake City, UT	VF/VT, Asys	Retrospective cohort	BLS-D+ALS	66.9	4.4
Kette	1998	Fruilli, Italy	Wit Bys, Wit EMS	Prospective cohort	BLS+ALS+ALS-P	*	*
Lindholm	1998	Kansas City, MO	CPR, VF/VT, Asys, ROSC	Retrospective cohort	ALS	67	6.5
Tadel	1998	Slovenia	Wit Bys, Wit EMS, VF/VT, Asys	Retrospective cohort	BLS+ALS-P	*	10†
Waalewijn	1998	Amsterdam, Netherlands	Wit Bys, Wit EMS, CPR, VF/VT, Asys	Prospective cohort	ALS	64	10†
Absalom	1999	Norfolk, United Kingdom	Wit EMS, CPR, ROSC	Retrospective cohort	ALS	68	*
Bottinger	1999	Heidelberg, Germany	Wit Bys, Wit EMS, CPR, VF/VT, Asys	Prospective cohort	BLS+ALS+ALS-P	67	8

(Continued)

Table 1. Continued

Author	Year	Location	Meta-Analysis Variable Reported	Study Design	EMS System	Age Mean, y	Response Time Mean, min
Kuilman	1999	Rotterdam, Netherlands	VF/VT, Asys	Retrospective cohort	ALS-P	64.8	*
Lui	1999	Hong Kong	Wit Bys, Wit EMS, CPR, VF/VT, Asys	Retrospective cohort	BLS-D	68.7	6.42
Stiell	1999	Canada-OPALS 1	CPR, VF/VT, Asys	Prospective cohort	BLS-D	68	6.7
Sunde	1999	Oslo, Norway	Wit Bys, Wit EMS	Prospective cohort	ALS+ALS-P	69.5	7†
Swor	2000	Oakland County, MI	Wit EMS, VF/VT, CPR	Prospective cohort	BLS+ALS	66.5	6.1
Valenzuela	2000	casinos	VF/VT, Asys	Prospective cohort	D at public sites	64	9.8
Finn	2001	Perth, Australia	Wit Bys, Wit EMS	Prospective cohort	BLS-D+ALS	65.1	*
Groh	2001	Indiana	VF/VT, CPR	Prospective cohort	BLS-D+ALS	65.9	6.3
Jennings	2001	Victoria, Australia	VF/VT, Asys	Retrospective cohort	BLS+ALS	68.2	8
Rea	2001	Kings County, WA	CPR	Prospective cohort	BLS-D+ALS	68.7	5.2
Citerio	2002	Lombardia, Italy	VF/VT, Asys	Prospective cohort	BLS+ALS+ALS-P	70.1	8.5
Fan	2002	Hong Kong	VF/VT	Prospective cohort	BLS-D	73†	9†
Lim	2002	Singapore	VF/VT, Asys, ROSC	Retrospective cohort	BLS-D	65.1	11.9
Myerberg	2002	Miami, FL	Wit Bys, VF/VT	Prospective cohort	BLS-D+ALS	68.5	4.88
Smith	2002	Melbourne, Australia	Wit Bys, Wit EMS	Prospective cohort	BLS+BLS-D+ALS	*	8.75
Goto	2003	Akita, Japan	Wit Bys, Wit EMS, VF/VT, Asys	Prospective cohort	BLS-D	63.7	*
Grmec	2003	Slovenia	Wit Bys, VF/VT, Asys	Prospective cohort	BLS-D+ALS	63.9	10.6
Haukoos	2003	Los Angeles, CA	VF/VT, Asys	Retrospective cohort	BLS-D+ALS	70†	*
Nishiuchi	2003	Osaka, Japan	VF/VT	Prospective cohort	BLS-D	67.5	5.9
Ong	2003	Singapore	Wit Bys, Wit EMS, CPR	Prospective cohort	BLS-D	62.2	10.2
Horsted	2004	Copenhagen, Denmark	Wit Bys, Wit EMS, VF/VT, Asys	Prospective cohort	BLS-D+ALS-P	68	5
Rudner	2004	Katowice, Poland	Wit Bys, Wit EMS, CPR, VF/VT, Asys	Prospective cohort	BLS+ALS	63	7
Davies	2005	London, England	VF/VT, Asys	Prospective cohort	D at public sites	63.1	9.1
Handel	2005	Reading, OH	CPR, VF/VT, Asys, ROSC	Retrospective cohort	BLS+ALS	65.3	*
Hayashi	2005	Okayama, Japan	Wit Bys, Wit EMS, VF/VT, Asys	Prospective cohort	BLS-D	67.1	11
White	2005	Rochester, MN	Wit Bys, VF/VT	Prospective cohort	BLS-D+ALS	64.3	6.2
Drezner	2006	Multicenter	VF/VT	Retrospective cohort	D at public sites	21	*
Kellum	2006	Wisconsin	Wit Bys, VF/VT	Prospective cohort	BLS-D+ALS	*	6
Pleskot	2006	East Bohemia, Czech Republic	Wit Bys, CPR, VF/VT, Asys	Prospective cohort	BLS+ALS-P	67	7.4
Davis	2007	San Diego, CA	VF/VT, Asys, ROSC	Prospective cohort	BLS+ALS	66.3	7
Daya	2007	Resuscitation Outcomes Consortium	ROSC	Prospective cohort	BLS-D+ALS	*	*
Dunne	2007	Detroit, MI	Wit Bys, Wit EMS, VF/VT, Asys, ROSC	Retrospective cohort	ALS	63.3	8.36
Estner	2007	Dachau, Germany	Wit Bys, Wit EMS, CPR, VF/VT, Asys	Prospective cohort	BLS+ALS-P	63.9	7.74
Fairbanks	2007	Rochester, NY	Wit Bys, CPR, VF/VT, Asys	Retrospective cohort	BLS-D+ALS	67	5
Herlitz	2007	Sweden	Wit Bys, Wit EMS, VF/VT, CPR	Prospective cohort	BLS-D+ALS	67	6
Hostler	2007	Resuscitation Outcomes Consortium	Wit Bys, Wit EMS, CPR	Prospective cohort	BLS-D+ALS	*	*

(Continued)

Table 1. Continued

Author	Year	Location	Meta-Analysis Variable Reported	Study Design	EMS System	Age Mean, y	Response Time Mean, min
Iwami	2007	Osaka, Japan	Wit Bys	Prospective cohort	BLS+BLS-D	69.5	9.2
Jasinskis	2007	Lithuania	VF/VT, Asys	Prospective cohort	ALS-P	67	6
Ma	2007	Taipei, Taiwan	CPR, VF/VT, Asys	Prospective cohort	BLS-D+ALS	68.6	4†
Morrison	2007	Canada-OPALS 3	Wit Bys, Wit EMS, VF/VT, CPR	Prospective cohort	BLS-D+ALS	*	*
Vadeboncoeur	2007	Arizona	CPR	Prospective cohort	BLS+BLS-D+ALS	*	*
Fleischhackl	2008	Austria	VF/VT	Prospective cohort	D at public sites	62.5	*

BLS indicates basic life support; ALS, advanced life support; D, defibrillator capable; D at public sites, publicly available defibrillator studies; P, physicians onboard EMS; Wit Bys, witnessed by bystander; Wit EMS, witnessed by EMS; CPR, cardiopulmonary resuscitation; VF/VT, ventricular fibrillation/ventricular tachycardia; Asys, asystole; ROSC, return of spontaneous circulation.

