Citation

Maconochie I, Aickin R, Atkins D, Bingham B, Chong KC, Couto T, De Van Voorde P, Guerguerian A, Hazinski M, Meaney P, Nadkarni V, Nuthall G, Ong G, Reis A, Shimizu N, Schexnayder S, Tijssen J, De Caen A. CPR : Chest Compression to Ventilation Ratio-Bystander-Pediatric Consensus on Science and Treatment Recommendation [Internet]. Brussels, Belgium: International Liaison Committee on Resuscitation (ILCOR), Pediatric Life Support Task Force, 2017 June 30. Available from: <u>http://www.ilcor.org</u>

CPR: Compression to Ventilation PICOST

The PICOST (Population, Intervention, Comparator, Outcome, Study Designs and Timeframe) **Population**: Patients of all ages (i.e., neonates, children, adults) with cardiac arrest from any cause and across all settings (in-hospital and outof-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-toventilation ratios. CO-CPR included compression with no ventilations, while CC-CPR included compression with asynchronous ventilations or minimally-interrupted cardiac resuscitation (MICR) 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 favorable 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 (nonrandomised 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. **Timeframe:** Published studies in English searched on January 15, 2016

The continuous evidence process for the production of Consensus of Science and Treatment Recommendations (CoSTR) started with a systematic review of basic life support (Ashoor, 2017, 50300) conducted by the Knowledge Synthesis Unit at St Michael's Hospital, Toronto, Canada with involvement of clinical content experts. Evidence for adult and pediatric literature was sought and considered by the Basic Life Support Adult Task Force and the Pediatric Task Force groups respectively. Additional scientific literature was identified after the completion of the systematic review by the Pediatric Task Force, and is described before the Values and Preferences section of this CoSTR. These data were taken into account when formulating the Treatment Recommendations.

The Pediatric Task Force looked at the following outcomes:

- a. favorable neurological function at the following time intervals: at hospital discharge and at one month
- b. survival to hospital discharge and to one month
- c. return of spontaneous circulation

The results of the systematic review on the pediatric literature showed 2 papers revealed bystander cardiopulmonary resuscitation (CPR) from the All Japan Utstein OHCA registry (Kitamura, 2010, 1347, Goto, 2014, 1).

For the critical outcome of favorable neurological function (PCPC 1 or 2) *at hospital discharge,* there were no data to assist with providing evidence for this outcome from the systematic review completed in 2016 by the Knowledge Synthesis Unit.

For the critical outcome of favorable neurological function at one month, very low quality evidence (downgraded for serious risk of bias, serious indirectness and serious imprecision) from two cohort studies (Kitamura, 2010, 1347, Goto, 2014, 1) was identified. The Kitamura study (Kitamura, 2010, 1347) used Japanese national OHCA registry data (which included OHCA of non-cardiac origin) to compare bystander delivery of chest compression only CPR with CPR with ventilation in 2439 infants and children during 2005-2007, when guidelines were transitioning from a chest compression: ventilation (C: V) ratio of 15:2 to 30:2 for pediatric OHCA. Favorable neurological function (PCPC 1 or 2) was seen less often with chest compression only CPR (relative risk (RR) 0.46 (95% CI 0.29-0.73), risk difference (RD) 3.02% (95% CI 1.47%-4.57)) than with CPR with ventilation.

When the results were further analyzed based on age, patients between 1-17 years had poorer outcomes with chest compression only (RR 0.46 (95% CI 0.28-0.75), RD 4.34 percentage points (95% CI 1.95-6.73)) than CPR with ventilation. In infants, there was no demonstrable difference in favorable neurological function (RR 0.39 (95% CI 0.11-1.36), RD 1.31% (95% CI -0.17%+2.80%)) between chest compression only CPR as compared with CPR with ventilation. A second Japanese OHCA registry study (Goto, 2014, 1) compared outcomes from bystander chest compression only CPR with ventilation in 2722 infants and children with OHCA (including traumatic causes) between 2008-2010. During this time adult bystander CPR guidelines encouraged chest compression only CPR whilst pediatric CPR guidelines advised CPR with ventilation with a C: V ratio of 30:2. This period also overlapped the period of national implementation of a dispatcher assisted-CPR program.

