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Compression-only or standard cardiopulmonary resuscitation for out-of-hospital cardiac arrest: a systematic review and meta-analysis of randomized controlled trials

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Abstract

This meta-analysis aims to compare chest compression-only cardiopulmonary resuscitation (CO-CPR) with standard CPR (sCPR), which includes mouth-to-mouth ventilation, as potential strategies for managing out-of-hospital cardiac arrest (OHCA). We systematically searched various databases and registries such as MEDLINE, Embase, The Cochrane Library, and Clinicaltrials.gov to retrieve relevant studies. We used the revised Cochrane "Risk of Bias" tool for randomized trials (RoB 2.0) to assess the risk of bias in included studies. Revman 5.4 was used to pool dichotomous outcomes under a random effects model. A total of 4 randomized controlled trials were included in our meta-analysis. Our results indicate that CO-CPR was associated with a significantly increased survival to hospital discharge compared to sCPR [relative risk (RR) 1.22, 95% confidence interval (CI): 1.01 to 1.46] with minimal heterogeneity (I^2=0%). No significant difference was observed between the two groups regarding 1-day survival (RR 1.07, 95% CI: 0.94 to 1.23), survival to hospital admission with a good neurological outcome (cerebral performance category 1 or 2) (RR 1.10, 95% CI: 0.80 to 1.51), return of spontaneous circulation (RR 1.05, 95% CI: 0.95 to 1.17), and survival to hospital admission (RR 1.08, 95% CI: 0.93 to 1.25). This meta-analysis found that chest CO-CPR significantly improves survival to hospital discharge compared to sCPR for managing OHCA, while yielding comparable results for other resuscitation outcomes.

Key words: CPR, OHCA, cardiac arrest, cardiopulmonary resuscitation.

Introduction

An out-of-hospital cardiac arrest (OHCA) is defined as cessation of cardiac mechanical activity, confirmed by the absence of signs of circulation, which occurs outside the hospital setting [1]. The global worldwide average of OHCA incidence in adults is 95.9/100,000/year [1]. In the USA, it ranks among the top six causes of death. Annually, around 300,000 OHCA patients receive treatment in North America [2]. Several factors are linked to poor outcomes in OHCA patients, including older age, unwitnessed arrest, absence of bystander cardiopulmonary resuscitation (CPR), delayed ROSC (over 30 minutes), non-shockable initial rhythm, high lactate levels, and low pH (<7.2) [3]. The most common predictors are initial rhythm, age, and CPR duration [4]. OHCA is swiftly recognized and addressed through the prompt activation of 911, bystander-initiated CPR, layperson use of an automated external defibrillator (AED) before the arrival of emergency medical services (EMS), advanced life support (ALS), and post-resuscitation care [2]. Despite improvements in OHCA survival, the rate of survival to hospital discharge and survival with good neurological outcomes remains below 10%. There are notable variations in OHCA survival to discharge (3.4–22%) and survival with functional recovery (0.8–21%) across the US [4].

CPR is crucial for survival in cardiac arrest, with outcomes heavily dependent on early recognition, rapid emergency response, and the quality of CPR delivered. The current guidelines from the American Heart Association (AHA) and the European Resuscitation Council (ERC) strongly emphasize the importance of high-quality CPR, which includes effective chest compressions and rescue breaths [4]. Despite being inherently, inefficient, providing only 10% to 40% of normal blood flow to the heart and brain even when performed according to guidelines, studies show that effective CPR significantly impacts survival [5]. Today basic life support typically consists of performing cycles based on 30 compressions with a pause for two ventilations (30:2) which is also known as standard CPR (sCPR) [6]. Traditionally, layperson CPR has included both chest compressions and rescue breathing to ensure circulation and oxygenation [6]. Given the historical reluctance of bystanders to perform CPR due to the resistance associated with mouth-to-mouth ventilation [6], it is critical to explore the efficacy of an alternative form of CPR that focuses solely on chest compressions, minimizing or eliminating the need for rescue breathing. Compression-only CPR (CO-CPR) has emerged as an easier alternative for laypersons who are not trained in CPR or are unwilling to perform rescue breaths [7]. In patients with OHCA, CO-CPR provides similar survival and neurological outcomes compared to sCPR [8]. Research by Berg and colleagues in animal models, supported by a clinical study where dispatchers

randomly assigned callers to CO-CPR or sCPR, found that both methods have similar efficacy and survival rates [9].
Overall, CPR started prior to EMS arrival has repeatedly been shown to be associated with survival rates 2–3 times higher compared with no such initiation [10]. Our goal in this systematic review was to compare the efficacy of CO-CPR and sCPR in outcomes of patients with OHCA.

