Effectiveness of Different Compression-to-Ventilation Methods for Cardiopulmonary Resuscitation: A Systematic Review

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ABSTRACT

Aim: To compare the effectiveness of different compression-to-ventilation methods during cardiopulmonary resuscitation (CPR) in patients with cardiac arrest.

Methods: We searched MEDLINE and Cochrane Central Register of Controlled Trials from inception until January 2016. We included experimental, quasi-experimental, and observational studies that compared different chest compression-to-ventilation ratios during CPR for all patients and assessed at least one of the following outcomes: favourable neurological outcomes, survival, return of spontaneous circulation (ROSC), and quality of life. Two reviewers independently screened literature search results, abstracted data, and appraised the risk of bias. Random-effects meta-analyses were conducted separately for randomised and non-randomised studies, as well as study characteristics, such as CPR provider.

Results: After screening 5,703 titles and abstracts and 229 full-text articles, we included 41 studies, of which 13 were companion reports. For adults receiving bystander or dispatcher-instructed CPR, no significant differences were observed across all comparisons and outcomes. Significantly less adults receiving bystander-initiated or plus dispatcher-instructed compression-only CPR experienced favourable neurological outcomes, survival, and ROSC compared to CPR 30:2 (compression-to-ventilation) in un-adjusted analyses in a large cohort study. Evidence from emergency medical service (EMS) CPR providers showed significantly more adults receiving CPR 30:2 experiencing improved favourable neurological outcomes and survival versus those receiving CPR 15:2. Significantly more children receiving CPR 15:2 or 30:2 experienced favourable neurological outcomes, survival, and greater ROSC compared to compression-only CPR. However, for children <1 years of age, no significant differences were observed between CPR 15:2 or 30:2 and compression-only CPR.

Conclusions: Our results demonstrated that for adults CPR 30:2 is associated with better survival and favourable neurological outcomes when compared to CPR 15:2. For children, more patients receiving CPR with either 15:2 or 30:2 compression-to ventilation ratio experienced favourable neurological function, survival, and ROSC when compared to CO-CPR for children of all ages, but for children <1 years of age, no statistically significant differences were observed.

INTRODUCTION

Out-of-hospital cardiac arrest (OHCA) is a leading cause of mortality worldwide with millions of lives lost every year.[1] Less than 10% of people with OHCA who receive treatment survive to hospital discharge.[2] Cardiopulmonary resuscitation (CPR) is important for patient survival of sudden cardiac arrest; however, bystander CPR rates remain very low globally.[3]

CPR involves chest compressions and ventilations to maintain cardio-cerebral perfusion while attempting to restart the heart.[4] Although CPR is undoubtedly life-saving, it can be challenging to learn and difficult to perform. A barrier to attempting CPR is the administration of rescue breaths (i.e., mouth-to-mouth ventilation).[5] In addition, evidence suggests that prolonged interruptions in chest compressions to deliver ventilations may be harmful. Attempts to overcome these problems have led to the development of compression-only resuscitation and minimally-interrupted chest compression techniques. However, uncertainty exists about the effectiveness of these newer techniques, and whether effects differ depending on the CPR provider, setting, and characteristics of recipients.

We aimed to determine the effectiveness of different compression-to-ventilation methods during CPR regarding favourable neurological outcomes, survival, return of spontaneous circulation (ROSC), and quality of life among patients experiencing cardiac arrest, and whether this differed by CPR provider, setting, and characteristics of recipients.

METHODS

Protocol

The protocol was drafted using the Preferred Reporting Items for Systematic Reviews and Meta-analysis Protocols (PRISMA-P)[6] in collaboration with clinical experts from the International Liaison Committee on Resuscitation (ILCOR) (Appendix A) and registered with PROSPERO (CRD42016047811).

Eligibility criteria

The eligibility criteria based on PICOST (Population, Intervention, Control, Outcomes, Study design and Timeframe) were:[7]

Population: Patients of all ages (i.e., neonates, children, adults) with cardiac arrest from any cause and across all settings (in-hospital and out-of-hospital). Studies that included animals were not eligible.

Intervention: All manual CPR methods including Compression-only CPR (CO-CPR), Continuous Compression CPR (CC-CPR), and CPR with different compression-to-ventilation ratios. CO-CPR included compression with no ventilations, while CC-CPR included compression with asynchronous ventilations or minimally-interrupted cardiac resuscitation (MICR) (Appendix B). Studies that mentioned the use of a mechanical device during CPR were only considered if the same device was used across all relevant intervention arms and would therefore not confound the observed effect.

Comparators: Studies had to compare at least two different CPR methods from the eligible interventions; studies without a comparator were excluded.

Outcomes: The primary outcome was favourable neurological outcomes, measured by cerebral performance or a modified Rankin Score. Secondary outcomes were survival, ROSC, and quality of life.

Study designs: 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. Study designs without a comparator group (e.g., case series, cross-sectional studies), reviews, and pooled analyses were excluded.

Other: We excluded unpublished studies (e.g., conference abstracts, trial protocols), and non-English papers.

Information sources and literature search

MEDLINE and the Cochrane Central Register of Controlled Trials were searched from inception until January 2016. An experienced librarian developed the original search strategy.

The final search strategy was conducted on January 15, 2016 (Appendix C). The unique results from the literature search were uploaded to proprietary online screening software, Synthesi.SR.[8] The literature search was supplemented by scanning the references of all studies included in the previous ILCOR reviews, and additional studies identified by the ILCOR content experts.

Study selection

A training exercise was conducted prior to commencing study selection using the predefined eligibility criteria (Appendix D) on a random sample of 25 titles and abstracts (i.e., level 1 screening). A similar training exercise was conducted for the screening of a random sample of 24 potentially relevant full-text articles (i.e., level 2 screening). The team established 75% agreement among all reviewers for level 1 screening and 83% for level 2 screening.

Subsequently, pairs of reviewers screened citations independently for inclusion at level 1 (EL, FY, HMA, JI, MG, PAK, RC, TL, VN) and level 2 (FY, JI, MG, PAK, RC, VN) screening. All discrepancies were resolved by discussion or the involvement of a third reviewer (HMA, ACT) and/or clinical expert (GDP, ADC).

Data items and data abstraction

A standardized data abstraction form was developed and pilot-tested prior to beginning data abstraction. Data items were study characteristics (e.g., study design, year of conduct), patient characteristics (e.g., number of patients, mean age, and initial rhythm), CPR methods and outcomes (e.g., compressions-to-ventilations ratios, scale used, time point, results). Outcomes were abstracted according to the Utstein-style guidelines for resuscitation research.[9]

Companion reports (i.e., multiple publications reporting results from the same study participants) were identified by discerning overlap in study period, geographic location, setting, and type of CPR method. The publication with the longest follow-up period was considered the main publication and companion reports were only used to supplement the data abstracted from the main publication.

