



This template guides the expert systematic reviewer or the knowledge synthesis lead on how to draft the first consensus on science with treatment recommendation (CoSTR) for their respective task force(s) based on the derived evidence profile tables and discussion with the writing group. The task force chair or their delegate uses the draft CoSTR and with the help of the task force members creates a final draft for review and approval by the Continuous Evidence Evaluation working group (CEE WG) and then by ILCOR executive prior to posting on ILCOR.org.

**User Instructions:**

Please maintain header size (14) and font calibri size (10) and bolded as per the template and the references should be formatted as per the ILCOR pre-specifications. Examples are italicized in the template however it not necessary to italicize when completing the sections in the template

V 2.4 November 26 2018 CEE WG approved

## Consensus on Science with Treatment Recommendations (CoSTR)

### Template for [www.ilcor.org](http://www.ilcor.org) posting

#### Header: Insert Title for ILCOR CoSTR (preferably short and similar to published SR)

Insert disclaimer for why the CoSTR is marked 'DRAFT' *Note to Webmaster – this preamble about draft can be removed when you are notified by ILCOR that the CoSTR label of draft is no longer required.*

*This CoSTR is a final version prepared by ILCOR and is labelled "draft" to comply with copyright rules of journals. The 'draft label' will be removed from this website once a summary article has been published in a scientific journal.*

#### Header: CoSTR Citation

Insert citation for ILCOR.org posting of CoSTR – section in yellow is standard across all citations

Example

*Soar J, Donnino MW, Andersen LW, Berg KM, Böttiger BW, Callaway CW, Deakin CD, Drennan J, Neumar RW, Nicholson TC, O'Neil BJ, Paiva EF, Parr MJ, Reynolds JC, Ristagno G, Sandroni C, Wang TL, Welsford M, Nolan JP, Morley PT (if not all members of the TF contributed sufficiently to be authors please include the caveat -on behalf of the International Liaison Committee on Resuscitation (insert) Life Support Task Force(s).  
Antiarrhythmic Drugs for Cardiac Arrest in Adults and Children Consensus on Science with Treatment Recommendations [Internet] Brussels, Belgium: International Liaison Committee on Resuscitation (ILCOR) Advanced Life Support Task Force, 2018 May 30. Available from: <http://ilcor.org>*

#### Header - Methodological Preamble and Link to Published Systematic Review

Insert this methodological brief overview and TF chair will adjust specific for the TF and ILCOR priority team that did the work:

Example:

*The continuous evidence evaluation process for the production of Consensus on Science with Treatment Recommendations (CoSTR) started with a systematic review of basic life support (Ashoor, 2017, 50300 – PROSPERO citation) 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 published after the completion of the systematic review and identified 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.*

#### Header -Systematic Review

Webmaster to insert the Systematic Review citation and link to Pubmed using this format

Example

*Usman M, Fitzpatrick-Lewis D, Kenny M, Parminder R, Atkins DL, Soar J, Nolan J, Ristagno G, Sherifali D Effectiveness of antiarrhythmic drugs for shockable cardiac arrest: A systematic review Resuscitation 132:November 2018 63-72 PMID:30179691  
DOI:[10.1016/j.resuscitation.2018.08.025](https://doi.org/10.1016/j.resuscitation.2018.08.025)*

#### Header - PICOST

Insert the PICOST (TF chairs uses the CEE WG approved PICOST and in line with what was published in PROSPERO)

Example

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### The PICOST (Population, Intervention, Comparator, Outcome, Study Designs and Timeframe)

**Population:** Adults and children in any setting (in-hospital or out-of-hospital) with cardiac arrest and a shockable rhythm at any time during cardiopulmonary resuscitation (CPR) or immediately after return of spontaneous circulation (ROSC).

**Intervention:** Administration (intravenous or intra-osseous) of an antiarrhythmic drug during CPR and immediately (within 1 hour) after ROSC.

