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| Question |
| **Question: In adults and children with cardiac arrest treated by emergency medical services, does continuous chest compressions with or without ventilations compared with standard CPR improve patient outcomes?** |
| **Population:** | Adults and children in any setting (in-hospital or out-of-hospital) with cardiac arrest |
| **Intervention:** | Continuous chest compressions delivered by emergency medical services (EMS) with or without ventilations |
| **Comparison:** | Standard CPR, defined as any compression-to-ventilation ratio delivered by EMS. Comparator groups that receive no CPR or compared manual CPR with mechanical CPR were excluded from the review. Studies including automated CPR or any use of mechanical devices were only be included if administered to all treatment arms. |
| **Main outcomes:** | Favourable neurological survival (as measured by cerebral performance category or modified Rankin Score) at discharge or 30-days and at any time interval after 30-days; Survival to discharge or 30 days survival; Survival to any time interval after discharge or 30 days survival; Return of spontaneous circulation (ROSC); Quality of life as measured by any indicator or score. |
| **Setting:** | Out-of-hospital |
| **Perspective:** |  |
| **Background:** |  |
| **Conflict of interests:** | BLS TF Members Laurie Morrison and Christian Vaillancourt are co-authors on the ROC CCC trial (Nichol 2015 2203)  |

# Assessment

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| ProblemIs the problem a priority? |
| Judgement | Research evidence | Additional considerations |
| ○ No○ Probably no○ Probably yes**X** Yes○ Varies○ Don't know | Conventional cardiopulmonary resuscitation (CPR) consists of manual chest compressions and positive-pressure ventilation to maintain oxygenation until return of spontaneous circulation is achieved. Ventilations result in frequent interruptions in chest compressions, however, which can reduce coronary and aortic blood flow during cardiac arrest and has been associated with poorer survival in animal models (Kern 2002 645). Similarly, higher chest compression fraction (total resuscitation time spent performing chest compressions) has been associated with improved outcomes in observational studies (Christenson 2009 1241). One strategy to improve chest compression fraction and reduce interruptions in chest compression is to perform continuous chest compression with 1) asynchronous ventilations or 2) passive oxygenation via face mask. However, there is also concern that continuous chest compression may be harmful for patients who require more effective ventilations, such as asphyxial arrests or drowning (Berg 2000 1743).  | In resource-limited environments including the prehospital setting, there is value in limiting resuscitation logistics wherever possible. Some systems have achieved this by performing continuous chest compression with passive oxygenation which may help prioritise other treatments. There has also been widespread adoption of high-performance CPR among EMS systems which focus on providing minimally interrupted chest compressions.  |
| Desirable EffectsHow substantial are the desirable anticipated effects? |
| Judgement | Research evidence | Additional considerations |
| ○ Trivial**X** Small○ Moderate○ Large○ Varies○ Don't know | Interruptions in chest compressions have been associated with poorer clinical outcomes in observational studies (Christenson 2009 1241). Pauses for ventilations are a significant source of interruptions in chest compressions and may have negative impacts on coronary and aortic blood flow (Berg 2001 2465). Asynchronous positive pressure ventilation may achieve similar oxygenation without compromising chest compression quality. However, based on a large cluster RCT undertaken in North America (Nichol 2015 2203) the likely benefit to patient outcomes is small. In this RCT, adherence to protocol was low and it is possible that larger differences in patient outcomes exist with greater compliance to CCC strategy. Studies adopting minimally interrupted cardiac resuscitation (Bobrow 2008 1158) have demonstrated larger impacts on patient outcomes, particularly in patients with witnessed shockable OHCA. These studies, however, have typically examined minimally interrupted cardiac resuscitation as a bundle with other resuscitation practice changes and therefore the directness of evidence is uncertain. |  A strategy of CCC has been shown to significantly improve chest compression fraction in a large cluster RCT (Nichol 2015 2203). |
| Undesirable EffectsHow substantial are the undesirable anticipated effects? |
| Judgement | Research evidence | Additional considerations |
| ○ Large○ Moderate**X** Small○ Trivial○ Varies○ Don't know | Based on a large cluster RCT undertaken in North America (Nichol 2015 2203), CCC was not inferior to standard CPR in the intention-to-treat analysis. However, in the per-protocol population, the survival rate was significantly lower in the CCC group compared to the standard CPR group (adjusted difference, −2.0 percentage points; 95% CI, −2.9 to −1.1; P<0.001), although the groups were imbalanced and larger numbers of patients were excluded due to noncompliance. Adjustment for pretreatment confounders attenuated the difference in the survival rate between the treatment groups in the per protocol analysis (difference, −0.3 percentage points; 95% CI, −1.1 to 0.4; P = 0.38). In another large observational study (Schmicker 2021 31) from the Resuscitation Outcomes Consortium, the association between treatment groups was attenuated by adherence to the intended strategy. For the intended strategy of CCC, survival was significantly lower when adhered to (adjusted OR: 0.72 [95% CI: 0.64, 0.81]), while for the intended strategy of 30:2, survival was higher when adhered to (adjusted OR: 1.05 [95% CI: 0.90, 1.22]). This may suggest some harm with a CCC strategy.  | Presently, there is a lack of scientific evidence to support the use passive oxygenation during OHCA. It is possible that passive oxygenation may be inferior to PPV, which may be more clinically important in OHCA precipitated by asphyxia or drowning. It is also possible that PPV may be more effective for oxygenation but too difficult to achieve in practice. As such, the net benefit of PPV may be smaller than passive oxygenation or asynchronous ventilations using PPV.  |