*Not reported in study.

†Median value (age or response time).

Results

Search Results

There were 909 citations retrieved from the original search, 631 of which were excluded based on a priori exclusion criteria (Figure 1). Of the 278 articles chosen for full text review, 204 articles met inclusion criteria and were evaluated in detail. Studies were included if they had reported at least one of the five variables that are included in this meta-analysis.^{2,3,19,27–30,40–109} One article by Valenzuela et al⁶⁷ contrasted OHCA cases that occurred in Washington State from those that occurred in Arizona, so it was analyzed as 2 separate studies. One study did not specify the total number of survivors, so it was only included in the sensitivity analysis of bystander CPR.³⁰

Study Characteristics

Tables 1 and 2 display the study characteristics and variables used in the meta-analysis. All 79 articles were cohort studies. All documented the presence of at least 1 of the 5 variables in both survivors and nonsurvivors, with the primary outcome being survival to hospital discharge. The year of publication ranged from 1984 to 2008. Forty-six studies were conducted outside the United States. Twenty studies had less than 20% of their patients who were below the age of 18 years, whereas the remaining studies included adult patients only. Collectively, the 79 studies reported the outcomes of 142 740 patients.

The overall crude survival rate to hospital discharge in all the studies was 7.1% (10 017 survivors of 141 581 cases of OHCA). One study was not included because the total number of survivors was not reported.³⁰ The pooled rate of survival to hospital discharge in these studies was 7.6% (95% CI, 6.7 to 8.4). Of those studies that reported survival to hospital admission (n=49), the overall crude rate was 17.6%. The pooled survival to hospital admission rate was 23.4% (95% CI, 20.7 to 26.1).

Survival rates to hospital discharge, over 5-year time periods, are illustrated in Figure 2. There was no significant difference in survival rates over time ($P=0.152$) after adjustment for location (international versus United States), mean age of the patients, mean response interval, and type of EMS.

The results for each of the 5 clinical criteria are presented in the same manner (Figures 3 through 8). The studies were stratified into quintiles (tertiles for ROSC) based on the baseline survival rate. The vertical line marks the aggregate measure of the odds ratios across all studies.

Witnessed by Bystander

Thirty-six studies contained sufficient data to assess the association of an OHCA witnessed by a bystander (Figure 3). Collectively, these studies reported the outcomes of 95 539 cases. In these studies, the crude rate of survival to hospital discharge was 7.6% (7214 survivors). The pooled odds ratio for surviving to hospital discharge if a bystander witnessed the arrest (compared to unwitnessed events) ranged from 0.34 (95% CI, 0.07 to 1.66) among those with the highest baseline survival rates to 4.42 (95% CI, 1.81 to 10.80) in studies with the lowest baseline rates.

Witnessed by EMS

Thirty articles reported sufficient data to assess the association between OHCA being witnessed by EMS personnel and survival (Figure 4). In total, these studies reported on the outcomes of 83 229 cases, with a crude overall survival rate to hospital discharge rate of 6.1% (5056 survivors). The pooled odds ratio for survival among OHCA patients witnessed by EMS compared to all other arrests, ranged from 1.65 (95% CI, 0.63 to 4.34) in those with the highest baseline rates to 6.04 (95% CI, 4.12 to 8.85) in the studies with the lowest baseline rates of survival.

Bystander CPR

Odds ratios for the association between bystander CPR and survival are given in Figure 5 (n=32 studies). Collectively, these studies reported on the outcomes of 76 485 cases. In studies reporting overall rates of survival to hospital discharge, the crude rate was 6.7% (5094 survivors out of 75 388 patients). The pooled odds ratio for survival among patients receiving bystander CPR compared with those who did not ranged from 1.23 (95% CI, 0.71 to 2.11) in the studies with the highest baseline survival rates to 5.01 (95% CI, 2.57 to 9.78) in the studies with the lowest baseline rates. One study³⁰ was not included in the overall pooled odds ratio for by-

Table 2. Determination of Study Survival Rates

Author	Year	Total Adult Cardiac Arrests With Resuscitation Attempted	Resuscitation Not Attempted (Includes DNR, Obvious Death)	Survive to Admission	Survive to Discharge	Survival Rate to Hospital Discharge, %
Wilson	1984	126	0	28	11	8.7
Smith	1985	893	0	79	29	3.2
Aprahamian	1986	319	126	94	42	13.2
Bachman	1986	512	*	24	14	2.7
Bonnin	1989	232	7	56	22	9.5
Becker	1991	3221	*	241	55	1.7
Brisson	1992	1510	*	143	38	2.5
Bonnin	1993	1461	0	*	92	6.3†
Kellermann	1993	1068	0	267	85	8.0
Pepe	1993	2404	0	*	193	8.0
Richless	1993	96	0	14	3	3.1
Tresch	1993	196	0	37	10	5.1
Van der Hoeven	1993	257	0	39	6	2.3
Kass	1994	599	0	113	24	4.0§
Lombardi	1994	2329	*	*	52	2.2
Schneider	1994	211	125	50	19	9.0
Crone	1995	1069	0	240	135	12.6
Hodgetts	1995	100	82	*	2	2.0
Rainer	1995	455	0	105	52	11.4
Giraud	1996	113	146	22	8	7.1
Killien	1996	78	2	31	17	21.8
Kuisma	1996	255	68	98	44	17.3
Adams	1997	8651	*	*	612	7.1
Fischer	1997	464	82	185	74	15.9
Kuisma	1997	162	43	45	8	4.9
Mitchell	1997	275	*	*	27	9.8
Stapczynski	1997	311	0	46	19	6.1
Valenzuela	1997	7635	0	*	1086	14.2
Valenzuela	1997	665	0	*	46	6.9
De Vreede	1998	288	350	*	47	16.3
Joyce	1998	322	0	83	26	8.1
Kette	1998	344	*	60	23	6.7
Lindholm	1998	832	0	*	67	8.1
Tadel	1998	337	511	78	19	5.6
Waalwijk	1998	1046	400	165	134	12.8
Absalom	1999	260	0	59	26	10.0
Bottinger	1999	338	243	129	48	14.2
Kuilman	1999	898	0	441	276	30.7
Lui	1999	744	0	89	12	1.6
Stiell	1999	5335	0	366	197	3.7
Sunde	1999	326	573	96	30	9.2
Swor	2000	2608	108	538	189	7.2
Valenzuela	2000	148	0	71	56	37.8†
Finn	2001	1293	*	*	85	6.6‡
Groh	2001	388	0	61	21	5.4
Jennings	2001	115	96	22	6	5.2
Rea	2001	7265	*	*	1112	15.3

(Continued)

