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Title: A Systematic Review and Meta-Analysis of the Effect of Dispatcher-Assisted CPR on Outcomes from Sudden Cardiac Arrest in Adults and Children.

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Abstract: BACKGROUND: Dispatcher-assisted cardiopulmonary resuscitation (DA-CPR) has been reported in individual studies to significantly increase the rate of bystander CPR and survival from cardiac arrest.

METHODS: We undertook a systematic review and meta-analysis to evaluate the impact of DA-CPR programs on key clinical outcomes following out-of-hospital cardiac arrest. We searched the PubMED, EMBASE, CINAHL, ERIC and Cochrane Central Register of Controlled Trials databases from inception until July 2018. Eligible studies compared systems with and without dispatcher-assisted CPR programs. Included studies were divided into three groups: comparison of outcomes in systems providing DA-CPR; comparison of cases where DA-CPR was provided to cases where bystander CPR was ongoing, and DA-CPR was not provided; and comparison of cases where DA-CPR was provided to cases where no bystander CPR was provided (patient level comparisons). The GRADE system was used to assess certainty of evidence at an outcome level. We used random-effects models to produce summary effect sizes across all outcomes.

RESULTS: Of 5,531 citations screened, 33 studies were eligible for inclusion. All included studies were observational. Evidence certainty across all outcomes was assessed as low or very low. In system-level and patient-level comparisons, the provision of DA-CPR compared with no DA-CPR was consistently associated with improved outcome across all analyses. Comparison of DA-CPR to bystander CPR produced conflicting results. Findings were consistent across sensitivity analyses and the pediatric sub-group.

CONCLUSION: These results support the recommendation that dispatchers provide CPR instructions to callers for adults and children with suspected OHCA.

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A Systematic Review and Meta-Analysis of the Effect of Dispatcher-Assisted CPR on Outcomes from Sudden Cardiac Arrest in Adults and Children.

Running Title: **Nikolaou – DA-CPR systematic review**

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ABSTRACT (348 words)

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RESULTS: Of 5,531 citations screened, 33 studies were eligible for inclusion. All included studies were observational. Evidence certainty across all outcomes was assessed as low or very low. In system-level and patient-level comparisons, the provision of DA-CPR compared with no DA-CPR was consistently associated with improved outcome across all analyses. Comparison of DA-CPR to bystander CPR

produced conflicting results. Findings were consistent across sensitivity analyses and the pediatric sub-group.

CONCLUSION: These results support the recommendation that dispatchers provide CPR instructions to callers for adults and children with suspected OHCA.

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INTRODUCTION

Out-of-hospital cardiac arrest (OHCA) is a significant cause of death world wide[1] with an annual rate of between 55 and 113/100,000 person-years.[2] The immediate commencement of cardiopulmonary resuscitation (CPR) by bystanders increases the likelihood of a meaningful neurological recovery.[3,4] The majority of cardiac arrests are witnessed by someone that could initiate this life-saving intervention, yet rates of bystander CPR in many systems are disappointingly low. [5,6]

A key challenge is that bystanders may be untrained or uncomfortable in performing CPR without assistance.[7] Dispatcher-assisted CPR (DA-CPR), also known as telecommunicator-assisted CPR (T-CPR), is a system in which dispatchers provide CPR instructions to emergency callers over the telephone. The goal of this approach is to increase the performance of bystander CPR, and ultimately improve survival.[8]

In 2010, Bohm et al conducted a systematic review which concluded that evidence supporting the use of DA-CPR was limited.[9] The subsequent publication of additional studies led to clinical experts within the International Liaison Committee on Resuscitation (ILCOR) recommending the re-examination of this question as a key research priority within their continuous evidence evaluation process[10].

METHODS

We conducted a systematic review and meta-analysis to evaluate the effect of DA-CPR provision, compared with no DA-CPR provision, on key clinical outcomes in cases of suspected OHCA.

The review was performed in accordance with and funded by the ILCOR continuous evidence evaluation process.[10] This report complies with the PRISMA checklist for reporting systematic reviews.[11] We used the GRADE (Grading of Recommendations, Assessment, Development and Evaluation) approach to categorise certainty of evidence.[12] Our protocol was registered with the PROSPERO database (PROSPERO - CRD42018091427).

Inclusion and Exclusion Criteria

All primary research studies including human participants, adult and pediatric patients, with cardiac arrest outside a hospital setting, and which reported outcomes of interest were included. Randomised controlled trials (RCTs) and non-randomised studies (non-randomised controlled trials, interrupted time series, controlled before-and-after studies, cohort studies) were eligible for inclusion.

Studies including animals, simulated patients and humans without a comparator group were not eligible. We also excluded commentaries, reviews, and studies not published in peer-reviewed journals or only as abstracts.

Information Sources and Search Strategies

In collaboration with an expert information specialist, we conducted a comprehensive search of five electronic databases: PubMED, EMBASE, CINAHL, ERIC, and the Cochrane Library from inception to July 1, 2018. The search strategy combined MESH and free text terms to describe the population and the intervention/comparator. No language or geographic restrictions were applied. A full

search strategy is included in the electronic supplement. Search results from all five databases were merged and duplicate references were manually discarded. Additional citations were identified through backward citation tracking of the included studies, consultation with clinical experts on ILCOR task forces, and a search of clinical trials registries.

Study Selection and Data Extraction

Titles and abstracts of all studies that resulted from the search were independently screened by two experienced reviewers (NN and KND) to determine eligibility for full-text review. The same reviewers reviewed full text articles of all potentially relevant articles and extracted data from eligible full-text articles. Data collection forms were developed and pilot-tested to capture relevant data. Each step of review was discussed, and any incongruence was resolved by consensus.

Outcomes

Outcomes were pre-defined and ranked by the ILCOR BLS and Pediatric Task Forces (see electronic supplement). The clinical outcomes of interest were: health related quality of life; favorable neurological outcomes; survival; rate of bystander CPR; return of spontaneous circulation (ROSC); initial shockable rhythm; and time to CPR.

Assessment of Risk of Bias and evidence certainty

Two reviewers (KND and JT) independently assessed each included study for risk of bias using the GRADE handbook[12] advice and the Cochrane Methods Group

template for observational studies.[13] For each outcome, two reviewers (KC, NN) also assessed publication bias according to the criteria defined by GRADE (study design, study size, lag bias, and comprehensiveness of search strategy).

We categorised the overall certainty of evidence for each outcome using the approach recommended by GRADE.

Data Synthesis and Analysis

The results of included studies were classified into 3 categories for the purposes of more accurate analysis: comparison of outcomes in systems with DA-CPR programs, case-based comparison of DA-CPR to bystander CPR, and case-based comparisons of DA-CPR to no CPR before EMS arrival. Summary effect sizes were produced across all outcomes and a subgroup analysis was pre-specified for pediatric studies.

Given the observational nature and the differences in settings and population of included studies we could not assume a common effect size, so we used a random effects model for meta-analysis, to avoid discounting a small study by giving it a very small weight (as in a fixed-effect analysis). We used Review Manager software (Version 5.1. Copenhagen: The Nordic Cochrane Centre, the Cochrane Collaboration, 2011), to calculate combined odds ratios (ORs) with 95% confidence intervals and measure statistical heterogeneity. Heterogeneity between studies was described using the I^2 statistic. The I^2 was categorized according to GRADE recommendations as low, moderate, substantial or considerable.[14] To avoid reducing the number of studies available for synthesis, mainstream analyses included studies reporting unadjusted data. When there were studies coming from the same region and with overlapping

populations, only the study (or combination of non-overlapping studies) that provided the largest number of participants was used.

We also performed a sensitivity analysis including only studies reporting ORs adjusted for the confounders that were deemed most important for each outcome by the study authors. These two analyses were presented in GRADE tables and the overall certainty of evidence was evaluated according to GRADE. Data from the pre-specified subgroup analysis for the pediatric group i.e. number and combined effect size of pediatric studies and heterogeneity with regard to the rest of the studies, were also presented in the summary of findings tables. Raw data were used in order to calculate unadjusted summary ORs while the generic inverse variance method was used in order to combine the reported adjusted odds.

Additional sensitivity analyses were performed replacing excluded studies with the next largest study and so on until all studies from the same region were entered. These analyses were not entered into GRADE tables and the overall certainty of evidence was not assessed but they are included in Appendix B. These analyses were used to assess robustness of the combined effect size that has been calculated for each outcome.

RESULTS

Overall Description of Included Studies

A total of 5,531 citations were identified through the search methods described above. Of these, 93 full text articles were reviewed, and 33 studies were included in this

191 systematic review.[15-47] Of the 60 studies excluded at the full text stage, the majority
192 were removed due to the lack of a comparison between DA-CPR and no DA-CPR (see
193 Figure 1 for the detailed PRISMA flowchart).
194
195 ***Study Characteristics***
196 A total of 33 studies reported on the effectiveness of dispatcher-assisted CPR in
197 out-of-hospital cardiac arrest. Geographically, the studies were conducted in a range of
198 countries with the majority from Japan (n = 10), United States (n = 6) and Korea (n=6)..
199 A total of 544,037 cases (Table 1) were included. The median number of participants
200 per study was 803 patients (IQR: 392 to 4,899 patients; Range: 145 to 193,914
201 patients). No RCTs were identified. All the included studies were observational and
202 included 11 retrospective cohort studies, 9 prospective cohort studies, 7 retrospective
203 before-after studies and 6 cross-sectional studies. The duration of follow-up ranged
204 from 1 month to 1 year following cardiac arrest. Of the 33 total studies, the number
205 included in each meta-analysis for the outcomes of interest was variable due to the
206 inconsistent nature of reporting in each of the studies. The way in which studies with
207 overlapping data were entered in the mainstream and sensitivity analyses is shown in
208 Appendix C.
209
210
211 ***Patient Characteristics***
212 Of the 33 included studies, 15 were conducted in the adult population
213 only[16,20,22,25,27,31,34,37,41-45,47,49], five were conducted in the pediatric population

214 only[15,18,26,33,40], and 13 included both adults and children[17,19,21,23,28-30,32,35-37,45,48]. The
215 proportion of males ranged from 52% to 85% (average 66%). The age reported for
216 adult-only studies ranged from 18 to >90 years and ranged between 0 to 19 years for
217 pediatric-only studies (Table 1).

218
219 ***Risk of Bias Assessment***

220 All of the included studies were observational cohort studies and most were
221 retrospective (18/33). With respect to overall risk of bias, 1 study was deemed at low
222 risk of bias, 16 were at moderate risk of bias, and 16 were at high risk of bias (Table 2).
223 The main methodological shortcoming was related to the comparability of cohorts on the
224 basis of the design or analysis, as the majority did not adjust for potential confounding
225 variables. In addition, some studies were not clear about their assessment of exposure
226 and the majority did not report the duration of follow-up or how they dealt with missing
227 data.

228
229 ***Outcomes***

230 The results of included studies were classified into 3 categories for the purposes
231 of more accurate analysis: comparison of outcomes in systems with DA-CPR programs,
232 comparison of DA-CPR to bystander CPR, and comparisons of DA-CPR to no CPR
233 before EMS arrival. For the comparisons of DA-CPR provided versus not provided, we
234 were able to compare 11 outcomes, 7 of which had adjusted analyses. For DA-CPR
235 compared to bystander CPR, we were able to compare 12 outcomes, 7 which had
236 adjusted analyses. For DA-CPR compared to no CPR, we were able to compare 11

outcomes, 5 which had adjusted analyses. The studies included in each analysis are indicated in Table 4-6. The outcomes of interest were then analyzed within each category and a summary of findings is outlined in Table 3 and Figure 2. The number of confounders that were adjusted for in the multivariable analyses ranged from 4 to 11. The most frequently used ones were: gender 11/ 14 (79% of studies), witnessed arrest 10/14 (71% of studies), location of arrest (public vs. home, 9/14- 64% of studies), call to response time 9/14 (64% of studies), shockable initial rhythm 6/14(43% of studies), and etiology of cardiac arrest 5/14 (36% of studies).

A. System Comparison

This analysis represents those published comparisons of before-after retrospective studies but also studies where emergency medical systems had DA-CPR programs in place but where the protocol was applied variably, ie. within an EMS system, outcomes for those patients who received DA-CPR compared to those who did not. A summary of findings for this group is outlined in Table 4. Evidence Profile tables for these comparisons appear in Appendix G.

Survival with Favourable Neurologic Outcome

Among the studies included, survival with favourable neurological outcome was recorded at hospital discharge (2 studies reported unadjusted analyses[17,42]; 1 study reported adjusted analyses[42]) and one-month (3 unadjusted[26,28,44] ; 2 adjusted[26,28]). In unadjusted analyses, DA-CPR was associated with improved survival with favourable neurological outcome at discharge and one-month (OR 1.10; [1.03,1.17]). Adjusted

analyses produced similar findings (AOR 1.47; [1.03,2.09]). Certainty of evidence was assessed as very low for all analyses.

Survival

Survival was reported at three time-points: hospital admission (unadjusted six studies[17,24,28,35,42,46] adjusted one study[28]); one-month (unadjusted two studies[26,28]; adjusted two studies[26,28]) and at hospital discharge (unadjusted seven studies[16,19,29,32,42,43,46]; adjusted one study[42]). Systems with Dispatcher-Assisted CPR programs were not associated with significantly improved survival at any time-point in unadjusted analyses, although the point estimate suggested benefit. In adjusted analyses, DA-CPR was associated with improved outcome at 1-month (AOR 1.40; [1.07,1.85]) and at hospital discharge (AOR 1.33; [1.07,1.66]), but not at hospital admission (AOR 0.97 [0.70, 1.34]). Certainty of evidence was assessed as very low in all analyses (Table 4 and Appendix G).