After approximately 75% agreement was achieved, pairs of reviewers (FY, JI, MG, PK, RC, VN) independently abstracted all relevant information from each article. All discrepancies were resolved by discussion or involvement of a third reviewer (EL, WZ). We contacted authors for relevant missing information and to provide clarification; for example, to obtain a breakdown of patient population by age. Clinical experts assisted in coding the appropriate CPR provider type, intervention and aetiology categories across the studies.

Risk of bias

The Cochrane Risk-of-Bias Tool[10] was used for appraising RCTs and quasi-RCTs; Cochrane Effective Practice and Organization of Care (EPOC) Risk-of-Bias Tool[11] was used for cluster-crossover RCTs, non-randomised controlled trials, interrupted time series, and controlled before-and-after studies; and Newcastle-Ottawa Scale was used for cohort studies.[12] Experienced pairs of reviewers (FY, JI, MG, PAK, RC, VN) independently appraised the risk of bias of all included studies with discrepancies resolved by a third reviewer (EL, WZ).

Synthesis of results

Intervention effects (e.g., CO-CPR versus CPR 30:2 compression-to-ventilation ratio) were summarized using un-adjusted risk ratios (RR) and risk differences (RD) and pooled via random-effects meta-analysis. We assessed statistical heterogeneity using the I^2 statistic,[13] with an I^2 value above 75% indicative of substantial heterogeneity.[13] All statistical analyses were conducted using the *metafor* package in R (version 3.2.3).[14]

For the main analysis, the intervention effect estimates were derived separately for RCTs and non-randomised studies, as well as for adults and children. For survival, the main analysis was conducted using the longest duration of follow-up, yet we also conducted a sensitivity analysis using the survival data closest to the timing of CPR. As well, a series of subgroup analyses were conducted exploring the impact of factors potentially affecting the intervention effect estimates, including aetiology of cardiac arrest, emergency medical service (EMS) response times, initial rhythm, and percentage of arrests that were witnessed.

Although not previously specified in the review protocol, we stratified overall results by CPR provider, (Appendix E) specifically: 1) Bystander plus dispatcher-instructed CPR, 2) dispatcher-

instructed CPR (telephone CPR), 3) bystander delivered CPR, 4) CPR delivered by EMS staff, and 5) CPR delivered by hospital staff.

GRADE appraisal

Using the Grading of Recommendation, Assessment, Development, and Evaluation (GRADE) guidance,[15] we assessed the quality (or certainty) of the available evidence. This was conducted by three reviewers (HMA, EL, WZ) and verified by the study guarantor and content experts (ACT, GDP, ADC). Studies looking at before-and-after guideline changes were considered "indirect evidence" because multiple aspects of treatment were likely to have changed over time, in addition to the prescribed compression-to-ventilation ratios.

RESULTS

Literature search

After screening 5,703 titles and abstracts and 229 potentially relevant full-text articles, 28 studies[2, 16-42] and 13 companion reports[39, 40, 43-54] fulfilled our eligibility criteria and were included (Figure 1).

Study characteristics

Included studies were published between 1993 and 2015 with a study period ranging from 1983 to 2015 (Table 1; Appendix F). We included one cluster-crossover RCT,[16] three RCTs,[20, 23, 24] and 24 cohort studies.[2, 17-19, 21, 22, 25-42] Most studies were conducted in the USA and Japan (n=16), involving OHCAs (n=27), while one[31] was conducted in a hospital setting.

Nine studies[17, 18, 20, 29, 33, 35, 37, 39, 41] included cardiac arrests with cardiac causes, 13 papers[2, 19, 24-28, 30, 34, 36, 38, 40, 42] included both cardiac and non-cardiac causes, and one paper[21] included non-cardiac causes. CPR was provided by: EMS personnel,[16-18, 25, 27, 29, 30, 32, 33, 36, 41] bystanders,[19, 21, 22, 26, 34, 35, 37, 38] bystanders receiving dispatcher instructions,[20, 23, 24] bystander alone or with dispatcher instructions,[2, 28] and emergency department staff.[31] Most studies (n=16)[2, 16, 17, 19, 20, 22, 23, 25, 30-33, 35, 36, 38, 40] did not restrict the study population by initial rhythm, six[24, 26, 29, 34, 39, 41] included only patients with initial shockable rhythm, and one [27] included patients with initial non-shockable rhythm.

Patient characteristics

Twenty studies[16-21, 24-34, 36, 39, 40] included adults, two[28, 38] included children, and six[2, 23, 35, 37, 41, 42] included both adults and children (Table 1; Appendix G). The overall number of CPR recipients in each study ranged from 181 to 350,439 and the proportion of males ranged from 59 to79%.

The mean age reported for adult-only studies ranged from 56.9 years (SD 18.6) to 74.1 years (SD 14.9), and was 4.9 years (SD 6.1) for paediatric-only studies.

Risk of bias results

Three RCTs were appraised with the Cochrane risk-of-bias tool (Appendix H). One trial[24] had an unclear random sequence generation, while another[20] had unclear allocation concealment, and the third trial[23] had a high risk of bias due to blinding of personnel, as well as incomplete outcome data bias. One cluster-crossover RCT[16] assessed using the EPOC risk-of-bias tool (Appendix I) had an unclear risk of bias for random sequence generation, as well as for allocation concealment; all other items were scored as low risk of bias.

For the 23 cohort studies, 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 (Appendix J). In addition, the majority of the cohort studies did not report the duration of follow-up.[17, 22, 25-28, 30-34, 36, 37, 40-42]

Reporting results

Results of the main analysis stratified by patient age, CPR comparisons, provider, and outcome are presented below, as well as in Table 2. Only statistically significant findings are presented in the text, but all results are presented in Table 1, where it can be observed that statistically significant results were not found for the following comparisons: CO-CPR versus CPR 15:2 in mostly adult patients and CO-CPR versus CPR 30:2 or CPR 15:2 in mostly adult patients. Unless otherwise noted, sub-group analyses (Table 3) and sensitivity analyses (Table 4) demonstrated consistent results with the main analyses. For all studies not included in the meta-analyses adjusted and un-adjusted estimates can be found in Appendix K.

CO-CPR vs. CPR 30:2 (adults)

For bystanders plus dispatcher-instructed CPR, one cohort study[2] of 350,439 mostly adult patients found that significantly less patients receiving CO-CPR experienced favourable neurological outcomes (RD -0.74, 95% CI: -0.85, -0.63), survived (RD -1.42, 95% CI: -1.58, -1.25), and experienced ROSC (RD -1.62, 95% CI: -1.81, -1.42) compared to CPR 30:2.