| Certainty of evidenceWhat is the overall certainty of the evidence of effects? |
| Judgement | Research evidence | Additional considerations |
| ○ Very low○ Low**X** Moderate○ High○ No included studies | The CoSTR included 4 studies; one large moderate-quality cluster RCT with crossover (Nichol 2015 2203) and 3 other very-low-quality cohort studies. The Task Force gave greater weight to the certainty of evidence derived from the cluster RCT as it addressed the PICOST directly. The certainty of evidence in the RCT was downgraded due to risk of bias from baseline differences (witness status and cluster), lack of blinding of intervention, lack of protection against contamination in the treatment strategies, and indirectness due to a low rate of protocol compliance. The certainty of evidence from the remaining cohort studies were also downgraded due to a high risk of residual confounding, high rates of non-adherence to treatments, and indirectness from the use of a bundled intervention.  |  |
| ValuesIs there important uncertainty about or variability in how much people value the main outcomes? |
| Judgement | Research evidence | Additional considerations |
| ○ Important uncertainty or variability**X** Possibly important uncertainty or variability○ Probably no important uncertainty or variability○ No important uncertainty or variability | There was only one study included that considered the impact of CCC and standard CPR on neurologically favourable survival, however, this was a large RCT (Nichol 2015 2203). No studies examined quality of life outcomes or longer-term patient outcomes. |  |
| Balance of effectsDoes the balance between desirable and undesirable effects favor the intervention or the comparison? |
| Judgement | Research evidence | Additional considerations |
| ○ Favors the comparison○ Probably favors the comparison○ Does not favor either the intervention or the comparison**X** Probably favors the intervention○ Favors the intervention○ Varies○ Don't know | Despite the theoretical risk of suboptimal ventilations in patients receiving CCC, there is limited data suggesting a negative impact on survival. Conversely, there is some observational data to indicate potential patient harm from interruptions in chest compressions. Furthermore, standard CPR involving a compression-to-ventilation ratio is hard to achieve, and in practice may result in asynchronous ventilations. |  |
| Resources requiredHow large are the resource requirements (costs)? |
| Judgement | Research evidence | Additional considerations |
| ○ Large costs○ Moderate costs**X** Negligible costs and savings○ Moderate savings○ Large savings○ Varies○ Don't know | Negligible impact on resources as both treatment strategies require similar investment in staff and resources. | It is possible the CCC is easier to teach and may be more practical in resource-limited environments. Data from one RCT (Nichol 2015 2203) and observation studies suggest that CCC is associated with more adherence to protocol compared to standard CPR (Bobrow 2008 1158; Schmicker 2021 31).  |
| Certainty of evidence of required resourcesWhat is the certainty of the evidence of resource requirements (costs)? |
| Judgement | Research evidence | Additional considerations |
| ○ Very low○ Low○ Moderate○ HighX No included studies | There were no economic evaluations of the two treatment strategies. |  |
| Cost effectivenessDoes the cost-effectiveness of the intervention favor the intervention or the comparison? |
| Judgement | Research evidence | Additional considerations |
| ○ Favors the comparison○ Probably favors the comparison**X** Does not favor either the intervention or the comparison○ Probably favors the intervention○ Favors the intervention○ Varies○ No included studies | CCC is likely to be as cost-effective as standard CPR. |  |
| EquityWhat would be the impact on health equity? |
| Judgement | Research evidence | Additional considerations |
| ○ Reduced○ Probably reduced**X** Probably no impact○ Probably increased○ Increased○ Varies○ Don't know | In the EMS setting, it is unlikely that CCC would improve treatment equity compared to standard CPR.  |  |
| AcceptabilityIs the intervention acceptable to key stakeholders? |
| Judgement | Research evidence | Additional considerations |
| ○ No○ Probably no○ Probably yes**X** Yes○ Varies○ Don't know | Many EMS systems around the world have already implemented CCC or minimally interrupted cardiac resuscitation.  |  |
| FeasibilityIs the intervention feasible to implement? |
| Judgement | Research evidence | Additional considerations |
| ○ No○ Probably no○ Probably yes**X** Yes○ Varies○ Don't know | The task force placed high value on the importance of providing high-quality chest compressions and simplifying resuscitation logistics for EMS systems and noted the support for the clinical benefit of bundles of care involving minimally interrupted cardiac resuscitation.  |  |