Other Outcomes

Data for ROSC, initial shockable rhythm and time to CPR all favoured DA-CPR (see Appendix G for details).

B. DA-CPR versus Bystander CPR (Table 5, Appendix H)

Survival with Favourable Neurologic Outcome

Survival with favourable neurologic outcome was reported at 1 month (unadjusted data was available in 2 studies[28,45], adjusted data from 1 study[31]) and at

hospital discharge (unadjusted data from 3 studies[18,37,48], adjusted data from 1 study[40]). Unadjusted data at both time points suggested less favourable outcomes and showed an association between DA-CPR and less favourable outcomes (OR 0.73; [0.68,0.77] and OR 0.83; [0.70,0.98]). The adjusted data suggest no difference between the groups at 1 month or at hospital discharge (AOR 1.0; [0.91,1.08] and AOR 1.12; [0.94,1.34]).

Survival

Survival was reported at three time points: at hospital admission (unadjusted data in 1 study[28]), at 1 month (unadjusted data from 5 studies[26,27,28,31,47], adjusted data from 2 studies[31,47]) and at hospital discharge (unadjusted data from 9 studies[16,18,22,29,36,37,38,41,48], adjusted data from one study[40]). At hospital admission, DA-CPR was not associated with improved outcome (OR 0.71; [0.31,1.60]), but was associated with less favourable outcomes at 1 month (OR 0.75; [0.60,0.95]) and at hospital discharge (OR 0.73; [0.67,0.81]. The adjusted data indicated a potential survival benefit with DA-CPR at 1 month (AOR 1.13; [1.06, 1.20]) , but not at hospital discharge (AOR 0.95; [0.83-1.09]).

Other Outcomes

Data for ROSC, initial shockable rhythm and time to CPR all favoured DA-CPR (see Appendix G for details).

C. DA-CPR vs. No CPR (Table 6, Appendix I)

Survival with Favourable Neurologic Outcome

When comparing DA-CPR to no CPR with regard to survival with favourable neurologic outcome at hospital discharge, both unadjusted [20,34,37,48] from four studies (OR 2.21; [1.44,3.40]) and adjusted[18,40,48] data from three studies (AOR 1.54; [1.35, 1.76]) indicated a benefit with DA-CPR. The same was true for survival with favourable neurologic outcome at 1 month [26,28,45] (OR 1.45; [1.38,1.53] and AOR 1.81; [1.23, 267]).

Survival

Survival in this group was reported at hospital, hospital discharge and at 1 month. Unadjusted analyses at hospital admission [20,28,34] (OR 1.54; [0.62, 3.83]) and at 1 month [26,27,28] (OR 1.68; [0.63, 4.45]) indicated no survival benefit with DA-CPR, however adjusted analysis at 1 month[26] was associated with improved survival (AOR 1.63; [1.32, 2.01]). These studies had very low certainty with serious risk of bias. For survival at hospital discharge both unadjusted[16,18,20,22,29,34,36,37,38,40,41,48] (OR 1.67; [1.39, 2.0]) and adjusted[18,38,40,48] analysis (AOR 1.40; [1.09, 1.78]) indicated benefit with DA-CPR.

Other Outcomes

Data for ROSC, initial shockable rhythm and time to CPR all favoured DA-CPR (see Appendix G for details).

Pediatric Studies

Subgroup analyses were performed for all mainstream and sensitivity analyses where pediatric studies were available. Heterogeneity ranged from none to substantial.

For all critical outcomes where data were available any observed heterogeneity was due to larger magnitude of effect in the pediatric group while the direction of effect was always similar (Table 3). For the important outcome of shockable initial rhythm there was considerable heterogeneity in mainstream analysis for the system based comparison. The OR was 0.74 (0.54-1) for the pediatric group (1 study[26]) and 1.15 (1.10-1.19) for the adult studies[27,40,43,45]. The heterogeneity was not confirmed in a sensitivity analysis where Goto et al (2014)[25] was replaced by the overlapping study of Akahane et al (2012).[15]

For the same outcome, two sensitivity analyses for the comparison of DA-CPR vs. no CPR indicated lower rates of initial shockable rhythm with DA-CPR, while the mainstream analysis and the other 3 of 5 relevant sensitivity analyses indicated higher rates of shockable rhythm with DA-CPR

Sensitivity Analyses

In sensitivity analyses, we explored the impact of study selection in relation to overlapping study samples. These analyses showed that study selection did not affect our overall review findings (appendices D-F). The hierarchy of how overlapping studies were handled is outlined in Appendix C.

DISCUSSION

In this systematic review and meta-analysis which included 33 studies and

544,037,cases, we found evidence that the provision of DA-CPR, compared with no bystander CPR, is associated with improved patient outcome in cases of suspected OHCA. In our comparison of DA-CPR with Bystander CPR the unadjusted and adjusted analyses showed divergent results, with the unadjusted data actually showing an increased benefit of Bystander CPR without dispatcher assistance and the adjusted analysis showing increased benefit of dispatcher-assisted CPR. Across all analyses, certainty of evidence was assessed as either very low.

Previous Work in this Area

This updated review supports the 2017 International Consensus on Cardiopulmonary Resuscitation and Emergency Cardiovascular Care Science with Treatment Recommendations (COSTR) which recommended that dispatchers provide CPR instructions to callers for adults and children with suspected OHCA[48]. The systematic review on which that COSTR was based was conducted in 2015[49]. Since then several new studies have been added to the literature. This review significantly enhances the work previously completed in that it is based on a very robust search, reports both adjusted and unadjusted analyses and includes important subgroup and sensitivity analyses based on the nature of the included papers (i.e. accounting for several overlapping datasets, etc.) in order to ensure complete transparency about the meta-analyses.

Interpretation of Findings

The beneficial effects seen can likely be attributed to a few different reasons. Firstly, an increase in BCPR with DA-CPR (from 28.9% to 64% in unadjusted analysis)

was confirmed in all sensitivity analyses and analyses of adjusted odds. Secondly, there was an increase in sustained ROSC evident in unadjusted and sensitivity analyses. Lastly, there was also higher (but not significant) unadjusted odds for the presence of shockable rhythm on arrival of EMS (OR 1.1 (0.97-1.24). In terms of the diminished time to CPR, DA-CPR may increase time compared to BCPR but also decrease time to CPR if first provided by emergency response personnel. The existing evidence from 1 study indicates a shorter time to CPR[26]. The direction of effect for these patients has been confirmed by adjusted and sensitivity analyses for the majority of the outcomes.

There are several challenges for the generalizability of the magnitude of effect in this analysis. The effect was expected to be lower in cases where there is very rapid response time from EMS[19,45], to vary according to the baseline BCPR rates and to be affected by the quality of DA-CPR program and the existence of quality assurance programs. Such programs can impact the rates of recognition of OHCA, time to deliver DA-CPR, and how instructions for DA-CPR are delivered (DA protocol, dispatcher handling delays induced by the caller). The effect can also be affected by the previous training experience of bystanders, their likelihood to follow the DA-CPR instructions, and the quality of the CPR provided[41]. Across 21 European countries that participated in the EURECA-1 study, less than one third of patients received DA-CPR[50]. In light of our review findings, these data highlight the opportunity, to save more lives through the establishment of systems that ensure the effective delivery of DA-CPR in all cases of

OHCA, such as some of the recent work done on dispatcher training and changes in the language used on such calls[51,52].

Pediatric Findings

This systematic review added 3 pediatric studies (Ro 2016[33], Lee 2017[40], Chang[18]) to the 2 studies (Akahane 2012[15], Goto 2014[26]) from the previous iteration in 2015 and performed additional subgroup analyses comparing these to the adult studies. We found that the results of the meta-analysis of pediatric studies were consistent in direction of effect with the adult studies for the 3 grouped analyses and for sensitivity analyses for all critical outcomes. When heterogeneity was substantial (DA-CPR vs no CPR and select sensitivity analyses), it was due to a larger magnitude of effect in pediatric studies.

Analytic Challenges with Data Quality

This was a very complex meta-analysis due to the variability in data reporting, lack of proper adjustment for confounders and the low certainty of evidence. It may be difficult to conduct a true randomized trial given the known benefits of bystander CPR and therefore we are likely to be left with observational studies of varying quality on which to base our advice. We chose to report both unadjusted and adjusted analyses in order to be transparent about the data on which our recommendations are based. There were several reasons for doing so. Only 14 of the 31 studies reported adjusted data. Reporting only studies with adjusted data would have led to the exclusion of studies with 205,382 patients. Most of the studies reported adjusted data only for their

primary outcomes. Therefore, study participants are even fewer for secondary outcomes (critical or important for this meta-analysis). Studies with adjusted data often had fewer participants across all outcomes; a median 7,639 fewer (range: 0 to 92,541 fewer). The unadjusted and adjusted data were equal in number to crude OR for only 2 outcomes. Also, studies reporting adjusted odds did not always provide higher overall certainty of evidence when compared with those reporting crude ORs. This was due to the presence of serious or very serious risk of bias in both adjusted and unadjusted data, leading to a very low overall certainty of evidence. Downgrading for inconsistency was more often present in the adjusted analyses. Upgrading for large magnitude of effect and plausible confounding occurred more often in the unadjusted data.

Adjusting for confounders confirmed benefit for system-based comparisons and in patient-based comparisons when DA-CPR was compared to No CPR. For patient-based comparisons, the combined adjusted ORs for DA-CPR vs. BCPR tended to offset the increased benefit that was observed with BCPR. In all publications where this information was provided, patients who received bystander CPR often had a witnessed cardiac arrest occurring in public locations with shorter time to CPR. Therefore, it is possible that the increased benefit with BCPR may be due the effect of these confounders on unadjusted ORs.

Strengths & Limitations

The strengths of this systematic review include its rigorous methods including collaboration with an experienced information scientist to develop and conduct the

search, the use of double screening, data extraction and risk of bias assessment, consultation with world experts from the ILCOR BLS and Pediatric Task Forces throughout the process and the presentation of both unadjusted and adjusted data for transparency.

As with all research, the current work also has some limitations including the incongruity and complexity of the data, overlap of datasets in several studies, the high risk of bias and confounding. The included cohort studies were methodologically flawed because most did not adjust for confounding variables in their analysis. The adjusted ORs remained similar to that of the crude ORs for system-based comparisons and for patient-based comparisons where DA-CPR was compared to no CPR. Adjustment for confounders tended to reduce confidence in unadjusted ORs only when DA-CPR was compared to cases with bystander CPR. Consequently, we present both unadjusted and adjusted data here to be clear about why results might not be reliable and should be interpreted with caution.

CONCLUSIONS

Dispatcher-assisted CPR is associated with a beneficial effect on patient outcomes following out-of-hospital cardiac arrest. When comparing DA-CPR to no CPR, both the unadjusted and adjusted analyses show DA-CPR provides better results in terms of survival with favourable neurologic outcome, survival to hospital discharge, and return of spontaneous circulation. Findings were consistent across sensitivity and sub-group analyses, however evidence certainty for all outcomes was assessed as low or

very low.

In terms of areas identified for future research, only one study to date has reported long-term outcomes (past 1 month) and we did not find any studies that measured survivor quality of life post-arrest. This should be a key consideration in the design of future studies/trials, as per the recommendations of the recent Core Outcomes in Sudden Cardiac Arrest (COSCA) statement.[53]

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List of Tables, Figures and Appendices

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A Systematic Review and Meta-Analysis of the Effect of Dispatcher-Assisted CPR on Outcomes from Sudden Cardiac Arrest in Adults and Children.

Running Title: **Nikolaou – DA-CPR systematic review**

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ABSTRACT (348 words)

BACKGROUND: Dispatcher-assisted cardiopulmonary resuscitation (DA-CPR) has been reported in individual studies to significantly increase the rate of bystander CPR and survival from cardiac arrest.

METHODS: We undertook a systematic review and meta-analysis to evaluate the impact of DA-CPR programs on key clinical outcomes following out-of-hospital cardiac arrest. We searched the PubMED, EMBASE, CINAHL, ERIC and Cochrane Central Register of Controlled Trials databases from inception until July 2018. Eligible studies compared systems with and without dispatcher-assisted CPR programs. The results of included studies were classified into 3 categories for the purposes of more accurate analysis: comparison of outcomes in systems with DA-CPR programs, case-based comparison of DA-CPR to bystander CPR, and case-based comparisons of DA-CPR to no CPR before EMS arrival. The GRADE system was used to assess certainty of evidence at an outcome level. We used random-effects models to produce summary effect sizes across all outcomes.

RESULTS: Of 5,531 citations screened, 33 studies were eligible for inclusion. All included studies were observational. Evidence certainty across all outcomes was assessed as low or very low. In system-level and patient-level comparisons, the provision of DA-CPR compared with no DA-CPR was consistently associated with improved outcome across all analyses. Comparison of DA-CPR to bystander CPR

produced conflicting results. Findings were consistent across sensitivity analyses and the pediatric sub-group.

CONCLUSION: These results support the recommendation that dispatchers provide CPR instructions to callers for adults and children with suspected OHCA.

