Circulation

# Part 2: Evidence Evaluation and Guidelines Development

## 2020 American Heart Association Guidelines for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care

**ABSTRACT:** The *2020 American Heart Association* (AHA) *Guidelines for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care* is based on the extensive evidence evaluation performed in conjunction with the International Liaison Committee on Resuscitation. The Adult Basic and Advanced Life Support, Pediatric Basic and Advanced Life Support, Neonatal Life Support, Resuscitation Education Science, and Systems of Care Writing Groups drafted, reviewed, and approved recommendations, assigning to each recommendation a Class of Recommendation (ie, strength) and Level of Evidence (ie, quality). The 2020 Guidelines are organized in knowledge chunks that are grouped into discrete modules of information on specific topics or management issues. The 2020 Guidelines underwent blinded peer review by subject matter experts and were also reviewed and approved for publication by the AHA Science Advisory and Coordinating Committee and the AHA Executive Committee. The AHA has rigorous conflict-of-interest policies and procedures to minimize the risk of bias or improper influence during development of the guidelines. Anyone involved in any part of the guideline development process disclosed all commercial relationships and other potential conflicts of interest.

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## INTRODUCTION

This Part describes the process of creating the *2020 American Heart Association* (AHA) *Guidelines for Cardiopulmonary Resuscitation* (CPR) *and Emergency Cardiovascular Care* (ECC). The process of evidence evaluation, the format of the guideline document; the formation of the AHA writing groups; the guideline development, review, and approval process; and the management of potential conflicts of interest are described.

## METHODOLOGY AND EVIDENCE REVIEW

The 2020 Guidelines are designed to present a comprehensive yet succinct compilation of guidance for CPR and ECC. These adult basic and advanced life support, pediatric basic and advanced life support, neonatal life support, resuscitation education science, and systems of care guidelines are based on the extensive evidence evaluation performed in conjunction with the International Liaison Committee on Resuscitation (ILCOR), as detailed in the *2020 International Consensus on CPR and ECC Science With Treatment Recommendations* (CoSTR).[1–7]

**Key Words:** AHA Scientific Statements ■ cardiac arrest ■ evidence evaluation ■ resuscitation



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**Table 1. GRADE Terminology for Strength of Recommendation and Criteria for Evidence Certainty Assessment[34]**

| Strength of Recommendation | | | |
|---|---|---|---|
| Strong Recommendation = We Recommend | | Weak Recommendation = We Suggest | |
| Assessment Criteria for Certainty of Effect | | | |
| Study Design | Certainty of Effect Begins at This Level | Lower if | Higher if |
| Randomized trial | High or moderate | Risk of bias<br>Inconsistency<br>Indirectness<br>Imprecision<br>Publication bias | Large effect<br>Dose response<br>All plausible confounding would reduce demonstrated effect or would suggest a spurious effect when results show no effect |
| Observational trial | Low or very low | | |

GRADE indicates Grading of Recommendations, Assessment, Development, and Evaluation.

The AHA partnered with the ILCOR task forces, as well as with other ILCOR member councils, in the evidence review process. The ILCOR Scientific Advisory Committee, consisting of methodological experts, created a methodological governance process for evidence evaluation. Although the *2015 AHA Guidelines Update for CPR and ECC* relied primarily on systematic reviews, the 2020 Guidelines used 3 types of evidence reviews (systematic reviews, scoping reviews, and evidence updates), each of which resulted in a description of the published evidence that facilitated guideline development.[4,8]

## Systematic Review

The first type of evidence review is the systematic review, conducted according to the recommendations of the National Academy of Medicine,[9] by using the methodological approach proposed by the Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) Working Group.[10] Each ILCOR task force identified and prioritized questions to be addressed by using the PICOST (population, intervention, comparator, outcome, study design, time frame) format[11] and determined the important outcomes to be reported. A detailed search for relevant publications was performed on MEDLINE, Embase, and Cochrane Library databases, with identified publications screened for further evaluation.