Materials and Methods

This meta-analysis was conducted following the recommendations of the Cochrane Handbook for Systematic Reviews of Interventions [11] and reported according to the Preferred Reporting Items for Systematic Review and Meta-Analysis Protocols (PRISMA) checklist [12]. We registered the protocol for this review with the International Prospective Register of Systematic Reviews (PROSPERO) under the identifier CRD42024547144.

Eligibility criteria

Inclusion criteria

1) Population: Patients with OHCA
2) Intervention: CO-CPR
3) Comparator: sCPR
4) Outcome: reporting at least 1 outcome of interest (long-term outcomes are to be assessed at a 3 to 5-year follow-up period)
5) Study design: Randomized Controlled Trials (RCTs) only

Exclusion criteria

1) All the study designs other than RCTs such as observational studies, including case-control and cohort studies, case reports, and letters to the editor
2) animal or in vitro studies.

Information sources

We performed a systematic search of the online resources from inception up to July 2024 with no language or geographical restrictions: (1) Electronic databases: the Cochrane Central Register of Controlled Trials (CENTRAL, via The Cochrane Library), MEDLINE (via PubMed), and Embase (via Ovid); (2) International trial registers: ClinicalTrials.gov; (3) Grey literature sources: ProQuest Dissertations and Theses Global (PQDT). We also screened the reference lists of included studies and relevant systematic reviews to identify potential studies for our review. Forward citation searching using the Web of Science was performed to identify further eligible articles. The detailed search strategy is given in *Supplementary Table 1*.

Selection process

All the literature search results were uploaded to Rayyan, a software tool for screening articles. After the de-duplication of articles, two reviewers independently performed screening based on title and abstracts. The remaining articles were subjected to full-text screening according to our inclusion criteria. Any disagreement between the two reviewers was settled through discussion.

Data collection process and data items

We constructed a structured excel spreadsheet for data extraction. Two reviewers independently extracted data into the sheet. Data items included study and patient characteristics (author name, year of publication, number of patients, age, sex, country, location of arrest, study arms, frequency of witnessed event, first cardiac rhythm, time to ACLS, and time to EMS response) and outcomes.

Type of Interventions

The control group was sCPR (rescue breathing and chest compressions as per standard BLS guidelines). The intervention group was continuous CO-CPR without rescue breathing.

Outcomes

Our study's primary outcomes were survival to hospital discharge, and 1 day survival. Secondary outcomes included survival to hospital discharge with a good neurological outcome (CPC 1 or 2), return of spontaneous circulation (ROSC), and survival to hospital admission.

Risk of bias assessment

We assessed the risk of bias in the included RCTs using the revised Cochrane Risk of Bias tool for randomized trials (RoB 2.0), which assesses bias in the following 5 domains: (1) bias arising from the randomization process; (2) bias caused by deviations from intended interventions; (3) bias caused by missing outcome data; (4) bias in the measurement of the outcome, and (5) bias in the selection of the reported result. Two review authors independently applied the tool to the studies. Any conflict between them was resolved through discussion.

Data synthesis

We carried out the meta-analyses using Review Manager (RevMan, version 5.4; The Cochrane Collaboration, Copenhagen, Denmark). A random effects model with the DerSimonian-Laird variance estimator was used. Dichotomous outcomes and continuous outcomes were pooled as risk ratios (RR) and mean difference (MD) along with 95% confidence intervals respectively. We planned to assess publication bias using a funnel plot if the number of studies was more than 10 in a meta-analysis.

The chi-square test and I^2 statistic were employed for each synthesis to detect the presence of heterogeneity and quantify it, respectively. We interpreted I^2 values according to the Cochrane Handbook for Systematic Reviews of Interventions, section 10.10. P< 0.10 will be considered statistically significant for the t^2 test.

Results

Study selection

A total of 174 studies were retrieved through our database search. Following deduplication and initial screening based on title and abstracts, 24 studies underwent full-text screening. Four articles met the inclusion criteria and were included in our meta-analysis [6,7,9,13]. The detailed study selection process is illustrated using a PRISMA flowchart (Figure 1).