Review registration: PROSPERO- CRD42018091427

INTRODUCTION

Out-of-hospital cardiac arrest (OHCA) is a significant cause of death world wide[1] with an annual rate of between 55 and 113/100,000 person-years.[2] The immediate commencement of cardiopulmonary resuscitation (CPR) by bystanders increases the likelihood of a meaningful neurological recovery.[3,4] The majority of cardiac arrests are witnessed by someone that could initiate this life-saving intervention, yet rates of bystander CPR in many systems are disappointingly low. [5,6]

A key challenge is that bystanders may be untrained or uncomfortable in performing CPR without assistance.[7] Dispatcher-assisted CPR (DA-CPR), also known as telecommunicator-assisted CPR (T-CPR), is a system in which dispatchers provide CPR instructions to emergency callers over the telephone. The goal of this approach is to increase the performance of bystander CPR, and ultimately improve survival.[8]

In 2010, Bohm et al conducted a systematic review which concluded that evidence supporting the use of DA-CPR was limited.[9] The subsequent publication of additional studies led to clinical experts within the International Liaison Committee on Resuscitation (ILCOR) recommending the re-examination of this question as a key research priority within their continuous evidence evaluation process[10].

METHODS

We conducted a systematic review and meta-analysis to evaluate the effect of DA-CPR provision, compared with no DA-CPR provision, on key clinical outcomes in cases of suspected OHCA.

The review was performed in accordance with and funded by the ILCOR continuous evidence evaluation process.[10] This report complies with the PRISMA checklist for reporting systematic reviews.[11] We used the GRADE (Grading of Recommendations, Assessment, Development and Evaluation) approach to categorise certainty of evidence.[12] Our protocol was registered with the PROSPERO database (PROSPERO - CRD42018091427).

Inclusion and Exclusion Criteria

All primary research studies including human participants, adult and pediatric patients, with cardiac arrest outside a hospital setting, and which reported outcomes of interest were included. Randomised controlled trials (RCTs) and non-randomised studies (non-randomised controlled trials, interrupted time series, controlled before-and-after studies, cohort studies) were eligible for inclusion.

Studies including animals, simulated patients and humans without a comparator group were not eligible. We also excluded commentaries, reviews, and studies not published in peer-reviewed journals or only as abstracts.

Information Sources and Search Strategies

In collaboration with an expert information specialist, we conducted a comprehensive search of five electronic databases: PubMED, EMBASE, CINAHL, ERIC, and the Cochrane Library from inception to July 1, 2018. The search strategy combined MESH and free text terms to describe the population and the intervention/comparator. No language or geographic restrictions were applied. A full

search strategy is included in the electronic supplement. Search results from all five databases were merged and duplicate references were manually discarded. Additional citations were identified through backward citation tracking of the included studies, consultation with clinical experts on ILCOR task forces, and a search of clinical trials registries.

Study Selection and Data Extraction

Titles and abstracts of all studies that resulted from the search were independently screened by two experienced reviewers (NN and KND) to determine eligibility for full-text review. The same reviewers reviewed full text articles of all potentially relevant articles and extracted data from eligible full-text articles. Data collection forms were developed and pilot-tested to capture relevant data. Each step of review was discussed, and any incongruence was resolved by consensus.

Outcomes

Outcomes were pre-defined and ranked by the ILCOR BLS and Pediatric Task Forces (see electronic supplement). The clinical outcomes of interest were: health related quality of life; favorable neurological outcomes; survival; rate of bystander CPR; return of spontaneous circulation (ROSC); initial shockable rhythm; and time to CPR.

Assessment of Risk of Bias and evidence certainty

Two reviewers (KND and JT) independently assessed each included study for risk of bias using the GRADE handbook[12] advice and the Cochrane Methods Group

template for observational studies.[13] For each outcome, two reviewers (KC, NN) also assessed publication bias according to the criteria defined by GRADE (study design, study size, lag bias, and comprehensiveness of search strategy).

We categorised the overall certainty of evidence for each outcome using the approach recommended by GRADE.

Data Synthesis and Analysis

The results of included studies were classified into 3 categories for the purposes of more accurate analysis: comparison of outcomes in systems with DA-CPR programs, case-based comparison of DA-CPR to bystander CPR, and case-based comparisons of DA-CPR to no CPR before EMS arrival. Summary effect sizes were produced across all outcomes and a subgroup analysis was pre-specified for pediatric studies.

Given the observational nature and the differences in settings and population of included studies we could not assume a common effect size, so we used a random effects model for meta-analysis, to avoid discounting a small study by giving it a very small weight (as in a fixed-effect analysis). We used Review Manager software (Version 5.1. Copenhagen: The Nordic Cochrane Centre, the Cochrane Collaboration, 2011), to calculate combined odds ratios (ORs) with 95% confidence intervals and measure statistical heterogeneity. Heterogeneity between studies was described using the I^2 statistic. The I^2 was categorized according to GRADE recommendations as low, moderate, substantial or considerable.[14] To avoid reducing the number of studies available for synthesis, mainstream analyses included studies reporting unadjusted data. When there were studies coming from the same region and with overlapping

populations, only the study (or combination of non-overlapping studies) that provided the largest number of participants was used.

We also performed a sensitivity analysis including only studies reporting ORs adjusted for the confounders that were deemed most important for each outcome by the study authors. These two analyses were presented in GRADE tables and the overall certainty of evidence was evaluated according to GRADE. Data from the pre-specified subgroup analysis for the pediatric group i.e. number and combined effect size of pediatric studies and heterogeneity with regard to the rest of the studies, were also presented in the summary of findings tables. Raw data were used in order to calculate unadjusted summary ORs while the generic inverse variance method was used in order to combine the reported adjusted odds.

Additional sensitivity analyses were performed replacing excluded studies with the next largest study and so on until all studies from the same region were entered. These analyses were not entered into GRADE tables and the overall certainty of evidence was not assessed but they are included in Appendix B. These analyses were used to assess robustness of the combined effect size that has been calculated for each outcome.

RESULTS

Overall Description of Included Studies

A total of 5,531 citations were identified through the search methods described above. Of these, 93 full text articles were reviewed, and 33 studies were included in this

systematic review.[15-47] Of the 60 studies excluded at the full text stage, the majority were removed due to the lack of a comparison between DA-CPR and no DA-CPR (see Figure 1 for the detailed PRISMA flowchart).

Study Characteristics

A total of 33 studies reported on the effectiveness of dispatcher-assisted CPR in out-of-hospital cardiac arrest. Geographically, the studies were conducted in a range of countries with the majority from Japan (n = 10), United States (n = 6) and Korea (n=6).. A total of 544,037 cases (Table 1) were included. The median number of participants per study was 803 patients (IQR: 392 to 4,899 patients; Range: 145 to 193,914 patients). No RCTs were identified. All the included studies were observational and included 11 retrospective cohort studies, 9 prospective cohort studies, 7 retrospective before-after studies and 6 cross-sectional studies. The duration of follow-up ranged from 1 month to 1 year following cardiac arrest. Of the 33 total studies, the number included in each meta-analysis for the outcomes of interest was variable due to the inconsistent nature of reporting in each of the studies. The way in which studies with overlapping data were entered in the mainstream and sensitivity analyses is shown in Appendix C.

Patient Characteristics

Of the 33 included studies, 15 were conducted in the adult population only[16,20,22,25,27,31,34,37,41-45,47,49], five were conducted in the pediatric population

only[15,18,26,33,40], and 13 included both adults and children[17,19,21,23,28-30,32,35-37,45,48]. The proportion of males ranged from 52% to 85% (average 66%). The age reported for adult-only studies ranged from 18 to >90 years and ranged between 0 to 19 years for pediatric-only studies (Table 1).

Risk of Bias Assessment

All of the included studies were observational cohort studies and most were retrospective (18/33). With respect to overall risk of bias, 1 study was deemed at low risk of bias, 16 were at moderate risk of bias, and 16 were at high risk of bias (Table 2). The main methodological shortcoming was related to the comparability of cohorts on the basis of the design or analysis, as the majority did not adjust for potential confounding variables. In addition, some studies were not clear about their assessment of exposure and the majority did not report the duration of follow-up or how they dealt with missing data.

Outcomes

The results of included studies were classified into 3 categories for the purposes of more accurate analysis: comparison of outcomes in systems with DA-CPR programs, comparison of DA-CPR to bystander CPR, and comparisons of DA-CPR to no CPR before EMS arrival. For the comparisons of DA-CPR provided versus not provided, we were able to compare 11 outcomes, 7 of which had adjusted analyses. For DA-CPR compared to bystander CPR, we were able to compare 12 outcomes, 7 which had adjusted analyses. For DA-CPR compared to no CPR, we were able to compare 11

outcomes, 5 which had adjusted analyses. The studies included in each analysis are indicated in Table 4-6. The outcomes of interest were then analyzed within each category and a summary of findings is outlined in Table 3 and Figure 2. The number of confounders that were adjusted for in the multivariable analyses ranged from 4 to 11. The most frequently used ones were: gender 11/ 14 (79% of studies), witnessed arrest 10/14 (71% of studies), location of arrest (public vs. home, 9/14- 64% of studies), call to response time 9/14 (64% of studies), shockable initial rhythm 6/14(43% of studies), and etiology of cardiac arrest 5/14 (36% of studies).

A. System Comparison

This analysis represents those published comparisons of before-after retrospective studies but also studies where emergency medical systems had DA-CPR programs in place but where the protocol was applied variably, ie. within an EMS system, outcomes for those patients who received DA-CPR compared to those who did not. A summary of findings for this group is outlined in Table 4. Evidence Profile tables for these comparisons appear in Appendix G.

Survival with Favourable Neurologic Outcome

Among the studies included, survival with favourable neurological outcome was recorded at hospital discharge (2 studies reported unadjusted analyses[17,42]; 1 study reported adjusted analyses[42]) and one-month (3 unadjusted[26,28,44] ; 2 adjusted[26,28]). In unadjusted analyses, DA-CPR was associated with improved survival with favourable neurological outcome at discharge and one-month (OR 1.10; [1.03,1.17]). Adjusted

analyses produced similar findings (AOR 1.47; [1.03,2.09]). Certainty of evidence was assessed as very low for all analyses.

Survival

Survival was reported at three time-points: hospital admission (unadjusted six studies[17,24,28,35,42,46] adjusted one study[28]); one-month (unadjusted two studies[26,28]; adjusted two studies[26,28]) and at hospital discharge (unadjusted seven studies[16,19,29,32,42,43,46]; adjusted one study[42]). Systems with Dispatcher-Assisted CPR programs were not associated with significantly improved survival at any time-point in unadjusted analyses, although the point estimate suggested benefit. In adjusted analyses, DA-CPR was associated with improved outcome at 1-month (AOR 1.40; [1.07,1.85]) and at hospital discharge (AOR 1.33; [1.07,1.66]), but not at hospital admission (AOR 0.97 [0.70, 1.34]). Certainty of evidence was assessed as very low in all analyses (Table 4 and Appendix G).

Other Outcomes

Data for ROSC, initial shockable rhythm and time to CPR all favoured DA-CPR (see Appendix G for details).

B. DA-CPR versus Bystander CPR (Table 5, Appendix H)

Survival with Favourable Neurologic Outcome

Survival with favourable neurologic outcome was reported at 1 month (unadjusted data was available in 2 studies[28,45], adjusted data from 1 study[31]) and at

hospital discharge (unadjusted data from 3 studies[18,37,48], adjusted data from 1 study[40]). Unadjusted data at both time points suggested less favourable outcomes and showed an association between DA-CPR and less favourable outcomes (OR 0.73; [0.68,0.77] and OR 0.83; [0.70,0.98]). The adjusted data suggest no difference between the groups at 1 month or at hospital discharge (AOR 1.0; [0.91,1.08] and AOR 1.12; [0.94,1.34]).

Survival

Survival was reported at three time points: at hospital admission (unadjusted data in 1 study[28]), at 1 month (unadjusted data from 5 studies[26,27,28,31,47], adjusted data from 2 studies[31,47]) and at hospital discharge (unadjusted data from 9 studies[16,18,22,29,36,37,38,41,48], adjusted data from one study[40]). At hospital admission, DA-CPR was not associated with improved outcome (OR 0.71; [0.31,1.60]), but was associated with less favourable outcomes at 1 month (OR 0.75; [0.60,0.95]) and at hospital discharge (OR 0.73; [0.67,0.81]. The adjusted data indicated a potential survival benefit with DA-CPR at 1 month (AOR 1.13; [1.06, 1.20]) , but not at hospital discharge (AOR 0.95; [0.83-1.09]).

Other Outcomes

Data for ROSC, initial shockable rhythm and time to CPR all favoured DA-CPR (see Appendix G for details).

C. DA-CPR vs. No CPR (Table 6, Appendix I)

Survival with Favourable Neurologic Outcome

When comparing DA-CPR to no CPR with regard to survival with favourable neurologic outcome at hospital discharge, both unadjusted [20,34,37,48] from four studies (OR 2.21; [1.44,3.40]) and adjusted[18,40,48] data from three studies (AOR 1.54; [1.35, 1.76]) indicated a benefit with DA-CPR. The same was true for survival with favourable neurologic outcome at 1 month [26,28,45] (OR 1.45; [1.38,1.53] and AOR 1.81; [1.23, 267]).

Survival

Survival in this group was reported at hospital, hospital discharge and at 1 month. Unadjusted analyses at hospital admission [20,28,34] (OR 1.54; [0.62, 3.83]) and at 1 month [26,27,28] (OR 1.68; [0.63, 4.45]) indicated no survival benefit with DA-CPR, however adjusted analysis at 1 month[26] was associated with improved survival (AOR 1.63; [1.32, 2.01]). These studies had very low certainty with serious risk of bias. For survival at hospital discharge both unadjusted[16,18,20,22,29,34,36,37,38,40,41,48] (OR 1.67; [1.39, 2.0]) and adjusted[18,38,40,48] analysis (AOR 1.40; [1.09, 1.78]) indicated benefit with DA-CPR.