Two systematic reviewers conducted a risk-of-bias assessment for each relevant study by using Cochrane and GRADE criteria for randomized controlled trials (RCTs),[12] Quality Assessment of Diagnostic Accuracy Studies (QUADAS)-2 for studies of diagnostic accuracy,[13] and GRADE criteria for observational and interventional studies informing therapy or prognosis questions.[10] In addition to assessing scientific bias, the Cochrane risk-of-bias tool also considers both the source of funding and potential conflicts of interest of authors of the study. The reviewers created evidence profile tables containing information on all study outcomes.[14] The quality of the evidence (ie, confidence in the estimate of the effect) was categorized as high, moderate, low, or very low[15] on the basis of the study methodologies and the GRADE domains of bias, inconsistency, indirectness, imprecision, and publication bias[10] (Tables 1 and 2). Any unresolved disparity between reviewer assessments was resolved through discussions and consensus with the task force representative of the Scientific Advisory Committee and, if disagreement remained, by the larger ILCOR task force.

The ILCOR task forces reviewed, discussed, and debated the studies and systematic review analyses, drafting a consensus on science statement and a written summary of identified evidence and evidence quality for each outcome. When there was consensus, the task force developed consensus treatment recommendations, labeled as strong or weak and either for or against a therapy, prognostic tool, or diagnostic test, noting the certainty of the evidence. In addition, each topic summary included the PICOST question and a justification and evidence-to-decision framework section, capturing the values and preferences considered by the task force as well as a list of knowledge gaps. Public input was sought at multiple stages, including PICOST development and draft CoSTR statements.[4] The task forces considered all public comments when finalizing the CoSTR statements. All 2020 CoSTR statements underwent peer review by at least 5 subject matter experts and were endorsed by the ILCOR board before publication.

## Scoping Review

The second type of evidence review is the scoping review. The purpose of a scoping review is to provide an overview of the available research evidence related to a specific topic and to determine if sufficient evidence is identified to recommend performance of a systematic review. One difference between scoping reviews and systematic reviews is that scoping reviews have broader inclusion criteria, whereas traditional systematic reviews address a narrow, clearly defined question. Unlike the treatment recommendations that can arise from a systematic review, scoping reviews cannot result in a new ILCOR treatment recommendation or modification of an existing ILCOR treatment recommendation.

The methodology for the scoping review was based on the Preferred Reporting Items for Systematic Reviews

**Table 2. GRADE Terminology[34]**

| | |
|---|---|
| Risk of bias | Study limitations in randomized trials include lack of allocation concealment, lack of blinding, incomplete accounting of patients and outcome events, selective outcome reporting bias, and stopping early for benefit. Study limitations in observational studies include failure to apply appropriate eligibility criteria, flawed measurement of exposure and outcome, failure to adequately control confounding, and incomplete follow-up. |
| Inconsistency | Criteria for inconsistency in results include the following: Point estimates vary widely across studies; CIs show minimal or no overlap; statistical test for heterogeneity shows a low *P* value; and the $I^2$ is large (a measure of variation in point estimates resulting from among-study differences). |
| Indirectness | Sources of indirectness include data from studies with differences in population (eg, OHCA instead of IHCA, adults instead of children), differences in the intervention (eg, different compression-ventilation ratios), differences in outcome, and indirect comparisons. |
| Imprecision | Low event rates or small sample sizes will generally result in wide CIs and therefore imprecision. |
| Publication bias | Several sources of publication bias include tendency not to publish negative studies and the influence of industry-sponsored studies. An asymmetrical funnel plot increases suspicion of publication bias. |
| Good practice statements | Guideline panels often consider it necessary to issue guidance on specific topics that do not lend themselves to a formal review of research evidence. The reason might be that research into the topic is unlikely to be located or would be considered unethical or infeasible. Criteria for issuing a nongraded good practice statement include the following: There is overwhelming certainty that the benefits of the recommended guidance will outweigh harms, and a specific rationale is provided; the statements should be clear and actionable to a specific target population; the guidance is deemed necessary and might be overlooked by some providers if not specifically communicated; and the recommendations should be readily implementable by the specific target audience to which the guidance is directed. |