Study characteristics

A total of 4,987 patients (2,482 in the CO-CPR group, and 2,505 in the sCPR group) were included in the four RCTs included in this systematic review and meta-analysis. The included RCTs were conducted in Sweden (50%) and the USA (50%). Most of the patients included in the RCTs had witnessed OHCA. The study and patient characteristics of the included RCTs are summarized in Table 1. A male preponderance was noted across all studies, with 64-68% of OHCA patients being male. This proportion was conserved in both the treatment (CO-CPR) and comparator (sCPR) group, with no statistically significant difference between the two.

Risk of bias assessment

Two of the four included RCTs were assessed to be at low risk of bias using the RoB2 tool. Two studies had a moderate risk of bias on account of potential bias due to deviations from the intended intervention and missing outcome data (Figure 2).

Pooled analysis of all studies

Primary outcomes

Survival to hospital discharge

Three of the 4 RCTs included in this meta-analysis assessed survival to hospital discharge. The survival to hospital discharge was significantly increased in the CO-CPR group compared to the sCPR group (RR = 1.22; 95% CI [1.01, 1.46]) (Figure 3). The interstudy heterogeneity was estimated to be minimal (I^2 = 0%).

1-day survival

A meta-analysis of 2 studies showed no significant difference between the CO-CPR and sCPR groups with respect to 1-day survival (RR = 1.07; 95% CI [0.94, 1.23]) (Figure 4) with minimal heterogeneity (I^2= 0%).

Secondary outcomes

There was no significant difference observed in the survival to hospital admission (RR = 1.08; 95% CI [0.93, 1.25]; I^2 = 7%; *Supplementary Figure 1*); ROSC (RR = 1.05; 95% CI [0.95, 1.17]; I^2 = 16% *Supplementary Figure 2*), and survival to hospital discharge with a good neurological outcome (RR = 1.10; 95% CI [0.80, 1.51]; I^2 = 37%; *Supplementary Figure 3*) between the 2 groups.

Discussion and Conclusions

Our systematic review and meta-analysis synthesized evidence from four RCTs regarding the effectiveness of CO-CPR versus sCPR in OHCA patients. We found a statistically significant increase in survival to hospital discharge in patients who were administered CO-CPR compared to sCPR. CO-CPR was found to be non-inferior to sCPR with respect to other outcomes such as 1-day survival, survival to hospital admission, survival with good neurological outcome (CPC 1 or 2), ROSC, and 30-day survival. Our results suggest that amendments to bystanders-led resuscitation guidelines for OHCA might be considered.

The finding that CO-CPR is non-inferior to sCPR is supported by a growing body of evidence that explores why rescue breathing may be less useful than previously considered. Firstly, CO-CPR results in a greater number of chest compressions (average 88 ± 5 per minute) in the first several minutes of OHCA compared to sCPR (average 44 ± 2 per minute) [14]. Since survival from cardiac arrest improves considerably with more than 80 compressions per minute [15], CO-CPR clearly improves circulatory consistency. Secondly, most sCPR providers (even when trained) pause chest compressions for too long when attempting rescue breaths [14]. This leads to poorer coronary and cerebral perfusion, thus compromising cardiac and neurological outcomes [16]. Thirdly, the psychomotor complexity of balancing both compressions and rescue breaths has been posited to reduce the quality of both chest compressions and rescue breaths. In contrast, CO-CPR is undoubtedly easier to learn and perform due to its simplicity [16]. Multiple bystanders can participate in providing chest compressions, which is crucial for maintaining the quality of compressions by allowing fatigued providers to switch with others [17]. Finally, time to initiation of sCPR is longer compared to CO-CPR, in part due to its psychomotor complexity, as well as fears of the potential risk of infection transmission associated with mouth-to-mouth rescue breaths [18].

The most recent, similar meta-analysis by Bielski et al. included 3 RCTs and 12 observational studies [4]. A key difference in data inclusion is that their review included 12 observational studies in addition to 3 RCTs, which we also included in our review. However, we focused exclusively on RCTs, and, therefore included the Riva et al. trial, which was published after Bielski et al. meta-analysis [7]. By limiting our review to RCTs, the risk of randomization bias was minimal. When broadly comparing our results with those of Bielski et al., they found no significant differences between the outcomes of both CPR types. In contrast, our review revealed that, although most outcomes showed no significant differences, survival to hospital discharge was comparatively higher among patients receiving CO-CPR. The factors contributing to this difference include the inclusion of the most recent RCT in our review and the identification of a data calculation error in the number of patients in the RCT groups receiving CO-CPR vs sCPR in the Bielski et al. review [4].