# Summary of judgements

|  | **Judgement** |
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| **Problem** | No | Probably no | Probably yes | **Yes** |  | Varies | Don't know |
| **Desirable Effects** | Trivial | **Small** | Moderate | Large |  | Varies | Don't know |
| **Undesirable Effects** | Large | Moderate | **Small** | Trivial |  | Varies | Don't know |
| **Certainty of evidence** | Very low | Low | **Moderate** | High |  |  | No included studies |
| **Values** | Important uncertainty or variability | **Possibly important uncertainty or variability** | Probably no important uncertainty or variability | No important uncertainty or variability |  |  |  |
| **Balance of effects** | Favors the comparison | Probably favors the comparison | Does not favor either the intervention or the comparison | **Probably favors the intervention** | Favors the intervention | Varies | Don't know |
| **Resources required** | Large costs | Moderate costs | **Negligible costs and savings** | Moderate savings | Large savings | Varies | Don't know |
| **Certainty of evidence of required resources** | Very low | Low | Moderate | High |  |  | **No included studies** |
| **Cost effectiveness** | Favors the comparison | Probably favors the comparison | **Does not favor either the intervention or the comparison** | Probably favors the intervention | Favors the intervention | Varies | No included studies |
| **Equity** | Reduced | Probably reduced | **Probably no impact** | Probably increased | Increased | Varies | Don't know |
| **Acceptability** | No | Probably no | Probably yes | **Yes** |  | Varies | Don't know |
| **Feasibility** | No | Probably no | Probably yes | **Yes** |  | Varies | Don't know |

# Type of recommendation

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| Strong recommendation against the intervention | Conditional recommendation against the intervention | Conditional recommendation for either the intervention or the comparison | Conditional recommendation for the intervention | Strong recommendation for the intervention |
| ○  | ○  | **X** | ○  | ○  |