Other Outcomes

Data for ROSC, initial shockable rhythm and time to CPR all favoured DA-CPR (see Appendix G for details).

Pediatric Studies

Subgroup analyses were performed for all mainstream and sensitivity analyses where pediatric studies were available. Heterogeneity ranged from none to substantial.

For all critical outcomes where data were available any observed heterogeneity was due to larger magnitude of effect in the pediatric group while the direction of effect was always similar (Table 3). For the important outcome of shockable initial rhythm there was considerable heterogeneity in mainstream analysis for the system based comparison. The OR was 0.74 (0.54-1) for the pediatric group (1 study[26]) and 1.15 (1.10-1.19) for the adult studies[27,40,43,45]. The heterogeneity was not confirmed in a sensitivity analysis where Goto et al (2014)[25] was replaced by the overlapping study of Akahane et al (2012).[15]

For the same outcome, two sensitivity analyses for the comparison of DA-CPR vs. no CPR indicated lower rates of initial shockable rhythm with DA-CPR, while the mainstream analysis and the other 3 of 5 relevant sensitivity analyses indicated higher rates of shockable rhythm with DA-CPR

Sensitivity Analyses

In sensitivity analyses, we explored the impact of study selection in relation to overlapping study samples. These analyses showed that study selection did not affect our overall review findings (appendices D-F). The hierarchy of how overlapping studies were handled is outlined in Appendix C.

DISCUSSION

In this systematic review and meta-analysis which included 33 studies and

544,037,cases, we found evidence that the provision of DA-CPR, compared with no bystander CPR, is associated with improved patient outcome in cases of suspected OHCA. In our comparison of DA-CPR with Bystander CPR the unadjusted and adjusted analyses showed divergent results, with the unadjusted data actually showing an increased benefit of Bystander CPR without dispatcher assistance and the adjusted analysis showing increased benefit of dispatcher-assisted CPR. Across all analyses, certainty of evidence was assessed as either very low.

Previous Work in this Area

This updated review supports the 2017 International Consensus on Cardiopulmonary Resuscitation and Emergency Cardiovascular Care Science with Treatment Recommendations (COSTR) which recommended that dispatchers provide CPR instructions to callers for adults and children with suspected OHCA[48]. The systematic review on which that COSTR was based was conducted in 2015[49]. Since then several new studies have been added to the literature. This review significantly enhances the work previously completed in that it is based on a very robust search, reports both adjusted and unadjusted analyses and includes important subgroup and sensitivity analyses based on the nature of the included papers (i.e. accounting for several overlapping datasets, etc.) in order to ensure complete transparency about the meta-analyses.

Interpretation of Findings

The beneficial effects seen can likely be attributed to a few different reasons. Firstly, an increase in BCPR with DA-CPR (from 28.9% to 64% in unadjusted analysis)

was confirmed in all sensitivity analyses and analyses of adjusted odds. Secondly, there was an increase in sustained ROSC evident in unadjusted and sensitivity analyses. Lastly, there was also higher (but not significant) unadjusted odds for the presence of shockable rhythm on arrival of EMS (OR 1.1 (0.97-1.24). In terms of the diminished time to CPR, DA-CPR may increase time compared to BCPR but also decrease time to CPR if first provided by emergency response personnel. The existing evidence from 1 study indicates a shorter time to CPR[26]. The direction of effect for these patients has been confirmed by adjusted and sensitivity analyses for the majority of the outcomes.

There are several challenges for the generalizability of the magnitude of effect in this analysis. The effect was expected to be lower in cases where there is very rapid response time from EMS[19,45], to vary according to the baseline BCPR rates and to be affected by the quality of DA-CPR program and the existence of quality assurance programs. Such programs can impact the rates of recognition of OHCA, time to deliver DA-CPR, and how instructions for DA-CPR are delivered (DA protocol, dispatcher handling delays induced by the caller). The effect can also be affected by the previous training experience of bystanders, their likelihood to follow the DA-CPR instructions, and the quality of the CPR provided[41]. Across 21 European countries that participated in the EURECA-1 study, less than one third of patients received DA-CPR[50]. In light of our review findings, these data highlight the opportunity, to save more lives through the establishment of systems that ensure the effective delivery of DA-CPR in all cases of

OHCA, such as some of the recent work done on dispatcher training and changes in the language used on such calls[51,52].

Pediatric Findings

This systematic review added 3 pediatric studies (Ro 2016[33], Lee 2017[40], Chang[18]) to the 2 studies (Akahane 2012[15], Goto 2014[26]) from the previous iteration in 2015 and performed additional subgroup analyses comparing these to the adult studies. We found that the results of the meta-analysis of pediatric studies were consistent in direction of effect with the adult studies for the 3 grouped analyses and for sensitivity analyses for all critical outcomes. When heterogeneity was substantial (DA-CPR vs no CPR and select sensitivity analyses), it was due to a larger magnitude of effect in pediatric studies.

Analytic Challenges with Data Quality

This was a very complex meta-analysis due to the variability in data reporting, lack of proper adjustment for confounders and the low certainty of evidence. It may be difficult to conduct a true randomized trial given the known benefits of bystander CPR and therefore we are likely to be left with observational studies of varying quality on which to base our advice. We chose to report both unadjusted and adjusted analyses in order to be transparent about the data on which our recommendations are based. There were several reasons for doing so. Only 14 of the 31 studies reported adjusted data. Reporting only studies with adjusted data would have led to the exclusion of studies with 205,382 patients. Most of the studies reported adjusted data only for their

primary outcomes. Therefore, study participants are even fewer for secondary outcomes (critical or important for this meta-analysis). Studies with adjusted data often had fewer participants across all outcomes; a median 7,639 fewer (range: 0 to 92,541 fewer). The unadjusted and adjusted data were equal in number to crude OR for only 2 outcomes. Also, studies reporting adjusted odds did not always provide higher overall certainty of evidence when compared with those reporting crude ORs. This was due to the presence of serious or very serious risk of bias in both adjusted and unadjusted data, leading to a very low overall certainty of evidence. Downgrading for inconsistency was more often present in the adjusted analyses. Upgrading for large magnitude of effect and plausible confounding occurred more often in the unadjusted data.

Adjusting for confounders confirmed benefit for system-based comparisons and in patient-based comparisons when DA-CPR was compared to No CPR. For patient-based comparisons, the combined adjusted ORs for DA-CPR vs. BCPR tended to offset the increased benefit that was observed with BCPR. In all publications where this information was provided, patients who received bystander CPR often had a witnessed cardiac arrest occurring in public locations with shorter time to CPR. Therefore, it is possible that the increased benefit with BCPR may be due the effect of these confounders on unadjusted ORs.

Strengths & Limitations

The strengths of this systematic review include its rigorous methods including collaboration with an experienced information scientist to develop and conduct the

search, the use of double screening, data extraction and risk of bias assessment, consultation with world experts from the ILCOR BLS and Pediatric Task Forces throughout the process and the presentation of both unadjusted and adjusted data for transparency.

As with all research, the current work also has some limitations including the incongruity and complexity of the data, overlap of datasets in several studies, the high risk of bias and confounding. The included cohort studies were methodologically flawed because most did not adjust for confounding variables in their analysis. The adjusted ORs remained similar to that of the crude ORs for system-based comparisons and for patient-based comparisons where DA-CPR was compared to no CPR. Adjustment for confounders tended to reduce confidence in unadjusted ORs only when DA-CPR was compared to cases with bystander CPR. Consequently, we present both unadjusted and adjusted data here to be clear about why results might not be reliable and should be interpreted with caution.

CONCLUSIONS

Dispatcher-assisted CPR is associated with a beneficial effect on patient outcomes following out-of-hospital cardiac arrest. When comparing DA-CPR to no CPR, both the unadjusted and adjusted analyses show DA-CPR provides better results in terms of survival with favourable neurologic outcome, survival to hospital discharge, and return of spontaneous circulation. Findings were consistent across sensitivity and sub-group analyses, however evidence certainty for all outcomes was assessed as low or

very low.

In terms of areas identified for future research, only one study to date has reported long-term outcomes (past 1 month) and we did not find any studies that measured survivor quality of life post-arrest. This should be a key consideration in the design of future studies/trials, as per the recommendations of the recent Core Outcomes in Sudden Cardiac Arrest (COSCA) statement.[53]

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List of Tables, Figures and Appendices
(listed in the order they appear in the manuscript)

TABLE 1 – Characteristics of Included Studies (organized alphabetically by Country)

Country, region	Author/Year	Sample Size	Study duration	Patient characteristics	Design	Comparisons	CPR instructions as reported in paper	Outcomes
Belgium, Liege	Stipulante 2014[43]	392	Before: 1 November 2008 - 31 January 2009; After: November 1, 2010, to January 31, 2011	Adults; all OHCA resulting in calls to the EMCC, not due to trauma or asphyxia	Retrospective before-after	DI vs. no DI	CCO	B-CPR, Survival to hospital discharge, no flow time
Canada, Ottawa	Vaillancourt 2007[46]	529	Before: 1 July 2003-April 2004; After: April 2004 - 31 December 2004	Age>16; presumed cardiac origin, not witnessed by EMS; received CPR	Retrospective before-after	DI vs. no DI	CC + Ventilation	B-CPR, first recorded rhythm VF/VT, ROSC, survival to hospital admission, survival to hospital discharge
Denmark, Capital Region	Viereck 2017[47]	548	01 January 2013– 31 December 2013	All OHCA treated by EMS, not witnessed by EMS, received CPR	Prospective cohort	DA-CPR vs. Bystander CPR	Not reported	ROSC, Survival at 1 month
Finland	Kuisma 2005[32]	373	1 Jan 1997-31 Dec 2002	Witnessed VF; cardiac origin CPR; CPR attempted	Retrospective cohort	DI vs. no DI	1 January 1997 to September 2000 : CC + Ventilation September 2000 tp December 2002: CCO	Survival to hospital discharge

TABLE 1 – Characteristics of Included Studies (organized alphabetically by Country)

Country, region	Author/Year	Sample Size	Study duration	Patient characteristics	Design	Comparisons	CPR instructions as reported in paper	Outcomes
Finland, southern and eastern Finland	Hiltunen 2015[29]	164	1 March 2010-31Aug 2010	All OHCA before hospital admission;	Prospective cohort	DI vs. no DI; DA-CPR vs. Bystander CPR vs. NO CPR	CCO	B-CPR, ROSC, survival at HD and 1 year, (CPC) status at 6 months
France, Rouen	Besnier 2015[17]	245	Before: from 1 January 2009 - 15 August 2009. After: 1 July 2011 to 30 June 2012.	All non-traumatic, <90 years, patient not at end of life, no flow time < 10 min, CPR possible, regulated by EMS centre	Retrospective before-after	DI vs. no DI	CCO or CCO+Ventilation , to the discretion of the dispatcher	Survival to hospital admission, favorable neurologic outcome at discharge
Austria, Graz	Gotz 2017[27]	173	01 Sep 2014 to 30 Oct 2015	All nonclinical cardiac arrest cases	Retrospective cohort	DA-CPR vs. Bystander CPR / NO CPR	CCO (73.3%) or CC + Ventilation	Survival at 1 month
Ireland, 1 National Ambulance Service region	Oman 2016[36]	145	1 January 2011 -31 December 2012.	Potential rescuer nearby who could deliver CPR.	Retrospective cohort	DA-CPR vs. Bystander CPR / NO CPR	Adults CCO, PAEDS CC + Ventilation	Survival to hospital discharge
Japan, Iwaki	Fujie 2014[23]	559	1 Jan 2004-31 Dec 2009	Adults; not because of trauma, asphyxia, drowning, drugs, or fire; received CPR by EMS; transported to hospital	Retrospective cohort	DI vs. no DI	CCO or CC + Ventilation according to the local protocols	B-CPR, favorable neurologic outcome at 1 month

TABLE 1 – Characteristics of Included Studies (organized alphabetically by Country)

Country, region	Author/Year	Sample Size	Study duration	Patient characteristics	Design	Comparisons	CPR instructions as reported in paper	Outcomes
Japan, Nara	Fukushima 2015[24]	283	1 Jan 2007-31 Dec 2012	Adults; witnessed; collapse before emergency call	Retrospective cohort	DI vs. no DI	CCO or CC + Ventilation according to the local protocols	B-CPR, ROSC, survival to hospital admission, favorable neurological outcome at 1 month
Japan, Nara, Chuwa, Yamato-Koriyama	Fukushima 2017[25]	368	1 November 2013 - 31 March 2015	Adults; non-traumatic; not witnessed by EMS; no DNAR orders; not in medical facilities	Retrospective cohort	DI vs. no DI	CCO or CC + Ventilation according to previous training of callers	Ongoing CPR, quality of CPR
Japan, Nationwide	Akahane 2012	1780	Jan 2005-Dec 2008	Age < 20 years; not witnessed by EMS; call to the EMS to arrival on the scene of <60 min; known etiology; no malignancy	Retrospective cohort	DI vs. no DI	CCO or CC+V according to previous training of callers	B-CPR, first recorded rhythm VT/VF, Survival at 1 month, favorable neurologic outcome at 1 month
Japan, Nationwide	Goto 2014[26]	5009	Jan 2008-Dec2010	Age <18;received EMS; received CPR; not witnessed by EMS	Prospective cohort	DI vs. no DI; DA-CPR vs. Bystander CPR / NO CPR	CCO or CC + Ventilation according to previous training of callers	B-CPR, first recorded rhythm VT/VF, Survival at 1 month, favorable neurological outcome at 1 month, time to first CPR