Table 2. Continued

Author	Year	Total Adult Cardiac Arrests With Resuscitation Attempted	Resuscitation Not Attempted (Includes DNR, Obvious Death)	Survive to Admission	Survive to Discharge	Survival Rate to Hospital Discharge, %
Citerio	2002	178	0	*	10	5.6‡
Fan	2002	320	82	*	4	1.3
Lim	2002	93	0	15	1	1.1
Myerberg	2002	738	0	*	51	6.9
Smith	2002	436	778	82	35	8.0
Goto	2003	203	227	*	20	9.9
Grmec	2003	216	*	128	44	20.4
Haukoos	2003	575	0	*	25	4.3
Nishiuchi	2003	974	176	236	50	5.1‡
Ong	2003	351	*	30	7	2.0
Horsted	2004	219	233	82	25	11.4
Rudner	2004	147	150	43	15	10.2
Davies	2005	172	4	*	39	22.7
Handel	2005	84	79	26	12	14.3‡
Hayashi	2005	179	0	*	2	1.1
White	2005	326	0	158	85	26.1
Drezner	2006	9	0	*	1	11.1†
Kellum	2006	358	169	*	39	10.9
Pleskot	2006	560	144	149	53	9.5
Davis	2007	1095	46	197	47	4.3
Daya	2007	7478	6052	*	568	7.6†
Dunne	2007	471	51	28	1	0.2‡
Estner	2007	412	277	180	47	11.4
Fairbanks	2007	539	277	*	27	5.0§
Herlitz	2007	38 413	*	*	2114	5.5‡
Hostler	2007	9886	*	*	727	7.4
Iwami	2007	12 437	*	*	433	3.5§
Jasinskas	2007	62	10	11	*	*
Ma	2007	1423	86	242	80	5.6
Morrison	2007	4673	40	671	239	5.1
Vadeboncoeur	2007	1097	*	*	*	*
Fleischhackl	2008	62	*	*	17	27†

Survival Rate to hospital admission and discharge is for all presenting rhythms.

*Not reported in study.

†Not included in overall survival rate.

‡Survival at 1-month reported.

§Survival at 1-year reported.

stander CPR because no information was provided on the community's baseline survival percentage.

The reporting of bystander CPR differed among studies. Because a patient who arrested in the presence of EMS personnel was never "eligible" to receive bystander CPR, we stratified studies by whether the arrest was witnessed by EMS. For the 19 studies that did not include EMS witnessed arrests in the total, the odds ratio for bystander CPR was 2.44 (95% CI, 1.69 to 3.19). This compared with an odds ratio of 1.69 (95% CI, 1.10 to 2.28) for studies in which all arrests, including EMS witnessed arrests, were included.

Ventricular Fibrillation/Ventricular Tachycardia

Fifty-eight studies contained sufficient data to assess the association between VF/VT as the presenting cardiac rhythm and OHCA survival (Figure 6). Outcomes were reported in 82 854 cases, with an overall crude survival rate to hospital discharge in these studies of 7.2% (5972 survivors). The pooled odds ratio for survival to hospital discharge among patients found in VF/VT compared to those found in all other rhythms ranged from 2.91 (95% CI, 1.10 to 7.66) in the studies with the highest baseline rates of survival to 20.62 (95% CI, 12.61 to 33.72) in the studies with the lowest baseline survival.

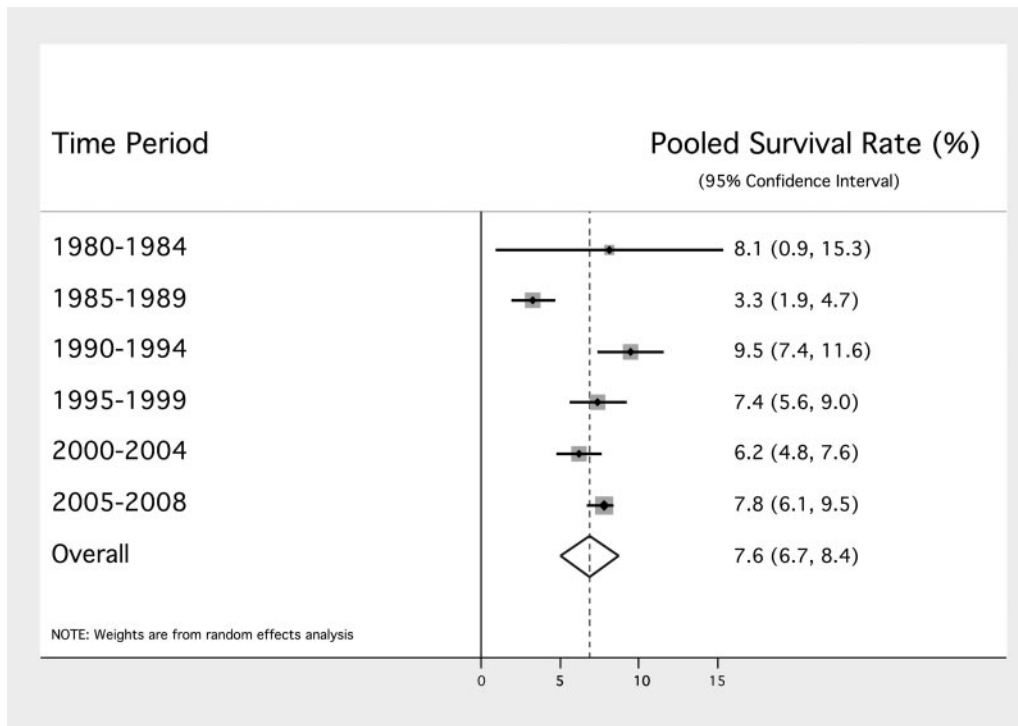


Figure 2. OHCA survival to hospital discharge by 5-year time periods (based upon final year of patient enrollment into study).

Asystole

Odds ratios for the relationship between asystole as the presenting cardiac rhythm and OHCA survival are shown in Figure 7 (n=40 studies). In total, outcomes were reported on 23 202 cases, with an overall crude survival rate in these studies of 8.1% (1870 survivors). The pooled odds ratio for survival to hospital discharge among those patients found in asystole compared with those patients found in all other cardiac rhythms ranged from 0.10 (95% CI, 0.03 to 0.31) in the studies with the lowest baseline rates of survival to 0.15 (95% CI, 0.09 to 0.25) in studies with the highest baseline rates.

Return of Spontaneous Circulation

Twelve studies reported data on the relationship between achieving prehospital ROSC and survival to hospital discharge (Figure 8). These studies reported the outcomes of 17 697 patients. Overall, the crude rate of survival to hospital discharge in these studies was 6.6% (1,162 survivors). The pooled odds ratio for survival to hospital discharge among patients who achieved ROSC in the field (compared to those who did not) ranged from 20.96 (95% CI, 7.43 to 59.13) in those with the highest baseline survival rates to 99.84 (95% CI, 14.30 to 696.89) in the studies with the lowest baseline rates of survival.

Study-specific odds ratios for ROSC were considerably elevated above the null in all strata; no point estimate was less than 8.49. Three of the 12 studies required ROSC to be “sustained” (patient had a pulse on leaving the scene of the OHCA). The other 9 considered any restoration of a palpable pulse, no matter how transient, to represent ROSC. One study did not document whether ROSC occurred in the prehospital

setting versus in the emergency department.²⁰ The others defined ROSC as occurring before transport from the scene.