For the critical outcome of survival to hospital discharge, no evidence was found in the systematic review (Ashoor, 2017, 50300) but subsequently there was evidence published after completion of the systematic review that assisted with the Pediatric Task Force's making its recommendations.

For the critical outcome of survival to one month very low quality evidence (downgraded for serious risk of bias, serious indirectness and serious imprecision) from two cohort studies (Kitamura, 2010, 1347, Goto, 2014, 1) was identified.

The Kitamura study showed poorer outcomes with chest compression only CPR when compared to CPR with ventilation (RR 0.76 (95% CI 0.60-0.97), RD 2.98% (95% CI 0.45%-5.51)).

When the results were further analyzed based upon age, patients between 1-17 years had worse outcomes with chest compression-only CPR (RR 0.70 (95% CI 0.53-0.93), RD 4.74% (95% CI 1.17%-8.31)) than CPR with ventilation. Infants showed no demonstrable difference in survival to one month (RR 0.90 (95% CI 0.56-1.45), RD 0.74% (95% CI -2.61%-+4.09%)) between chest compression only CPR and CPR with ventilation. The Goto study showed worse survival amongst children who received chest compression only CPR compared to those receiving CPR with ventilation, (RR 0.56 (95% CI 0.45-0.69), RD 7.04% (95% CI 4.50%-9.58%)). There was no subgroup analysis for different ages.

For the important outcome of return of spontaneous circulation (ROSC), very low quality evidence (downgraded for serious risk of bias, serious indirectness and serious imprecision) from two cohort studies (Kitamura, 2010, 1347) was identified. The Kitamura study did not show a statistically significant difference in ROSC whether chest compression only CPR or CPR with ventilation was used (RR 0.74 (95% CI 0.53-1.02), RD 1.96% (95% CI -0.03%- +3.95%)). When the results were further analyzed based upon age, patients between 1-17 years of age had worse outcomes with the provision of chest compression only CPR (RR 0.67 (95% CI 0.47-0.96), RD 3.53% (95% CI 0.58%-6.48)). Infants did not show a statistically significant difference in ROSC (RD--0.04% (95% CI -2.31%- +2.22%), RR 1.01 (95% CI 0.49-2.09)) if compression only CPR or I CPR or if CPR with ventilation was delivered.

Treatment Recommendation

We suggest that bystanders provide CPR with ventilation for infants and children younger than 18 years with OHCA (weak recommendation, very low quality evidence) We continue to recommend that if bystanders can't provide rescue breaths as part of CPR for infants and children younger than 18 years with OHCA (Good Practice statement), they should at least provide chest compressions. In 2015, this was cited as a strong recommendation based on very low quality evidence (Maconochie, 2015, e147, de Caen, 2015, S177).

Additional science since the systematic review was completed

Additional science since the systematic review by the Knowledge Synthesis Unit (Ashoor, 2017, 10) is provided in the following paragraphs as it has informed the Pediatric Task Force in making their treatment recommendation (Fukuda, 2016, 2060, Naim, 2017, 133). They are included in this section as other data may have been published but may not have come to the attention of the Pediatric Task Force. When the systematic review comes to be repeated, these data with other data will be included in the Science section of the CoSTR, provided that such data assist in determining the recommendations for Bystander CPR.

For the critical outcome of favorable neurological function (PCPC 1 or 2) at hospital discharge,

we identified very low quality evidence (downgraded for serious risk of bias, serious indirectness) from one cohort study (Naim, 2017, 133). This study (Naim, 2017, 133) is an USA non-traumatic OHCA registry study that compared 1411 infants and children who received either bystander chest compression or bystander CPR with ventilation between 2013-2015. This cohort included <1 yr. age and 1-18 yrs. age subgroups. In infants, there was no difference in favorable neurological function at hospital discharge for those who received chest compression

only CPR when compared with those received CPR with ventilation (p=0.083;). Children 1-17 yrs. of age had comparable neurological outcomes (PCPC 1 or 2) when chest compression only CPR was compared to CPR with ventilation (p = 0.117).