**Comparators:** Another anti-arrhythmic drug or placebo or no drug during CPR or immediately after ROSC.

**Outcomes:** Survival to hospital discharge with good neurological outcome and survival to hospital discharge were ranked as critical outcomes. Return of spontaneous circulation (ROSC) was ranked as an important outcome. For antiarrhythmic drugs after ROSC – re-arrest was included as an important outcome.

**Study Designs:** Randomized controlled trials (RCTs) and non-randomized studies (non-randomized controlled trials, interrupted time series, controlled before-and-after studies, cohort studies) are eligible for inclusion.

**Timeframe:** All years and all languages were included as long as there was an English abstract; unpublished studies (e.g., conference abstracts, trial protocols) were excluded. Literature search updated to August 15, 2017.

PROSPERO Registration CRD42017080475

## Header- Consensus on Science<sup>1</sup>

COS template

The recommended standard Consensus on Science format for questions that relate to interventions is as follows when a meta-analysis or network meta-analysis is possible. Please note that we standardize the reporting of all COS as Relative Risk (RR) and Risk Differences (RD) or Absolute Risk Reduction (ARR) and patients with outcome/1000 patients not Odds Ratio (OR)

Example:

*For the important outcome (O) (e.g., return of spontaneous circulation), we have identified very-low-certainty evidence (downgraded for risk of bias and imprecision) from 2 observational studies (first author last name year of publication first page number= ILCOR format Smith 2018 123) enrolling 421 adult out-of-hospital cardiac arrests (P), which showed no benefit from the use of the intervention (I) when compare with standard care (C) (RR, 2.12; 95%CI, 0.75–6.02; P = 0.16; absolute risk reduction [ARR], 2.14%; 95% CI, –0.91% to 5.38%, or 21 more patients/1000 survived with the intervention [95% CI, 9 fewer patients/1000 to 54 more patients/1000 survived with the intervention])*

The recommended standard Consensus on Science format for questions that relate to interventions is as follows when a meta-analysis is not possible.

Example:

*For the critical outcomes of survival to hospital discharge/one month (n=12 studies and reference ILCOR format), long-term survival (n=6 studies and add references using the ILCOR format, i.e. Smith 2018 123), favorable neurological outcome at hospital discharge/one month (n=8 studies and reference ILCOR format), and long-term favorable neurological outcomes (n=6 studies), we identified only observational studies. The overall quality of evidence was rated as very low for all outcomes primarily due to a very serious risk of bias. The individual studies were all at a critical risk of bias due to confounding. Because of this and a high degree of heterogeneity, no meta-analyses could be performed and individual studies are difficult to interpret.*

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## Header – Treatment Recommendations<sup>2</sup>

Treatment Recommendations Template for Task Force Chairs

The recommended standard treatment recommendation format is as follows:

*We suggest/recommend for/against (I) in comparison with (C) for out-of-hospital cardiac arrest (P) (weak/strong recommendation, very low/low/moderate/high certainty of evidence).*

## Header- Justification and Evidence to Decision Framework Highlights<sup>3</sup>

Narrative Reporting of the Evidence to Decision Framework Incorporating Values and Preferences and other domains included in the framework, by Task Force Chairs. Technical Remarks refers to details that helps to provide specificity for the recommendation based on the current science i.e. dosing or timing.

Example

- *This topic was prioritized by the ALS Task Force based on a large RCT comparing amiodarone, lidocaine and placebo ('ROC ALPS') (Kudenchuk 2016 1711) that was published after the previous CoSTR in 2015 (Callaway 2015 s84, Soar 2015 e71).*
- *In considering the importance of this topic we noted that in a large RCT (n= 23,711) of continuous or interrupted chest compressions during cardiopulmonary resuscitation (CPR) for out-of-hospital cardiac arrest (OHCA) (Nichol 2015 2203), 22.5% of patients had an initial rhythm of VF/pVT and about 6.7% of all patients received an antiarrhythmic drug (amiodarone 4.7%, lidocaine 2.0%) during CPR. A large observational study (n= 108,079) on airway management using data from the American Heart Association Get With The Guidelines Registry of in-hospital cardiac arrest (IHCA) reported that about 18% of all patients had an initial rhythm of VF/pVT, and 25% of all patients received an antiarrhythmic drug (amiodarone 17%, lidocaine 8%) during CPR (Andersen 2017 494).*
- *Given the availability of comparative data from large RCTs, we did not include non-RCTs in establishing our confidence in the estimated effect size of these drugs.*