Excluding the one study²⁰ that did not limit ROSC to the prehospital setting reduced the subgroup OR (lowest baseline survival) from 99.84 (95% CI 14.30 to 696.89) to 35.29 (95% CI, 5.54 to 224.94). The overall pooled survival rate (absolute risk) of all subjects included in this analysis decreased from 15.5% (95% CI 0.0 to 33.3) to 5.1% (95% CI, 0.0 to 12.9) following exclusion of this study.

Number Needed to Treat to Save One Life

Survival rates to hospital discharge are listed by each of the 5 main clinical criteria in Table 3. The results indicate that 53% of all OHCA cases were witnessed by a bystander, 10% were witnessed by EMS, and 36% were unwitnessed. In addition, 32% of patients received bystander CPR, 40% were found in VF/VT arrest, 42% were found in asystole, and 22% achieved ROSC in the prehospital setting. Reported rates of survival to hospital discharge ranged from 0.1% to 33.6% across these groups, depending on the baseline survival rate (Table 3). The strongest predictor of survival to hospital discharge was ROSC in the field. In this group as many as 1 in 3 survived.

The number needed to treat (NNT) to save one life is also shown in Table 3. The data indicate that 17 persons experiencing OHCA would need to be witnessed by a bystander to save the life of one person in those areas where baseline survival rates were low. The corresponding NNT for areas with high baseline survival was 71. For regions in which baseline survival rates were high, 16 persons with OHCA would need to be witnessed by EMS to save the life of one person and in locations where baseline survival rates are low,

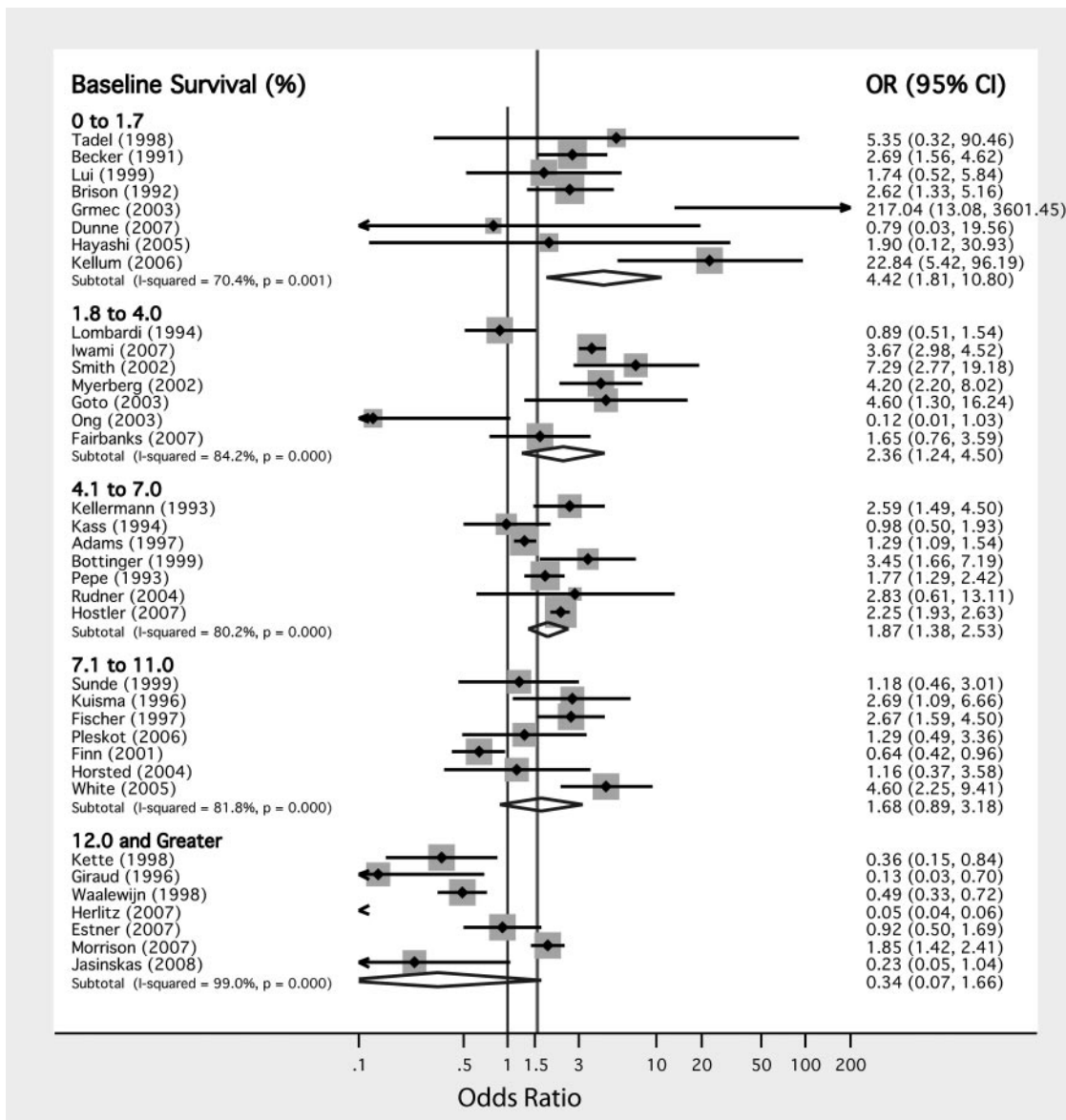


Figure 3. Forest plot of studies reporting witnessed by bystander stratified by baseline survival.

23 persons with OHCA would require an EMS witnessed event to save the life of one person. For bystander CPR, the NNT was 24 in areas with high baseline survival rates and 36 in areas with low rates.

Regression Analyses

Meta-regression analyses were conducted to assess predictors of heterogeneity among odds ratios. The only factor that significantly explained the heterogeneity in odds ratios for all 5 clinical criteria was baseline survival rate and therefore, analyses were stratified by this variable. In addition, the results of the weighted multivariate linear regression indicated that baseline survival significantly explained differences in survival rates. For example, as the baseline survival rate increased, the difference in survival between bystander-witnessed and unwitnessed arrests decreased (β coefficient = -0.7617 ; $P=0.023$).

The type of EMS system significantly explained heterogeneity in the odds ratio for VF/VT ($P<0.05$); the largest

pooled OR was evident at those locations in which a defibrillator was available at public sites (OR=12.5) and the smallest pooled OR was at sites in which both basic and advanced life support were available (OR=5.1). The type of EMS system also significantly explained the heterogeneity in odds ratio for asystole; locations with basic life support only and locations with public access defibrillation yielded the greatest reduction in the odds ratios ($P<0.05$). Variation in the odds ratios could also be significantly explained by differences in case mix (ie, some studies included arrests of all etiologies) and length of follow-up (ie, some studies reported survival 1 month postevent). Mean response interval was a significant predictor of heterogeneity for arrests that were witnessed by EMS ($P<0.05$); for those locations in which the mean response time interval was less than 8 minutes, the pooled OR was 5.9, it was 2.4 in locations with a mean response time interval of 8 minutes or longer.