TABLE 1 – Characteristics of Included Studies (organized alphabetically by Country)

Country, region	Author/Year	Sample Size	Study duration	Patient characteristics	Design	Comparisons	CPR instructions as reported in paper	Outcomes
Japan, Nationwide	Moriwaki 2016[35]	803	Sep 2007-Feb 2010	Non-traumatic; not witnessed by EMS	Retrospective cohort	DI vs. no DI	CCO or CC + Ventilation according to the will of callers	B-CPR, ROSC, Survival to hospital admission, Survival at 7 days, Survival at 7 days with good recovery & mild neurological deficits
Japan, Nationwide	Takei 2016[45]	193914	2007-2012	Witnessed (not by EMS); no pre-hospital involvement of a physician	Prospective cohort	DA-CPR vs. Bystander CPR / NO CPR	CCO or CC + Ventilation according to previous training and will of callers	First recorded rhythm VT/VF, survival with favorable neurological outcome at 1Month, time to CPR
Japan, Nationwide	Takahashi 2017[44]	37899	Jan 2005-Dec 2012	Age >15; Cardiogenic; witnessed (not by EMS)	Cross-sectional	DI vs. no DI;DA-CPR vs. Bystander CPR / NO CPR	CCO or CC + Ventilation	B-CPR, ROSC, first recorded rhythm VT/VF, favorable neurologic outcome at 1 month
Japan, Nationwide	Japanese Circulation Society Resuscitation Science Study Group (JCSRSSG)[31] 2013	173565	1 Jan 2006-31 Dec 2010	Age ≥ 18witnessed (not by EMS); confirmed by EMS; received CPR by EMS; transported to hospital	Prospective cohort	DA-CPR vs. Bystander CPR	CCO or CC + Ventilation according to previous training and will of callers	B-CPR, Public defibrillation with failed ROSC, first recorded rhythm VT/VF, ROSC on arrival to hospital, favorable neurological outcome at 30 days, survival at 30 days, time to CPR

TABLE 1 – Characteristics of Included Studies (organized alphabetically by Country)

Country, region	Author/Year	Sample Size	Study duration	Patient characteristics	Design	Comparisons	CPR instructions as reported in paper	Outcomes
Japan, Saga	Iwamura 2013[30]	800	1 July 2010-31 June 2011	Transported to hospital, received CPR, carotid pulse could be checked	Retrospective cohort	DI vs. no DI		B-CPR
Korea, Nationwide	Chang 2018[18]	1953	Jan 2012- Dec 2016	Age<19 but > 1 year; not witnessed by EMS, received CPR by EMS	Cross-sectional	DA-CPR vs. Bystander CPR / NO CPR	The dispatcher follows the American Heart Association guidelines	First recorded rhythm VT/VF,ROSC , survival to discharge, favorable neurologic outcome at discharge
Korea, Nationwide	Lee 2017[33]	1013	Jan 2012- Dec 2013	Age<19; not witnessed by EMS, received CPR by EMS	Cross-sectional	DA-CPR vs. Bystander CPR / NO CPR	CCO for general OHCA caused by cardiac etiology, trauma, and poisoning, and CC + Ventilation for respiratory OHCA caused by asphyxia, hanging, and drowning	ROSC, first recorded rhythm VT/VF, ROSC, survival to discharge, favorable neurologic outcome at discharge
Korea, Nationwide	Park 2018[37]	53240	Jan 2012-Dec2015	Age ≥18; presumed cardiac cause, received CPR, non EMS witnessed,	Cross-sectional	DA-CPR vs. Bystander CPR / NO CPR	According to the 2010 American Heart Association guidelines	First recorded rhythm VT/VF,ROSC to arrival at the ED, survival to discharge, favorable neurologic outcome at discharge

TABLE 1 – Characteristics of Included Studies (organized alphabetically by Country)

Country, region	Author/Year	Sample Size	Study duration	Patient characteristics	Design	Comparisons	CPR instructions as reported in paper	Outcomes
Korea, Nationwide	Ro 2017[40]	37924	2012-2013	Age ≥18; presumed cardiac cause, received CPR, non EMS witnessed,	Cross-sectional study	DA-CPR vs. Bystander CPR / NO CPR	According to 2010 American Heart Association guidelines	First recorded rhythm VT/VF,ROSC, Survival to discharge, favorable neurologic outcome at discharge, Time to CPR
Korea, Nationwide	Ro 2016[39]	1529	Jan 2012-Dec 2014	Age ≤18 ; not witnessed by EMS; received CPR by EMS	Cross-sectional study	DA-CPR vs. Bystander CPR / NO CPR	-Two-finger chest compression technique and rescue ventilation in infants (aged 1 year or younger) - One- hand chest compression and rescue ventilation in children (aged 1-8 years) Two-hand chest-compression-only technique in adolescents (aged 9 years or older).	B-CPR, first recorded rhythm VT/VF, ROSC , survival and good neurological recovery at discharge from the hospital, time to CPR

TABLE 1 – Characteristics of Included Studies (organized alphabetically by Country)

Country, region	Author/Year	Sample Size	Study duration	Patient characteristics	Design	Comparisons	CPR instructions as reported in paper	Outcomes
Korea, Seoul	Song 2014[42]	8144	Before: Jan 2009-Dec 2010; After: Jan 2012-Dec 2012	Age >15; presumed cardiac cause	Retrospective before-after	DI vs. no DI	CCO for cardiac aetiology; CC + Ventilation for non-cardiac and pediatric victims.	B-CPR, first recorded rhythm VT/VF, ROSC, survival to hospital admission and discharge, favorable neurologic outcome at discharge
Singapore, City of Singapore	Harjanto 2016[28]	2968	Before: April 2010-Dec 2011; After: Jan 2012-feb 2013	Adults; transported by ambulance, presumed to be of cardiac origin, no DNAR orders, received CPR by EMS,	Retrospective before-after	DI vs. no DI; DA-BCPR vs. non DA-CPR / no CPR	*CCO:* For adult victims and children > 8 year old *CCO +* Ventilation *for*: children 1-8 years old **OR** adults whose SCA has a respiratory cause such as drowning **OR** people who collapsed > 15 minutes before	B-CPR, ROSC, first recorded rhythm VT/VF, Survival to hospital admission, survival at 30 days, favorable neurologic outcome at 1 month
Sweden, Gothenburg	Bang 1999[16]	475	1 Jan 1994-31 March 1996	All arrests; death was not anticipated	Prospective cohort	DI vs. no DI; DA-CPR vs. Bystander CPR / NO CPR	CC+ Ventilation	Survival to hospital discharge

TABLE 1 – Characteristics of Included Studies (organized alphabetically by Country)

Country, region	Author/Year	Sample Size	Study duration	Patient characteristics	Design	Comparisons	CPR instructions as reported in paper	Outcomes
Switzerland.	Dami 2015[20]	683	1 January 2011 -31 December 2013.	Age ≥18; non- traumatic, not witnessed by EMS,	Prospective cohort	DA-CPR vs. NO CPR	Not reported	Survival to hospital admission and hospital discharge and favorable neurologic outcome at discharge
USA, 20 State based registries (CARES)	Shah 2017[41]	3335	1 Jan 2014 to 31 Dec 2015	Age >19; not witnessed by EMS, no CPR prior to 911 call, caller transferred to a dispatcher trained to perform CPR instruction, the caller physically present with the patient	Prospective cohort	DA-CPR vs. NO CPR	Not reported	Survival to hospital discharge
USA, Arizona	Wu 2018[48]	2310	1 January 2011- 31 December 2014	Age ≥18 years; presumed cardiac origin	Retrospective cohort	DA-CPR vs. Bystander CPR / NO CPR	75% according to American Heart Association (AHA) guidelines [2,7]	First recorder rhythm VT/VF, ROSC, Survival to hospital admission, survival to hospital discharge, favorable neurologic outcome at discharge.
USA, King County	Culley 1991[19]	4899	Before=1976-1981; After=1982-1988	Witnessed (not by EMS);non-traumatic; outside nursing homes or physicians' offices	Retrospective before-after	DI vs. no DI	CC+ Ventilation	B-CPR, Survival to hospital discharge

TABLE 1 – Characteristics of Included Studies (organized alphabetically by Country)

Country, region	Author/Year	Sample Size	Study duration	Patient characteristics	Design	Comparisons	CPR instructions as reported in paper	Outcomes
USA, King County	Eisenberg 1985[22]	446	6 May 1981 -31 December 1982	Underlying heart disease; received cardiopulmonary resuscitation; not witnessed by EMS	Retrospective before-after	DI vs. no DI	CC + Ventilation	B-CPR, survival to hospital discharge
USA, King County	Lewis 2013[34]	304	1 January 2011-December 31, 2011	Age > 17; not witnessed by EMS	Retrospective cohort	DA-CPR vs. NO CPR	Children CC + Ventilation ; Adults: CCO	First recorded rhythm VT/VF, survival to hospital admission, survival and good neurological recovery at hospital discharge
USA, King County	Rea 2001[38]	7265	1983 - 2000.	Age ≥ 18; cardiac causes, not witnessed by EMS	Prospective cohort	DA-CPR vs. Bystander CPR / NO CPR	CC + Ventilation	Survival to hospital discharge; time to CPR

Table 2 – Risk of Bias Assessment Listed Alphabetically by Author

			Quality assessment (GRADE handbook)			
Study #	Study (Author/year)	Primary Outcome	Risk of Bias			
			Eligibility Criteria	Exposure & Outcome Measurement	Control for Confounding	Incomplete Follow-up
1	Akahane 2012 (Paeds)	Survival at 1 month & survival w CPC 1,2	Low	Low	High	Low
2	Bang 1999	Undetermined	Unclear	High	High	Low
3	Besnier	favorable neurologic outcome at discharge	Unclear	High	High	High
4	Chang 2018	Survival to HD & good neurologic outcome	Low	Unclear	Low*	Low
5	Culley 1991	Rate of Bystander CPR	High	High	High	Low

Study #	Study (Author/year)	Primary Outcome	Risk of Bias			
			Eligibility Criteria	Exposure & Outcome Measurement	Control for Confounding	Incomplete Follow-up
6	Dami 2015	Survival	Unclear	High	High	Unclear
7	Eisenberg 1985	Rate of Bystander CPR; survival	Low	Unclear	High	Unclear
8	Fujie 2014	Rate of bystander CPR	Unclear	High	High	Unclear
9	Fukushima 2015	Survival at 1 month & survival with CPC 1,2	Unclear	High	High	Unclear
10	Fukushima 2017	Survival at 1 month & survival with CPC 1,2	Low	High	High	N/a
11	Goto 2014 (Paeds)	Survival at 1 month & survival with CPC 1,2	Low	Unclear	Unclear*	Low
12	Harjanto 2016	Survival to admission; 30 day and good neurologic outcome	Unclear	Low	Unclear*	Low
13	Hiltunen 2015	Survival at 1 year	Unclear	High	High	Unclear
14	Iwamura 2013	Rate of ROSC	High	High	High	High

Study #	Study (Author/year)	Primary Outcome	Risk of Bias			
			Eligibility Criteria	Exposure & Outcome Measurement	Control for Confounding	Incomplete Follow-up
15	JCSRSSG 2013	Survival at 1 month & survival with CPC 1,2	Unclear	Unclear	Unclear*	Low
16	Kuisma 2005	Survival to hospital discharge	High	Unclear	High	High
17	Lee 2017	Survival to hospital discharge	Low	Unclear	Unclear	Low
18	Lewis 2103	Recognition of Cardiac Arrest	Low	Low	High	High
19	Moriwaki 2016	Bystander CPR rate	Low	High	High	High
20	Oman 2016	Frequency of TCPR and call times	Low	Unclear	High	High
21	Park 2018	Survival with CPC 1,2 at hospital discharge	Low	Unclear	Low*	Low
22	Rea 2001	Survival to hospital discharge	Low	Low	Low*	Low
23	Ro 2016 (Paeds)	Survival to HD & good neurologic outcome	Low	Unclear	Low*	Low

Study #	Study (Author/year)	Primary Outcome	Risk of Bias			
			Eligibility Criteria	Exposure & Outcome Measurement	Control for Confounding	Incomplete Follow-up
24	Ro 2017	Survival with CPC 1,2 at hospital discharge	Low	Unclear	Low*	Low
25	Shah 2017	Survival to hospital discharge	Unclear	Unclear	Low*	Low
26	Song 2014	Survival to hospital discharge	Low	Unclear	Low*	Low
27	Stipulante	FLow time; survival to admission	Unclear	Low	High	High
28	Takahashi 2017	Rate of shockable rhythm on initial ECG; field ROSC	Low	Unclear	Low*	Unclear
29	Takei 2016	Survival with CPC 1,2 at 1 month	Low	Unclear	Unclear	Unclear
30	Vaillancourt	Recognition of Cardiac Arrest	Low	Low	High	Low
31	Viereck 2017	ROSC; Survival at 1 month	Low	Unclear	Unclear*	Low

Study #	Study (Author/year)	Primary Outcome	Risk of Bias			
			Eligibility Criteria	Exposure & Outcome Measurement	Control for Confounding	Incomplete Follow-up
32	Wu 2018	Survival to hospital discharge	Unclear	Low	Low*	Low
33	Gotz 2017 (In German)	Survival at 1 month	Low	High	High	Low

* Assessment is relevant for outcomes where adjusted estimates for effect size are provided.
Risk of bias for confounding high in case of unadjusted estimates for effect size.