*In making these recommendations, the ALS Task Force considered the following:*

*Amiodarone or lidocaine*

- *We considered the predefined and reported subgroup analysis of the ROC ALPS study (Kudenchuk 2016 1711) that showed an improvement in the critical outcome of survival to hospital discharge with amiodarone or lidocaine compared with placebo in those patients who had a bystander witnessed cardiac arrest. In addition, survival rate was also higher among amiodarone recipients than placebo recipients with EMS-witnessed arrest – this was associated with earlier drug use: the time from cardiac arrest to the first dose of trial drug was 11.7±5.8 min for EMS-witnessed arrest versus a time from 911-call to the first study drug of 19.3±7.1 for non-EMS-witnessed cardiac arrest.*
- *We did not identify any RCTs for in-hospital cardiac arrest (IHCA). The EMS-witnessed subgroup analysis data from a large OHCA RCT does suggest the use of antiarrhythmic drugs in the hospital setting could be useful as drugs tend to be given much earlier after IHCA. We acknowledge the lack of RCT data for IHCA in our knowledge gaps.*
- *In making a weak recommendation, we considered the reported increase in the important but short-term outcome of ROSC of both amiodarone (Kudenchuk 1999 871) or lidocaine (Kudenchuk 2016 1711) with no evidence of improved or worse longer-term outcomes ranked as critical: survival or good neurological survival to hospital discharge.*
- *We considered that in the ROC ALPS study there was no difference between amiodarone and lidocaine in ROSC, survival or good neurological survival to hospital discharge.*
- *We considered the differences between the two amiodarone versus 'placebo' RCTs (Kudenchuk 1999 871, Kudenchuk 2016 1711), and also the two amiodarone versus lidocaine RCTs (Dorian 2002 884, Kudenchuk 2016 1711). We discussed the benefits of pooling or keeping the studies separate in the systematic review and meta-analyses. The benefits of increasing precision of an estimate of effect were weighed against the detrimental effects of combining distinctly different studies. We have provided both pooled estimates based on combining studies and also just those from the individual studies.*
- *The earlier RCTs (Kudenchuk 1999 871, Dorian 2002 884) used polysorbate 80 as placebo in the amiodarone v placebo study (Kudenchuk 1999 871), and mixed polysorbate 80 with lidocaine (Dorian 2002 884) in the amiodarone v lidocaine study. The effects of polysorbate 80 on the outcome of these studies is uncertain.*

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## Header – Knowledge Gaps<sup>4</sup>

Knowledge Gaps Template for Task Force chairs

The statements regarding the knowledge gaps could include wording such as:

*There were no studies identified that evaluated this question in the paediatric/in-hospital setting.*

*No RCTs compared intervention with standard care in any patient population*

*Only short term/surrogate outcomes were evaluated, future studies should document survival/neurologically intact survival to hospital discharge/30days.*

**Note to Webmaster: CoSTR posting should be linked to ETD summary table**

## Header – References

**References listed alphabetically by first author last name in this citation format**

### **(Circulation)**

Paradis NA, Martin GB, Rivers EP, Goetting MG, Appleton TJ, Feingold M, Nowak RM. Coronary perfusion pressure and the return of spontaneous circulation in human cardiopulmonary resuscitation. JAMA. 1990;263:1106–1113.