CPR 30:2 vs CPR 15:2 (adults)

For EMS CPR, a meta-analysis of two cohort studies[25, 27] with 4,877 adults found that significantly more patients receiving CPR 30:2 experienced favourable neurological outcomes (RD 1.72, 95% CI: 0.52, 2.91) compared to CPR 15:2. A meta-analysis of six cohort studies[17, 25, 27, 30, 33, 36] with 13,962 adults revealed that significantly more patients receiving CPR 30:2 survived (RD 2.48, 95% CI: 1.57, 3.38) compared to CPR 15:2. The results for ROSC were not statistically significant.

CPR 50:2 vs CPR 15:2 (adults)

For EMS CPR, one cohort study[29] of 200 adults found that significantly more patients receiving CPR 50:2 survived (RD 21.48, 95% CI: 6.90, 36.06) and experienced ROSC (RD 21.89, 95% CI: 6.88, 36.90) compared to CPR 15:2.

CC-CPR (with asynchronous ventilations at a rate of 10 per minute) vs. CPR 30:2 (adults)

For EMS CPR, one cluster-crossover RCT[16] including 23,711 adults found significantly less patients receiving CC-CPR experienced ROSC (RD -1.15, 95% CI: -2.25, -0.05) compared to CPR 30:2 in un-adjusted analysis. However, results for favourable neurological outcomes and

survival were not statistically significant. Results were also found not to be significant for ROSC (RD −1.1, 95% CI:-2.4, 0.1) when adjusted for confounding variables.

CC-CPR (with minimally interrupted cardiac resuscitation) vs. CPR 15:2 (adults)

For EMS CPR, one cohort study[18] of 181 adults found that significantly more patients receiving CC-CPR experienced favourable neurological outcomes (RD 24.11, 95% CI: 11.58, 36.63) compared to CPR 15:2.

CC-CPR (with minimally interrupted cardiac resuscitation) vs. CPR 15:2 or 30:2 (adults)

For EMS CPR, one cohort study[41] with 2,460 mostly adult patients found that significantly more patients receiving CC-CPR survived (RD 5.24, 95% CI: 2.88, 7.6) and experienced ROSC (RD 10.64, 95% CI: 6.80, 14.49) compared to CPR 15:2 or 30:2. The results for favourable neurological outcomes were not statistically significant.

CC-CPR (with asynchronous positive-pressure ventilations delivered by a Thumper device) vs. CPR 5:1(adults)

For in-hospital CPR, one cohort study[31] of 515 adults found that significantly more patients receiving CC-CPR survived (RD 5.86 95% CI: 1.19, 10.53), and experienced ROSC (RD 11.64, 95% CI: 3.61, 19.68) compared to CPR 5:1. The results for favourable neurological outcomes were not statistically significant.

CO-CPR vs. CPR 30:2 (Paediatrics)

For bystander plus dispatcher-instructed CPR, one cohort study[28] of 2,617 children (mean age: NR) found significantly less patients receiving CO-CPR experienced favourable neurological

outcomes (RD -3.30, 95% CI: -4.88, -1.71), and survived (RD -7.04, 95% CI: -9.58, -4.50) compared to CPR 30:2.

CO-CPR vs. CPR 15:2 or 30:2 (Paediatrics)

For bystander CPR, one cohort study[38] of 2,439 paediatric (mean age: 4.9yrs) patients found significantly less patients receiving CO-CPR experienced favourable neurological outcomes (RD -3.02, 95% CI: -4.57, -1.47) or survived (RD -2.98, 95% CI: -5.51, -0.45) compared to CPR 15:2 or 30:2. The results for ROSC were not statistically significant.

Quality of life

None of the included studies reported data on quality of life.

GRADE (Appendix L)

The only results of high certainty in this systematic review were those for favourable neurological outcomes, survival, and ROSC, in one cluster-crossover RCT[16] which compared CO-CPR to CPR 30:2 provided by EMS. All other results were of low or very low certainty.

DISCUSSION

For adults, our results suggest no statistically significant differences across all outcomes and comparisons for those receiving bystander-initiated CPR alone or dispatcher-instructed CPR with or without ventilations. Significantly less adults receiving bystander plus dispatcher-instructed CO-CPR experienced favourable neurological outcomes, survival, and ROSC compared to CPR 30:2. As well, significantly more patients receiving EMS CPR 30:2 experienced favourable neurological outcomes and survival compared to CPR 15:2.

For children, the results varied by the patients' age. CPR 15:2 or 30:2 compression-to-ventilation ratios showed more children with favourable neurological outcomes, survival, and ROSC when compared to CO-CPR for children of all ages. However, no statistically significant differences were observed across these outcomes for children less than one year old. In addition, only two studies with small sample sizes of children were identified for inclusion in our review. As such, our results might be affected by a lack of power to show a true effect in this population. Two additional studies have been published since our literature search was conducted and should be considered to inform guidelines for paediatric population. The studies by Fukuda and Naim examined CO-CPR compared to conventional CPR for paediatric population and both found conventional CPR to be associated with improved outcomes for paediatrics, which was consistent with our results.[55, 56]

The findings from this review and meta-analysis require interpretation in the context of the settings where the interventions were applied. The 2015 consensus on science and treatment recommendations for dispatcher instructions noted that CPR instructions are associated with increased performance of CPR and better patient outcomes.[57] The finding of no statistically significant difference between CPR with a synchronous compression-to-ventilation ratio and

316 dispatcher-instructed CO-CPR[58] supports ILCOR's recommendation for dispatcher-instructed
317 CO-CPR. For bystander-initiated CPR, Iwami found that any CPR is better than no CPR,[2] in un-
318 adjusted analyses CPR 30:2 compression-to-ventilation was associated with the best outcomes in
319 adults. Iwami adjusted for measured confounding variables for no CPR versus CO-CPR or
320 conventional CPR and found similar odds ratios across the two comparisons. Iwami eloquently
321 notes "the most important result from this nationwide registry of OHCA is not the comparison of
322 odds ratios (ORs) between CCCPR and conventional CPR but the increase in the total incidence
323 of survival with favourable neurological outcomes attributed to either type of bystander CPR".[2]
324 This review supports ILCOR's current recommendation that all victims of cardiac arrest should
325 receive chest compressions. For those trained and willing to give rescue-breaths, our findings
326 support that additional benefits can be achieved from CPR with a synchronous compression-to-
327 ventilation ratio.

328 Of note, a meta-analysis by Hupfl[59] compared CO-CPR to conventional CPR and found the same
329 three RCTs[20, 23, 24] as our systematic review with the same findings for survival at discharge.
330 Also a recent Cochrane review[60] which included four studies demonstrated the same findings as
331 our review.

332 There are some limitations of the included studies worth noting. All three RCTs had unclear risk
333 of bias for at least one important criterion, and one of the RCTs had a high risk of bias for two
334 components. In the discussion of one trial publication,[23] authors observed that some dispatchers
335 seemed to have had a prejudice against CO-CPR and a preference for standard CPR, while some
336 callers indicated a preference for a CPR technique irrespective of the randomised intervention.
337 This issue may also have impacted the other studies. The included cohort studies were
338 methodologically flawed because most did not adjust for confounding variables in their analysis.