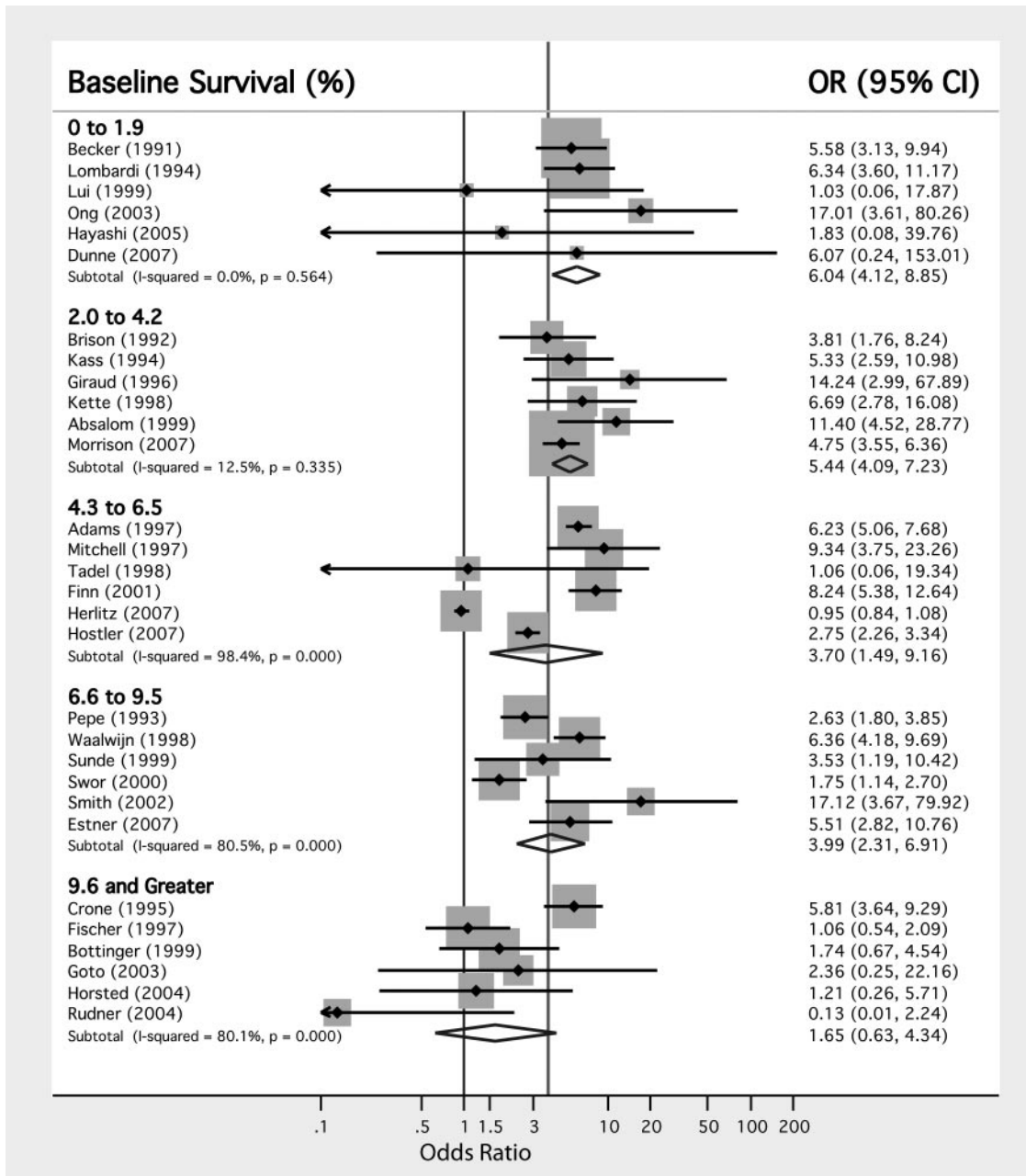


Figure 4. Forest plot of studies reporting witnessed by EMS stratified by baseline survival.

Sensitivity Analyses

We limited our analyses to adult cardiac arrest patients for whom resuscitation was attempted in the prehospital setting. Because having a consistent denominator (ie, total number of resuscitations attempted in the prehospital setting) was important, we conducted a sensitivity analysis that excluded four studies that described patients who sustained OHCA but failed to include information on patients who were treated but not transported to the emergency department.^{29,51,57,86} Excluding these articles did not appreciably change our results. For example, the pooled odds ratio for VF/VT changed from 20.62 (95% CI, 12.61 to 33.72) to 22.69 (95% CI, 13.54 to 38.87) in the lowest baseline survival group, and from 2.91 (95% CI, 1.10 to 7.66) to 2.91 (95% CI, 1.10 to 7.67) in the highest baseline survival group.

In further sensitivity analyses, studies that contained elements which deviated from other studies were excluded. Four studies limited their analysis to OHCA cases that were not witnessed by EMS providers^{78,97,99,103}; 6 studies reported survival at 1 month rather than at hospital discharge^{2,81,85,90,95,108}; 3 studies reported survival 1 year post OHCA^{52,103,105}; and 2 studies grouped pulseless electric activity and asystole together.^{55,95} Excluding these studies did not appreciably alter our final pooled results.

Publication Bias

The Begg’s test for publication bias was conducted. For all 5 criteria of interest, the Begg test was not significant ($P>0.05$). Visual inspection of funnel plots did not suggest publication bias.

