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# Effects of cardiopulmonary resuscitation training on mortality rates after out-of-hospital cardiac arrest: protocol for a systematic review and meta-analysis

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## ABSTRACT

**Introduction** An out-of-hospital cardiac arrest occurs at a rate of 67–170 cases per 100 000 inhabitants per year in Europe. The early recognition of the occurrence of a cardiac arrest, placing an emergency call, performing cardiopulmonary resuscitation (CPR) and performing defibrillation are the most important response measures. The objective of this systematic review and meta-analysis is to assess the effects of laypersons' CPR training with respect to CPR initiation rates, cardiovascular mortality rates, survival rate and the use of an automated external defibrillator.

**Methods and analysis** The literature search will be performed in the following databases: MEDLINE, Web of Science, the Cochrane Central Register of Controlled Studies, CINAHL, HBI, TESEO and NTX. Intervention studies and quasi-experimental studies in which CPR training interventions were performed will be included. We will exclude studies in which the participants do not meet the inclusion criteria, without a control group and in which the methodology of the intervention applied is unclear. There will be no restrictions on publication date or language of publication. The risk of bias will be assessed using the Risk of Bias in Non-randomized Studies of Interventions tool for randomised controlled trials (RCT), non-RCT and quasi-experimental trials. Data analysis and synthesis will be performed using RevMan V.5.4.1 software. The findings will be reported in accordance with Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidance.

**Ethics and dissemination** Ethical approval is not required, as only secondary data will be used. The findings will be published in a journal and presented at conferences.

**PROSPERO registration number** CRD42022365288.

## STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ This work will allow us to understand the influence that cardiopulmonary resuscitation training has on mortality rates after out-of-hospital cardiac arrest and thereby determine which are the most effective measures.
⇒ The methodological quality and risk of bias of clinical trials will be evaluated using the Cochrane Risk of Bias 2.0 and Risk of Bias in Non-randomized Studies of Interventions tools for randomised and non-randomised studies, respectively.
⇒ A meta-analysis may not be possible for certain outcomes due to a limited number of eligible studies and due to heterogeneity of the studies.

## INTRODUCTION

Out-of-hospital cardiac arrest (OHCA) is a major global health problem, with more than 300 000 cases occurring annually in the USA and between 1.5 and 2.8 per 1000 hospital admissions in Europe.[1 2] A high variability exists in the incidence and survival from an OHCA across Europe, according to the EuReCa TWO Study.[3] As of 2021, the overall incidence of OHCA where cardiopulmonary resuscitation (CPR) was attempted was 56 per 100 000 individuals per year, with a range of 21–91 per 100 000 individuals per year. In one-third of the cases (33%), return of spontaneous circulation was achieved, and 8% of patients were discharged from the hospital alive.[1]

The survival rate varies depending on the cause of cardiac arrest, the location where the cardiac arrest occurred and how quickly CPR was initiated.[3 4] As stated in the European guidelines by the European Resuscitation Council (ERC), the most important response measures that can currently be taken outside a hospital setting are: early recognition that a cardiac arrest is occurring, placing an emergency call, performing CPR and performing defibrillation.[2]

Decreasing the time to treatment is crucial for improving outcomes in cases of cardiac arrest.[5] The speed with which CPR is initiated is an important factor in the survival rate, and the International Liaison Committee on

Resuscitation, in its 2023 update, recommended that CPR be initiated within the first 4–6 min after cardiac arrest to maximise the chances of survival.[5]

In Spain, according to the Out-of-Hospital Spanish Cardiac Arrest Registry report, the first link in the chain of survival, which is the presence of bystanders and the performance of early CPR, is critical for improving the survival rate of patients who suffer an OHCA.[6] The report highlights the increase in prior resuscitation by bystanders, including the use of automated external defibrillators (AEDs), perhaps due to the increased instances of telephone-aided CPR from coordination centres. The percentage of patients who survived and were discharged in good neurological condition was 11.1% of the total number of patients included in the study (n=8133). In addition, the report indicated an overall improvement in aspects related to the first links in the chain of survival, suggesting a positive trend in the survival rate.[6]

Despite efforts to generate recommendations on CPR, such as the Life-Saving Systems Guide from the ERC, only an average of 58% of bystanders initiate CPR. AED use is even lower, with an average of 28%.[1] These data contribute to an average survival rate to hospital discharge between 0% and 18%. This is why the ERC recommends CPR training for the general population, from school-age children to adults.

