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

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- 54 supplementary files.

55 **ABSTRACT**

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

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

66 **Results:** After screening 5,703 titles and abstracts and 229 full-text articles, we included 41
67 studies, of which 13 were companion reports. For adults receiving bystander or dispatcher-
68 instructed CPR, no significant differences were observed across all comparisons and outcomes.
69 Significantly less adults receiving bystander-initiated or plus dispatcher-instructed compression-
70 only CPR experienced favourable neurological outcomes, survival, and ROSC compared to CPR
71 30:2 (compression-to-ventilation) in un-adjusted analyses in a large cohort study. Evidence from
72 emergency medical service (EMS) CPR providers showed significantly more adults receiving
73 CPR 30:2 experiencing improved favourable neurological outcomes and survival versus those
74 receiving CPR 15:2. Significantly more children receiving CPR 15:2 or 30:2 experienced
75 favourable neurological outcomes, survival, and greater ROSC compared to compression-only
76 CPR. However, for children <1 years of age, no significant differences were observed between
77 CPR 15:2 or 30:2 and compression-only CPR.

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

83 **INTRODUCTION**

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

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

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

101 **METHODS**

102 **Protocol**

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

107 **Eligibility criteria**

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

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

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

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

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

125 **Study designs:** Randomised controlled trials (RCTs) and non-randomised studies (non-
126 randomised controlled trials, interrupted time series, controlled before-and-after studies, cohort
127 studies) were eligible for inclusion. Study designs without a comparator group (e.g., case series,
128 cross-sectional studies), reviews, and pooled analyses were excluded.

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

131 **Information sources and literature search**

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

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

138 **Study selection**

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

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

148 **Data items and data abstraction**

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

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

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

165 **Risk of bias**

166 The Cochrane Risk-of-Bias Tool¹⁰ was used for appraising RCTs and quasi-RCTs; Cochrane
167 Effective Practice and Organization of Care (EPOC) Risk-of-Bias Tool¹¹ was used for cluster-
168 crossover RCTs, non-randomised controlled trials, interrupted time series, and controlled before-
169 and-after studies; and Newcastle-Ottawa Scale was used for cohort studies.¹² Experienced pairs
170 of reviewers (FY, JI, MG, PAK, RC, VN) independently appraised the risk of bias of all included
171 studies with discrepancies resolved by a third reviewer (EL, WZ).

172 *Synthesis of results*

173 Intervention effects (e.g., CO-CPR versus CPR 30:2 compression-to-ventilation ratio) were
174 summarized using un-adjusted risk ratios (RR) and risk differences (RD) and pooled via random-
175 effects meta-analysis. We assessed statistical heterogeneity using the I² statistic,¹³ with an I²
176 value above 75% indicative of substantial heterogeneity.¹³ All statistical analyses were
177 conducted using the *metafor* package in R (version 3.2.3).¹⁴

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

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

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

189 **GRADE appraisal**

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

196 **RESULTS**

197 **Literature search**

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

201 **Study characteristics**

202 Included studies were published between 1993 and 2015 with a study period ranging from 1983
203 to 2015 (Table 1; Appendix F). We included one cluster-crossover RCT,¹⁶ three RCTs,^{20, 23, 24}
204 and 24 cohort studies.^{2, 17-19, 21, 22, 25-42} Most studies were conducted in the USA and Japan (n=16),
205 involving OHCAs (n=27), while one³¹ was conducted in a hospital setting.