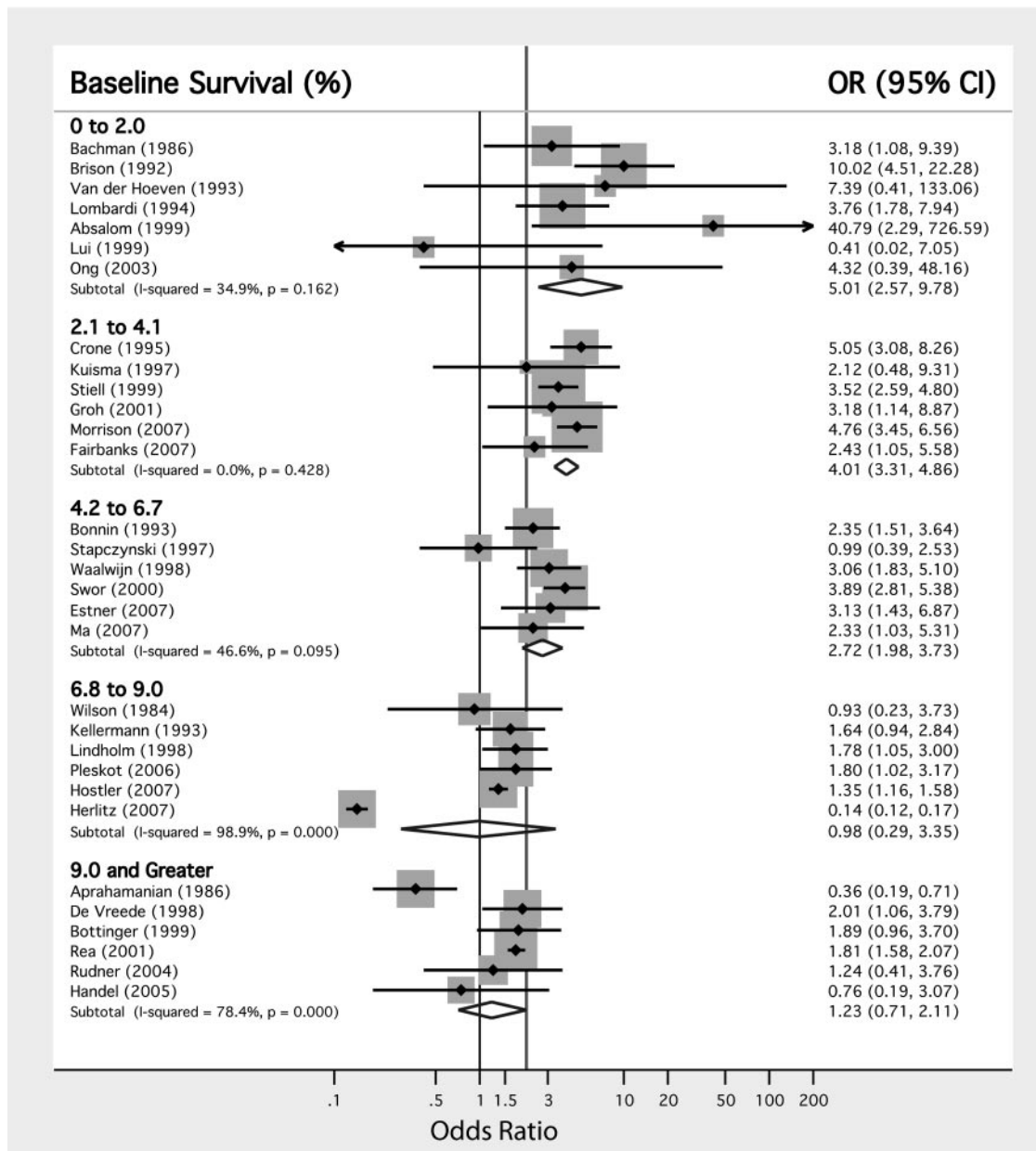


Figure 5. Forest plot of studies reporting bystander CPR stratified by baseline survival.

Discussion

Survival from OHCA has not significantly improved in almost 30 years. The aggregate survival rate, recorded across various populations, is between 6.7% and 8.4%. This lack of progress, despite enormous efforts in research spending, the introduction of novel drugs and devices, and periodic evidence-based revisions to clinical guidelines may be attributable, in part, to the offsetting influence of declining incidence of ventricular fibrillation arrests,¹¹⁰⁻¹¹² increasing age of the population,¹¹³ and longer EMS response time intervals attributable to urbanization and population growth.¹¹⁴ Breaking this barrier to achieve decisive improvements in OHCA survival represents a challenging and worthwhile goal for emergency cardiac care.

Recognizing the importance of several clinical predictors of OHCA survival may help communities and research

scientists focus their efforts to achieve this goal. We found that OHCA victims who receive CPR from a bystander or an EMS provider, and those who are found in VF or VT, are much more likely to survive than those who do not. Moreover, we found that the strength of association between VF/VT and survival was greatest in locations in which a defibrillator is available at public sites. To put these observations in context, approximately 1 of every 4 to 7 patients with a presenting rhythm of VF/VT survive to hospital discharge, compared to only 1 of every 21 to 500 patients found in asystole. Because prompt provision of CPR delays the degradation of tachyarrhythmias to asystole, this may explain why bystander CPR and prehospital defibrillation have such a positive impact on survival.¹¹⁵

By far the most powerful criterion associated with survival from OHCA is ROSC in the field. The odds of sur-

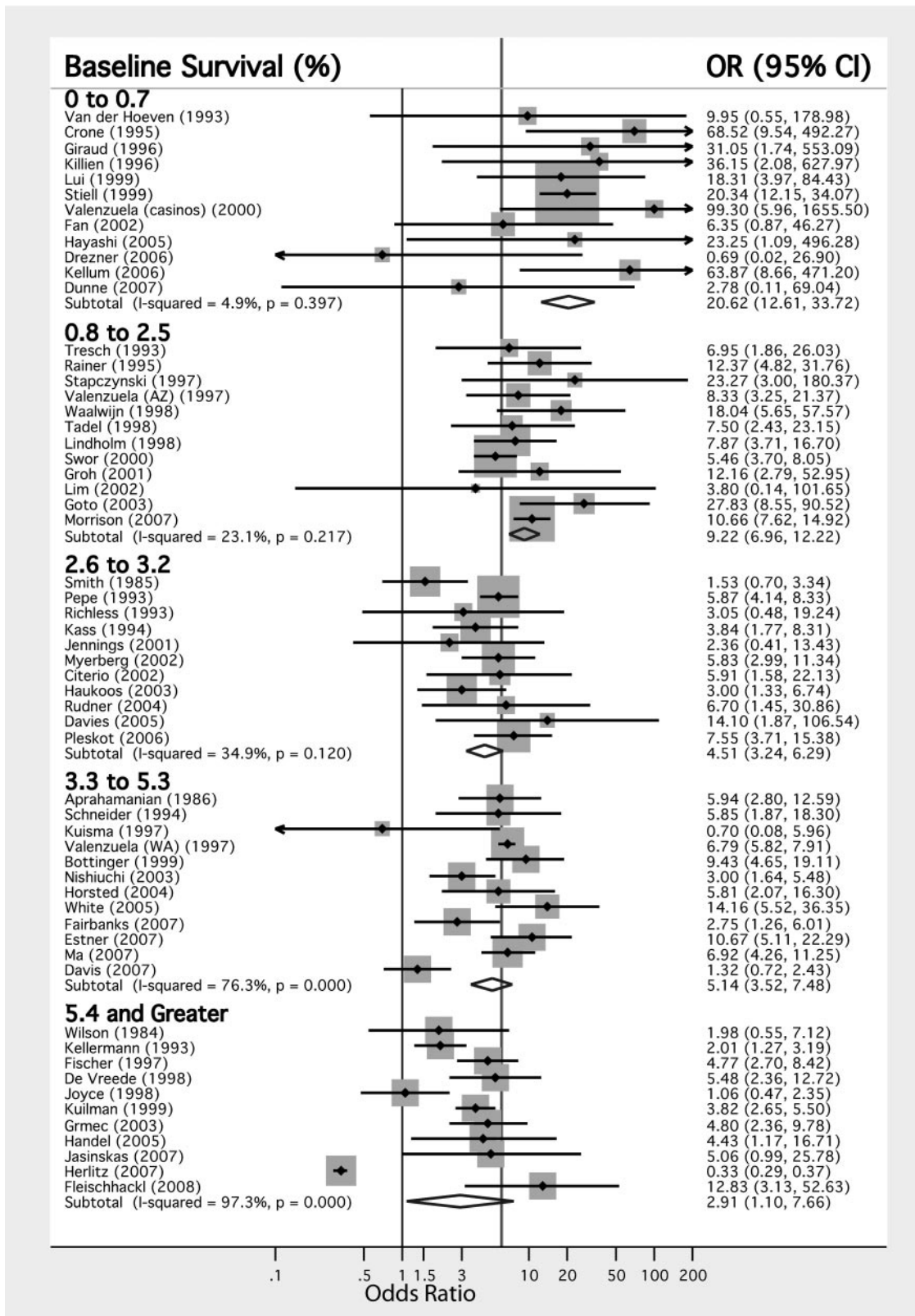


Figure 6. Forest plot of studies reporting ventricular fibrillation/tachycardia stratified by baseline survival.