TABLE 3 – Brief Table of Findings by Analysis

	UNADJUSTED ANALYSIS			ADJUSTED ANALYSIS		
	Studies (n patients)	**Evidence quality**	**Odds ratio [95% CI]**	**Studies (n patients)**	**Evidence quality**	**Odds ratio [95% CI]**
Systems Comparisons						
Survival with GNO-1 month	3 (44698)	Very Low	1.10 [1.03, 1.17]	2 (6799)	Very Low	1.47 [1.03, 2.09]
Survival with GNO-hospital discharge	2 (5533)	Very Low	1.70 [1.21, 2.37]	1 (5288)	Very Low	1.67 [1.13, 2.47]
Survival–1 month	2 (6799)	Very Low	1.20 [0.99, 1.45]	2 (6799)	Very Low	1.40 [1.07, 1.85]
Survival–hospital discharge	7 (14139)	Very Low	1.23 [0.99, 1.53]	1 (5288)	Very Low	1.33 [1.07, 1.66]
Survival-hospital admission	6 (9548)	Very Low	1.08 [0.95, 1.23]	1 (2493)	Very Low	0.97 [0.70, 1.34]
ROSC	5 (49229)	Very Low	1.17 [1.08, 1.27]	1 (2493)	Very Low	1.14 [0.88, 1.48]
Initial Shockable Rhythm	5 (53371)	Very Low	1.13 [1.03, 1.23]	No data		
Time to CPR	1 (4306)		Median 4 min (IQR 1-9) vs. 11 min (IQR 7-16); p<0.0001			
DA-CPR versus Bystander CPR						
Survival with GNO-1 month	2 (90889)	Low	0.73 [0.68,0.77]	1 (78112)	Very Low	1.0 [0.91,1.08]
Survival with GNO-hospital D/C	3 (28618)	Low	0.83 [0.70,0.98]	1 (17209)	Very Low	1.12 [0.94,1.34]
Survival – 1 month	5 (82295)	Low	0.76 [0.60, 0.95]	2 (78697)	Very Low	1.13 [1.06, 1.20]
Survival–hospital discharge	9 (34528)	Low	0.73 [0.67,0.81]	1 (17209)	Very Low	0.95 [0.83-1.09]
Survival–hospital admission	1 (821)	Very Low	0.71 [0.31,1.60]	No data		
ROSC	7 (38271)	Low	0.79 [0.63, 0.98]	3 (34811)	Very Low	1.04 [0.94, 1.14]
Initial Shockable Rhythm	4 (118686)	Very Low	0.74 [0.61,0.90]	1 (17054)	Very Low	1.02 [0.95, 1.09]
Time to CPR	2 (82198)	Very Low	Mean difference 1.47 [0.37, 2.53] mins more with DA-CPR)			
DA-CPR versus No CPR						
Survival with GNO-1 month	2 (164371)	Very Low	1.45 [1.38, 1.53]	1 (4306)	Very Low	1.81 [1.23, 2.67]
Survival with GNO-hospital discharge	5 (50895)	Moderate	2.21 [1.44, 3.40]	3 (35921)	Very Low	1.54 [1.35, 1.76]
Survival–1 month	3 (6619)	Very Low	1.68 [0.63, 4.45]	1 (4306)	Very Low	1.63 [1.32, 2.01]
Survival-hospital discharge	11 (59250)	Low	1.67 [1.39,2.0]	5 (43550)	Very Low	1.40 [1.09,1.78]
Survival – hospital admission	3 (3186)	Very Low	1.54 [0.62,3.83])	No data		
ROSC	6 (69495)	Very Low	1.63 [1.22, 2.18]	1 (32506)	Very Low	1.51 [1.32, 1.73]
ROSC (hospital arrival)	1 (46487)	Very Low	2.03 [1.87,2.20]	No data		
Initial Shockable Rhythm	6 (85787)	Very Low	1.51 [1.36, 1.67]	No data		
Time to CPR	4 (43194)	Very Low	**Goto 2014** n=4306 (pediatric), 2min (0-5 min) vs 11 (7-15); **Ro 2016** n=1265, 4 min (0-13 min), vs 10 min (6-18), reported p<0.01; **Ro 2017** n=32506: 3 min (0-11 min) vs 12 min (7-22 min): median time 1 min (IQR 0 -5 min) vs. median time 11 (IQR 7-15 min); reported p<0.0001. **Rea 2001 n=5072-** reported means (SD); (2.9 [2.4] vs. 6.4 [3.1]); MD [95% CI] = -3.5 [-3.7, -3.3]			

Table 3 - Summary of findings: Systems Based Comparisons

EMS systems where dispatch assisted CPR is offered compared to EMS systems where dispatch assisted CPR is not offered in adults and children with presumed cardiac arrest in out-of-hospital settings (unadjusted data)

Patient or population: adults and children with presumed cardiac arrest in out-of-hospital settings (unadjusted data)
Setting:
Intervention: EMS systems where dispatch assisted CPR is offered
Comparison: EMS systems where dispatch assisted CPR is not offered

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with EMS systems where dispatch assisted CPR is not offered	Risk with EMS systems where dispatch assisted CPR is offered				
Survival with CPC 1-2 or mRS (Survival with CPC 1-2 or mRS) follow up: 1 months	102 per 1,000	**111 per 1,000** (105 to 118)	**OR 1.10** (1.03 to 1.17)	44698 (3 observational studies) Harjanto 2016 Takahashi, 2017 Goto 2014	⊕◯◯◯ VERY LOW [a]	Prespecified subgroup analysis for the PAEDs group: 1 study, (Goto 2014); NO heterogeneity compared to 2 adult studies (I2:0%). PAEDS OR: 1.03 (0.72, 1.48), AMPS: 1.10 (1.03, 1.17). Prespecified analysis of studies reporting adjusted ORs (2 studies 6799 patients), yielded VERY LOW quality evidence (SERIOUS RISK OF BIAS); OR 1.47 (1.03 to 2.09),
Survival with CPC 1-2 or mRS (Survival with CPC 1-2 or mRS) follow up: to hospital discharge	21 per 1,000	**35 per 1,000** (25 to 48)	**OR 1.70** (1.21 to 2.37)	5533 (2 observational studies) Besnier 2015 Song 2014	⊕◯◯◯ VERY LOW [b]	Prespecified analysis of studies reporting adjusted ORs (1 study 5288 patients) yielded VERY LOW quality evidence (SERIOUS RISK OF BIAS); OR 1.67 (1.13 to 2.47)
Survival (Survival to hospital admission) follow up: to hospital admission	183 per 1,000	**195 per 1,000** (175 to 216)	**OR 1.08** (0.95 to 1.23)	9548 (6 observational studies) Besnier 2015 Fukushima2015 Harjanto 2016 Moriwaki,2016 Song 2014 Vaillancourt 2007	⊕◯◯◯ VERY LOW [a,c,d]	Prespecified analysis of studies reporting adjusted ORs (1 study 2493 patients) yielded VERY LOW quality evidence (SERIOUS RISK OF BIAS, VERY SERIOUS IMPRECISION); OR 0.97 (0.70 TO 1.34)
Survival (Survival at 1 month) follow up: 1 months	61 per 1,000	**72 per 1,000** (60 to 86)	**OR 1.20** (0.99 to 1.45)	6799 (2 observational studies) Harjanto 2016 Goto 2014	⊕◯◯◯ VERY LOW [a,c]	Prespecified subgroup analysis for the PAEDs group: 1 study, (Goto 2014); NO heterogeneity compared to 1 adult study (I2:0%). PAEDS OR: 1.17 (0.95, 1.45), AMPS OR: 1.30 (0.84, 2.02). Prespecified analysis of studies reporting adjusted ORs (2 studies, 6799 patients) yielded VERY LOW quality evidence (SERIOUS RISK OF BIAS); OR 1.40 (1.07 to 1.85)

Table 3 - Summary of findings: Systems Based Comparisons

EMS systems where dispatch assisted CPR is offered compared to EMS systems where dispatch assisted CPR is not offered in adults and children with presumed cardiac arrest in out-of-hospital settings (unadjusted data)

Patient or population: adults and children with presumed cardiac arrest in out-of-hospital settings (unadjusted data)
Setting:
Intervention: EMS systems where dispatch assisted CPR is offered
Comparison: EMS systems where dispatch assisted CPR is not offered

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with EMS systems where dispatch assisted CPR is not offered	Risk with EMS systems where dispatch assisted CPR is offered				
Survival follow up: to hospital discharge	186 per 1,000	**219 per 1,000** (184 to 259)	**OR 1.23** (0.99 to 1.53)	14139 (7 observational studies) Bang 1999 Culley 1991 Hilltunen 2015 Kuisma 2005 Song 2014 Stipulante 2014 Vaillancourt 2007	⨁◯◯◯ VERY LOW [c,e,f]	Prespecified Analysis of studies reporting adjusted ORs (1 study 5288 patients) yielded VERY LOW quality evidence (SERIOUS RISK OF BIAS); OR 1.33 (1.07 to 1.66)
Sustained ROSC (Sustained ROSC)	204 per 1,000	**231 per 1,000** (217 to 246)	**OR 1.17** (1.08 to 1.27)	49229 (5 observational studies) Harjanto 2016 Hilltunen 2015 Song 2014 Takahashi, 2017 Vaillancourt 2007	⨁◯◯◯ VERY LOW [a]	Prespecified Analysis of studies reporting adjusted ORs (1 study 2493 patients) yielded VERY LOW quality evidence (SERIOUS RISK OF BIAS, SERIOUS IMPRECISION); OR 1.14 (0.88 to 1.48)
Bystander CPR (Bystander CPR)	289 per 1,000	**558 per 1,000** (478 to 633)	**OR 3.10** (2.25 to 4.25)	192734 (9 observational studies) Culley 1991 Harjanto 2016 Hilltunen 2015 JCSRSSG 2013 Song 2014 Stipulante Vaillancourt 2007 Akahane 2012 Ro 2016	⨁◯◯◯ VERY LOW [a]	Prespecified subgroup analysis for the PAEDs group: 2 studies, (Akahane 2012,Ro 2016); LOW heterogeneity (due to magnitude-not direction of effect)compared to 7 adult and mixed studies (I2:12%). PAEDS OR: 4.05 (2.43, 6.75), AMPS OR: 2.84 (1.91, 4.23). Prespecified Analysis of studies reporting adjusted ORs (3 studies, 9877 patients) yielded VERY LOW quality evidence (VERY SERIOUS RISK OF BIAS, STRONG ASSOCIATION); OR 5.74 (2.40 to 13.72)
Shockable rhythm	329 per 1,000	**357 per 1,000** (342 to 377)	**OR 1.13** (1.03 to 1.23)	53371 (5 observational studies) Harjanto 2016 Song 2014 Takahashi 2017 Vaillancourt Goto 2014	⨁◯◯◯ VERY LOW [a,f]	Prespecified subgroup analysis for the PAEDs group: 1 study, (Goto 2014); CONSIDERABLE heterogeneity compared to 4 adult and mixed population studies (I2:79%); Different directions of effects. PAEDS OR: 0.81 (0.60, 1.10), AMPS OR: 1.15 (1.10, 1.14)

Table 3 - Summary of findings: Systems Based Comparisons

EMS systems where dispatch assisted CPR is offered compared to EMS systems where dispatch assisted CPR is not offered in adults and children with presumed cardiac arrest in out-of-hospital settings (unadjusted data)

Patient or population: adults and children with presumed cardiac arrest in out-of-hospital settings (unadjusted data)
Setting:
Intervention: EMS systems where dispatch assisted CPR is offered
Comparison: EMS systems where dispatch assisted CPR is not offered

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with EMS systems where dispatch assisted CPR is not offered	**Risk with EMS systems where dispatch assisted CPR is offered**				
Time to CPR (Time to CPR)	1 STUDY, 4306 patients; reporting medians (IQR); Shorter times to CPR if DA-CPR is offered: 4 (1-9) vs. 11 (7-16); reported p<0.0001			(1 observational study) Goto 2014	⨁◯◯◯ VERY LOW [a]	
Survival follow up: 1 years	315 per 1,000	**322 per 1,000** (190 to 488)	**OR 1.03** (0.51 to 2.07)	164 (1 observational study) Hiltunen 2015	⨁◯◯◯ VERY LOW [e,g]	
Survival with CPC 1-2 or mRS (Survival with CPC 1-2 or mRS) follow up: 90 days	207 per 1,000	**264 per 1,000** (143 to 370)	**OR 1.37** (0.64 to 2.25)	164 (1 observational study) Hiltunen 2015	⨁◯◯◯ VERY LOW [e,g,h]	

***The risk in the intervention group** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: Confidence interval; **OR:** Odds ratio

GRADE Working Group grades of evidence
High certainty: We are very confident that the true effect lies close to that of the estimate of the effect
Moderate certainty: We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different
Low certainty: Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect
Very low certainty: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

Explanations

a. Crucial limitation for 1 criterion; some limitations for other criteria
b. Crucial limitation for 1 criterion
c. 95% CI for effect size includes null effect
d. Lag bias; asymmetry in funnel plot
e. Crucial limitation for multiple criteria
f. Substantial heterogeneity; differences in the direction of effects
g. Few events; 95% CI for effect size includes both appreciable benefit and harm
h. Follow up duration: 6 months

Table 5 - DACPR vs BCPR SOF table

Summary of findings: DA-CPR versus Bystander CPR

Patients/cases where dispatch assisted CPR is offered compared to patients/cases where bystander CPR without dispatch assist is offered in adults and children with presumed cardiac arrest in out-of-hospital settings (unadjusted data)

Patient or population: adults and children with presumed cardiac arrest in out-of-hospital settings (unadjusted data)
Setting:
Intervention: Patients/cases where dispatch assisted CPR is offered
Comparison: patients/cases where bystander CPR without dispatch assist is offered