206 Nine studies^{17, 18, 20, 29, 33, 35, 37, 39, 41} included cardiac arrests with cardiac causes, 13 papers^{2, 19, 24-}
207 ^{28, 30, 34, 36, 38, 40, 42} included both cardiac and non-cardiac causes, and one paper²¹ included non-
208 cardiac causes. CPR was provided by: EMS personnel,^{16-18, 25, 27, 29, 30, 32, 33, 36, 41} bystanders,^{19, 21,}
209 ^{22, 26, 34, 35, 37, 38} bystanders receiving dispatcher instructions,^{20, 23, 24} bystander alone or with
210 dispatcher instructions,^{2, 28} and emergency department staff.³¹ Most studies (n=16)^{2, 16, 17, 19, 20, 22,}
211 ^{23, 25, 30-33, 35, 36, 38, 40} did not restrict the study population by initial rhythm, six^{24, 26, 29, 34, 39, 41}
212 included only patients with initial shockable rhythm, and one²⁷ included patients with initial
213 non-shockable rhythm.

214 **Patient characteristics**

215 Twenty studies^{16-21, 24-34, 36, 39, 40} included adults, two^{28, 38} included children, and six^{2, 23, 35, 37, 41, 42}
216 included both adults and children (Table 1; Appendix G). The overall number of CPR recipients
217 in each study ranged from 181 to 350,439 and the proportion of males ranged from 59 to 79%.

218 The mean age reported for adult-only studies ranged from 56.9 years (SD 18.6) to 74.1 years (SD
219 14.9), and was 4.9 years (SD 6.1) for paediatric-only studies.

220 **Risk of bias results**

221 Three RCTs were appraised with the Cochrane risk-of-bias tool (Appendix H). One trial²⁴ had an
222 unclear random sequence generation, while another²⁰ had unclear allocation concealment, and
223 the third trial²³ had a high risk of bias due to blinding of personnel, as well as incomplete
224 outcome data bias. One cluster-crossover RCT¹⁶ assessed using the EPOC risk-of-bias tool
225 (Appendix I) had an unclear risk of bias for random sequence generation, as well as for
226 allocation concealment; all other items were scored as low risk of bias.

227 For the 23 cohort studies, the main methodological shortcoming was related to the comparability
228 of cohorts on the basis of the design or analysis, as the majority did not adjust for potential
229 confounding variables (Appendix J). In addition, the majority of the cohort studies did not report
230 the duration of follow-up.^{17, 22, 25-28, 30-34, 36, 37, 40-42}

231 **Reporting results**

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

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

241 For bystanders plus dispatcher-instructed CPR, one cohort study² of 350,439 mostly adult
242 patients found that significantly less patients receiving CO-CPR experienced favourable
243 neurological outcomes (RD -0.74, 95% CI: -0.85, -0.63), survived (RD -1.42, 95% CI: -1.58, -
244 1.25), and experienced ROSC (RD -1.62, 95% CI: -1.81, -1.42) compared to CPR 30:2.

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

246 For EMS CPR, a meta-analysis of two cohort studies^{25, 27} with 4,877 adults found that
247 significantly more patients receiving CPR 30:2 experienced favourable neurological outcomes
248 (RD 1.72, 95% CI: 0.52, 2.91) compared to CPR 15:2. A meta-analysis of six cohort studies^{17, 25,}
249 ^{27, 30, 33, 36} with 13,962 adults revealed that significantly more patients receiving CPR 30:2
250 survived (RD 2.48, 95% CI: 1.57, 3.38) compared to CPR 15:2. The results for ROSC were not
251 statistically significant.

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

253 For EMS CPR, one cohort study²⁹ of 200 adults found that significantly more patients receiving
254 CPR 50:2 survived (RD 21.48, 95% CI: 6.90, 36.06) and experienced ROSC (RD 21.89, 95% CI:
255 6.88, 36.90) compared to CPR 15:2.

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

257 For EMS CPR, one cluster-crossover RCT¹⁶ including 23,711 adults found significantly less
258 patients receiving CC-CPR experienced ROSC (RD -1.15, 95% CI: -2.25, -0.05) compared to
259 CPR 30:2 in un-adjusted analysis. However, results for favourable neurological outcomes and

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

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

263 For EMS CPR, one cohort study¹⁸ of 181 adults found that significantly more patients receiving
264 CC-CPR experienced favourable neurological outcomes (RD 24.11, 95% CI: 11.58, 36.63)
265 compared to CPR 15:2.