When trained, the general population will take on the role of the first responder in these situations, making their training and education essential. Globally, CPR is taught to millions of people each year. In Sweden, more than 3 million people (of a population of 9.7 million) have undergone CPR training during the past three decades.[7]

However, in recent years, the value of bystander CPR has been debated in the medical community. Only a few studies have examined trends in survival from OHCA using population-based cohorts. Some studies have shown that OHCA survival has most consistently improved among witnessed arrests with shockable rhythms, while others show no change in survival rates over time.[4] We therefore set out to investigate the effects of CPR training of students and laypersons on mortality rate, CPR initiation rate and AED use.

## METHODS AND ANALYSIS

### Study registration

This study was registered on the International Prospective Register of Systematic Reviews (PROSPERO) database on 22 October 2022 (CRD42022365288). The results will be reported in accordance with Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 guidance.[8]

The present protocol encompasses a systematic review and meta-analysis that will review the main effects of CPR training on the use of an AED, on mortality rate after OHCA and on resuscitation initiation rates.

### Eligibility criteria

#### Types of studies

Intervention studies (clinical trials—randomised or non-randomised) and quasi-experimental studies that report interventions using CPR training will be included. The latter must necessarily include a control group. Observational studies (cross-sectional and cohort) will be considered as well.

#### Participants

We will include studies whose sample is composed of undergraduate students, primary and secondary school students, general population, laypersons, and community participants with or without prior CPR training and/or CPR guided by dispatcher assistance.

#### Types of interventions

Studies will be included in which training interventions in basic life support with the use of AEDs and studies explicitly addressing the differentiation between trained bystanders, those guided by the dispatcher, and those with training and dispatcher assistance were carried out.

#### Outcome measures

The main expected outcome is the effects of CPR training on CPR initiation rates, mortality rates after OHCA, survival rate after OHCA and use of an AED. The studies to be included must present at least one of the expected outcomes.

#### Exclusion criteria

A study will be excluded:

- If it included participants with physical disabilities, intellectual disabilities, neuroendocrine disorders, chronic diseases (cardiovascular diseases, diabetes) and pregnant women.
- If there is no control group, non-school-based comparisons, intervention or undergoing interventions other than CPR training.
- If the methodology of the applied intervention is not clear.

### Search strategy

The reviews will follow these steps:

- Apply the inclusion and exclusion criteria during searches in the databases by reading the titles and abstracts.
- Apply the eligibility criteria after the complete reading of the articles selected in the initial stage.
- Assess the methodological quality and the risk of bias of the articles included in the previous step.
- Qualitative synthesis of data from selected articles (narrative synthesis or meta-analysis).
- Quantitative synthesis of data from selected articles (meta-analysis).

The research questions guiding the proposal are as follows: What are the effects of CPR training on the rates of using an AED?; What are the effects of CPR training on

Table 1 Data extraction table

| Data to be extracted | Item |
|---|---|
| Publication ID | Title, first author, publication year, country, study name, population |
| Study design | Randomised controlled trials (RCTs)<br>Non-RCTs<br>Quasi-experimental studies |
| Participants' characteristics | Sex<br>Age<br>Sample size<br>Prior CPR training<br>CPR guided by dispatcher assistance |
| Control group | No intervention<br>Other interventions (no CPR) |
| Intervention characteristics | Duration of intervention<br>Follow-up period<br>Intervention description<br>CPR training approach<br>Associated social factors |
| Outcome measurements | CPR initiation rates<br>Mortality rate after OHCA<br>Survival rate after OHCA<br>Use of automated external defibrillator |
| Analysis methods | Statistical methods used<br>Qualitative synthesis |

CPR, cardiopulmonary resuscitation; OHCA, out-of-hospital cardiac arrest.

mortality rate after OHCA? and What are the effects of CPR training on resuscitation initiation rates?

### Electronic search

The search will be performed from database inception in the following databases: MEDLINE (via PubMed), Web of Science-Clarivate Analytics, the Cochrane Central Register of Controlled Studies, CINAHL, EMBASE and SCOPUS.

A free combination of Medical Subject Headings terms and keywords will be performed, as shown in table 1. The search equation will be defined considering the following items: participants (undergraduate students, primary and secondary school students; general population; laypersons, community participants with or without CPR training and/or CPR guided by dispatcher assistance), intervention (CPR training), outcomes (effects of CPR training on CPR initiation rates; mortality rates after OHCA; survival rate after OHCA; AED use rate and the ability of the trained individuals to transmit the knowledge acquired in the training; studies with details from the interventions) and study design (clinical trial, intervention, observational).