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with patients/cases where bystander CPR without dispatch assist is offered	Risk with Patients/cases where dispatch assisted CPR is offered				
Survival with CPC 1-2 or mRS follow up: 1 months	60 per 1,000	**44 per 1,000** (42 to 47)	**OR 0.73** (0.68 to 0.77)	90889 (2 observational studies) Harjanto 2016 Takei 2016	⊕⊕◯◯ LOW [a]	Prespecified Analysis of studies reporting adjusted ORs (1 study, 78112 patients) yielded VERY LOW quality evidence (SERIOUS RISK OF BIAS, SERIOUS IMPRECISION); OR 1 (0.91 to 1.08)
Survival with CPC 1-2 or mRS (follow up: to hospital discharge)	63 per 1,000	**52 per 1,000** (45 to 61)	**OR 0.83** (0.70 to 0.98)	28618 (3 observational studies) Park 2018 Wu 2018 Chang 2018	⊕⊕◯◯ LOW [a]	Prespecified subgroup analysis for the PAEDs group: 1 study, (Chang 2018); NO heterogeneity compared to 2 adult studies (I2:0%). PAEDS OR: 0.97 (0.58-1.62), ADULTS OR: 0.79(0.61-1.02). Prespecified Analysis of studies reporting adjusted ORs (1 study, 17209 patients) yielded VERY LOW quality evidence (SERIOUS RISK OF BIAS, SERIOUS IMPRECISION); OR 1.12 (0.94 TO 1.34)
Survival follow up: to hospital admission	181 per 1,000	**135 per 1,000** (64 to 261)	**OR 0.71** (0.31 to 1.60)	821 (1 observational study) Harjanto 2016	⊕◯◯◯ VERY LOW [b,c]	
Survival follow up: 1 months	93 per 1,000	**72 per 1,000** (58 to 89)	**OR 0.76** (0.60 to 0.95)	82295 (5 observational studies) Gotz Harjanto 2016 JCSRSSG 2013 Viereck 2017 Goto 2014	⊕⊕◯◯ LOW [a]	Prespecified subgroup analysis for the PAEDs group: 1 study (Goto 2014); NO heterogeneity compared to 4 adult / mixed population studies (AMPS),(I2:0%). PAEDS OR: 0.74 (0.58-0.95), AMPS OR: 0.71 (0.47-1.08). Prespecified Analysis of studies reporting adjusted ORs (2 studies, 78697 patients) yielded VERY LOW quality evidence (SERIOUS RISK OF BIAS); OR 1.13 (1.06 to 1.20)
Survival follow up: to hospital discharge	129 per 1,000	**97 per 1,000** (90 to 107)	**OR 0.73** (0.67 to 0.81)	34528 (9 observational studies) Bang 1999 Eisenberg 1985 Hiltunen 2015 Oman 2016 Rea 2001 Park 2018 Shah 2017 Wu 2018 Chang 2018	⊕⊕◯◯ LOW [a]	Prespecified subgroup analysis for the PAEDs group: 1 study, (Chang 2018); MODERATE heterogeneity compared to 8 adult and mixed population studies (AMPS), (I2:49%). PAEDS OR: 0.98 (0.65-1.48), AMPS OR: 0.73 (0.67-0.79). Prespecified Analysis of studies reporting adjusted ORs (1 study, 17209 patients) yielded VERY LOW quality evidence (SERIOUS RISK OF BIAS, SERIOUS IMPRECISION); OR 0.95 (0.83 TO 1.09)

Summary of findings: DA-CPR versus Bystander CPR

Patients/cases where dispatch assisted CPR is offered compared to patients/cases where bystander CPR without dispatch assist is offered in adults and children with presumed cardiac arrest in out-of-hospital settings (unadjusted data)

Patient or population: adults and children with presumed cardiac arrest in out-of-hospital settings (unadjusted data)
Setting:
Intervention: Patients/cases where dispatch assisted CPR is offered
Comparison: patients/cases where bystander CPR without dispatch assist is offered

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with patients/cases where bystander CPR without dispatch assist is offered	Risk with Patients/cases where dispatch assisted CPR is offered				
Sustained ROSC	173 per 1,000	**142 per 1,000** (116 to 170)	**OR 0.79** (0.63 to 0.98)	38271 (7 observational studies) Harjanto 2016 Hiltunen 2015 Ro 2017 Takahashi 2017 Viereck 2017 Wu 2018 Chang 2017	⨁⨁◯◯ LOW [a]	Prespecified subgroup analysis for the PAEDs group: 1 study, (Chang 2018); NO heterogeneity compared to 6 adult / mixed population studies (AMPS) (I2:0%). PAEDS OR: 0.82 (0.56-1.19), AMPS OR: 0.79 (0.62-1). Prespecified analysis of studies reporting adjusted ORs (3 studies, 34811 patients) yielded VERY LOW quality evidence (SERIOUS RISK OF BIAS, SERIOUS IMPRECISION); OR 1.04 (0.94 TO 1.14)
ROSC to hospital arrival	115 per 1,000	**110 per 1,000** (106 to 114)	**OR 0.95** (0.91 to 0.99)	104246 (2 observational studies) JCSRSSG 2013 Park 2018	⨁⨁◯◯ LOW [b]	Prespecified analysis of studies reporting adjusted ORs (1 study 78150 patients) yielded VERY LOW quality evidence (SERIOUS RISK OF BIAS); OR 1.09 (1.04-1.14)
Shockable rhythm	516 per 1,000	**441 per 1,000** (394 to 490)	**OR 0.74** (0.61 to 0.90)	118686 (4 observational studies) Park 2018 Takei 2016 Wu 2018 Chang 2018	⨁◯◯◯ VERY LOW [a,d]	Prespecified subgroup analysis for the PAEDs group: 1 study, (Chang 2018); LOW heterogeneity compared to 3 adult and mixed population studies (AMPS), (I2:8.4%). PAEDS OR: 0.61 [0.43, 0.88] AMPS: 0.77 (0.62-0.94). Prespecified analysis of studies reporting adjusted ORs (1 study, 17054 patients) yielded VERY LOW quality evidence (SERIOUS RISK OF BIAS, SERIOUS IMPRECISION); OR 1.02 (0.95 TO 1.09)
Time to CPR-continuous	The mean time to CPR-continuous was **0** min	The mean time to CPR-continuous in the intervention group was 1.47 min more (0.37 more to 2.53 more)	-	82198 (2 observational studies) JCSRSSG 2013 Rea 2001	⨁◯◯◯ VERY LOW [d,e]	
Time to CPR-narrative	3 studies reporting median (IQR). All report increased medians for DA-CPR compared to B-CPR: Ro 2017 n=17209 3 (0 to 11) vs. 2 (0-9); Ro 2016 (PAEDS): n=766, 4 (0-13) vs. 2 (0-10); Goto 2014: n=4306, 2 (0-5) VS. 1 (0-5). Another study (Takei 2016, n=88068) reported longer time from call to CPR 1 (0,3) vs. 0 (-2,3)			(3 observational studies) Goto 2014 Ro 2016 Ro 2017 Takei 2016	⨁◯◯◯ VERY LOW [e]	
Survival follow up: 1 years	375 per 1,000	**322 per 1,000** (182 to 505)	**OR 0.79** (0.37 to 1.70)	117 (1 observational study) Hiltunen 2015	⨁◯◯◯ VERY LOW [c,e]	

Summary of findings: DA-CPR versus Bystander CPR

Patients/cases where dispatch assisted CPR is offered compared to patients/cases where bystander CPR without dispatch assist is offered in adults and children with presumed cardiac arrest in out-of-hospital settings (unadjusted data)

Patient or population: adults and children with presumed cardiac arrest in out-of-hospital settings (unadjusted data)
Setting:
Intervention: Patients/cases where dispatch assisted CPR is offered
Comparison: patients/cases where bystander CPR without dispatch assist is offered

Outcomes	**Anticipated absolute effects*** (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with patients/cases where bystander CPR without dispatch assist is offered	**Risk with Patients/cases where dispatch assisted CPR is offered**				
Survival with CPC 1-2 or mRS follow up: 90 days	188 per 1,000	**265 per 1,000** (130 to 463)	**OR 1.56** (0.65 to 3.73)	117 (1 observational study) Hiltunen 2015	⨁◯◯◯ VERY LOW [c,e,f]	

***The risk in the intervention group** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: Confidence interval; **OR:** Odds ratio; **MD:** Mean difference

GRADE Working Group grades of evidence
High certainty: We are very confident that the true effect lies close to that of the estimate of the effect
Moderate certainty: We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different
Low certainty: Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect
Very low certainty: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

Explanations

a. Crucial limitation for 1 criterion; some limitations for other criteria
b. Some limitations for multiple criteria
c. 95% CI for effect size includes both appreciable benefit and harm
d. Considerable heterogeneity; differences in the direction of effects
e. Crucial limitation for multiple criteria
f. Follow up duration: 6 months

Table 6 - DACPR vs NO CPR SOF table

Summary of findings: DA-CPR versus NO CPR

Patients/cases where dispatch assisted CPR is offered compared to patients/cases where no bystander CPR is offered in adults and children with presumed cardiac arrest in out-of-hospital settings (unadjusted data)

Patient or population: adults and children with presumed cardiac arrest in out-of-hospital settings (unadjusted data)
Setting:
Intervention: Patients/cases where dispatch assisted CPR is offered
Comparison: patients/cases where no bystander CPR is offered

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with patients/cases where no bystander CPR is offered	Risk with Patients/cases where dispatch assisted CPR is offered				
Survival with CPC 1-2 or mRS follow up: 1 months	31 per 1,000	**44 per 1,000** (42 to 46)	**OR 1.45** (1.38 to 1.53)	164371 (2 observational studies) Harjanto 2016 Takei 2016	⨁◯◯◯ VERY LOW [a]	Prespecified analysis of studies reporting adjusted ORs (1 study,4306 patients) yielded VERY LOW quality evidence (SERIOUS RISK OF BIAS); OR 1.81 (1.23 to 2.67)
Survival with CPC 1-2 or mRS (follow up: to hospital discharge)	24 per 1,000	**51 per 1,000** (34 to 76)	**OR 2.21** (1.44 to 3.40)	50895 (5 observational studies) Dami 2015 Lewis 2103 Park 2018 Wu 2018 Chang 2018	⨁⨁⨁◯ MODERATE [a]	Prespecified subgroup analysis for the PAEDs group: 1 study, (Chang 2018); SUBSTANTIAL heterogeneity (I2:65.7%) compared to with 4 AMPS. PAEDS OR: 3.63 (2.18-6.03), AMPS OR: 1.96 (1.19-3.24). Prespecified analysis of studies reporting adjusted ORs (3 studies, 35921 patients) yielded VERY LOW quality evidence (SERIOUS RISK OF BIAS); OR 1.54 (1.35 to 1.76)
Survival follow up: to hospital admission	143 per 1,000	**204 per 1,000** (94 to 390)	**OR 1.54** (0.62 to 3.83)	3186 (3 observational studies) Dami 2015 Harjanto 2016 Lewis 2103	⨁◯◯◯ VERY LOW [b,c,d]	
Survival follow up: 1 months	57 per 1,000	**93 per 1,000** (37 to 213)	**OR 1.68** (0.63 to 4.45)	6619 (3 observational studies) Gotz Harjanto 2016 Goto 2014	⨁◯◯◯ VERY LOW [a,d,e]	Prespecified subgroup analysis for the PAEDs group: 1 study, (Goto 2014); NO heterogeneity with 2 adult and mixed population studies (I2:0%). PAEDS OR: 1.42 (1.16-1.74), AMPS OR: 2.14 (0.18-2.25) Prespecified analysis of studies reporting adjusted ORs (1 study, 4306 patients) yielded VERY LOW quality evidence (SERIOUS RISK OF BIAS); OR 1.63 (1.32 to 2.01)
Survival follow up: to hospital discharge	57 per 1,000	**92 per 1,000** (78 to 108)	**OR 1.67** (1.39 to 2.00)	59250 (11 observational studies) Bang 1999 Dami 2015 Eisenberg 1985 Hiltunen 2015 Lewis 2103 Oman 2016 Rea 2001 Park 2018 Shah 2017 Wu 2018 Chang 2018	⨁⨁◯◯ LOW [a]	Prespecified subgroup analysis for the PAEDs group: 1 study, (CHANG 2018); CONSIDERABLE heterogeneity for PAEDs compared with 10 adult and mixed population studies (I^2 = 92.3%); effect size larger for PAEDS 3.14 (2.16, 4.58) vs. 1.50 (1.31, 1.73). Prespecified analysis of studies reporting adjusted ORs (5 studies, 43550 patients) yielded VERY LOW quality evidence (SERIOUS RISK OF BIAS); OR 1.40 (1.09 to 1.78)

Summary of findings: DA-CPR versus NO CPR

Patients/cases where dispatch assisted CPR is offered compared to patients/cases where no bystander CPR is offered in adults and children with presumed cardiac arrest in out-of-hospital settings (unadjusted data)

Patient or population: adults and children with presumed cardiac arrest in out-of-hospital settings (unadjusted data)
Setting:
Intervention: Patients/cases where dispatch assisted CPR is offered
Comparison: patients/cases where no bystander CPR is offered