Consequently, those results might not be reliable and should be interpreted with caution. Additionally, a small number of studies where the focus was not to compare different compression-to-ventilation ratios (though these data were featured in sub-group analyses) were included, after having been identified by the content experts. It is possible that similar studies could have been missed during our screening process. Also we identified several studies examining minimally-interrupted cardiac resuscitation delivered by EMS from Arizona. In some of these cases, the evaluation appeared to run concurrently with a community campaign of bystander compression-only CPR.[21, 39] It was difficult to precisely determine the overlap in patient populations reported in these studies. For example, whilst it was clear that some studies examined specific sub-groups who received MICR (e.g. age),[61, 62] there appeared to be overlap in the patient populations evaluated between reports.[18, 41, 43] To minimize the risk of including individual patients more than once in our meta-analysis, we limited our analysis to the Bobrow, 2008[41] paper as we judged this to be the most comprehensive study that was aligned with our specific PICO question. Finally, the studies we evaluated included a variety of settings where EMS systems and response times may vary and for some studies it was not possible to separate paediatric from adult cases.

There are strengths that are worth noting in our review approach. Our team is multidisciplinary, including content experts, systematic review methodologists, a statistician, and trained systematic review staff. All levels of screening and data abstraction were conducted after a pilot-test and were done in duplicate, with discrepancies verified by a third reviewer. We also assessed the quality of the totality of the evidence using GRADE. However, there are some limitations to be noted, such as limiting to published studies only written in English. The majority of studies identified in this review were observational in nature and thereby at risk of bias from measured

and unmeasured confounding factors. In our analyses we only included un-adjusted estimates because only four of the included papers[16, 28, 31, 41] undertook analyses which adjusted for potentially confounding variables (Appendix K). Also, since there were fewer than 10 studies in the meta-analyses[63], we were unable to statistically assess for publication bias.

In terms of areas identified for future research, we did not find any studies that measured quality of life. This is an important patient-related outcome that needs to be considered in future studies. In addition, none of the included studies provided data on neonates. Thus, for this population it might be necessary to use indirect evidence from paediatric studies or animal models to extrapolate results.

CONCLUSIONS

For adults, our results demonstrated that CPR 30:2 is associated with better survival and favourable neurological outcomes when compared to CPR 15:2. For children, more patients receiving CPR with either 15:2 or 30:2 compression-to ventilation ratio experienced favourable neurological function, survival, and ROSC when compared to CO-CPR for children of all ages, but for children <1 years of age, no statistically significant differences were observed.

CONFLICTS OF INTEREST

Dr. Gavin Perkins and Dr. Allan deCaen are both affiliated with ILCOR, the commissioning committee of this review. All other authors have no known conflicts of interest to declare.

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LIST OF ABBREVIATIONS

CA – cardiac arrest; CC-CPR – continuous compression CPR; CI – confidence interval; CO-CPR – compression-only CPR; CPR – cardiopulmonary resuscitation; EMS – emergency medical service; EPOC – Effective Practice and Organization of Care; GRADE – Grading of Recommendation, Assessment, Development, and Evaluation; ILCOR BLS – International Liaison Committee on Resuscitation Basic Life Support; MICR – minimally-interrupted cardiac resuscitation; OHCA – out-of-hospital cardiac arrest; OR – odds ratio; PICOST – Population,

Intervention, Control, Outcomes, Study design and Timeframe; PRESS – Peer Review of Electronic Search Strategies; PRISMA-P – Preferred Reporting Items for Systematic Reviews and Meta-analysis Protocols; RCTs – randomised controlled trials; RD – risk differences; ROSC – return of spontaneous circulation; RR – risk ratio; SD – standard deviation

LEGENDS TO FIGURES

Table 1: Summary characteristics

Table 2: Main analysis stratified by patient age, CPR comparisons, provider, and outcome

Table 3. Subgroup Analysis - Favourable Neurological Outcomes

Table 4. Sensitivity Analysis

Figure 1. Flow chart

Figure 2. Forest plots of risk ratio for favourable neurological outcomes, ROSC and survival with CO-CPR vs. CPR 15:2. Treatment effect is measured using risk ratio estimate (95% confidence interval), with values ≥1 indicating that treatment is more effective than control.

Figure 3. Forest plots of risk ratio for favourable neurological outcomes and survival with CO-CPR vs. CPR 15:2 or 30:2 Treatment effect is measured using risk ratio estimate (95% confidence interval), with values ≥1 indicating that treatment is more effective than control.)

Figure 4. Forest plots of risk ratio for favourable neurological outcomes, ROSC and survival with CPR 30:2 vs. CPR 15:2. Treatment effect is measured using risk ratio estimate (95% confidence interval), with values ≥1 indicating that treatment is more effective than control.

SUPPLEMENTARY FILES

Supplementary File 1: Appendix (A-L)

Supplementary File 2: PRISMA Checklist

Table 1. Summary Characteristics

Study and patient characteristics	Number of studies (%)
Population	
Adults	20 (71 %)
Paediatrics	2 (7 %)
All (adults and paediatrics)	6 (21 %)
Study region	
Australia and New Zealand	2 (7 %)
Europe	8 (29 %)
Asia	7 (25 %)
North America	11 (39 %)
Aetiology	
Cardiac	9 (32 %)
Non-cardiac	1 (4 %)
Cardiac and Non-cardiac	13 (46 %)
Not specified	5 (18 %)
Study design	
Cohorts	24 (86 %)
RCTs	3 (11 %)
NRCTs	1 (4 %)
Sample size	181 to 350,439
Male (range of %)	59 to 79
Patient age	
Range of mean (SD)	4.9 (6.1) to 74.1 (14.9)
Range of median (IQR)	1.1 (0 to 9) to 79.0 (66 to 86)
Intervention characteristics	**Number of studies (%)**
Type of CPR method	
CPR 5:1	1 (4 %)
CPR 15:2	19 (68 %)
CPR 30:2	11 (39 %)
CPR15:2 or 30:2	4 (14 %)
CPR 50:2	1 (4 %)
CO-CPR	16 (57 %)
CC-CPR[a]	4 (14%)
Initial rhythm	
Shockable	6 (21 %)
Non-shockable	1 (4 %)
Shockable and Non-shockable	16 (57 %)
Not specified	5 (18 %)
Setting	
Out-of hospital CA	27 (96 %)
In-of hospital CA	1 (4 %)
Provider	
Bystander CPR only	11 (39 %)
Bystander CPR + Dispatcher-instructed CPR	2 (7 %)
Dispatcher-instructed CPR only	3 (11 %)
EMS CPR only	11 (39 %)
In-hospital CPR	1 (4 %)
Arrest witnessed (range of %)	7 to 50
EMS Response time	
Range of mean (SD)	3.7 (2) to 12.2 (5)
Range of median (IQR)	5.0 (4 to 7) to 12.2 (6 to 11)
Outcomes characteristics	**Number of studies (%)**
Favourable neurological outcomes	17 (61 %)
Survival	26 (93 %)
Return of spontaneous circulation	18 (64 %)