The search terms for creating the equations will be combined with specific filters in each database, as shown in the draft search strategy in the online supplemental material. There will be no restrictions on publication date or language in the searches. In cases where articles are published in languages other than those the researchers are fluent in, the authors will use translation services.

### Additional search

To ensure the wide scope of this research, we will complement the electronic searches with a manual search in the reference lists of the retrieved studies or relevant reviews that are related to the topic.

### Data extraction

For all the studies identified, at least two authors will independently select and review titles and abstracts using the Rayyan QCRI tool.[9] The articles that meet the inclusion criteria will be obtained for a full review. Any disagreement will be resolved by discussion with a third reviewer. A manual search will be performed if any relevant studies are found using the defined search strategies. All the researchers will then review the full text of all eligible studies. The information on the phases of the selection process will be described through a PRISMA flow diagram[8] (figure 1).

Two reviewers will extract the following information from the selected relevant studies: publication identity (ID), participant characteristics, control group, intervention characteristics, outcome measures and analysis methods. The data to be extracted are available in table 1. Any disagreement will be resolved through a discussion and review of the article, and a third researcher will be consulted.

## Data synthesis

### Evaluation of methodological quality

Two independent researchers will carry out the evaluation, and in case of doubts or discrepancies, a third researcher will be consulted. The methodological quality of randomised clinical trials will be assessed using the Revised Cochrane risk of bias tool for randomized trials.[10] The following criteria will be evaluated in intervention studies: random sequence generation, allocation concealment, blinding of participants and those responsible for the intervention, and evaluation of results. In addition, incomplete outcome data, selective reporting, funding and the potential for conflicts of interest associated with individual trials will also be considered. The risk of bias will be ranked using predetermined criteria such as: low, high or clear.

For non-randomised, before–after controlled studies, the risk of bias will be assessed using the Risk of Bias in Non-randomized Studies of Interventions (ROBINS-I) tool. The ROBINS-I was developed to assess the risk of bias in the results of non-randomised studies that compare the effects of two or more interventions on the health of the study population.[11]