It is also important to note that the RCTs included in our meta-analysis were done in developed countries with good health literacy and infrastructure. These trials took place in nations where EMS response times are very short, and telephonic CPR instructions are comparatively more accessible due to the availability of well-established EMS systems [19]. The demonstrated superiority of CO-CPR in survival to hospital discharge, along with its non-inferiority in other outcomes, has even more positive implications for developing countries where sCPR is more challenging due to poor health literacy and lack of established EMS systems.

The limitations of this systematic review and meta-analysis arise from some of the inherent limitations in the included RCTs including some issues with blinding, inconsistencies in determining the neurological status of survivors, inconsistent adherence to intention-to-treat analysis, and the limited applicability of dispatcher-directed bystander CPR to CPR performed by healthcare professionals or bystanders with prior BLS training. Additionally, the findings are not applicable to the pediatric population due to the mean age of the study populations in the included RCTs. As pediatric cardiac arrests are more commonly hypoxic, the need for rescue breaths may be preserved [20]. This may also be true in specific OHCA aetiologies including drowning, drug overdoses with respiratory depression, or asphyxia. Further study in these specific populations is warranted.

While data from all four studies confirms the known male preponderance for OHCA [21], none of the studies reported on whether there were any treatment differences between men and women. This precludes any meta-analysis of this topic and constitutes an additional limitation. However, given it is known that women have lower unadjusted resuscitation and survival rates (due to a lower incidence of ventricular fibrillation rhythms) [21], understanding whether CO-CPR versus sCPR has different impacts on men versus women is an important area for future research.

Among the four RCTs included, only three evaluated survival to hospital discharge, and other outcomes were reported by only two trials. Due to the limited number of RCTs, the total number of patients involved was relatively small (n=4987). Hallstorm et al. had the smallest data size, with approximately 250 patients included in each category whereas Rea et al. had the largest data size having approx. of 1000 patients in each category [6,13]. Another limitation is that while CPR instructions were provided to bystanders in the Rea et al. and Riva et al. trials, they were not provided in the Svenson et al. and Hallstrom et al. trials before EMS arrival, which may have compromised the initial quality of CPR. Additionally, lack of sufficient data prevented us from conducting a subgroup analysis based on clinically relevant characteristics such as the type of first cardiac rhythm (shockable vs non-shockable), which could significantly influence survival outcomes [22].

The American Heart Association's BLS guidelines, widely followed across the world, recommend chest compressions combined with rescue breaths (sCPR) for adults experiencing OHCA. There is a growing need for additional RCTs to compare outcomes such as time to ROSC, long-term survival, and the occurrence of cardiac arrhythmias during OHCA. Future studies should particularly focus on rural populations or countries where EMS systems are less advanced and where the number of trained CPR providers is likely to be lower. Conducting RCTs in these settings would provide valuable insights into the effectiveness of different CPR methods in diverse environments [23].

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Online supplementary material:
Supplementary Table 1. Search Strategy for MEDLINE.
Supplementary Figure 1. Forest plot of survival to hospital admission.
Supplementary Figure 2. Forest plot of return of spontaneous circulation.
Supplementary Figure 3. Forest plot of survival to hospital discharge with a good neurological outcome (cerebral performance category 1 or 2).

PRISMA 2020 flow diagram for new systematic reviews which included searches of databases and registers only