Abbreviations: CA – cardiac arrest; CC-CPR - continuous compression CPR; CO-CPR – compression-only CPR; CPR – cardiopulmonary resuscitation; EMS – emergency medical service; IQR – interquartile range; NRCT – non-randomised controlled trials; RCT – randomised controlled trial; SD – standard deviation

[a]Includes cardiocerebral resuscitation and minimally interrupted cardiac resuscitation

428 **Table 2. Main analysis stratified by patient age, CPR comparisons, provider, and outcome**

Study ID	# of studies (# of patients)	CPR Provider	Outcome	Treatment %: (# events/n)	Control %: (# events/n)	Risk Ratio (95% CI)	Risk Difference % (95% CI)	I^2
Adults + All (both adult and paediatric) Patients								
CO-CPR vs. CPR 30:2								
Iwami T, 2015[2a]	1 Cohort (350,439)	Bystander + Dispatcher-instructed CPR	Favourable neurological outcomes	1.94 (4846/249970)	2.68 (2690/100469)	0.72 (0.69, 0.76)†	-0.74 (-0.85, -0.63)	NA
			Survival*	4.27 (10685/249970)	5.69 (5717/100469)	0.75 (0.73, 0.78)†	-1.42 (-1.58, -1.25)	NA
			ROSC	6.33 (15818/249970)	7.94 (7982/100469)	0.80 (0.78, 0.82)†	-1.62 (-1.81, -1.42)	NA
CO-CPR vs. CPR 15:2								
Rea TD, 2010[24]	1 RCT (1,941)	Dispatcher-instructed CPR	Favourable neurological outcomes	14.40 (94/653)	11.53 (73/633)	1.25 (0.94, 1.66)	2.86 (-0.80, 6.53)	NA
Hallstrom A, 2000[20]; Rea TD, 2010[24]; Svensson L, 2010[23a]	3 RCTs (3,737)	Dispatcher-instructed CPR	Survival*	11.48 (211/1838)	9.52 (180/1890)	1.20 (1.00, 1.45)	1.88 (-0.05, 3.82)	0%
SOS-KANTO Study group, 2007[19]; Ong MEH, 2008[22]	2 Cohorts (1,592)	Bystander CPR	Favourable neurological outcomes	4.89 (29/593)	3.60 (36/999)	1.34 (0.82, 2.20)	0.51 (-2.16, 3.18)	1%
Van Hoeyweghen 1993[35]; Ong MEH, 2008[22]; Iwami T, 2007[26]	3 Cohorts (2,185)	Bystander CPR	ROSC	30.95 (251/811)	32.67 (411/1258)	0.89 (0.68, 1.16)	-4.19 (-13.68, 5.31)	64%
SOS-KANTO Study group, 2007[19]; Ong, MEH, 2008[22]; Iwami, T, 2007[26]; Bohm, K, 2007[34]; Waalewijn, RA, 2001[37a]; Holmberg, 2001[42a]	6 Cohorts (15,476)	Bystander CPR	Survival*	6.00 (156/2601)	7.55 (924/12240)	0.88 (0.74, 1.04)	-0.83 (-1.85, 0.19)	0%
CO-CPR vs. CPR 15:2 or 30:2								
Panchal, 2013[21]; Bobrow, 2010[39]; Olasveengen 2008[40]	3 Cohorts (2,193)	Bystander CPR	Favourable neurological outcomes	6.65 (76/1142)	6.36 (67/1053)	1.12 (0.71, 1.77)	0.28 (-2.33, 2.89)	29%
			Survival*	11.58 (132/1140)	8.64 (91/1053)	1.16 (0.64, 2.09)	1.27 (-3.70, 6.23)	63%
Olasveengen, 2008[40]	1 Cohort (426)	Bystander CPR	ROSC	36.55 (53/145)	37.37 (105/281)	0.98 (0.75, 1.27)	-0.81 (-10.48, 8.85)	NA
CPR 30:2 vs. CPR 15:2								
Olasveengen TM, 2009[25]; Kudenchuk P, 2012[27]	2 Cohorts (4,877)	EMS CPR	Favourable neurological outcomes	6.33 (169/2668)	4.75 (105/2209)	1.34 (1.02, 1.76)†	1.72 (0.52, 2.91)	24%
Olasveengen TM, 2009[25]; Kudenchuk	6 Cohorts (14,044)	EMS CPR	Survival*	10.01 (746/7449)	7.66 (499/6513)	1.37 (1.19, 1.59)†	2.48 (1.57, 3.38)	25%

P, 2012[27]; Steinmetz J, 2008[30]; Robinson S, 2010[33]; Sayre M, 2009[36]; Deasy C, 2011[17]								
Olasveengen TM, 2009[25]; Kudenchuk P, 2012[27]; Steinmetz J, 2008[30]; Sayre M, 2009[36]; Robinson S, 2010[33]; Deasy C, 2011[17]; Hostler D, 2007[32]	7 Cohorts (15,287)	EMS CPR	ROSC	34.99 (2404/6870)	32.40 (2151/6639)	1.11 (1.00, 1.23)	3.45 (0.10, 6.80)	64%
CPR 50:2 vs. CPR 15:2								
Garza A, 2009[29]	1 Cohort (200)	EMS CPR	Survival*	43.86 (25/57)	22.38 (32/143)	1.96 (1.28, 2.99)†	21.48 (6.90, 36.06)	NA
			ROSC	59.65 (34/57)	37.76 (54/143)	1.58 (1.17, 2.13)†	21.89 (6.88, 36.90)	NA
CC-CPR[b] vs. CPR 30:2								
Nichol G, 2015[16]	1 Cluster-crossover RCT (23,711)	EMS CPR	Favourable neurological outcomes	7.03 (883/12560)	7.68 (844/10995)	0.92 (0.84, 1.00)	-0.65 (-1.31, 0.02)	NA
			Survival*	8.95 (1129/12613)	9.71 (1072/11035)	0.92 (0.85, 1.00)	-0.76 (-1.51, -0.02)	NA
			ROSC	24.18 (3058/12646)	25.33 (2799 /11051)	0.955 (0.913, 0.998)†	-1.15 (-2.25, -0.05)	NA
CC-CPR[c] vs. CPR 15:2								
Kellum MJ, 2008[18]	1 Cohort (181)	EMS CPR	Favourable neurological outcomes	39.33 (35/89)	15.22 (14/92)	2.58 (1.50, 4.47)†	24.11 (11.58, 36.63)	NA
CC-CPR[c] vs. CPR 15:2 or 30:2								
Bobrow, 2008[41a]	1 Cohort (2,460)	EMS CPR	Favourable neurological outcomes	46.67 (28/60) ‡	57.97 (40/69) ‡	0.81 (0.57, 1.13)	-11.30 (-28.48, 5.87)	NA
			Survival*	9.08 (60/661)	3.84 (69/1799)	2.37 (1.69, 3.31)†	5.24 (2.88, 7.60)	NA
			ROSC	27.99 (185/661)	17.34 (312/1799)	1.61 (1.38, 1.89)†	10.64 (6.80, 14.49)	NA
CC-CPR[d] vs. CPR 5:1								
Lee IH, 2013[31 a]	1 Cohort (515)	In-hospital CPR	Favourable neurological outcomes	1.92 (4/208)	1.63 (5/307)	1.18 (0.32, 4.35)	0.29 (-2.05, 2.64)	NA
			Survival*	10.10 (21/208)	4.23 (13/307)	2.38 (1.22, 4.65)†	5.86 (1.19, 10.53)	NA
			ROSC	35.10 (73/208)	23.45 (72/307)	1.50 (1.14, 1.97)†	11.64 (3.61, 19.68)	NA
Paediatric Patients								
CO-CPR vs. CPR 30 :2								
Goto Y, 2014[28]	1 Cohort (2,617)	Bystander + Dispatcher-instructed CPR	Favourable neurological outcomes	2.71 (38/1402)	6.01 (73/1215)	0.45 (0.31, 0.66)†	-3.30 (-4.88, -1.71)	NA
			Survival*	8.84 (124/1402)	15.88 (193/1215)	0.56 (0.45, 0.69)†	-7.04 (-9.58, -4.50)	NA
CO-CPR vs. CPR 15:2 or 30:2								
Kitamura T, 2010[38]	1 Cohort (2,439)	Bystander CPR	Favourable neurological outcomes	2.59 (23/888)	5.61 (87/1551)	0.46 (0.29, 0.73)†	-3.02 (-4.57, -1.47)	NA

