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Review

Incidence and outcomes of out-of-hospital cardiac arrest from initial asystole: a systematic review and meta-analysis

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Abstract

Aim: To examine global variation in the incidence and outcomes of Emergency Medical Services (EMS) attended and treated out-of-hospital cardiac arrest (OHCA) from initial asystole.

Data sources: We systematically reviewed electronic databases for studies between 1990 and August 2024 reporting EMS-attended or treated asystolic OHCA populations. The primary outcome was survival to hospital discharge or 30-days. Random-effects models were used to pool primary and secondary outcomes and meta-regression was used to examine sources of heterogeneity. Study quality was assessed using the Joanna Briggs Institute critical appraisal tool for prevalence studies.

Results: The search returned 4464 articles, of which 82 studies were eligible for inclusion encompassing 540,054 EMS-treated patients across 35 countries. Five studies reported on EMS attended populations (n = 35,561). The studies included in the review had high clinical and statistical heterogeneity. The pooled proportion of EMS-treated initial asystolic OHCA was 53.0% (95% CI: 49.0%, 58.0%; I^2 = 100%). The overall pooled proportion of survivors to hospital discharge or 30-days was 1.5% (95% CI: 1.2%, 1.8%, I^2 = 97%). The pooled proportion of event survivors was 11.6% (95% CI 6.5%, 17.8%, I^2 = 99%), the pooled proportion of prehospital ROSC was 16.0% (95% CI 14.0%, 17.0%, I^2 = 100%) and the pooled proportion of neurologically favourable survival at longest follow-up was 0.6% (95% CI 0.5%, 0.8%, I^2 = 100%). The overall pooled incidence of EMS-treated asystolic OHCA was 11.0 cases per 100,000 person-years (95% CI: 10.5, 11.5, I^2 = 100%). In stratified analysis of survival to hospital discharge or 30-days, population type, study duration, study design and aetiology were the only variables that were significantly associated with survival to hospital discharge or 30-days. In adjusted analysis, population type, study duration, highest EMS skill level and region were significantly associated with the primary outcome. In the multivariable analysis of incidence, study region, arrest aetiology, sample size, year of publication, study population, study duration and study quality significantly explained variation in incidence across studies.

Conclusion: Initial asystolic OHCA made up 53% of all EMS-treated patients and pooled survival rates were extremely poor. Research efforts in this population should focus on developing prevention strategies as well as adherence to termination or withholding of resuscitation guidelines for asystolic OHCA.

Keywords: Cardiac arrest, Asystole, Cardiopulmonary resuscitation, Emergency medical services, Outcomes, Systematic review

Introduction

Out-of-hospital cardiac arrest (OHCA) is a leading cause of global mortality,[1] claiming millions of lives worldwide each year.[2] Overall survival remains low after OHCA, with previous systematic reviews indicating a pooled survival rate of 7.6% to 8.8%.[3–6] OHCA can present with shockable, Ventricular Tachycardia (VT) or Ventricular Fibrillation (VF) as well as non-shockable rhythms, pulseless electrical activity (PEA) or asystole, and survival rates vary significantly across these rhythms.[4,6]

Historically, efforts to increase survival from OHCA have focussed primarily on patients presenting in shockable rhythms.[7,8] However, the reported incidence of shockable OHCA has declined in recent years, and an increasing proportion of treated OHCA patients are presenting in asystole.[2] In fact, initial asystolic OHCA

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makes up between 38.9% and 59.6% of all OHCA cases across developed countries.[9–11] Importantly, survival outcomes for asystolic OHCA patients do not appear to have changed significantly over time, and existing evidence suggests that long-term favourable neurological recovery is also considerably poorer for patients who present in asystole.[12,13]

To date, there has been a lack of synthesised data on the short-term and long-term survival and neurological outcomes of initial asystolic OHCA, and factors associated with survival. Although current guidelines recommend attempting resuscitation for asystolic OHCA, some studies have suggested the practice may be futile and costly,[14] or associated with poorer long-term neurological outcomes and life expectancy.[2,15,16] Hence, there is a need to examine global variation in survival and incidence, long-term neurological outcomes and factors associated with survival in asystolic OHCA.[15] The findings may help guide recommendations for current resuscitation guidelines.[17]

In this study, we systematically reviewed the literature on patients with asystolic OHCA to determine global pooled outcomes, incidence rates and factors associated with survival.

Methodology

This systematic review follows the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) reporting guideline.[18] Prior to its commencement, review methodology was registered in the International Prospective Register of Systematic Reviews (PROSPERO no. CRD42021265916). A preliminary literature search conducted through the Cochrane and Joanna Briggs Institute (JBI) databases of systematic reviews and PROSPERO did not identify any other completed or ongoing systematic review on this topic.

Data sources and search strategy

A systematic literature search was conducted using major electronic databases: Ovid MEDLINE, EMBASE, EMCARE, CINAHL, EBM and Cochrane reviews. The search was carried out on studies published between 1st January 1990 to 2nd August 2024. We chose 1990 as the start of our inclusion period as it aligned to the publication of the original Utstein template which sought to reduce variability in the reporting of OHCA.[19]

A health information specialist was consulted to construct and execute the search strategy, which incorporated subject headings and keywords. The initial search strategy was executed in Ovid MEDLINE before replication in the additional databases. The final optimised search strategies for Medline and Embase are presented in Tables S1 and S2 in the supplementary appendix.

Study selection and eligibility

Shortlisted studies from all electronic databases were imported into the Covidence online systematic review management tool and duplicates were removed. Two reviewers (DD and ZN) independently screened titles and abstracts for relevant eligibility criteria. Any discrepancies between the two reviewers were resolved through discussion.

Interventional and observational studies were eligible for inclusion if they reported an EMS attended or treated OHCA population, had a documented initial cardiac rhythm of asystole, and provided sufficient data to calculate the primary outcome of survival to hospital discharge or 30-days. We excluded articles if they were reviews, news, case reports, letters, opinions, conference abstracts or animal studies. We also excluded studies if they excluded patients who died on scene, such as those investigating admitted patients or patients with return of spontaneous circulation (ROSC) only. Where multiple studies presented significantly overlapping populations, we retained the study with the most representative sample for that region and timeframe. When reviewing articles, we adopted standard definitions as recommended in the Utstein guidelines.[20,21] An EMS treated OHCA case was defined as a patient with absent signs of circulation who received any attempt at cardiopulmonary resuscitation (CPR) or defibrillation by a member of an organised EMS agency.

Outcomes

The primary outcome was the pooled rate of survival to hospital discharge or 30-days. Secondary outcomes included the pooled proportion of event survivors, the pooled proportion of patients achieving ROSC, the pooled proportion of survivors with good neurological outcome at longest-follow-up, and pooled incidence of EMS-attended or EMS-treated cases per 100,000 person-years.