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with patients/cases where no bystander CPR is offered	Risk with Patients/cases where dispatch assisted CPR is offered				
Sustained ROSC	98 per 1,000	**150 per 1,000** (117 to 191)	**OR 1.63** (1.22 to 2.18)	69495 (6 observational studies) Harjanto 2016 Hiltunen 2015 Ro 2017 Takahashi 2017 Wu 2018 Chang 2018	⨁◯◯◯ VERY LOW [a]	Prespecified subgroup analysis for the PAEDs group: 1 study, (Chang 2018); CONSIDERABLE heterogeneity compared to 5 adult and mixed population studies (I2:89%). PAEDS OR: 2.95 (2.07-4.20), AMPS OR: 1.45 (1.07-1.96). Prespecified analysis of studies reporting adjusted ORs (1 study, 32506 patients) yielded VERY LOW quality evidence (SERIOUS RISK OF BIAS); OR 1.51 (1.32 to 1.73)
ROSC to hospital arrival (ROSC HA)	38 per 1,000	**74 per 1,000** (69 to 80)	**OR 2.03** (1.87 to 2.20)	46487 (1 observational study) Park 2018	⨁◯◯◯ VERY LOW [a]	
Shockable rhythm	226 per 1,000	**306 per 1,000** (284 to 328)	**OR 1.51** (1.36 to 1.67)	85787 (6 observational studies) Lewis 2103 Park 2018 Takahashi 2017 Wu 2018 Goto 2014 Chang 2018	⨁◯◯◯ VERY LOW [a]	Prespecified subgroup analysis for the PAEDs group: 2 studies, (GOTO 2014, Chang 2018); NO heterogeneity for PAEDs compared to 4 adult and mixed population studies (I^2 = 0). PAEDS OR: 1.59 (0.78-3.21), AMPS OR: 1.53 (1.40-1.66)
Time to CPR	Four studies were identified: Rea 2001 N=5072: reporting means (SD) indicating shorter time to CPR with DA 2.9 (2.4) vs. 6.4 (3.1). Mean difference =-3.5 95% CI [-3.7, -3.3]; And 3 studies reporting medians (IQR) indicating shorter time to CPR for DA-CPR: Goto 2014 n=4306, 2min (0-5min) vs 11 (7-15) ; Ro 2016 n=1265, 4 min (0-13 min), vs 10 min (6-18), reported p<0.01; Ro 2017n=32506: 3 min (0-11 min) vs 12 min (7-22 min)			(4 observational studies)	⨁◯◯◯ VERY LOW [a]	
Survival follow up: 1 years	234 per 1,000	**321 per 1,000** (164 to 535)	**OR 1.55** (0.64 to 3.76)	100 (1 observational study) Hiltunen 2015	⨁◯◯◯ VERY LOW [b,f]	
Survival with CPC 1-2 or mRS follow up: 90 days	234 per 1,000	**263 per 1,000** (126 to 472)	**OR 1.17** (0.47 to 2.92)	100 (1 observational study) Hiltunen 2015	⨁◯◯◯ VERY LOW [b,f,g]	

Summary of findings: DA-CPR versus NO CPR

Patients/cases where dispatch assisted CPR is offered compared to patients/cases where no bystander CPR is offered in adults and children with presumed cardiac arrest in out-of-hospital settings (unadjusted data)

Patient or population: adults and children with presumed cardiac arrest in out-of-hospital settings (unadjusted data)
Setting:
Intervention: Patients/cases where dispatch assisted CPR is offered
Comparison: patients/cases where no bystander CPR is offered

Outcomes	**Anticipated absolute effects*** (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with patients/cases where no bystander CPR is offered	**Risk with Patients/cases where dispatch assisted CPR is offered**				

***The risk in the intervention group** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: Confidence interval; **OR:** Odds ratio

GRADE Working Group grades of evidence
High certainty: We are very confident that the true effect lies close to that of the estimate of the effect
Moderate certainty: We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different
Low certainty: Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect
Very low certainty: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

Explanations

a. Crucial limitation for 1 criterion; some limitations for other criteria
b. Crucial limitation for multiple criteria
c. Considerable heterogeneity; differences in the direction of effects
d. 95% CI for effect size includes both appreciable benefit and harm
e. Moderate heterogeneity;differences in the direction of effects
f. Few events; 95% CI for effect size includes both appreciable benefit and harm
g. Follow up duration: 6 months

Figure 1 – PRISMA Diagram

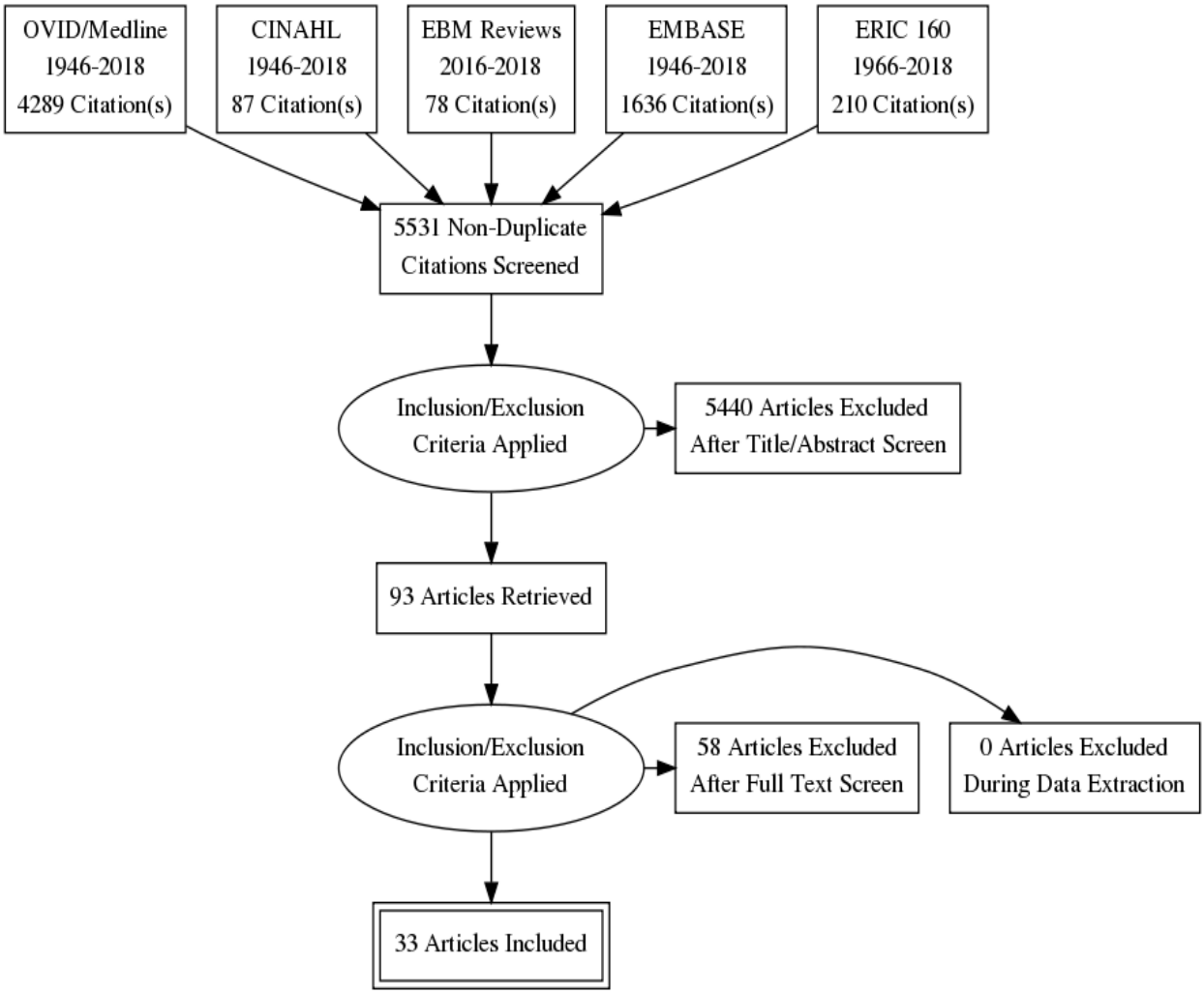
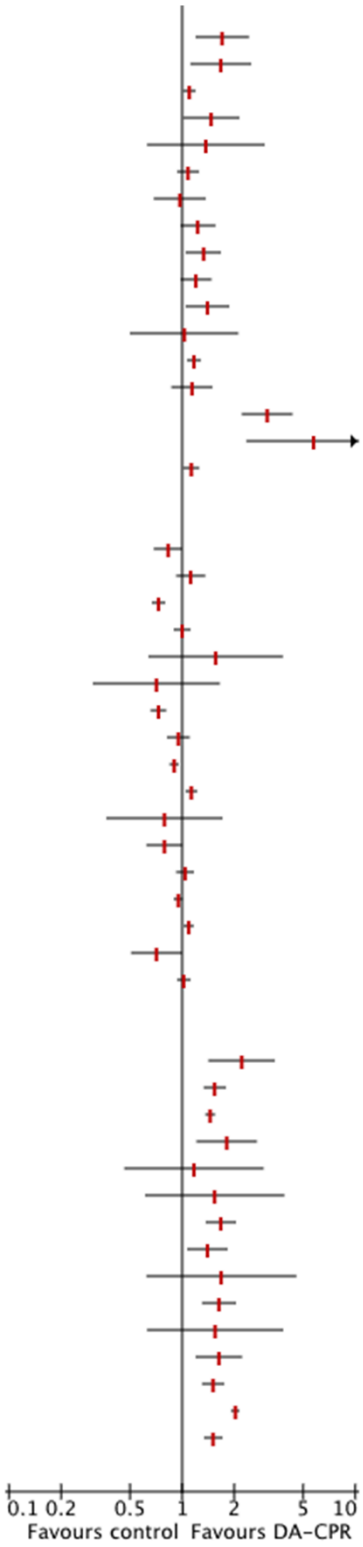


Figure 2 – Caterpillar Plot Diagram

System comparison
- Survival with GNO- Hospital D/C- unadjusted
- Survival with GNO- Hospital D/C- adjusted
- Survival with GNO- 1-month- unadjusted
- Survival with GNO- 1-month- adjusted
- Survival with GNO- 90-days- unadjusted
- Survival- hospital admission- unadjusted
- Survival- hospital admission- adjusted
- Survival- hospital discharge- unadjusted
- Survival- hospital discharge- adjusted
- Survival- 1-month- unadjusted
- Survival- 1-month- adjusted
- Survival- 1-year- unadjusted
- ROSC- unadjusted
- ROSC- adjusted
- Bystander CPR- unadjusted
- Bystander CPR- adjusted
- Shockable rhythm- unadjusted

DA-CPR versus bystander CPR
- Survival with GNO- Hospital D/C- unadjusted
- Survival with GNO- Hospital D/C- adjusted
- Survival with GNO- 1-month- unadjusted
- Survival with GNO- 1-month- adjusted
- Survival with GNO- 90-days- unadjusted
- Survival- hospital admission- unadjusted
- Survival- hospital discharge- unadjusted
- Survival- hospital discharge- adjusted
- Survival- 1-month- unadjusted
- Survival- 1-month- adjusted
- Survival- 1-year- unadjusted
- ROSC- unadjusted
- ROSC- adjusted
- ROSC to hospital admission- unadjusted
- ROSC to hospital admission- adjusted
- Shockable rhythm- unadjusted
- Shockable rhythm- adjusted

DA-CPR versus no CPR
- Survival with GNO- Hospital D/C- unadjusted
- Survival with GNO- Hospital D/C- adjusted
- Survival with GNO- 1-month- unadjusted
- Survival with GNO- 1-month- adjusted
- Survival with GNO- 90-days- unadjusted
- Survival- hospital admission- unadjusted
- Survival- hospital discharge- unadjusted
- Survival- hospital discharge- adjusted
- Survival- 1-month- unadjusted
- Survival- 1-month- adjusted
- Survival- 1-year- unadjusted
- ROSC- unadjusted
- ROSC- adjusted
- ROSC to hospital admission- unadjusted
- Shockable rhythm- unadjusted



Appendix A - Outcomes from Task Force

Click here to download Supplemental files for online publication only: Appendix A Outcomes from Task Force -010818.pdf

Appendix B - Final Search Strategies

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Appendix C - Hierarchy for including studies with overlapping da

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Appendix D - Sensitivity analyses- System based comparisons

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Appendix E - Sensitivity analyses- DA-CPR vs BCPR

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Appendix F - Sensitivity analyses- DA-CPR vs NOCPR

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Appendix G - Additional Outcomes

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We wish to draw the attention of the Editor to the following facts which may be considered as potential conflicts of interest and to significant financial contributions to this work.

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- CV has received peer-reviewed funding to study the topic of Dispatcher-Assisted CPR from the Canadian Institutes of Health Research, Heart & Stroke Foundation of Canada and the Canadian Arrhythmia Network.
- KC is supported by an NIHR post-doctoral research fellowship award.
- KND is supported by a Research Chair from North York General Hospital

We confirm that the manuscript has been read and approved by all named authors and that there are no other persons who satisfied the criteria for authorship but are not listed. We further confirm that the order of authors listed in the manuscript has been approved by all of us.

We confirm that we have given due consideration to the protection of intellectual property associated with this work and that there are no impediments to publication, including the timing of publication, with respect to intellectual property. In so doing we confirm that we have followed the regulations of our institutions concerning intellectual property.

We understand that the Corresponding Author is the sole contact for the Editorial process (including Editorial Manager and direct communications with the office). He/she is responsible for communicating with the other authors about progress, submissions of revisions and final approval of proofs. We confirm that we have provided a current, correct email address which is accessible by the Corresponding Author.

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And on behalf of the International Liaison Committee on Resuscitation's (ILCOR) Basic Life Support and Pediatric Task Forces