			Survival*	9.46 (84/888)	12.44 (193/1551)	0.76 (0.60, 0.97)†	-2.98 (-5.51, -0.45)	NA
			ROSC	5.52 (49/888)	7.48 (116/1551)	0.74 (0.53, 1.02)	-1.96 (-3.95, 0.03)	NA
Kitamura T, 2010[38e]	1 Cohort (1,444)	Bystander CPR	Favourable neurological outcomes	3.72 (20/538)	8.06 (73/906)	0.46 (0.28, 0.75)†	-4.34 (-6.73, -1.95)	NA
			Survival*	11.15 (60/538)	15.89 (144/906)	0.70 (0.53, 0.93)†	-4.74 (-8.31, -1.17)	NA
			ROSC	7.06 (38/538)	10.60 (96/906)	0.67 (0.47, 0.96)†	-3.53 (-6.48, -0.58)	NA
Kitamura T, 2010[38f]	1 Cohort (995)	Bystander CPR	Favourable neurological outcomes	0.86 (3/350)	2.17 (14/645)	0.39 (0.11, 1.36)	-1.31 (-2.80, 0.17)	NA
			Survival*	6.86 (24/350)	7.60 (49/645)	0.90 (0.56, 1.45)	-0.74 (-4.09, 2.61)	NA
			ROSC	3.14 (11/350)	3.10 (20/645)	1.01 (0.49, 2.09)	0.04 (-2.22, 2.31)	NA

Abbreviations: CC-CPR - continuous compression CPR; CI - confidence interval; CO-CPR - compression-only CPR; CPR - cardiopulmonary resuscitation; EMS – emergency medical service; NA – not applicable; RCT – randomized controlled trial; ROSC – Return of spontaneous circulation

* Survival data reported at the longest follow-up time. For example, if a study reported survival data at admission, at discharge or at 30 days, the survival data at 30 days was used.

† Results were found to be statistically significant

‡ Number of patients reported for favourable neurological outcomes and not the number of patients enrolled.[a] Combined population (includes both adults and paediatrics)

[b] All patients received positive-pressure ventilation

[c] Minimally interrupted cardiac resuscitation

[d] Mechanical Thumper device (model 1008) continuous CPR versus Thumper device (model 1007)

[e] Age 1 to 17years

[f] Age < 1 year

Table 3. Subgroup Analysis - Favourable Neurological Outcomes

Study ID	# of studies (# of patients)	CPR Provider	Aetiology	Mean EMS response (mins)	Initial Rhythm	% Arrest Witnessed (Rx; Ctrl)	ROB	Treatment % (# events /n)	Control % (# events /n)	Risk Ratio (95% CI)	Risk Difference % (95% CI)	I^2
Adults + All (both adult and paediatric) Patients												
CO-CPR vs. CPR 30:2												
Iwami T, 2015[2a]	1 Cohort (350,439)	Bystander + Dispatcher-instructed	Cardiac + noncardiac	8.00	shockable + nonshockable	35; 42	Moderate risk	1.94 (4846/249970)	2.68 (2690/100469)	0.72 (0.69, 0.76)*	-0.74 (-0.85, -0.63)	NA
CO-CPR vs. CPR 15:2												
Rea TD, 2010[24]	1 RCT (1,941)	Dispatcher-instructed CPR	Cardiac + noncardiac	6.50	shockable	43; 46	Low risk	14.40 (94/653)	11.53 (73/633)	1.25 (0.94, 1.66)	2.86 (-0.80, 6.53)	NA
SOS-KANTO Study group, 2007[19]; Ong MEH, 2008[22] [MAIN ANALYSIS]	2 Cohorts (1,592)	Bystander CPR	Combined	Combined	Combined	Combined	Combined	4.89 (29/593)	3.60 (36/999)	1.34 (0.82, 2.20)	0.51 (-2.16, 3.18)	1%
Ong MEH, 2008[22] [SENSITVITY ANALYSIS]	1 Cohort (441)	Bystander CPR	NR	11.50	shockable + nonshockable	77; 78	Unclear risk	1.30 (2/154)	2.09 (6/287)	0.62 (0.13, 3.04)	-0.79 (-3.23, 1.64)	NA
SOS-KANTO Study group, 2007[19] [SENSITVITY ANALYSIS]	1 Cohort (1,151)	Bystander CPR	Cardiac + noncardiac	NR	shockable + nonshockable	100; 100	Low risk	6.15 (27/439)	4.21 (30/712)	1.46 (0.88, 2.42)	1.94 (-0.75, 4.63)	NA
CPR 30:2 vs. CPR 15:2												
Olasveengen TM, 2009[25]; Kudenchuk P, 2012[27] [MAIN ANALYSIS]	2 Cohort (4,877)	EMS CPR	Combined	Combined	Combined	Combined	Combined	6.33 (169/2668)	4.75 (105/2209)	1.34 (1.02, 1.76)*	1.72 (0.52, 2.91)	24%
Olasveengen TM, 2009[25] [SENSITVITY ANALYSIS]	1 Cohort (917)	EMS CPR	Cardiac + noncardiac	9.00	shockable + nonshockable	59; 57	Unclear risk	11.83 (57/482)	10.34 (45/435)	1.14 (0.79, 1.65)	1.48 (-2.58, 5.54)	NA
Kudenchuk P, 2012[27] [SENSITVITY ANALYSIS]	1 Cohort (3,960)	EMS CPR	Cardiac + noncardiac	5.50	nonshockable	39; 39	Unclear risk	5.12 (112/2186)	3.38 (60/1774)	1.51 (1.11, 2.06)*	1.74 (0.49, 2.99)	NA
CC-CPR[b] vs. CPR 30:2												
Nichol G, 2015[16]	1 Cluster-crossover RCT (23,711)	EMS CPR	NR	5.90	shockable + nonshockable	41; 43	Low risk	7.03 (883/12560)	7.68 (844/10995)	0.92 (0.84, 1.00)	-0.65 (-1.31, 0.02)	NA