vival ranged from 50% in communities where baseline survival rates are high to 20% (1 in 5) in areas where baseline survival is low. Failure to restore a pulse on scene indicates that the patient will not likely survive to hospital discharge,

irrespective of the subsequent sophistication of in-hospital care. This finding strongly suggests that future efforts to boost OHCA survival should focus on optimizing provision of prehospital emergency cardiac care.^{116,117} It is noteworthy

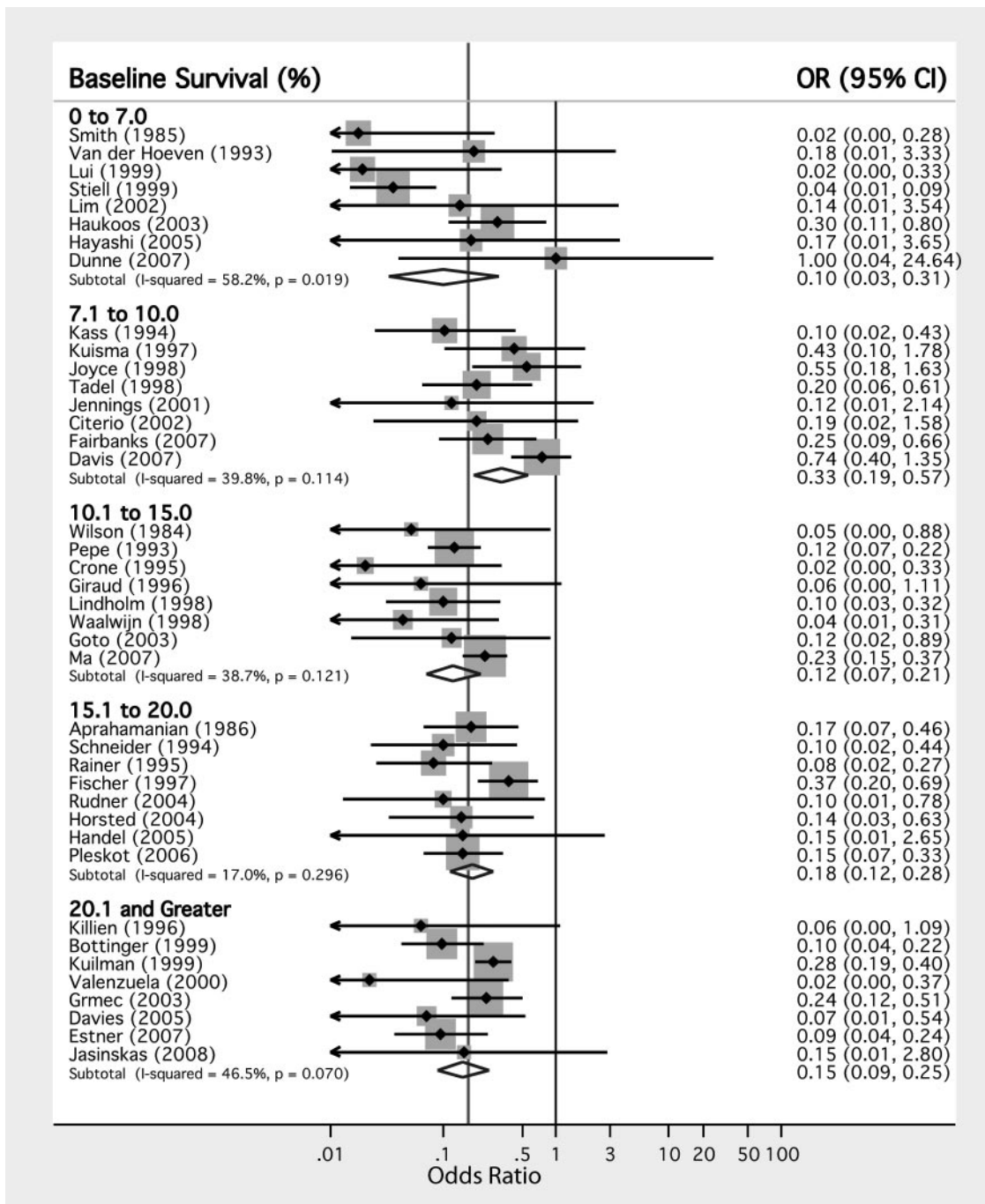


Figure 7. Forest plot of studies reporting asystole stratified by baseline survival.

that 40% of patients with OHCA were found with VF/VT, yet only 22% achieved ROSC. This group may be a priority population for future efforts to improve ROSC and survival to hospital discharge.

Although our analysis focused on 5 key variables, we examined several potentially confounding factors (eg, type of EMS system, United States versus international study, mean response time interval) to determine whether they introduced an unacceptable degree of heterogeneity to the main estimates of effect. The only external factor that was consistently significant across the 5 clinical factors was the baseline performance of the community's EMS system. In

systems with lower baseline survival rates, the magnitude of effect sizes for the 5 clinical factors such as provision of bystander CPR and an initial rhythm of VF/VT, were higher than in communities that had high baseline survival rates. This suggests that efforts such as targeted CPR training to increase bystander CPR rates will have their greatest effect in communities with low baseline rates of survival. A corollary hypothesis is that the return on investment for focusing on these characteristics may diminish as the overall performance of a community's EMS system improves. It is important to note, however, that certain factors, most notably VF/VT arrest and ROSC,