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

267 For EMS CPR, one cohort study⁴¹ with 2,460 mostly adult patients found that significantly more
268 patients receiving CC-CPR survived (RD 5.24, 95% CI: 2.88, 7.6) and experienced ROSC (RD
269 10.64, 95% CI: 6.80, 14.49) compared to CPR 15:2 or 30:2. The results for favourable
270 neurological outcomes were not statistically significant.

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

273 For in-hospital CPR, one cohort study³¹ of 515 adults found that significantly more patients
274 receiving CC-CPR survived (RD 5.86 95% CI: 1.19, 10.53), and experienced ROSC (RD 11.64,
275 95% CI: 3.61, 19.68) compared to CPR 5:1. The results for favourable neurological outcomes
276 were not statistically significant.

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

278 For bystander plus dispatcher-instructed CPR, one cohort study²⁸ of 2,617 children (mean age:
279 NR) found significantly less patients receiving CO-CPR experienced favourable neurological

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

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

283 For bystander CPR, one cohort study³⁸ of 2,439 paediatric (mean age: 4.9yrs) patients found
284 significantly less patients receiving CO-CPR experienced favourable neurological outcomes (RD
285 -3.02, 95% CI: -4.57, -1.47) or survived (RD -2.98, 95% CI: -5.51, -0.45) compared to CPR 15:2
286 or 30:2. The results for ROSC were not statistically significant.

287 **Quality of life**

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

289 **GRADE (Appendix L)**

290 The only results of high certainty in this systematic review were those for favourable
291 neurological outcomes, survival, and ROSC, in one cluster-crossover RCT¹⁶ which compared
292 CO-CPR to CPR 30:2 provided by EMS. All other results were of low or very low certainty.

293 **DISCUSSION**

294 For adults, our results suggest no statistically significant differences across all outcomes and
295 comparisons for those receiving bystander-initiated CPR alone or dispatcher-instructed CPR with
296 or without ventilations. Significantly less adults receiving bystander plus dispatcher-instructed
297 CO-CPR experienced favourable neurological outcomes, survival, and ROSC compared to CPR
298 30:2. As well, significantly more patients receiving EMS CPR 30:2 experienced favourable
299 neurological outcomes and survival compared to CPR 15:2.

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

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

316 dispatcher-instructed CO-CPR⁵⁸ 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 Hupfl⁵⁹ 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 review⁶⁰ 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.

339 Consequently, those results might not be reliable and should be interpreted with caution.
340 Additionally, a small number of studies where the focus was not to compare different
341 compression-to-ventilation ratios (though these data were featured in sub-group analyses) were
342 included, after having been identified by the content experts. It is possible that similar studies
343 could have been missed during our screening process. Also we identified several studies
344 examining minimally-interrupted cardiac resuscitation delivered by EMS from Arizona. In some
345 of these cases, the evaluation appeared to run concurrently with a community campaign of
346 bystander compression-only CPR.^{21, 39} It was difficult to precisely determine the overlap in
347 patient populations reported in these studies. For example, whilst it was clear that some studies
348 examined specific sub-groups who received MICR (e.g. age),^{61, 62} there appeared to be overlap in
349 the patient populations evaluated between reports.^{18, 41, 43} To minimize the risk of including
350 individual patients more than once in our meta-analysis, we limited our analysis to the Bobrow,
351 2008⁴¹ paper as we judged this to be the most comprehensive study that was aligned with our
352 specific PICO question. Finally, the studies we evaluated included a variety of settings where
353 EMS systems and response times may vary and for some studies it was not possible to separate
354 paediatric from adult cases.

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

362 and unmeasured confounding factors. In our analyses we only included un-adjusted estimates
363 because only four of the included papers^{16, 28, 31, 41} undertook analyses which adjusted for
364 potentially confounding variables (Appendix K). Also, since there were fewer than 10 studies in
365 the meta-analyses⁶³, we were unable to statistically assess for publication bias.