CC-CPR[c] vs. CPR 15 :2												
Kellum MJ, 2008[18]	1 Cohort (181)	EMS CPR	Cardiac	8.60	shockable	100; 100	High risk	39.33 (35/89)	15.22 (14/92)	2.58 (1.50, 4.47)*	24.11 (11.58, 36.63)	NA
CC-CPR vs. CPR 5:1												
Lee IH, 2013[31]	1 Cohort (515)	In-hospital CPR	NR	4.50	shockable + nonshockable	14; 15	Unclear risk	1.92 (4/208)	1.63 (5/307)	1.18 (0.32, 4.35)	0.29 (-2.05, 2.64)	NA
Paediatrics Patients												
CO-CPR vs. CPR 30 :2												
Goto Y, 2014[28]	1 Cohort (2,617)	Bystander + Dispatcher-instructed CPR	Cardiac + noncardiac	NR	NR	NA	Moderate risk	2.71 (38/1402)	6.01 (73/1215)	0.45 (0.31, 0.66)*	-3.30 (-4.88, -1.71)	NA
CO-CPR vs. CPR 15:2 or 30:2												
Kitamura T, 2010[38]	1 Cohort (2,439)	Bystander CPR	Cardiac + noncardiac	8.50	shockable + nonshockable	25; 24	Moderate risk	2.59 (23/888)	5.61 (87/1551)	0.46 (0.29, 0.73)*	-3.02 (-4.57, -1.47)	NA
Kitamura T, 2010[38d]	1 Cohort (1,444)	Bystander CPR	Cardiac + noncardiac	8.50	shockable + nonshockable	25; 24	Moderate risk	3.72 (20/538)	8.06 (73/906)	0.46 (0.28, 0.75)*	-4.34 (-6.73, -1.95)	NA
Kitamura T, 2010[38e]	1 Cohort (995)	Bystander CPR	Cardiac + noncardiac	8.50	shockable + nonshockable	25; 24	Moderate risk	0.86 (3/350)	2.17 (14/645)	0.39 (0.11, 1.36)	-1.31 (-2.80, 0.17)	NA

Abbreviations: CC-CPR - continuous compression CPR; CI – confidence interval; CO-CPR – compression-only CPR; CPR – cardiopulmonary resuscitation; EMS – emergency medical service; NA – not applicable; RCT – randomised controlled trial; ROB – risk of bias

* Results were found to be statistically significant

[a] Combined population (includes both adults and paediatrics)

[b] All patients received positive-pressure ventilation.

[c] Mechanical Thumper device (model 1008) continuous CPR versus Thumper device (model 1007)

[d] Age 1 to 17years

[e] Age < 1 year

Table 4. Sensitivity Analysis

Study ID	# of studies (# of patients)	CPR Provider	Outcome	Treatment %: (# events/n)	Control %: (# events/n)	Risk Ratio (95% CI)	Risk Difference % (95% CI)	I^2
Sensitivity analysis for age group: Adults + All (both adult and paediatric) Patients								
CO-CPR vs. CPR 15:2								
Hallstrom A, 2000[20]; Rea TD, 2010[24]; Svensson L, 2010[23a] [MAIN ANALYSIS]	Adults + All 3 RCTs (3,737)	Dispatcher-instructed CPR	Survival*	11.48 (211/1838)	9.52 (180/1890)	1.20 (1.00, 1.45)	1.88 (-0.05, 3.82)	0%
Hallstrom A, 2000[20]; Rea TD, 2010[24] [SENSITVITY ANALYSIS]	Adults 2 RCTs (2,461)	Dispatcher-instructed CPR	Survival*	12.89 (157/1218)	10.86 (134/1234)	1.19 (0.96, 1.48)	2.02 (-0.54, 4.59)	0%
Svensson L, 2010[23] [SENSITVITY ANALYSIS]	All (both adult and paediatric) 1 RCT (1,276)	Dispatcher-instructed CPR	Survival*	8.71 (54/620)	7.01 (46/656)	1.24 (0.85, 1.81)	1.70 (-1.26, 4.65)	NA
SOS-KANTO Study group, 2007[19]; Ong, MEH, 2008[22]; Iwami, T, 2007[26]; Bohm, K, 2007[34]; Waalewijn, RA, 2001[37a]; Holmberg, 2001[42a] [MAIN ANALYSIS]	Adults + All 6 Cohorts (15,476)	Bystander CPR	Survival*	6.00 (156/2601)	7.55 (924/12240)	0.88 (0.74, 1.04)	-0.83 (-1.85, 0.19)	0%
SOS-KANTO Study, 2007[19]; Ong MEH, 2008[22]; Iwami T, 2007[26]; Bohm K, 2007[34] [SENSITVITY ANALYSIS]	Adults 4 Cohorts (12,273)	Bystander CPR	Survival*	5.74 (131/2282)	6.88 (687/9991)	0.91 (0.75, 1.09)	-0.62 (-1.70, 0.45)	0%
Waalewijn RA, 2001[37]; Holmberg, 2001[42] [SENSITVITY ANALYSIS]	All (both adult and paediatric) 2 Cohort (3,203)	Bystander CPR	Survival*	7.84 (25/319)	10.54 (237/2249)	0.78 (0.53, 1.16)	-2.60 (-5.74, 0.53)	0%
Sensitivity analysis for age group: Paediatrics Patients								
CO-CPR vs. CPR 15:2 or 30:2								
Kitamura T, 2010[38] [MAIN ANALYSIS]	1 Cohort (2,439)	Bystander CPR	Favourable neurological outcomes	2.59 (23/888)	5.61 (87/1551)	0.46 (0.29, 0.73)†	-3.02 (-4.57, -1.47)	NA