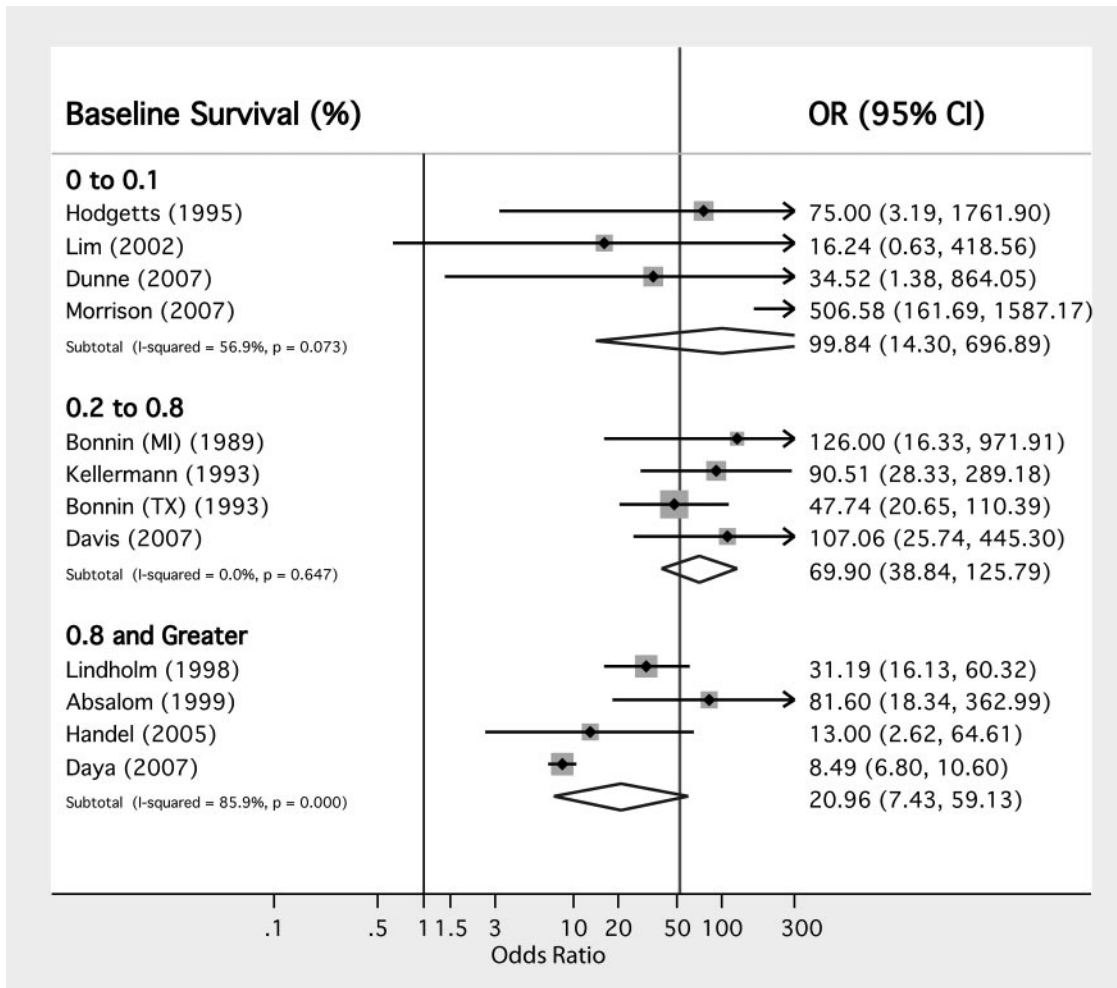


Figure 8. Forest plot of studies reporting return of spontaneous circulation stratified by baseline survival.

were significantly associated with OHCA survival in even the highest-performing EMS systems.

Some of the remaining heterogeneity between studies may be attributable to the highly variable nature of EMS systems in the United States and worldwide.¹¹⁸ For example, many

EMS agencies use locally-created protocols to determine whether and when to cease efforts if an OHCA patient does not respond to prehospital advanced cardiac life support.¹¹⁹ Some communities provide their first responders with Basic Life Support training and an automated external defibrillator,

Table 3. Survival Rates and Number Needed to Treat by Clinical Criteria

Variable	Pooled Percentage of Cardiac Arrests With Attribute	Low Baseline Survival		High Baseline Survival	
		Pooled Survival Rate, %	NNT	Pooled Survival Rate, %	NNT
Witnessed by bystander	53% (45.0–59.9)	6.4 (3.5–9.3)	17	13.5 (5.6–21.5)	71
Witnessed by EMS	10% (8.0–11.3)	4.9 (1.3–8.4)	23	18.2 (3.7–32.8)	16
Not witnessed	36% (30.4–40.8)	0.5 (0.2–0.9)		12.1 (7.5–16.7)	
Bystander CPR	32% (26.7–37.8)	3.9 (1.8–6.0)	36	16.1 (11.5–20.7)	24
No bystander CPR	68% (62.6–74.8)	1.1 (0.5–1.8)		12.0 (10.0–14.0)	
Ventricular fibrillation/tachycardia	40% (36.6–43.3)	14.8 (9.4–20.2)		23.0 (13.8–32.2)	
No ventricular fibrillation/tachycardia	60% (56.2–62.9)	0.4 (0.2–0.6)		7.4 (6.1–8.7)	
Asystole	42% (36.0–46.8)	0.2 (0–0.3)		4.7 (1.0–8.4)	
No asystole	58% (52.9–63.8)	4.4 (2.1–6.6)		30.1 (23.8–36.4)	
Return of spontaneous circulation	22% (17.7–25.5)	15.5 (0.0–33.3)		33.6 (24.9–42.2)	
No return of spontaneous circulation	78% (74.5–82.3)	0.1 (0.0–0.2)		1.8 (1.5–2.1)	

NNT indicates number needed to treat to save 1 life.

whereas others rely on paramedics trained to provide Advanced Life Support. A few U.S. systems and many foreign countries routinely employ nurses or physicians in prehospital settings.¹²⁰ It is not clear whether different approaches to provider training affect survival rates from OHCA.^{4,121}

Our study is limited in certain respects. Because individual-level patient data were not reported for each study, we could not adequately assess all patient characteristics and potential confounding factors which may influence survival. The studies in our meta-analysis did not contain enough data to simultaneously evaluate the effect of all 5 key criterion, so combined effects could not be assessed.

Despite our effort to apply quality criteria, it is possible that the reporting of predictor and outcome variables was inconsistent in some studies. The Utstein guidelines, designed by EMS leaders in 1991 and subsequently revised in 1996 and 2002, created a standardized approach to data collection.^{120,122,123} Research has shown that even in the era of Utstein-guided reporting of OHCA care and outcomes, marked variations in survival from one community to the next persist.¹²⁴ This variability probably reflects persistent differences in approach. For example, although 57 of the 79 studies included in our meta-analysis were published after 1996, some articles did not consistently report the length of prehospital resuscitation intervals (ie, call to ambulance response time and first defibrillation), the range of pharmaceutical interventions, the training level of EMS providers, the duration of resuscitation efforts, or policies permitting termination of unsuccessful resuscitations in the field. We chose not to report our findings using the Utstein definition of survival (witnessed VF arrest surviving to hospital discharge), as this has been summarized in previous studies.^{72,124,125}

We did not include studies that assessed investigational devices or emerging therapies that were outside the standard of care at the time these studies were conducted. Pulseless electric activity (or idioventricular rhythm) was not included in the meta-analysis, because the definitions applied to this type of rhythm were highly nonuniform across studies. And, although the articles included in our meta-analysis were limited to English publications, the information was gathered from 26 countries and represents a variety of populations and EMS systems. Finally, our analysis was restricted to studies with primarily adult patients. Cardiac arrest in pediatric populations differs in fundamental ways from OHCA in adults.

Although the overall rate of OHCA survival has not improved, the field of cardiac and cerebral resuscitation is rapidly evolving. Most of the studies incorporated in our meta-analysis were conducted before the advent of therapeutic hypothermia. This treatment has been shown to benefit resuscitated patients.^{7,34,35} Patients treated under the recently revised AHA guidelines for CPR, which emphasize rapid compressions and deemphasize ventilation, could not be distinguished from earlier studies included in the meta-analysis.³⁶ However, there is hope that these recent changes in technique and emphasis will improve outcomes.^{126–129} Future studies will need to take such changes into account to assess their impact on survival.

This meta-analysis brings together almost 30 years of research, involving more than 142 000 patients. Our findings conclusively affirm the value of bystander CPR, the critical importance of “shockable” rhythms, and the predictive value of ROSC in the field. Focused strategies designed to boost rates of bystander CPR, deliver earlier defibrillation, and achieve ROSC before transport are likely to do more to improve aggregate rates of OHCA survival than interventions applied later in a patient’s treatment. Currently, 92% of individuals who experience OHCA each year do not survive to hospital discharge. This dismal statistic can be improved.

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Disclosures

None.

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