Data extraction and quality assessment

A minimum of two reviewers (DD with ZN/JB) reviewed the full text of eligible studies, extracted study data and performed quality assessments. A standardised data extraction form was developed, tested and refined comprising the following study variables: lead author, study setting, country, region, study design (e.g. observational, experimental), registry-based data collection, inclusion criteria, exclusion criteria, age definition, EMS personnel type, publication year, study duration, number of patients (EMS-attended and EMS-treated), serviceable population, arrest characteristics (age, proportion of male sex, proportion of asystole, presumed cardiac aetiology, witnessed by EMS or bystander, location of the arrest, bystander CPR, endotracheal intubation, intravenous/intraosseous (IV/IO) epinephrine administration, EMS response time and EMS transport time to hospital and study outcomes.

The JBI critical appraisal tool for studies reporting prevalence data was used to assess the quality of the included studies across nine domains[22] including: sample frame, recruitment of study participants, sample size, study subjects and setting, coverage of the identified sample, validity of the methods used in the assessment of the condition, standardised and reliable measuring of the condition, appropriateness of statistical analysis and the adequacy of response rate. Reviewers answered yes or no/unclear to each of the nine domains, and the total sum of yes responses was used to define study quality (0–3 points = high risk of bias, 4–6 points = moderate risk of bias, or 7–9 points = low risk of bias). Any disagreements were resolved through discussion.

Data synthesis

All data were analysed using Stata statistical software version 18 (Statacorp, College Station, Texas, USA). All statistical tests used a two-sided p-value < 0.05. The primary outcome of survival to hospital discharge or 30-days was calculated by dividing the total number of survivors over the total number of EMS-treated cases with known outcome. A similar approach was used for the remaining patient outcomes such as event survival, prehospital return of spontaneous circulation (ROSC), and neurologically favourable survival. To calculate the incidence rate, we used the number of EMS attended or treated cases divided by population and study time in years, where population refers to the study's serviceable population.

If the serviceable population was not reported, we used national online sources to estimate the resident population for that region and time. The 95% confidence intervals for the incidence rate were then estimated assuming a Poisson distribution. The measurement of neurological outcome was based on the tool used by individual studies.

As significant heterogeneity was expected when pooling the incidence and outcomes of initial asystolic OHCA populations, we used DerSimonian & Laird random-effects models to calculate the pooled primary and secondary outcomes. For patient outcomes, we pooled proportions using a Freeman-Tukey double arcsine transformation procedure to allow for the inclusion of studies whose survival proportions are clustered or close to zero.[23] Heterogeneity for all meta-analyses were assessed using the I^2 statistic. The I^2 values of 25%, 50% and 75% indicate low, moderate and high heterogeneity, respectively. Publication bias was assessed by visually inspecting a funnel plot of the log odds of the proportion of survivors to hospital discharge or 30 days against the inverse standard error. For studies with zero events, where the log odds and its standard error were undefined, we added 0.5 to the number of survivors and 1 to the study size to enable inclusion in the funnel plot.[24]

To identify potential sources of heterogeneity in the primary outcome, we performed stratified analyses and unadjusted and adjusted meta-regression, examining for interactions between survival and the following variables: year of publication, sample size, study duration, study design, registry-based data collection, highest EMS skill level, region, aetiology, and study quality. In the subgroup of studies with sufficient data, we also examined the impact of baseline characteristics such as the mean/median age, the proportion of male sex, presumed cardiac aetiology, any witness, EMS-witness, bystander witness, bystander CPR, public location, endotracheal intubation, IV/IO epinephrine administration, EMS response and EMS transport time to hospital. These characteristics were categorised into approximately equal tertiles for analysis.

We also explored variation in event survival and the incidence of EMS-treated OHCA per 100,000 person-years using the same approach.

Results

Study selection

The study selection flow chart is shown in Fig. 1. The search strategy returned 4464 titles, of which 2162 were duplicates, leaving 2302 studies for title and abstract screening. A total of 456 potentially relevant articles underwent full-text review, which resulted in 82 studies being included in the quantitative synthesis.

Study characteristics

The characteristics of the 82 included studies are presented in Table 1. A total of 540,054 EMS-treated patients across 35 countries from all continents except Africa and Antarctica were included. The pooled rate of initial asystole in the included populations was 53.0% (95% CI: 49.0%, 58.0%; I^2 = 100%). Only 5 of these studies reported on EMS-attended populations (i.e. populations with both treated and untreated patients), totalling 35,561 patients across 3 countries. Thirty-six studies examined both paediatric and adult populations, while 39 studies examined adult populations only. The remaining 7 studies examined paediatric populations. Publication dates for all studies ranged between 1990 and 2024 and the length of studies ranged from 2 months to 27 years. The majority of studies were retrospective cohort studies (75.6%). Registry-based methods of data collection were reported in thirty (36.5%) studies. Patients with all OHCA aetiologies were included in 38 (46.3%) studies, while the others involved either presumed cardiac (*n* = 29), non-traumatic (*n* = 5) or traumatic (*n* = 6) aetiologies only. Among the five studies where both EMS-attended and EMS-treated data were available, two each were from Australia and Europe, and one from Korea. Specifically, the EMS attempted resuscitation rate in these studies ranged between 30% and 53%, with the highest rate observed in the Korean study.

The baseline characteristics of the included populations were infrequently reported. The mean/median age was reported in 21.9% studies and ranged between 1 and 79 years. Among the adult-only cohorts, different age thresholds were reported with the median or mean age ranging between 58 years and 79 years. The proportion of males was reported in 25.6% of studies and the proportion of presumed cardiac aetiology was reported in 57.3% of studies. The proportion of bystander witnessed status, the proportion of bystander CPR status and the proportion of any witnessed status was reported in 29.2%, 29.2% and 39.0% of the studies respectively. The proportion of EMS-witnessed status and the proportion of public location of arrest was reported in 28.0% and 7.3% of studies respectively. The proportion of patients who had endotracheal intubation and IV/IO epinephrine administration was reported in 7.0% of studies. EMS response time and transport time to hospital was reported in 17.0% and 5.0% of studies respectively.

Quality assessment

The quality assessment results are shown in Table 1 and Fig. 2. The median score according to JBI criteria was 6 out of a possible 9 points (interquartile range [IQR], 2–7), and only 5 studies (6.1%) were deemed to be at high risk of bias (≤3 points). The most significant issues identified were related to the level of detail describing the study subjects and the setting, the definitions used to identify EMS-treated OHCA patients, lack of validity of methods for identification and lack of consistent and reliable measurement of initial rhythm. The sample frame was impacted by significant patient exclusions (e.g. non-cardiac aetiologies) or involved the collection of data from limited geographical regions (e.g. single-centre studies) and time-frames. The majority of EMS-treated asystolic OHCA were reported as a subgroup of a broader population (e.g. all EMS-treated patients) and the documentation of baseline characteristics were poor. Very few of the included studies reported methods of verifying the initial arrest rhythm or the criteria used to define initial asystole.