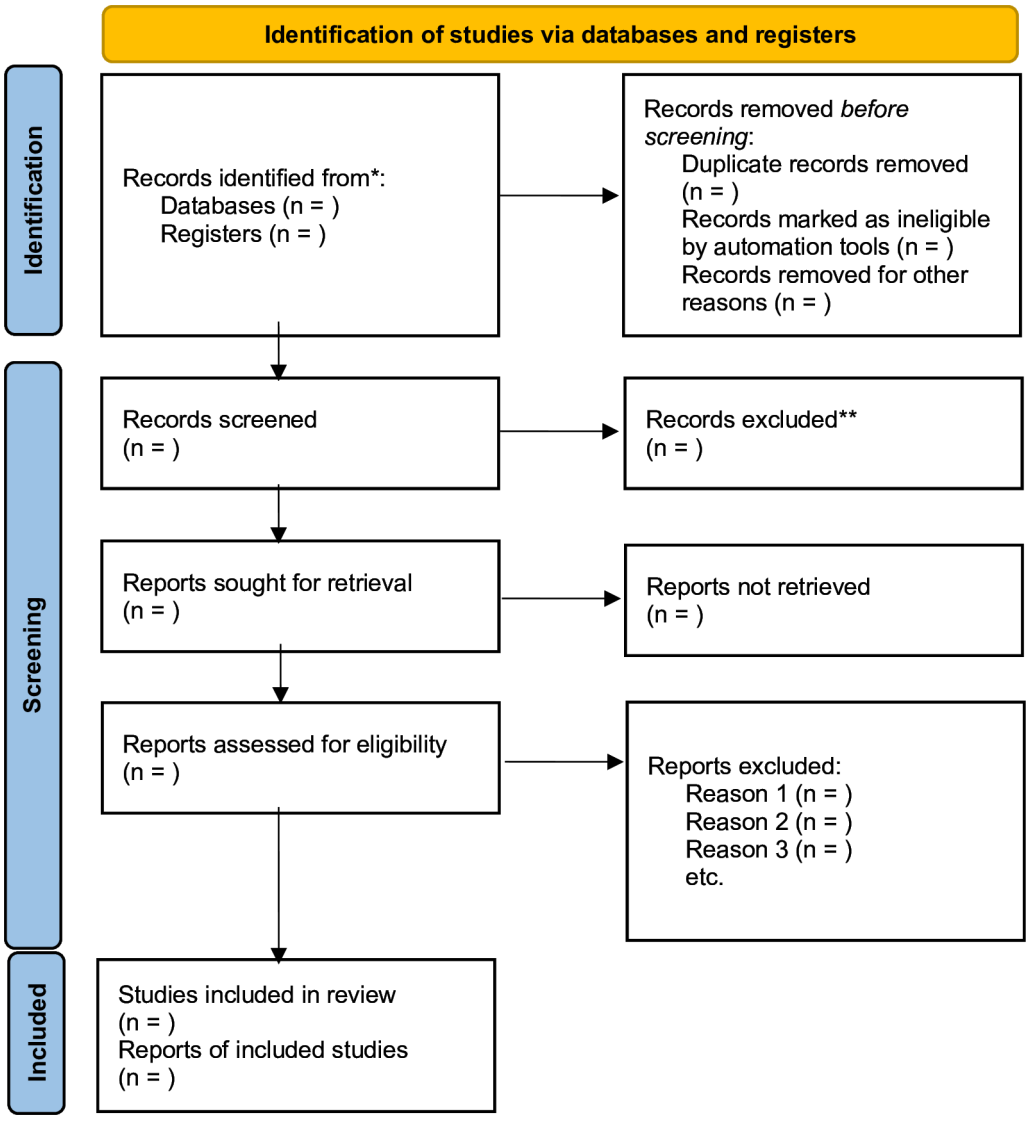


**Figure 1** Preferred Reporting Items for Systematic Reviews and Meta-Analyses flow chart of study selection.

For qualitative studies, the Critical Appraisal Skills Program will be used to analyse the risk of bias. This instrument corresponds to a checklist of 10 questions, 9 referring to quality and 1 to 'value' (contribution to the existing literature),[12] and its use is recommended by the Cochrane Collaboration for qualitative literature.[13]

The overall strength of evidence for each outcome will be analysed using the Grading of Recommendations Assessment, Development and Evaluation tool.[14]

### Data analysis

A narrative approach will be used to summarise the effects of CPR training. If the studies are sufficiently homogeneous, a quantitative synthesis will be performed.

The meta-analysis of the included studies will be performed using statistical software (RevMan V.5.4.1). The heterogeneity between assay results will be evaluated by performing a standard $X^2$ test with a significance level of 0.05. To assess heterogeneity, the $I^2$ statistic will be calculated, corresponding to a quantitative measure of inconsistency between studies. A value of 0% indicates that no heterogeneity was observed, $I^2$ values of 50% indicate a moderate level, and 75% or higher indicate a substantial level of heterogeneity.

If possible, funnel plots will be used to assess the presence of potential reporting biases. A linear regression will be performed to evaluate the asymmetry of the funnel plot. If the studies are very heterogeneous, a narrative synthesis will be carried out. If studies with a qualitative approach are analysed, a meta-synthesis will be performed to synthesise the data from the included studies.

### Missing data

In case of missing or unclear data—with an uncertain risk of bias—considered possibly important for this evaluation, an attempt will be made to contact the researchers who authored the article. If it is not possible to resolve doubts regarding the article's data after contacting the authors, an analysis will be carried out with the available data and a discussion will be crafted on the possible impact of missing data.

### Subgroup analysis

If sufficient data are available, the following subgroup analyses will be performed: specific details of the interventions (eg, methodological strategy, components and duration) and research setting (family participation, influence of prior CPR training and CPR guided by dispatcher assistance and socioeconomic conditions).

## Patient and public involvement

None.

## ETHICS AND DISSEMINATION

Ethical approval and participant consent are not required, as only secondary data will be used. The findings will be published in a peer-reviewed journal and presented at conferences. In case of any changes to this protocol, the PROSPERO registration record will be updated and the modifications will be explained in the final report of this review.

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**Contributors** PMAA, TTdS, GP, DGM and MP-R conceptualised, designed and supervised the protocol. PMAA, TTdS, GP, DGM, MFP and MP-R will be responsible for methodology, data curation and formal analysis. PMAA, MFP and TTdS will be responsible for investigation. MP-R will be the third party and will host consensus meetings at each stage in case of disagreement. PMAA and TTdS were responsible for writing the original draft. PMAA, TTdS, GP DGM and MP-R are responsible for project administration and were responsible for reviewing and editing the manuscript. All authors read, reviewed and approved the final protocol.

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**Competing interests** None declared.

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