Christenson J, Andrusiek D, Everson-Stewart S, Kudenchuk P, Hostler D, Powell J, Callaway CW, Bishop D, Vaillancourt C, Davis D, Aufderheide TP, Idris A, Stouffer JA, Stiell I, Berg R; and the Resuscitation Outcomes Consortium Investigators. Chest compression fraction determines survival in patients with out-of-hospital ventricular fibrillation. Circulation. 2009;120:1241–1247. doi: 10.1161/CIRCULATIONAHA.109.852202.

Stiell IG, Brown SP, Nichol G, Cheskes S, Vaillancourt C, Callaway CW, Morrison LJ, Christenson J, Aufderheide TP, Davis DP, Free C, Hostler D, Stouffer JA, Idris AH; and the Resuscitation Outcomes Consortium Investigators. What is the optimal chest compression depth during out-of-hospital cardiac arrest resuscitation of adult patients? Circulation. 2014;130:1962–1970. doi: 10.1161/CIRCULATIONAHA.114.008671.

Cheskes S, Schmicker RH, Verbeek PR, Salcido DD, Brown SP, Brooks S, Menegazzi JJ, Vaillancourt C, Powell J, May S, Berg RA, Sell R, Idris A, Kampp M, Schmidt T, Christenson J; Resuscitation Outcomes Consortium (ROC) Investigators. The impact of peri-shock pause on survival from out-of-hospital shockable cardiac arrest during the Resuscitation Outcomes Consortium PRIMED trial. Resuscitation. 2014;85:336–342. doi: 10.1016/j.resuscitation.2013.10.014.

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## **Detailed Instructions to Chairs and Webmaster by superscript reference in template**

### **<sup>1</sup> Creation of Consensus on Science (COS) Statement**

Guidance to Task force Chairs

The completed GRADE evidence profile tables are used to create a written summary of evidence for each outcome: the Consensus on Science statements.

The structure of the Consensus on Science statement was developed as a means of providing an explicit narrative to communicate the evidence synthesis and certainty judgments found in the evidence profile tables.

These statements are made for each of the key outcomes, and are supported by the inclusion of:

- a categorization of the overall certainty of the evidence (high, moderate, low, or very low)
- the inclusion of reasons for certainty downgrading or upgrading,
- the specific population (P)
- the specific intervention (I) and comparison (C), and
- an estimate of the magnitude of effect (ideally as mean difference or risk difference) and certainty around that estimate (95% CI).

### **<sup>2</sup> Creation of Treatment Recommendations**

Guidance to Task force Chairs

Consensus-based treatment recommendations are created whenever possible. These recommendations are to be accompanied by an overall assessment of the evidence as well as a statement from the task force about the values and preferences that underlie their recommendations (see next section: Evidence to Decision framework).

These Treatment Recommendations are supported by the inclusion of:

- wording that reflects the strength of the recommendation (recommend/suggest)
- the direction of the recommendation (for/against)
- the specific population (P)
- the specific intervention (I)
- a statement of the strength of recommendation (strong or weak), and
- a categorization of the overall certainty of the evidence (high, moderate, low, or very low).

The GRADE process encourages organizations to commit to making a recommendation by using “we recommend” for strong recommendations and “we suggest” for weak recommendations in either a positive or negative direction (ie, “suggest/recommend,” “for/against”).

In the unusual circumstances in which task forces chose not to make recommendations, they were encouraged to specify whether this was because they had very low confidence in effect estimates (very limited data), because they felt that the balance between desirable and undesirable consequences was so close they could not make a recommendation (data exists, but no clear benefits), or because the two management options had very different undesirable consequences (and local values and preferences would decide which direction to take).

In some situations, the task forces may wish to make a strong recommendation, based on critical outcomes that are supported by low or very low levels of evidence (confidence in estimate of effect). In general, GRADE discourages guideline panels from making these discordant recommendations, but has identified 5 situations where this may be reasonable:

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- When low certainty evidence suggests benefit in a life threatening situation (evidence regarding harms can be low or high)
- When low certainty evidence suggests benefit and high certainty evidence suggests harm or a very high cost
- When low certainty evidence suggests equivalence of two alternatives, but high certainty evidence of less harm for one of the competing alternatives
- When high certainty evidence suggests equivalence of two alternatives and low certainty evidence suggests harm in one alternative
- When high certainty evidence suggests modest benefits and low/very low certainty evidence suggests possibility of catastrophic harm

It is expected that all treatment recommendations be accompanied by an Evidence to Decision framework (*vide infra*).