Survival to hospital discharge or 30 days

All 82 studies included sufficient data to calculate the primary outcome. In these studies, survival to hospital discharge or 30-days ranged between 0% and 23.0% with the crude survival rate being 1.9% (9931 survivors from 531,049 EMS treated patients with known outcome). The overall pooled proportion of survivors to hospital discharge or 30-days was 1.5% (95% CI: 1.2%, 1.8%, I^2 = 97%).

The results of the stratified and meta-regression analysis for survival to hospital discharge or 30-days is shown in Table 2. In the unadjusted analysis, population, study duration, study design and aetiology were the only variables that were significantly associated with survival to hospital discharge or 30-days. In adjusted analysis, population, study duration, highest EMS skill level and region were significantly associated with the primary outcome.

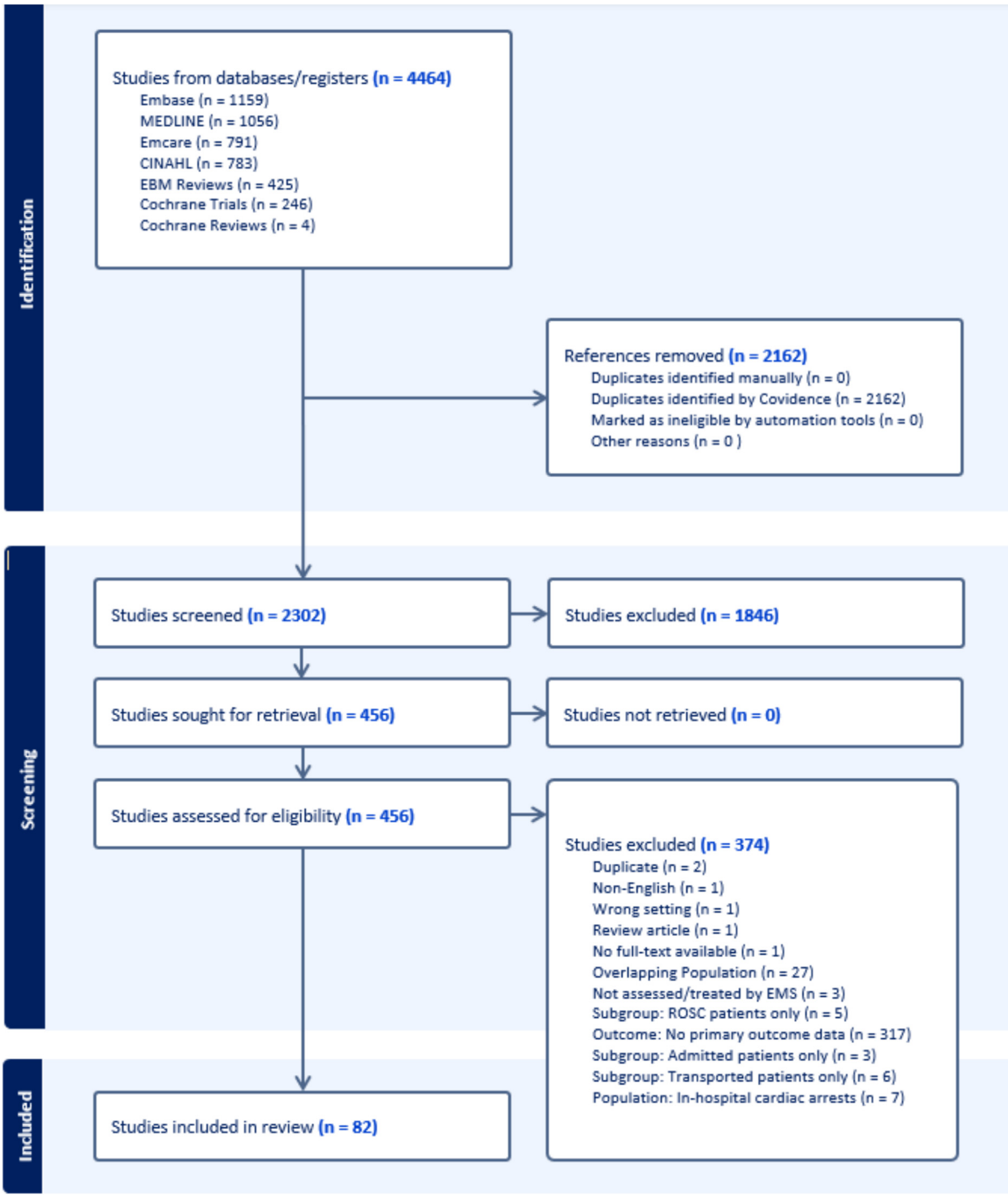

Fig. 1 – PRISMA chart.

Event survival and prehospital ROSC

The results of the stratified and meta-regression analysis for event survival is shown in Table 3. Twenty four (n = 24) studies reported rates of event survival, ranging between 0% and 60.0%, with the crude rate being 5.3% (3273 patients who survived the event from 62,213 EMS-treated patients with known outcome). The pooled rate of event survival was 11.6% (95% CI 6.5%, 17.8%, I^2 = 99%). For the unadjusted analysis, study design and aetiology were the only factors that were significantly associated with event survival. For the adjusted analysis, there were no variables that significantly explained the heterogenity in event survival.

Thirty eight (n = 38) studies reported rates of prehospital ROSC, ranging between 1.0% and 67.0% with the crude rate being 4.8% (20,178 patients who had prehospital ROSC from 421,078

Table 1 – Summary of study and patient characteristics.