366 In terms of areas identified for future research, we did not find any studies that measured quality
367 of life. This is an important patient-related outcome that needs to be considered in future studies.

368 In addition, none of the included studies provided data on neonates. Thus, for this population it
369 might be necessary to use indirect evidence from paediatric studies or animal models to

370 extrapolate results.

371 **CONCLUSIONS**

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

377 **CONFLICTS OF INTEREST**

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

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392 **LIST OF ABBREVIATIONS**

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

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

403 **LEGENDS TO FIGURES**

404 Table 1: Summary characteristics

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

406 Table 3. Subgroup Analysis - Favourable Neurological Outcomes

407 Table 4. Sensitivity Analysis

408 Figure 1. Flow chart

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

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

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

418 **SUPPLEMENTARY FILES**

419 Supplementary File 1: Appendix (A-L)

420 Supplementary File 2: PRISMA Checklist

421 **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 %) |

422 **Abbreviations:** CA – cardiac arrest; CC-CPR - continuous compression CPR; CO-CPR – compression-only CPR;
423 CPR – cardiopulmonary resuscitation; EMS – emergency medical service; IQR – interquartile range; NRCT – non-
424 randomised controlled trials; RCT – randomised controlled trial; SD – standard deviation
425

426 ^aIncludes cardiocerebral resuscitation and minimally interrupted cardiac resuscitation
427

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 ^{31a} | 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 ^{38c} | 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 |
| | | | Favourable neurological outcomes | 0.86 (3/350) | 2.17 (14/645) | 0.39 (0.11, 1.36) | -1.31 (-2.80, 0.17) | NA |
| Kitamura T, 2010 ^{38f} | 1 Cohort (995) | Bystander CPR | 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 |

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

431
432 * 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
433 30 days was used.

434 † Results were found to be statistically significant

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

437 ^b All patients received positive-pressure ventilation

438 ^c Minimally interrupted cardiac resuscitation

439 ^d Mechanical Thumper device (model 1008) continuous CPR versus Thumper device (model 1007)

440 ^e Age 1 to 17years

441 ^f Age < 1 year

442 **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 [SENSITIVITY 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 [SENSITIVITY 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 [SENSITIVITY 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 [SENSITIVITY 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 |

443 **Abbreviations:** CC-CPR - continuous compression CPR; CI – confidence interval; CO-CPR – compression-only CPR; CPR – cardiopulmonary resuscitation;
444 EMS – emergency medical service; NA – not applicable; RCT – randomised controlled trial; ROB – risk of bias
445

446 * Results were found to be statistically significant

447 ^a Combined population (includes both adults and paediatrics)

448 ^b All patients received positive-pressure ventilation.

449 ^c Mechanical Thumper device (model 1008) continuous CPR versus Thumper device (model 1007)

450 ^d Age 1 to 17years

451 ^e Age < 1 year

452 **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 [SENSITIVITY 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 [SENSITIVITY 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 [SENSITIVITY 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 [SENSITIVITY 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 [SENSITIVITY 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 [SENSITIVITY 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 [SENSITIVITY 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 [SENSITIVITY 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 [SENSITIVITY 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 [SENSITIVITY 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 [SENSITIVITY 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 [SENSITIVITY ANALYSIS] | 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) | | | | | | | |
|-----------|---------------------------|--|--|--|--|--|--|--|

453 **Abbreviations:** CC-CPR – continuous compression CPR; CI – confidence interval; CO-CPR – compression-only CPR; CPR – cardiopulmonary resuscitation;
454 EMS – emergency medical service; NA – not applicable; RCT – randomised controlled trial; ROSC – return of spontaneous circulation
455
456 * 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
457 used.
458 † Results were found to be statistically significant
459 ^a Minimally interrupted cardiac resuscitation
460 ^b Mechanical Thumper device (model 1008) continuous CPR versus Thumper device (model 1007)

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