GRADE indicates Grading of Recommendations, Assessment, Development, and Evaluation; IHCA, in-hospital cardiac arrest; and OHCA, out-of-hospital cardiac arrest.

and Meta-analyses (PRISMA) Extension for Scoping Reviews.[8,16,17] Each task force identified questions to be reviewed, presented in the PICOST format. The MEDLINE, Embase, and Cochrane databases were then searched to identify relevant publications. Those performing the scoping reviews extracted data to create summary tables. The task force then reviewed the studies and the evidence tables, developing a consensus narrative summary of the evidence and an overview of the task force insights. Each topic narrative summary and overview of task force insights as well as the complete scoping review were posted on the ILCOR website for public review and input,[4] with final versions included in the appendix and summarized in the body of the relevant task force CoSTR publication.

### Evidence Update

The evidence update is the third type of review supporting the 2020 CoSTR and the 2020 Guidelines. This review is used for questions not undergoing a systematic or scoping review. Evidence updates were performed by AHA writing group members, AHA volunteers, or other ILCOR member council volunteers. The evidence update reviewers used PubMed to conduct searches of English language publications indexed in the MEDLINE database. When the search strategies from previous reviews were available, these were repeated. Searching beyond the MEDLINE database was optional, at the discretion of the reviewer. Reviewers identified relevant new studies, guidelines, and systematic reviews, and completed an evidence update worksheet,[8] which included the research question, the search strategy, and a table summarizing any new evidence. After review by the ILCOR Science Advisory Committee Chair, the evidence update worksheet was included in the relevant 2020 CoSTR task force publication appendix and cited within the body of the manuscript.