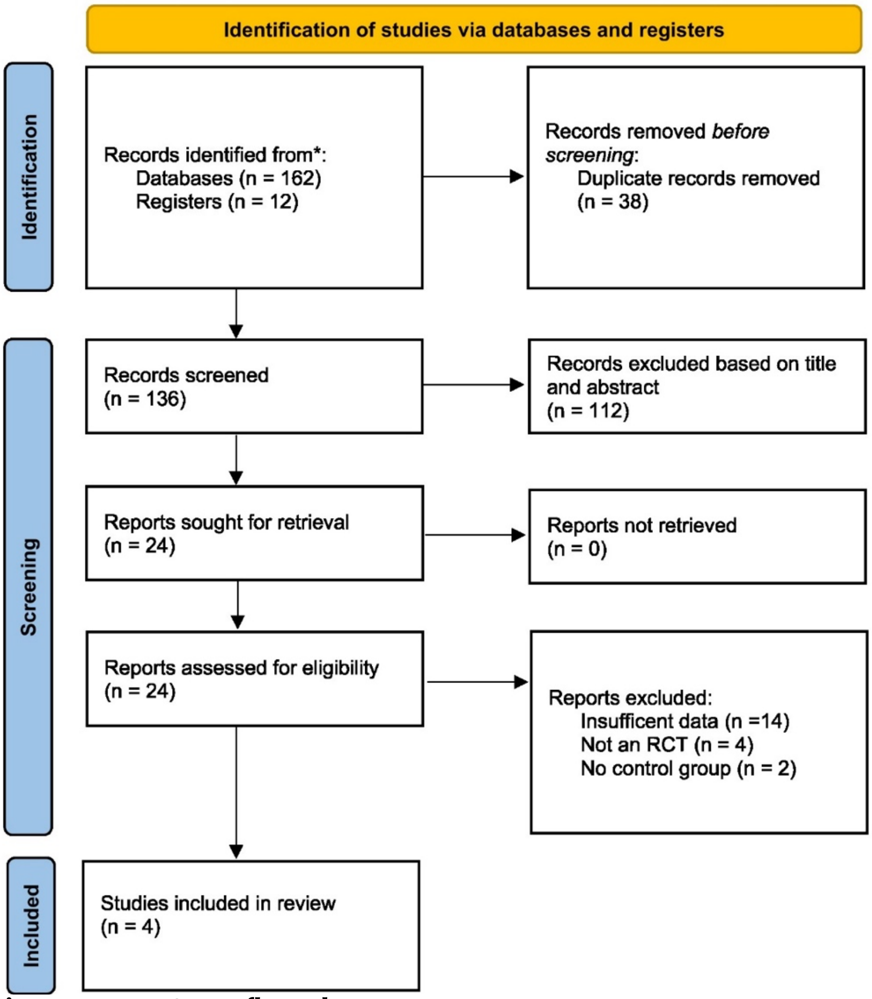

Figure 1. PRISMA flowchart.

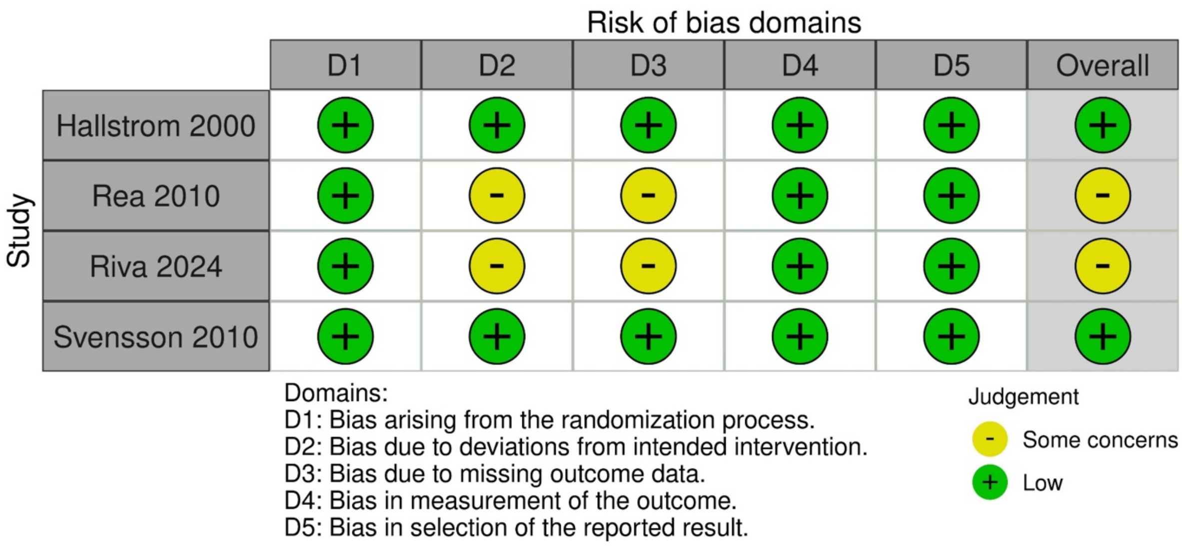

Figure 2. Summary of risk of bias assessment for each randomized control trial included in the meta-analysis.

