This template guides the Task Force ADOLOPMENT (TFA) team to create the consensus on science with treatment recommendation (CoSTR) for their respective task force(s), based on the derived evidence profile tables and discussion with the task force(s). The Scientific Advisory Committee representative for the team initially approves the document and then forwards this for approval by the Scientific Advisory Committee and then by ILCOR executive prior to posting on ILCOR.org.

This summary document includes some of the steps along the way, as it does not rely on that information to be published in a separate document (eg. published Systematic Review).

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

## 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)`

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: Conflict of Interest Declaration

The ILCOR Scientific Advisory Committee process is guided by a rigorous ILCOR Conflict of Interest policy. The following Task Force members and other authors were recused from the discussion as they declared a conflict of interest: (insert names or declare none applicable)

The following Task Force members and other authors declared an intellectual conflict of interest and this was acknowledged and managed by the Task Force Chairs and Conflict of Interest committees: (insert names or declare none applicable)

## Header: CoSTR Citation

Insert citation for ILCOR.org posting of CoSTR

Example

*Soar J, Donnino MW, Andersen LW, Berg KM, Böttiger BW, Callaway CW, Deakin CD, Drennan I, 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*](http://ilcor.org/)

**Header - Methodological Preamble (and if relevant, Link to Published Systematic Review)**

Insert brief methodological brief overview:

Example:

*The continuous evidence evaluation process for the production of Consensus on Science with Treatment Recommendations (CoSTR) started with a detailed review of a recently published systematic review/guideline based on a recently published systematic review (Finn, 2019, 50300). Additional scientific literature published after the completion of the published systematic review was identified by a subsequent search of the relevant literature, conducted by [insert either IS or TFA team members here] with involvement of clinical content experts. The totality of this identified evidence was considered by the [insert name] task force, and used to create/update bias assessment tables and evidence profile tables. These data were then used to formulate the Consensus on Science and Treatment Recommendations.*

## Header - PICOST

Insert the PICOST (TF chairs uses the SAC approved PICOST)

Example

**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.

NOTE FOR RISK OF BIAS: When possible, it is preferable methodology to compare the Risk of Bias (RoB) for a specific outcome across studies.  Rarely, the team may decide to assess RoB for all outcomes within a study for a specific comparison, rather than for a specific outcome across all studies, as long as the RoB for that outcome is very similar across all included studies. This will result in a RoB assessment per study rather than per outcome across studies.

Example

*“In most cases bias was assessed per comparison rather than per outcome, since there were no meaningful differences in bias across outcomes. In cases where differences in risk of bias existed between outcomes this was noted.”*

*“There are two studies addressing the comparison of interest however both have different risk of bias and too different to combine. You may choose to group the outcomes for each study under a single risk of bias as long as the risk of bias is similar across all outcomes within a study.”*

NOTE FOR SELECTING OUTCOMES: For both consistency in messaging and in approach, it is recommended to report on survival (and morbidity-free survival) preferentially over death (and death and/or disability), where the data in the literature allows this approach.

## [Header- Consensus on Science](#_1_Creation_of)[1](#_1_Creation_of)

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 either of the following options based on the available data:

Preferred Option 1:

1) Relative Risk (RR) with 95% confidence interval (95% CI) **AND**

2) Patients with outcome/1000 patients with 95% CI when there are small differences (<1%) **OR** Absolute Risk Difference (ARD) with 95% CI when there are larger differences **AND**

3) Number needed to treat or Number needed to harm should be reported when the differences are statistically different and clinically meaningful.

Preferred Option 2:

1. Risk Differences (RD) with 95% CI **AND**
2. 2) Patients with outcome/1000 patients with 95% CI when there are small differences (<1%) **OR** Absolute Risk Difference (ARD) with 95% CI when there are larger differences **AND**
3. 3) Number needed to treat or Number needed to harm should be reported when the differences are statistically different and clinically meaningful.

***SAC prefers either of these combined approaches over using an Odds Ratio when a meta-analysis is possible.***

Odds Ratio Option:

While these are the preferred analyses, SAC recognizes that the information available in the literature may not support this approach.  In situations where this is not possible, it is reasonable to use a different approach, such as calculating adjusted Odds Ratios (95% CI) with the accompanying outcomes/1000 patients (95% CI).

 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])

Meta-analysis Not Possible Option:

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.*

[**Header – Treatment Recommendations2**](#_2_Creation_of)

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 3](#_3Creation_of_the)

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 recent systematic review (Finn, 2019, 50300) that was published after the previous CoSTR in 2015 (Callaway 2015 s84, Soar 2015 e71).*
* *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.*

## [Header – Knowledge Gaps4](#_4_Creation_of)

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](#_4_Creation_of)

**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. \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

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

## 1 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).

## 2 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:

* 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)*.](#_Additional_Resources_for)

## 3Creation of the Justification and Evidence to Decision Framework Highlights 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). 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. A TFA team member 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 EtD tables can also be created using the word templates exported from GRADEPro. 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

1. EtD experience in 15 guideline groups

<https://implementationscience.biomedcentral.com/articles/10.1186/s13012-016-0462-y>

1. GRADE guidance articles

<https://www.ncbi.nlm.nih.gov/pubmed/26931285>

https://www.ncbi.nlm.nih.gov/pubmed/27713072

## 4 Creation of Knowledge Gaps

Guidance to Task force Chairs

The ILCOR Task Force Adolopment 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. 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.

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.

Schünemann HJ, Wiercioch W, Brozek J, Etxeandia-Ikobaltzeta I, Mustafa RA, Manja V, Brignardello-Petersen R, Neumann I, Falavigna M, Alhazzani W, Santesso N. GRADE Evidence to Decision (EtD) frameworks for adoption, adaptation, and de novo development of trustworthy recommendations: GRADE-ADOLOPMENT. Journal of clinical epidemiology. 2017 Jan 1;81:101-10.