			Survival*	9.46 (84/888)	12.44 (193/1551)	0.76 (0.6, 0.97)†	-2.98 (-5.51, -0.45)	NA
			ROSC	5.52 (49/888)	7.48 (116/1551)	0.74 (0.53, 1.02)	-1.96 (-3.95, 0.03)	NA
Kitamura T, 2010[38] [SENSITVITY ANALYSIS]	Age 1-17 years 1 Cohort (1,444)	Bystander CPR	Favourable neurological outcomes	3.72 (20/538)	8.06 (73/906)	0.46 (0.28, 0.75)†	-4.34 (-6.73, -1.95)	NA
			Survival*	11.15 (60/538)	15.89 (144/906)	0.70 (0.53, 0.93)†	-4.74 (-8.31, -1.17)	NA
			ROSC	7.06 (38/538)	10.60 (96/906)	0.67 (0.47, 0.96)†	-3.53 (-6.48, -0.58)	NA
Kitamura T, 2010[38] [SENSITVITY ANALYSIS]	Age < 1 year 1 Cohort (995)	Bystander CPR	Favourable neurological outcomes	0.86 (3/350)	2.17 (14/645)	0.39 (0.11, 1.36)	-1.31 (-2.80, 0.17)	NA
			Survival*	6.86 (24/350)	7.60 (49/645)	0.90 (0.56, 1.45)	-0.74 (-4.09, 2.61)	NA
			ROSC	3.14 (11/350)	3.10 (20/645)	1.01 (0.49, 2.09)	0.04 (-2.22, 2.31)	NA
Sensitivity analysis for survival data closest to CPR								
CO-CPR vs. CPR 15:2								
SOS-KANTO Study group, 2007[19]; Ong, MEH, 2008[22]; Iwami, T, 2007[26]; Bohm, K, 2007[34]; Waalewijn, RA, 2001[37a]; Holmberg, 2001[42a] [MAIN ANALYSIS]	Longest follow-up time 6 Cohorts (15,476)	Bystander CPR	Survival	6.00 (156/2601)	7.55 (924/12240)	0.88 (0.74, 1.04)	-0.83 (-1.85, 0.19)	0%
SOS-KANTO Study group, 2007[19]; Ong, MEH, 2008[22]; Iwami, T, 2007[26]; Bohm, K, 2007[34]; Waalewijn, RA, 2001[37]; Holmberg, 2001[42] [SENSITVITY ANALYSIS]	Closest follow-up time 6 Cohorts (15,476)	Bystander CPR	Survival	12.42 (323/2601)	16.72 (2047/12240)	0.93 (0.80, 1.08)	-0.97 (-2.22, 0.28)	16%
Hallstrom A, 2000[20]; Rea TD, 2010[24]; Svensson L, 2010[23a] [MAIN ANALYSIS]	Longest follow-up time 3 RCTs (3,737)	Dispatcher-instructed CPR	Survival	11.48 (211/1838)	9.52 (180/1890)	1.20 (1.00, 1.45)	1.88 (-0.05, 3.82)	0%
Hallstrom A, 2000[20]; Rea TD, 2010[24]; Svensson L, 2010[23] [SENSITVITY ANALYSIS]	Closest follow-up time 3 RCTs (3,737)	Dispatcher-instructed CPR	Survival	14.07 (211/1500)	11.63 (178/1531)	1.22 (1.01, 1.46)†	2.37 (0.00, 4.73)	0%
CO-CPR vs. CPR 15:2 or 30:2								
Panchal, 2013[21]; Bobrow, 2010[39]; Olasveengen 2008[40] [MAIN ANALYSIS]	Longest follow-up time 3 Cohorts	Bystander CPR	Survival	11.58 (132/1140)	8.64 (91/1053)	1.16 (0.64, 2.09)	1.27 (-3.70, 6.23)	63%

	(2,193)							
Panchal, 2013[21]; Bobrow, 2010[39]; Olasveengen, 2008[40] [SENSITVITY ANALYSIS]	Closest follow-up time 3 Cohorts (2,193)	Bystander CPR	Survival	15.26 (174/1140)	15.95 (168/1053)	1.21 (0.76, 1.95)	2.00 (-2.95, 6.94)	74%
CPR 30:2 vs. CPR 15:2								
Olasveengen TM, 2009[25]; Kudenchuk P, 2012[27]; Steinmetz J, 2008[30]; Robinson S, 2010[33]; Sayre M, 2009[36]; Deasy C, 2011[17] [MAIN ANALYSIS]	Longest follow-up time 6 Cohorts (14,044)	EMS CPR	Survival	10.01 (746/7449)	7.66 (499/6513)	1.37 (1.19, 1.59)†	2.48 (1.57, 3.38)	25%
Olasveengen TM, 2009[25]; Kudenchuk P, 2012[27]; Steinmetz J, 2008[30]; Robinson S, 2010[33]; Sayre M, 2009[36]; Deasy C, 2011[17] [SENSITVITY ANALYSIS]	Closest follow-up time 6 Cohorts (14,044)	EMS CPR	Survival	24.42 (1819/7449)	19.53 (1272/6513)	1.38 (1.21, 1.56)†	5.81 (2.99, 8.62)	50%
CC-CPR[a] vs. CPR 15:2 or 30:2								
Bobrow, 2008[41] [MAIN ANALYSIS]	Longest follow-up time 1 Cohort (2,460)	EMS CPR	Survival	9.08 (60/661)	3.84 (69/1799)	2.37 (1.69, 3.31)†	5.24 (2.88, 7.60)	NA
Bobrow, 2008[41] [SENSITVITY ANALYSIS]	Closest follow-up time 1 Cohort (2,460)	EMS CPR	Survival	21.94 (145/661)	15.06 (271/1799)	1.46 (1.22, 1.74)†	6.87 (3.31, 10.43)	NA
CC-CPR[b] vs. CPR 5:1								
Lee IH, 2013[31] [MAIN ANALYSIS]	Longest follow-up time 1 Cohort (515)	In-hospital CPR	Survival	10.10 (21/208)	4.23 (13/307)	2.38 (1.22, 4.65)†	5.86 (1.19, 10.53)	NA
Lee IH, 2013[31] [SENSITVITY	Closest follow-up	In-hospital CPR	Survival	32.21 (67/208)	23.13 (71/307)	1.39 (1.05, 1.85)†	9.08 (1.17, 16.99)	NA

ANALYSIS]	time 1 Cohort (515)							

Abbreviations: CC-CPR – continuous compression CPR; CI – confidence interval; CO-CPR – compression-only CPR; CPR – cardiopulmonary resuscitation; EMS – emergency medical service; NA – not applicable; RCT – randomised controlled trial; ROSC – return of spontaneous circulation

* Survival data reported closest to CPR. For example, if a study reported survival data at admission, at discharge or at 30 days, the survival data at admission was used.

† Results were found to be statistically significant

[a] Minimally interrupted cardiac resuscitation

[b] Mechanical Thumper device (model 1008) continuous CPR versus Thumper device (model 1007)

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