	All studies	By Population		
		All ages	Adults only	Paediatrics only
Total studies, n	82	36	39	7
Cumulative EMS-treated patients, n	540,054	107,640	415,888	16,526
Year of publication, n (%)				
1990–99	16 (19.5)	9 (5.0)	6 (15.3)	1 (14.2)
2000–09	25 (30.4)	13 (36.1)	11 (28.2)	1 (14.2)
2010–19	33 (40.2)	10 (27.7)	19 (48.7)	4 (57.1)
2020+	8 (9.7)	4 (11.1)	3 (7.6)	1 (14.1)
EMS-treated sample, n (%)				
<100 patients	19 (23.1)	12 (33.3)	3 (7.6)	4 (57.1)
100–1000 patients	37(45.1)	14 (38.8)	21 (53.8)	2 (28.5)
>1000 patients	26 (31.7)	10 (27.7)	15 (38.4)	1 (14.2)
Study duration, n (%)				
<1 year	13 (15.8)	9 (25.0)	4 (10.2)	0
1–5 years	41 (50.0)	17 (47.2)	22 (56.4)	2 (28.5)
>5 years	28 (34.1)	10 (27.7)	13 (33.3)	5 (71.4)
Study design, n (%)				
Prospective cohort	17 (20.7)	5 (13.8)	9 (23.0)	3 (42.8)
Retrospective cohort	62 (75.6)	31 (86.1)	27 (69.2)	4 (57.1)
Secondary Analysis	3 (3.7)	0	3 (7.7)	0
Registry-based data, n (%)	30 (36.5)	10 (27.7)	17 (43.5)	3 (42.8)
Highest EMS skill level, n (%)				
Physician	34 (41.4)	17 (47.2)	13 (33.3)	4 (57.1)
Paramedic	44 (53.6)	15 (41.6)	26 (66.7)	3 (42.9)
EMT	1 (1.2)	1 (2.7)	0	0
Nurse	3 (3.6)	3 (8.3)	0	0
Region, n (%)				
Asia	12 (14.6)	5 (13.8)	6 (15.3)	1 (14.2)
Australasia	10 (12.2)	2 (5.5)	5 (12.8)	3 (42.8)
Europe	36 (43.9)	22 (61.1)	13 (33.3)	1 (14.2)
North America	23 (28.0)	6 (16.6)	15 (38.4)	2 (28.0)
Other	1(1.2)	1(2.8)	0	0
Aetiologies included, n (%)				
All aetiologies	38 (46.3)	18 (50.0)	17 (43.5)	3 (42.8)
Non-traumatic	5 (6.1)	0	4 (10.2)	1 (14.2)
Other	4 (4.8)	2 (5.5)	1 (2.5)	1 (14.2)
Presumed Cardiac	29 (35.3)	14 (38.8)	15 (38.4)	0
Traumatic	6 (7.3)	2 (5.5)	2 (5.1)	2 (28.5)
Patient Characteristics, WM (95% CI)				
Age in Years	70.3 (62.9,77.7)	67.9 (66.9,68.9)	73.3 (70.5,76.2)	1.0 (NA+)
Proportion Male	58 (57,60)	61 (58,64)	58 (57,60)	61 (NA+)
Proportion Presumed Cardiac Aetiology	59 (54,65)	96 (89,100)	58 (51,65)	30 (23,38)
Study quality, n (%) §				
High risk of bias (<3 points)	5 (6.1)	2 (5.5)	2 (5.1)	1 (14.2)
Moderate risk of bias (4–6 points)	53 (64.6)	26 (72.2)	23 (58.9)	4 (57.1)
Low risk of bias (≥7 points)	24 (29.2)	8 (22.2)	14 (35.9)	2 (28.5)
Bystander witness				
≤28%	10 (41.7)	2 (22.2)	7 (50.0)	1 (100.0)
29–51%	7 (29.1)	3 (33.3)	4 (28.5)	NA+
>51%	7 (29.1)	4 (44.4)	3 (21.4)	NA+
Any witness				
≤32%	11 (34.3)	3 (20.0)	7 (43.7)	1 (100.0)
33–51%	11 (34.3)	7 (46.7)	4 (25.0)	0
>51%	10 (31.2)	5 (33.3)	5 (31.2)	0
EMS witness				
≤18%	7 (30.4)	4 (36.3)	3 (25.0)	NA+
19–63%	9 (39.1)	3 (27.2)	6 (50.0)	NA+
>63%	7 (30.4)	4 (36.3)	3 (25.0)	NA+
Public Location				
≤8%	3 (50.0)	0	3 (60.0)	NA+
9–13%	1 (16.7)	0	1 (20.0)	NA+
>13%	2 (33.3)	1 (100.0)	1 (20.0)	NA+

(continued on next page)

Table 1 (continued)

	All studies	By Population		
		All ages	Adults only	Paediatrics only
Bystander CPR				
≤22%	10 (41.7)	6 (60.0)	4 (30.7)	0
23–31%	7 (29.1)	2 (20.0)	5 (38.4)	0
>31%	7 (29.1)	2 (20.0)	4 (30.7)	1 (100.0)
Endotracheal intubation				
<24%	2 (33.3)	NA	1 (20.0)	1 (100.0)
24–65%	2 (33.3)	NA	2 (40.0)	0
>65%	2 (33.3)	NA	2 (40.0)	0
IV/IO Epinephrine administration				
<15%	2 (33.3)	NA	1 (20.0)	1 (100.0)
15–63%	2 (33.3)	NA	2 (40.0)	0
>63%	2 (33.3)	NA	2 (40.0)	0
EMS response time				
<6.1 min	4 (28.6)	1 (50.0)	3 (27.3)	0
6.1–6.9 min	2 (14.3)	0	2 (18.2)	0
>6.9 min	8 (57.1)	1 (50.0)	6 (54.5)	1 (100.0)
EMS transport time				
<26.8 min	1 (25.0)	1 (33.3)	0	0
26.8–31.6 min	2 (50.0)	1 (33.3)	1 (100.0)	0
>31.6 min	1 (25.0)	1 (33.3)	0	0

WM Weighted Mean.
EMS denotes emergency medical service, WM weighted mean, CI confidence interval.
Age- Estimated from 18 studies, involving 404,103 patients.
Proportion of male Sex estimated from 20 studies, involving 394,963 patients.
Proportion of cardiac aetiology estimated from 46 studies involving 416,263 patients.
§ Graded on a 9-point scale using the Joanna Briggs Institute critical appraisal tool for studies reporting prevalence data.

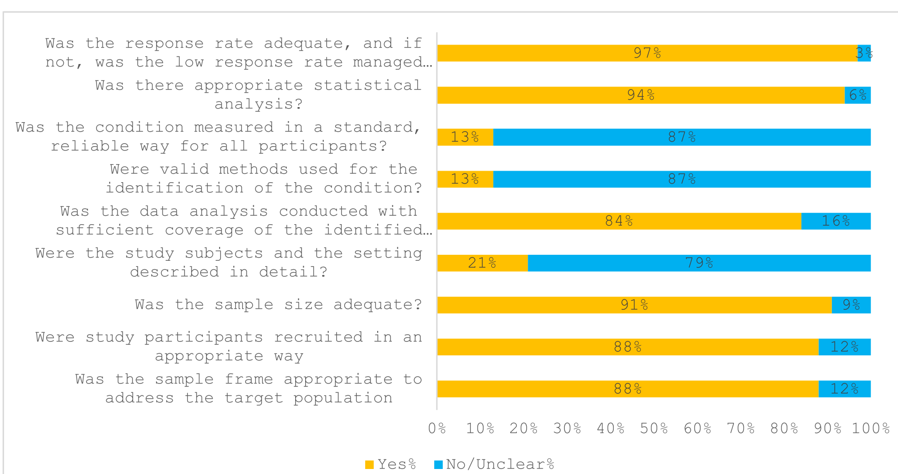

Fig. 2 – Assessment of study quality using the Joanna Briggs Institute critical appraisal tool for studies reporting prevalence and incidence data.

EMS-treated patients with known outcome). The pooled rate of prehospital ROSC was 16.0% (95% CI 14.0%, 17.0%, I^2 = 100%).