Study or Subgroup	cCPR Events	cCPR Total	sCPR Events	sCPR Total	Weight	Risk Ratio IV, Random, 95% CI
Hallstrom 2000	35	240	29	278	16.3%	1.40 [0.88, 2.22]
Rea 2010	122	978	105	956	57.5%	1.14 [0.89, 1.45]
Svensson 2010	54	282	44	297	26.2%	1.29 [0.90, 1.86]
Total (95% CI)		**1500**		**1531**	**100.0%**	**1.22 [1.01, 1.46]**
Total events	211		178			

Heterogeneity: Tau² = 0.00; Chi² = 0.76, df = 2 (P = 0.68); I² = 0%

Test for overall effect: Z = 2.06 (P = 0.04)

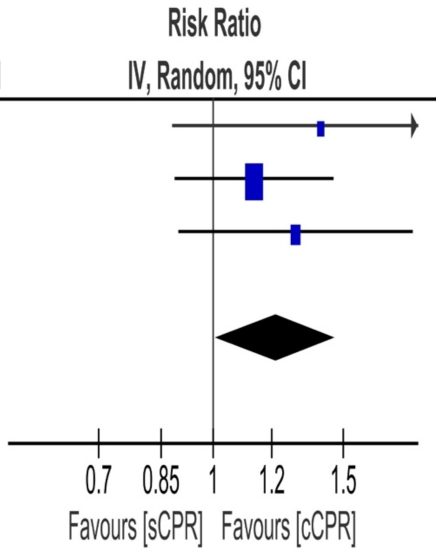

Figure 3. Forest plot of survival to hospital discharge.

Study or Subgroup	cCPR Events	cCPR Total	sCPR Events	sCPR Total	Weight	Risk Ratio IV, Random, 95% CI
Riva 2024	179	640	168	610	56.9%	1.02 [0.85, 1.21]
Svensson 2010	147	613	136	652	43.1%	1.15 [0.94, 1.41]
Total (95% CI)		**1253**		**1262**	**100.0%**	**1.07 [0.94, 1.23]**
Total events	326		304			

Heterogeneity: Tau² = 0.00; Chi² = 0.80, df = 1 (P = 0.37); I² = 0%

Test for overall effect: Z = 1.00 (P = 0.32)

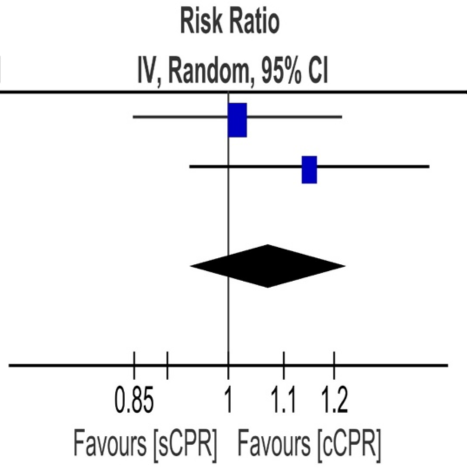

Figure 4. Forest plot of 1-day survival.

Table 1. Study characteristics of included studies.

Study	Country	Standard cardiopulmonary resuscitation							
		No.	**Age**	**Sex (male)**	**Arrest location**	**Witnessed arrest (%)**	**First cardiac rhythm**	**Time to ACLS (min)**	**Time to EMS response (min)**
Hallstrom *et al.* 2000	USA	279	68.5	65%	Home: 248 (90%); public indoors: 7 (3%); public outdoors: 11 (4%); other residence: 12 (4%)	158 (56%)	Shockable (VF): 116 (42%); unshockable (PEA, asystole): 159 (57%)	***N.A.***	4.0
Rea *et al.* 2010	Multi-country	960	63.9	64%	Home*: 837 (88%) Public: 86 (9%) Nursing Home: 34 (4%)	437 (46%)	Shockable: 304 (32%)	10	6.7
Svensson et al. 2010	Sweden	656	67	68%	Home: ___ (76%) Public: ___ (8%) Other: ___ (16%)	***N.A.***	Shockable (VF/VT): 37% Unshockable (Asystole): 54% Unshockable (PEA): 9%	***N.A.***	< 5min: 21.7% 6-8 min: 29.4% 9-15 min: 33.3% >15 min: 15.6%
Riva *et al.* 2024	Sweden	610	74	66%	Home: 421 (70%) Public: 128 (21%) Other: 57 (9%)	482 (81%)	Shockable (VF/VT): 180 (30%)	13.8	***N.A.***