For the critical outcome of favorable neurological function at one month, we identified very low quality evidence (downgraded for serious risk of bias, serious indirectness and very serious imprecision) from an additional cohort study (Fukuda, 2016, 2060). This Japanese OHCA registry study compared outcomes from bystander chest compression only CPR and CPR with ventilation in 1150 children >1 year of age with OHCA (including traumatic causes) between 2011-12, when CPR with ventilation guidelines advised a C: V ratio of 30:2, and an established national dispatcher-assisted CPR protocol existed. Favorable neurological function (PCPC 1 or 2) was no different whether CPR with ventilation or chest compression only CPR were provided (adjusted Odds Ratio (aOR) 1.52, (95% CI 0.93-2.49)).

For the critical outcome of survival to one month we identified very low quality evidence (downgraded for serious risk of bias, serious indirectness and very serious imprecision) from one cohort study (Fukuda, 2016, 2060). This study showed no difference in one-month survival in children (1-18 yrs. age) whether chest compression only CPR or CPR with ventilation was provided (aOR 1.38 (95% CI 0.98-1.96)).

For the critical outcome of survival to hospital discharge, we identified very low quality evidence (downgraded for serious risk of bias, serious indirectness) from one cohort study (Naim, 2017, 133). In infants with OHCA, survival to hospital discharge was worse in those infants who received chest compression only CPR when compared to those with CPR with ventilation (p = 0.002). For children >1 yr. of age, there was no statistical difference in survival to hospital discharge when comparing the use of chest compression only CPR with ventilation (p = 0.258).

For the important outcome of return of spontaneous circulation (ROSC), we identified very low quality evidence (downgraded for serious risk of bias, serious indirectness and serious imprecision) from one cohort study (Fukuda, 2016, 2060). This study did not show any statistically significant difference in ROSC whether CC-CPR or conventional CPR CC-CPR was provided (aOR 1.42 (95% CI0.95-2.12)).

Values, preferences, and Pediatric Task Force insights

In making these recommendations, we place a higher value on the importance of rescue breaths as part of CPR over a strategy that deemphasizes ventilation. Despite the very lowquality evidence, the Pediatric Task Force continue to advocate to at least provide 'any CPR' (including compression-only) in the out-of-hospital settings; this position is based on the former deliberations as seen in 2015 CoSTR Basic Life Support recommendations (Maconochie, 2015, e147, de Caen, 2015, S177). As the systematic review (Ashoor, 2017, 10) did not compare any modality of CPR with 'no' CPR', this position represents a Good Practice Statement in accord with GRADE evidence assessment for this CoSTR. While older registry data (Kitamura, 2010, 1347, Goto) showed that outcomes were improved if CPR with ventilation was used in comparison with compression-only CPR in all pediatric age groups, recent literature suggests that there is no difference in survival and neurologic outcomes (Naim, 2017, 133, Fukuda, 2016, 2060) when comparing compression-only CPR or CPR with ventilation children (older than infants). However, the Pediatric Task Force felt that there is still Insufficiently strong evidence to support a change to the current practice, emphasizing the delivery of chest compressions with ventilation.

Knowledge gaps

Current knowledge gaps include but are not limited to:

- The lack of corroborating or refuting data from other registries. The four papers providing evidence to date on bystander CPR come from Japan and North America. The Pediatric Task Force felt that other registries could provide helpful information either individually or in collaboration to supply further evidence in bystander CPR, ideally with long term outcomes that influence patient care and function, e.g. PCPC status at 3 months, 6 months and 1 year post CPR event.
- To ascertain if there is a need to stratify for age (as physiological adaptions may impact on resuscitation requirements to achieve ROSC and favorable neurological function.
- How can telephone dispatchers ensure that optimal delivery of CPR is provided for OHCA pediatric cases?