Favourable neurological survival

Twenty six (n = 26) studies reported neurologically favourable survival at longest follow-up, ranging in definitions from a Cerebral Performance Category ≤ 2 at hospital discharge or 30 days (*n* = 19), Modified Rankin Scale ≤ 3 at discharge (*n* = 2), Overall Performance Category 1–2 at discharge (*n* = 1), Paediatric Cerebral Performance Category 1 at 18 months (*n* = 1), Bloom category 1/2 at 12 months (*n* = 1), alive at one year (*n* = 1) or unspecified (*n* = 1). Among these studies, neurologically favourable survival at longest follow-up ranged between 0% and 15%, with the crude rate being 0.4% (1927 patients with favourable neurological outcome from 446,213

Table 2 – Stratified analysis and meta regression of survival to hospital discharge or 30 days among EMS treated OHCA with initial asystole.

	Number of studies	Pooled proportion of survivors (95% CI)	I^2	P value for interaction (unadjusted)	P Value for interaction (adjusted)
Total studies, n	82	1.5 (1.2, 1.8)	98%	–	–
Population					
All ages	36	1.4 (0.8, 2.2)	96%	Ref	Ref
Adults only	39	1.4 (1.1, 1.8)	98%	0.567	0.556
Paediatrics only	7	3.4 (1.4, 6.2)	84%	<0.001	0.012
Year of publication, n (%)					
1990–99	16	1.1 (0.5, 2.0)	69%	Ref	Ref
2000–09	25	2.1 (1.3, 2.9)	90%	0.813	0.943
2010–19	33	0.9 (0.5, 1.3)	98%	0.921	0.831
2020+	8	2.8 (1.1, 5.2)	99%	0.220	0.618
EMS-treated sample					
<100 patients	19	3.3 (1.4, 5.8)	51%	Ref	Ref
100–1000 patients	37	1.9 (1.3, 2.7)	82%	0.547	0.944
>1000 patients	26	1.4 (1.0, 1.8)	99%	0.477	0.755
Study duration					
<1 year	13	1.2 (0.0, 3.5)	90%	Ref	Ref
1–5 years	41	1.3 (1.0,1.6)	80%	<0.001	0.006
>5 years	28	1.7 (1.1, 2.3)	99%	<0.001	0.008
Study design, n (%)					
Retrospective cohort	62	1.3 (0.9,1.6)	98%	Ref	Ref
Prospective cohort	17	2.1 (0.9, 3.6)	92%	0.011	0.111
Secondary Analysis	3	1.9 (1.1, 2.9)	NA+	0.959	0.263
Registry-based data	30	1.7 (1.2, 2.2)	99%	0.526	0.732
Highest EMS skill level					
Physician	34	1.8 (1.3, 2.4)	97%	Ref	Ref
Paramedic	44	1.2 (0.8, 1.6)	97%	0.279	0.032
EMT	1	2.8 (1.3, 5.3)	NA+	0.846	0.641
Nurse	3	4.8 (1.5, 9.5)	NA+	0.692	0.849
Region					
North America	23	1.4 (0.7, 2.3)	97%	Ref	Ref
Europe	36	1.6 (1.1, 2.1)	85%	0.386	0.531
Asia	12	1.3 (0.6, 2.3)	99%	0.958	0.042
Australasia	10	1.7 (0.3, 3.8)	92%	0.609	0.721
Other	1	1.8 (0.5, 4.5)	NA+	0.954	0.955
All aetiologies					
All aetiologies	39	1.2 (0.7, 1.9)	97%	Ref	Ref
Presumed cardiac	28	1.2 (0.7, 1.9)	98%	0.003	0.751
Non-traumatic	5	1.9 (1.3, 2.7)	86%	0.569	0.767
Traumatic	6	1.0 (0.5, 1.5)	24%	0.882	0.203
Other*	4	7.0 (0.0, 22.2)	88%	0.931	0.525
Study quality, n (%)					
High risk of bias	5	7.7 (1.2, 17.6)	67%	Ref	Ref
Moderate risk of bias	53	1.3 (1.0,1.7)	97%	0.529	0.575
Low risk of bias	24	1.9 (1.1, 2.9)	98%	0.688	0.649
Age in years					
<66	7	1.1 (0.0, 3.3)	98%	Ref	NA+
66–69	4	1.7 (0.1, 4.8)	98%	0.836	NA+
>69	6	1.3 (0.5, 2.3)	99%	0.350	NA+
Male					
<58%	6	0.8 (0.0, 2.1)	99%	Ref	NA+
58–62%	8	1.7 (0.6, 3.4)	98%	NA+	NA+
>62%	6	1.0 (0.7, 1.4)	77%	NA+	NA+
EMS witnessed					
<18%	7	0.5 (0.1,1.1)	44%	Ref	Ref
18–63%	9	1.5 (0.6, 2.9)	99%	0.429	0.358
>63%	7	4.5 (2.9, 6.4)	91%	0.214	0.713
Any witnessed					
<32%	11	1.5 (0.4, 3.1)	99%	Ref	Ref
32–51%	11	0.9 (0.5, 1.5)	79%	0.311	0.212
>51%	10	3.0 (1.8, 4.3)	98%	0.996	0.437

(continued on next page)

Table 2 (continued)

	Number of studies	Pooled proportion of survivors (95% CI)	I^2	P value for interaction (unadjusted)	P Value for interaction (adjusted)
Bystander witnessed					
<28%	10	1.3 (0.5, 2.4)	99%	Ref	Ref
28-51%	7	0.5 (0.2, 0.9)	77%	0.417	0.848
>51%	7	2.7 (2.6, 2.8)	0%	0.367	0.946
Bystander CPR					
<22%	10	1.5 (0.4, 3.3)	99%	Ref	Ref
22–32%	7	0.9 (0.4,1.5)	69%	0.419	0.875
>32%	7	1.9 (1.0, 3.1)	99%	0.801	0.778
Public location					
<8%	3	1.4 (1.0, 1.9)	NA+	Ref	NA+
8–13%	1	1.8 (0.8, 3.6)	NA+	0.934	NA+
>13%	2	0.9 (0.7, 1.1)	NA+	0.726	NA+
Endotracheal intubation					
<24%	2	1.2 (1.1, 1.2)	NA+	Ref	NA+
24–65%	2	1.5 (1.2, 1.8)	NA+	0.372	NA+
>65%	2	2.5 (2.4, 2.6)	NA+	0.613	NA+
IV/IO Epinephrine administration					
<15%	2	3.2 (3.1, 3.3)	NA+	Ref	NA+
15–63%	2	0.9 (0.9, 1.0)	NA+	0.50	NA+
>63%	2	1.2 (1.1, 1.3)	NA+	0.126	NA+
EMS response time					
<6.1 min	4	1.5 (1.2, 1.9)	73%	Ref	NA+
6.1–6.9 min	2	1.1 (0.4, 2.0)	99%	0.933	NA+
>6.9 min	8	1.7 (0.8, 3.0)	NA+	0.467	NA+
EMS transport time					
<26.8 min	1	1.7 (1.5, 2.0)	NA+	Ref	NA+
26.8–31.6 min	2	1.2 (1.1, 1.2)	NA+	0.711	NA+
>31.6 min	1	3.0 (2.9, 3.0)	NA+	0.796	NA+

NA+- not available (calculation not possible).
*Other Aetiologies – Drowning, Hanging.