# Conclusions

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| Recommendation |
| We recommend that EMS providers perform CPR with 30 compressions to 2 ventilations or continuous chest compressions with positive pressure ventilations delivered without pausing chest compressions until a tracheal tube or supraglottic device has been placed (strong recommendation, moderate-certainty evidence). |
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| Justification |
| • Interruptions in chest compressions have been associated with poorer clinical outcomes in observational studies (Christenson 2009 1241). Pauses for ventilations are a significant source of interruptions in chest compressions and may have negative impacts on coronary and aortic blood flow (Berg 2001 2465). Asynchronous positive pressure ventilation may achieve similar oxygenation without compromising chest compression quality.• This topic was prioritised for review due to the time since the previous systematic review (Ashoor 2017 112) in which a number of additional cohort studies were published on the topic. We identified one large cluster RCT (Nichol 2015 2203) and three cohort studies including two post-hoc analyses of the earlier cluster RCT (Bobrow 2008 1158; Grunau 2017 e3386; Schmicker 2021 31). In the case of the RCT, there the review noted moderate risk of bias from baseline differences in groups, lack of blinding, and potential for contamination in the treatment effect. For the cohort studies, the risk of bias assessment noted serious risk of uncontrolled confounding. All studies were at risk of indirectness due to either a high rate of non-adherence to protocol (Nichol 2015 2203; Grunau 2017 e3386; Schmicker 2021 31) or before-and-after design which included bundled interventions after the introduction of the 2005 Resuscitation Guidelines (Bobrow 2008 1158). Post-hoc analyses of the Nichol (2017, 2203) RCT were also underpowered to detect meaningful differences (Grunau 2017 e3386).• Based on a large cluster RCT undertaken in North America (Nichol 2015 2203) the likely benefit of CCC on patient outcomes is small. In this RCT, adherence to protocol was low and it is possible that larger differences in patient outcomes exist with greater compliance to CCC strategy. Studies adopting minimally interrupted cardiac resuscitation (Bobrow 2008 1158) have demonstrated larger impacts on patient outcomes, particularly in patients with witnessed shockable OHCA. These studies, however, have typically examined minimally interrupted cardiac resuscitation as a bundle with other resuscitation practice changes and therefore the directness of evidence is uncertain.• In making these recommendations, the task force noted no high-quality evidence to support the superiority of either CCC or standard CPR for patient outcomes in OHCA. The task force took into consideration that although there was relative homogeneity in the CCC strategies, there was heterogeneity in the use of ventilation strategies, including both asynchronous PPV and passive oxygenation. The adequacy of ventilation were not assessed in any studies, although measures of chest compression quality (e.g. chest compression fraction) were reported. • The task force also placed a relatively high value on the importance of providing high-quality chest compressions and simplifying resuscitation logistics for EMS providers and noted support for the clinical benefit of bundles of care involving minimally interrupted cardiac resuscitation. There was some evidence to suggest that a CV ratio of 30:2 may be much harder to achieve in practice and would ultimately result in asynchronous ventilations. • The Task Force removed the 2017 recommendation in support of systems that have implemented minimally interrupted cardiac resuscitation for witnessed shockable OHCA. In doing so, it recognised there was a single retrospective study reporting adjusted estimates for the intervention (Bobrow 2008 1158) with a serious risk of bias from uncontrolled confounding. As the study implemented continuous chest compressions as part of a bundle consisting of other resuscitation practices, it was uncertain if the treatment effect was related to CCC or the other practices introduced. |

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| Subgroup considerations |
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| Implementation considerations |
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| Monitoring and evaluation |
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| Research priorities |
| Several knowledge gaps were identified in the review of this topic, including:1. What is the effect of delayed positive pressure ventilation versus 30:2 high-quality CPR?2. Which elements of minimally interrupted cardiac resuscitation (compressions, ventilations, delayed defibrillation) are most important for patient outcomes?3. How effective is passive oxygenation during resuscitation?4. How does adherence to CCC or a CV ratio of 30:2 influence patient outcomes? |