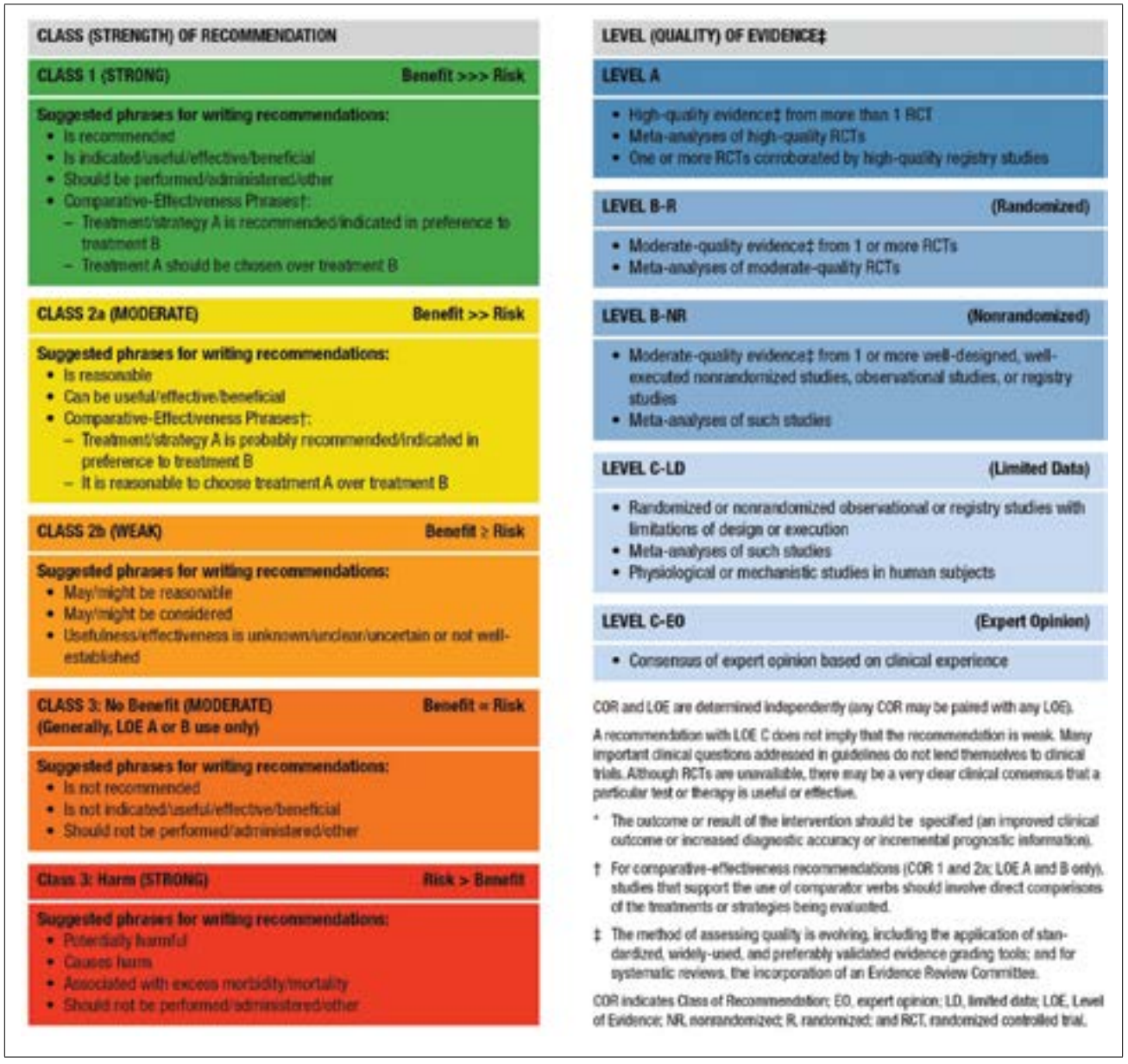
## GUIDELINE FORMAT

In contrast to prior ECC Guidelines, the 2020 Guidelines are organized in knowledge chunks, grouped into discrete modules of information on specific topics or management issues.[18] Each modular knowledge chunk includes a table of recommendations, a brief introduction or synopsis, recommendation-specific supportive text, and, when appropriate, figures, flow diagrams of algorithms, and additional tables. Hyperlinked references are provided to facilitate quick access and review.

## FORMATION OF THE AHA GUIDELINE WRITING GROUPS

The AHA strives to ensure that each guideline writing group includes requisite expertise and diversity, representative of the broader medical community by selecting experts from a wide array of backgrounds, geographic regions of North America, sexes, races, ethnicities, intellectual perspectives, and scopes of clinical practice. Volunteers with an interest and recognized expertise in resuscitation are nominated by the writing group chair, selected by the AHA ECC Committee and approved by the AHA Manuscript Oversight Committee. The Adult Basic and Advanced Life Support Writing Group included experts in emergency medicine, critical care, cardiology, toxicology, neurology, emergency medical services, education, research, and public health. The Pediatric Basic

**Table 3. Applying Class of Recommendation and Level of Evidence to Clinical Strategies, Interventions, Treatments, or Diagnostic Testing in Patient Care (Updated May 2019)***




This tool has been used in all AHA ECC Guidelines and focused updates since its initial publication in the 2015 Guidelines Update.[35]

and Advanced Life Support Writing Group consisted of pediatric clinicians including intensivists, cardiac intensivists, cardiologists, and emergency physicians and emergency medicine nurses. The Neonatal Life Support Writing Group included neonatal physicians and nurses with backgrounds in clinical medicine, education, research, and public health. The Resuscitation Education Science Writing Group consisted of experts in resuscitation education, clinical medicine (ie, pediatrics, intensive care, emergency medicine), nursing, prehospital care, and health services and education research. The Systems of Care Writing Group included experts in clinical medicine, education, research, and public health. Before appointment, writing group members completed a disclosure of relevant relationships with industry. Writing group members also adhered to all AHA requirements for management of any potential conflicts of interest.