EMS-treated patients with long term follow up). The pooled rate of neurologically favourable survival at longest follow-up was 0.6% (95% CI 0.5%, 0.8%, I^2 = 100%).

Incidence

Table 4 shows the pooled incidence of EMS-treated cases across the 82 studies and stratifications. The overall pooled incidence of EMS-treated asystolic cases was 11.0 cases per 100,000 person-years (95% CI: 10.5, 11.5, I^2 = 100%). In the unadjusted analysis, study population, year of publication, number of patients treated, study design, highest EMS skill level, region, aetiology and study quality explained the variation in the incidence. In the multivariable analysis, all variables except highest EMS skill level remained significantly associated with incidence across studies.

Publication bias

A funnel plot for the primary outcome of survival to hospital discharge or 30 day survival is shown in Fig. 3. Visual inspection of the funnel plot shows some evidence of asymmetry.

Discussion

We conducted a systematic review and meta-analysis of 82 studies, including over 540,000 EMS-treated asystolic OHCA patients from 35 countries. Survival to hospital discharge or 30 days was 1.5% (*n* = 9931), with 0.6% achieving favourable neurological outcomes at the longest follow-up. Our analysis identified study population, study duration, highest EMS skill level, and study continent as the only variables significantly associated with survival to hospital discharge or 30 days. No variables were significantly associated with event survival. Predictors such as bystander-witnessed arrest, any witnessed arrest, bystander CPR, arrest location, endotracheal intubation, IV/IO epinephrine administration, EMS response time and EMS transport time to hospital showed no significant association with survival to hospital discharge or 30-days. However, our review was limited by the clinical and statistical heterogeneity of included studies, and this should be considered when interpreting the results of our pooled estimates.

The incidence of EMS-treated asystolic OHCA varies globally, with a higher incidence in Asia compared to North America and Europe.[2,6,25] This disparity may be attributed to regional policies limiting the withholding of resuscitation in the field.[2,6,25] However, due to limited data on EMS-attended populations, we were unable to quantify the full incidence of asystolic OHCA cases assessed by EMS, which is likely higher than the reported EMS-treated cases. Our findings align with a previous systematic review by Sasson et al (2010), which analysed studies from 1950 to 2008.[3] Forty studies included data on asystolic arrest. The review reported a pooled survival rate of 0.2% (95% CI: 0%–0.3%) in EMS systems with low baseline survival and 4.7% (95% CI: 1.0%–8.4%) in systems with high baseline survival.[3] These results suggest that survival rates for asystolic OHCA remain persistently poor and have not improved significantly

Table 3 – Stratified analysis and meta regression of event survival for EMS-treated asystolic OHCA.

	Number of studies	Pooled proportion of survivors (95% CI)	I^2	P value for interaction (unadjusted)	P value for interaction (adjusted)
Total studies, n	24	11.6 (6.5, 17.8)	99%	–	–
Population					
All ages	9	11.8 (6.0, 18.9)	93%	Ref	Ref
Adults only	13	9.7 (3.9, 17.6)	99%	0.814	0.707
Paediatrics only	2	10.5 (8.2, 13.0)	NA+	0.755	0.894
Year of publication					
1990–99	4	13.0 (4.1, 25.8)	98%	Ref	Ref
2000–09	10	11.6 (5.1, 20.1)	98%	0.753	0.813
2010–19	8	12.1 (3.3, 24.9)	99%	0.724	0.640
2020+	2	9.8 (6.6, 13.5)	NA+	0.830	0.698
EMS-treated sample					
<100 patients	7	17.2 (4.9, 34.1)	91%	Ref	Ref
100–1000 patients	10	9.4 (6.1, 13.4)	91%	0.526	0.791
>1000 patients	7	11.1 (3.1, 23.0)	99%	0.751	0.716
Study duration					
<1 year	6	10.4 (4.7, 18.0)	91%	Ref	Ref
1–5 years	8	8.7 (3.3, 16.3)	97%	0.989	0.626
>5 years	10	14.8 (6.4, 25.7)	99%	0.886	0.680
Study design					
Retrospective cohort	18	11.7 (5.4, 19.9)	99%	Ref	Ref
Prospective cohort	5	10.4 (3.1, 21.0)	98%	0.039	0.220
Secondary Analysis	1	15.9 (11.1, 21.9)	NA+	0.769	0.346
Registry-based data	6	7.9 (0.9, 20.6)	99%	0.613	0.651
Highest EMS skill level					
Physician	5	17.2 (12.2, 22.7)	90%	Ref	Ref
Paramedic	16	8.5 (3.7, 15.0)	99%	0.147	0.943
EMT	1	13.4 (9.8, 17.7)	NA+	0.676	0.781
Nurse	2	17.1 (10.4, 25.0)	NA+	0.897	0.805
Region					
North America	7	16.1 (6.2, 29.4)	99%	Ref	Ref
Europe	9	9.6 (1.8, 22.0)	99%	0.555	0.599
Asia	3	7.3 (1.4, 17.1)	NA+	0.629	0.622
Australasia	5	11.1 (6.7, 16.3)	90%	0.841	0.679
Other	0	NA+	NA+	NA+	NA+
Aetiologies included					
All aetiologies	14	14.0 (10.9, 17.5)	95%	Ref	Ref
Presumed cardiac	6	2.7 (0.8, 5.4)	97%	<0.001	0.390
Non-traumatic	2	13.0 (11.5, 14.6)	NA+	0.372	0.735
Traumatic	1	13.4 (9.8, 17.7)	NA+	0.680	NA+
Other*	1	53.8 (25.1, 80.7)	NA+	0.170	0.540
Study quality					
High risk of bias	1	53.8 (25.1, 80.7)	NA+	Ref	
Moderate risk of bias	19	10.8 (5.0, 18.3)	99%	0.154	NA+
Low risk of bias	4	10.6 (1.5, 26.1)	99%	0.155	NA+
Other variables					
Age in years					
<66	3	11.4 (5.3, 19.5)	NA+	Ref	NA+
66–69	2	0.4 (0.3, 0.4)	NA+	0.063	NA+
>69	1	1.7 (1.3, 2.1)	NA+	0.058	NA+
Male					
<58%	5	6.6 (1.0, 16.3)	99%	NA+	NA+
58–62%	0	NA+	NA+	NA+	NA+
>62%	0	NA+	NA+	NA+	NA+
Any witness					
<32%	10	12.0 (2.9, 25.4)	97%	Ref	NA+
32–51%	11	12.8 (9.3, 16.8)	NA+	0.745	NA+
>51%	10	11.0 (0.6, 31.1)	100%	0.748	NA+
EMS witnessed					
<18%	1	10.6 (7.3, 14.7)	NA+	Ref	NA+
18–63%	3	2.6 (0.5, 5.8)	NA+	0.117	NA+
>63%	3	17.5 (13.6, 21.8)	NA+	0.259	NA+