### <sup>3</sup>**Creation of the Values and Preferences Section of the CoSTR**

Guidance to Task force Chairs

In 2015 ILCOR task forces were encouraged to create standardized “values and preferences” statements to capture perspectives related to the prioritization of outcomes in justifying Consensus on Science with Treatment Recommendations (CoSTR). Recently the GRADE working group has expanded this approach and developed a formalized framework designed to transparently and explicitly capture most if not all of the considerations a guideline panel would take into account when formulating a recommendation. This approach, called the Evidence to Decision (EtD) Framework captures concepts as diverse as feasibility, acceptability, resource utilization and even cost-effectiveness when possible. Context-specific guidance can be provided as well. The EtD is embedded into the online software that creates evidence profiles and generates distinct tables that capture the judgments and when possible, the evidence-based insights and justifications that support a recommendation. The ESR or KSU lead enters all the evidence profile tables into the online software and the EtD tables are generated by the software. The Task Force chair leads the discussion with the task force based on the EtD tables and enters the summary of judgements into the EtD tables. The online software generates the summary ETD tables. The summary ETD tables are designed to support decision-making by the task forces and the task force chair uses this information to generate the section on values and preferences in the CoSTR. The Task Force Chair provides the ETD summary tables as a separate document.

### **Additional Resources for Task Force Chairs on how to generate and use a EtD framework**

1. Evidence to Decision in GRADE Handbook  
<http://gdt.guidelinedevelopment.org/app/handbook/handbook.html#h.33qgws879zw>
2. EtD experience in 15 guideline groups  
<https://implementationscience.biomedcentral.com/articles/10.1186/s13012-016-0462-y>
3. GRADE guidance articles  
<https://www.ncbi.nlm.nih.gov/pubmed/26931285>  
<https://www.ncbi.nlm.nih.gov/pubmed/27713072>

### <sup>4</sup>**Creation of Knowledge Gaps**

Guidance to Task force Chairs

The ILCOR priority team members that are content experts and the liaison to the participating task forces should list deficiencies in the published literature as they are identified during the preparation of the Evidence Profile tables and the systematic review manuscript. This can occur at any stage during the process, but commonly occurs during the assessment for inclusion/exclusion of articles identified by the initial search.

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These gaps may be related to any of the elements of the PICO framework (population, intervention, comparison and outcome). The gaps may also include specific methodology or study types, or relate to time of assessment of outcomes (eg. duration of follow up).

#### **General References for TF chairs**

Alexander PE, Bero L, Montori VM, et al. World Health Organization recommendations are often strong based on low confidence in effect estimates. *J Clin Epidemiol* 2014;67:629–34

Andrews JC, Schünemann HJ, Oxman AD, et al. GRADE guidelines: 15. Going from evidence to recommendation-determinants of a recommendation's direction and strength. *J Clin Epidemiol* 2013;66:726–35.29.

GRADE handbook: 6.3.2 Confidence in best estimates of magnitude of effects (certainty of evidence). <https://gdt.gradepro.org/app/handbook/handbook.html#h.1yd7iwhn8pxp>

GRADE handbook: 6.3.3 Confidence in values and preferences.

<https://gdt.gradepro.org/app/handbook/handbook.html#h.i5hfweocv3qs>

Morley PT, Lang E, Aickin R, Billi JE, Eigel B, Ferrer JM, et al. Part 2: Evidence Evaluation and Management of Conflicts of Interest: 2015 International Consensus on Cardiopulmonary Resuscitation and Emergency Cardiovascular Care Science With Treatment Recommendations. *Circulation*. 2015;132(16 Suppl 1):S40-50.