## GUIDELINES DEVELOPMENT, REVIEW, AND APPROVAL

Each AHA writing group reviewed all relevant and current AHA guidelines for CPR and ECC,[19–30] pertinent 2020 CoSTR evidence and recommendations,[1–3,6,7] and all relevant evidence update worksheets to determine if current guidelines should be reaffirmed, revised, or retired, or if new recommendations were needed. The

writing groups then drafted, reviewed, and approved recommendations, assigning to each recommendation a Class of Recommendation (COR) (ie, strength) and Level of Evidence (LOE) (ie, quality) (Table 3). Each of the 2020 Guidelines articles was submitted for blinded peer review to 5 subject matter experts nominated by the AHA. Before appointment, all peer reviewers were required to disclose relationships with industry and any other potential conflicts of interest, and all disclosures were reviewed by AHA staff. Peer reviewer feedback was provided for guidelines in draft format and again in final format. All guidelines were reviewed and approved for publication by the AHA Science Advisory and Coordinating Committee and AHA Executive Committee.

## MANAGEMENT OF POTENTIAL CONFLICTS OF INTEREST

The AHA and ILCOR have rigorous conflict-of-interest policies and procedures to minimize the risk of bias or improper influence during development of the CoSTRs and the AHA guidelines. Both organizations followed these policies[31–33] throughout the 2020 evidence evaluation and document preparation process, and anyone involved in any part of this process was required to disclose all commercial relationships and other potential conflicts (including intellectual) both before joining the writing group and during writing group activities. These disclosures were reviewed before assignment of task force chairs and members, writing group chairs and members, consultants, and peer reviewers. In keeping with the AHA conflict of interest policy, the chair and most members of each ILCOR and AHA writing group had to be free of relevant conflicts. Writing group members do not draft text or vote on any recommendation for which they had a relevant conflict. Appendix 1 lists writing group members' disclosure information. Peer reviewers were also required to disclose relationships with industry and any other potential conflicts of interest; these disclosures appear in Appendix 2.

## ARTICLE INFORMATION

The American Heart Association requests that this document be cited as follows: Magid DJ, Aziz K, Cheng A, Hazinski MF, Hoover AV, Mahgoub M, Panchal AR, Sasson C, Topjian AA, Rodriguez AJ, Donoghue A, Berg KM, Lee HC, Raymond T, Lavonas EJ. Part 2: evidence evaluation and guidelines development: 2020 American Heart Association Guidelines for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care. *Circulation*. 2020;142(suppl 2):S358–S365. doi: 10.1161/CIR.0000000000000898

### Disclosures

**Appendix 1. Writing Group Disclosures**

| Writing Group Member | Employment | Research Grant | Other Research Support | Speakers' Bureau/ Honoraria | Expert Witness | Ownership Interest | Consultant/ Advisory Board | Other |
|---|---|---|---|---|---|---|---|---|
| David J. Magid | University of Colorado | NIH†; NHLBI†; CMS†; AHA† | None | None | None | None | None | American Heart Association (Senior Science Editor)† |
| Khalid Aziz | University of Alberta Pediatrics | None | None | None | None | None | None | Salary: University of Alberta† |
| Katherine M. Berg | Beth Israel Deaconess Medical Center Pulmonary and Critical Care | NHLBI Grant K23 HL128814† | None | None | None | None | None | None |
| Adam Cheng | Alberta Children's Hospital | None | None | None | None | None | None | None |
| Aaron Donoghue | The Children's Hospital of Philadelphia, University of Pennsylvania School of Medicine | None | None | None | Atkinson, Haskins, Nellis, Brittingham, Gladd & Fiasco* | None | None | None |
| Mary Fran Hazinski | Vanderbilt University School of Nursing | None | None | None | None | None | American Heart Association† | None |
| Amber V. Hoover | American Heart Association | None | None | None | None | None | None | None |