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Table 3 (continued)

	Number of studies	Pooled proportion of survivors (95% CI)	I^2	P value for interaction (unadjusted)	P value for interaction (adjusted)
Bystander witnessed					
<28%	2	1.2 (0.8, 1.6)	NA+	Ref	NA+
28–51%	3	6.9 (0.0, 25.8)	NA+	0.496	NA+
>51%	3	17.5 (13.6, 21.8)	NA+	0.153	NA+
Bystander CPR					NA+
<22%	5	13.6 (3.9, 27.4)	99%	Ref	
22%–32%	1	15.9 (11.1, 21.9)	NA+	0.704	NA+
>32%	1	0.4 (0.4, 0.5)	NA+	0.307	NA+
Public location			NA+	NA+	
<8%	1	15.3 (14.5, 16.1)	NA+	NA+	NA+
8%–13%	0	NA+	NA+	NA+	NA+
>13%	0	NA+	NA+	NA+	NA+
Endotracheal intubation					
<24%	0	NA+	NA+	NA+	NA+
24–65%	1	0.4 (0.4, 0.5)	NA+	NA+	NA+
65%	0	NA+	NA+	NA+	NA+
IV/IO Epinephrine administration					
<15%	0	NA+	NA+	NA+	NA+
15–63%	0	NA+	NA+	NA+	NA+
63%	1	0.4 (0.4. 0.5)	NA+	NA+	NA+
EMS response time					
<6.1	0	NA+	NA+	NA+	NA+
6.1–6.9	0	NA+	NA+	NA+	NA+
>6.9	4	15.3 (13.0, 17.8)	NA+	NA+	NA+
EMS transport time					
<26.8%	0	NA+	NA+	NA+	NA+
26.8–31.6%	0	NA+	NA+	NA+	NA+
>31.6%	0	NA+	NA+	NA+	NA+

NA+ – Not Possible.
* Other Aetiologies p– Drowning, Hanging.

over recent decades. Additionally, our findings indicate that over half of the survivors of asystolic OHCA either die or suffer significant neurological impairment at follow-up.

Given the extremely low survival and poor neurological outcomes, prevention should be prioritised. Efforts should focus on early detection and interventions to prevent the degradation of shockable rhythms (VF/VT) to asystole. This may be achieved through prompt CPR and early rhythm analysis with defibrillation not only by EMS personnel but also by citizen responders.[26] Primary prevention strategies should enhance public education on cardiac symptoms and encourage timely medical care, with mass media campaigns aimed at recognising and responding to symptoms of heart attack demonstrating a positive impact on OHCA incidence.[27] Secondary prevention should involve the use of implantable cardioverter-defibrillators (ICDs) for high-risk patients.[28]

Alongside preventive measures, improved implementation of termination of resuscitation (TOR) protocols for asystolic OHCA is essential.[29] The 2020 International Consensus on Cardiopulmonary Resuscitation and Emergency Cardiovascular Care also conditionally recommends the use of termination of resuscitation (TOR) rules to guide clinicians in deciding whether to discontinue out-of-hospital resuscitation efforts or continue CPR during transport, based on very low-certainty evidence.[30] It recognises that identifying futile cases is complex and typically relies on a combination of clinical guidelines and clinician judgement.[30] The International Liaison Committee on Resuscitation (ILCOR) task force emphasises that decisions should not rely solely on TOR rules but should also consider factors such as the patient's prior wishes, pre existing comorbidities, and quality of life, in addition to clinical guidelines and clinician judgment.[30] In situations where prehospital TOR is not feasible due to legal, cultural, or logistical factors, continuing CPR and transporting the patient to the hospital may be preferred.[30] However, adherence to these guidelines is inconsistent, leading to futile resuscitation attempts with poor survival and neurological outcomes.[12] Strengthening compliance with TOR guidelines could give clear guidance to EMS personnel about resuscitation in the field and could reduce unnecessary hospital transports and optimise resource allocation.[31]

TOR criteria have demonstrated high specificity and predictive value for mortality.[31,32] A systematic review by Smyth et al (2024) reported that the Universal Termination of Resuscitation (UTOR) rule has a 1% missed survival rate when the likelihood of survival is 8%.[29] Given our findings of 1.5% survival (0.6% neurologically favourable), treating asystolic OHCA cases that meet TOR criteria may be futile in most cases. Some argue that medical futility is defined by a <1% survival rate, supporting TOR rule application.[33] However, the European Resuscitation Council maintains that even <1% survival justifies resuscitation,[34] highlighting ongoing debate regarding futility in OHCA. Ardagh (2000) suggests avoiding the term "futile" in resuscitation decisions and instead evaluating the balance of benefits and harms from the patient's perspective.[35]

Despite their potential benefits, TOR rules face significant implementation barriers. A multicentre trial by Morrison et al (2014) found that 21% of eligible patients were transported despite meeting TOR criteria, with no survivors.[36] Reasons for noncompliance included

Table 4 – Stratified analyses and meta-regression of the incidence of EMS-treated asystolic OHCA per 100,000 person years.

	Number of studies	Pooled incidence per 100,000 person-years (95% CI)	I^2	P value for interaction (Unadjusted)	P value for interaction (adjusted)
Total studies, n	82	11.0 (10.5, 11.5)	100%	–	–
Population					
All ages	36	12.8 (11.9, 13.8)	100%	Ref	Ref
Adults only	39	12.2 (11.1, 13.3)	100%	0.014	<0.001
Paediatrics only	7	3.0 (0.6, 5.4)	100%	<0.001	0.294
Year of publication					
1990–99	16	10.8 (7.5, 14.1)	100%	Ref	Ref
2000–09	25	15.6 (12.4, 18.9)	100%	<0.001	0.912
2010–19	33	9.1 (7.7, 10.4)	100%	0.224	0.728
2020+	8	35.7 (31.8, 39.6)	100%	<0.001	<0.001
EMS-treated sample					
<100 patients	19	2.0 (1.7, 2.4)	97%	Ref	Ref
100–1000 patients	37	4.3 (4.1, 4.5)	100%	<0.001	0.262
>1000 patients	26	29.5 (26.1, 32.9)	100%	<0.001	<0.001
Study duration					
<1 year	13	58.5 (49.8, 67.2)	100%	Ref	Ref
1–5 years	41	8.7 (8.3, 9.0)	100%	<0.001	<0.001
>5 years	28	10.6 (8.0, 13.2)	100%	<0.001	<0.001
Study design, n (%)					
Retrospective cohort	62	11.0 (10.4, 11.5)	99%	Ref	Ref
Prospective cohort	17	12.3 (9.7, 14.9)	99%	0.039	0.280
Secondary Analysis	3	9.3 (8.2, 10.5)	69%	0.769	0.398
Registry-based data	30	11.7 (10.8, 12.7)	99%	0.361	0.023
Highest EMS skill level					
Physician	34	11.1 (9.5, 12.6)	99%	Ref	Ref
Paramedic	44	13.9 (12.8, 15.1)	99%	<0.001	0.0
EMT	1	0.0 (0.0, 0.1)	NA+	<0.001	0.682
Nurse	3	16.6 (10.2, 23.0)	80%	0.035	0.789
Region					
North America	23	12.0 (11.1, 12.9)	100%	Ref	Ref
Europe	36	12.1 (11.3, 13.0)	100%	<0.001	0.016
Asia	12	13.5 (8.9, 18.1)	100%	0.017	<0.001
Australasia	10	5.3 (3.3, 7.3)	100%	<0.001	0.021
Other	1	3.6 (3.1, 4.1)	NA+	0.002	0.402
Aetiologies included					
All aeitologies	39	12.9 (11.9, 14.0)	100%	Ref	Ref
Presumed cardiac	28	24.2 (20.9, 27.4)	100%	0.127	0.272
Non-traumatic	5	17.2 (9.0, 25.4)	100%	0.005	0.727
Traumatic	6	1.5 (0.9, 2.1)	100%	<0.001	0.005
Other	4	0.3 (0.2, 0.5)	100%	<0.001	<0.001
Study quality					
High risk of bias	5	1.4 (0.8, 2.0)	98%	Ref	ref
Moderate risk of bias	53	10.7 (10.2, 11.3)	100%	<0.001	<0.001
Low risk of bias	24	20.7 (18.4, 22.9)	100%	<0.001	0.015

location of arrest, family distress, patient age, and perceived short transport times.[36] Additional barriers include EMS provider training gaps, cultural and ethical concerns, challenges in family communication, regional guideline discrepancies, and legal uncertainties.[29,37]

Our review reinforces the persistently poor prognosis of asystolic OHCA and underscores the need for enhanced preventive strategies, adherence to TOR guidelines, and a nuanced approach to defining futility in resuscitation efforts. Addressing legal, ethical, and educational barriers will be critical in ensuring the effective implementation of TOR protocols across EMS systems.

Limitations

This review has several limitations. Population characteristics were frequently unreported, limiting our ability to analyse these factors comprehensively. Key variables such as CPR duration were not included, despite its potential impact on survival outcomes. Our search strategy may have missed studies where asystolic OHCA was not explicitly mentioned in the title or abstract or where primary outcome data were not reported. While we included studies from multiple regions, no studies from Africa or Antarctica were identified. Many studies lacked details on initial rhythm, confirmation or the cri-

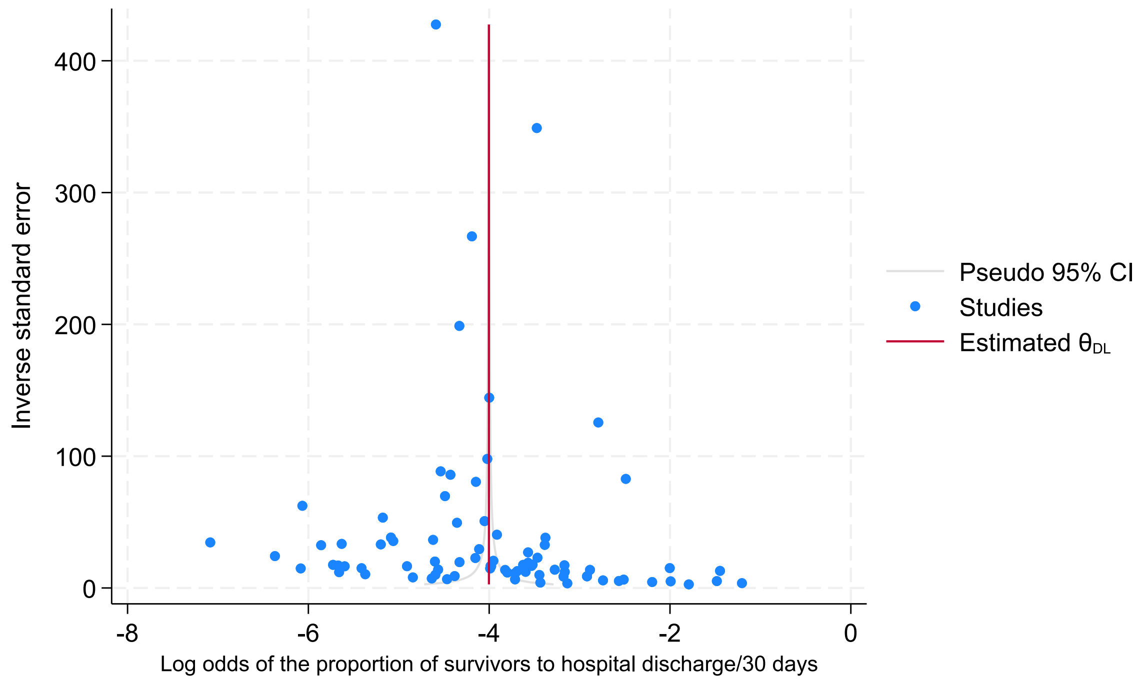

Fig. 3 – Funnel plot for the log odds of the proportion of survivors to hospital discharge or 30 day survival among EMS treated asystole studies.

teria used to define asystole. Additionally, missing outcome data was common, reducing the reliability of pooled estimates. Although our funnel plot suggested some asymmetry, this may not necessarily indicate publication bias, as funnel plots in single-group proportional meta-analyses have limited interpretability compared to interventional studies.[38]

Conclusion

This systematic review and meta-analysis highlights significant variability in outcomes for EMS-treated patients across a global cohort. With a pooled proportion of 53.0% of patients with asystolic OHCA, the overall survival rate to hospital discharge or 30-days was low at 1.5%. Additionally, the proportion of survivors to event, prehospital return of spontaneous circulation (ROSC), and neurologically favourable survival were relatively modest, with proportions of 11.6%, 16.0%, and 0.6%, respectively. These pooled results should be interpreted with caution, given the high clinical and statistical heterogeneity observed across the 82 studies included in the review. Further research in this population could consider novel preventive strategies for this population and the role of TOR guidelines.

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CRediT authorship contribution statement

Dhiraj Bhatia Dwivedi: Writing – review & editing, Writing – original draft, Visualization, Validation, Software, Resources, Project administration, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Jocasta Ball:** Writing – review & editing, Visualization, Validation, Supervision, Resources, Project administration, Methodology, Investigation, Data curation, Conceptualization. **Karen Smith:** Writing – review & editing, Visualization, Validation, Supervision, Resources, Project administration, Methodology, Investigation, Conceptualization. **Ziad Nehme:** Writing – review & editing, Writing – original draft, Visualization, Validation, Supervision, Software, Resources, Project administration, Methodology, Investigation, Funding acquisition, Formal analysis, Data curation, Conceptualization.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary material

Supplementary data to this article can be found online at https://doi.org/10.1016/j.resuscitation.2025.110629.

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