(*Continued*)

**Appendix 1. Continued**

| Writing Group Member | Employment | Research Grant | Other Research Support | Speakers' Bureau/ Honoraria | Expert Witness | Ownership Interest | Consultant/ Advisory Board | Other |
|---|---|---|---|---|---|---|---|---|
| Eric J. Lavonas | Denver Health Emergency Medicine | BTG Pharmaceuticals (Denver Health (Dr Lavonas' employer) has research, call center, consulting, and teaching agreements with BTG Pharmaceuticals. BTG manufactures the digoxin antidote, DigiFab. Dr Lavonas does not receive bonus or incentive compensation, and these agreements involve an unrelated product. When these guidelines were developed, Dr Lavonas recused from discussions related to digoxin poisoning.)† | None | None | None | None | None | American Heart Association (Senior Science Editor)† |
| Henry C. Lee | Stanford University | NICHD (PI of R01 grant examining intensive care for infants born at extremely early gestational age)* | None | None | None | None | None | None |
| Melissa Mahgoub | American Heart Association | None | None | None | None | None | None | None |
| Ashish R. Panchal | The Ohio State University Wexner Medical Center Emergency Medicine | None | None | None | None | None | None | None |
| Tia T. Raymond | Medical City Children's Hospital Congenital Heart Surgery Unit | None | None | None | None | None | None | None |
| Amber J. Rodriguez | American Heart Association National Center Emergency Cardiovascular Care | None | None | None | None | None | None | None |
| Comilla Sasson | American Heart Association | None | None | None | None | None | None | None |
| Alexis A. Topjian | The Children's Hospital of Philadelphia, University of Pennsylvania School of Medicine Anesthesia and Critical Care | None | None | None | None | None | None | None |

This table represents the relationships of writing group members that may be perceived as actual or reasonably perceived conflicts of interest as reported on the Disclosure Questionnaire, which all members of the writing group are required to complete and submit. A relationship is considered to be "significant" if (a) the person receives $10 000 or more during any 12-month period, or 5% or more of the person's gross income; or (b) the person owns 5% or more of the voting stock or share of the entity, or owns $10 000 or more of the fair market value of the entity. A relationship is considered to be "modest" if it is less than "significant" under the preceding definition.

*Modest.

†Significant.

**Appendix 2. Reviewer Disclosures**

| Reviewer | Employment | Research Grant | Other Research Support | Speakers' Bureau/ Honoraria | Expert Witness | Ownership Interest | Consultant/Advisory Board | Other |
|---|---|---|---|---|---|---|---|---|
| Fredrik Folke | Gentofte University Hospital (Denmark) | None | None | None | None | None | None | None |
| Joel Lexchin | University Health Network, Toronto (Canada) | None | None | None | None | None | None | None |
| Robert T. Mallet | University North Texas Health Science Center | None | None | None | None | None | AHA (service on study sections reviewing grant applications to support resuscitation research)* | None |
| Mary Ann McNeil | University of Minnesota | None | None | None | None | None | None | None |
| Taylor Sawyer | Seattle Children's Hospital/ University of Washington | None | None | None | None | None | None | None |
| Will Smith | Wilderness and Emergency Medicine Consulting (WEMC) | None | None | None | None | None | None | None |
| Lorrel E. B. Toft | University of Nevada Reno | None | None | None | None | None | None | None |

This table represents the relationships of reviewers that may be perceived as actual or reasonably perceived conflicts of interest as reported on the Disclosure Questionnaire, which all reviewers are required to complete and submit. A relationship is considered to be "significant" if (a) the person receives $10 000 or more during any 12-month period, or 5% or more of the person's gross income; or (b) the person owns 5% or more of the voting stock or share of the entity, or owns $10 000 or more of the fair market value of the entity. A relationship is considered to be "modest" if it is less than "significant" under the preceding definition.

*Modest.

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