

AHA FOCUSED UPDATE

2018 American Heart Association Focused Update on Pediatric Advanced Life Support

An Update to the American Heart Association Guidelines for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care

ABSTRACT: This 2018 American Heart Association focused update on pediatric advanced life support guidelines for cardiopulmonary resuscitation and emergency cardiovascular care follows the 2018 evidence review performed by the Pediatric Task Force of the International Liaison Committee on Resuscitation. It aligns with the International Liaison Committee on Resuscitation's continuous evidence review process, and updates are published when the group completes a literature review based on new published evidence. This update provides the evidence review and treatment recommendation for antiarrhythmic drug therapy in pediatric shock-refractory ventricular fibrillation/pulseless ventricular tachycardia cardiac arrest. As was the case in the pediatric advanced life support section of the "2015 American Heart Association Guidelines Update for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care," only 1 pediatric study was identified. This study reported a statistically significant improvement in return of spontaneous circulation when lidocaine administration was compared with amiodarone for pediatric ventricular fibrillation/pulseless ventricular tachycardia cardiac arrest. However, no difference in survival to hospital discharge was observed among patients who received amiodarone, lidocaine, or no antiarrhythmic medication. The writing group reaffirmed the 2015 pediatric advanced life support guideline recommendation that either lidocaine or amiodarone may be used to treat pediatric patients with shock-refractory ventricular fibrillation or pulseless ventricular tachycardia.

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This 2018 American Heart Association (AHA) focused update on the pediatric advanced life support (PALS) guidelines for cardiopulmonary resuscitation (CPR) and emergency cardiovascular care (ECC) is based on the systematic review of antiarrhythmic drugs for cardiac arrest and the resulting "2018 International Consensus on Cardiopulmonary Resuscitation and Emergency Cardiovascular Care Science With Treatment Recommendations" (CoSTR) from the Pediatric Task Force of the International Liaison Committee on Resuscitation (ILCOR). The draft pediatric CoSTR was posted online for public comment,¹ and a summary containing the final wording of the CoSTR has been published simultaneously with this focused update.²

AHA guidelines for CPR and ECC are developed in concert with the ILCOR systematic review process. In 2015, the ILCOR evidence evaluation process transitioned to a continuous one, with systematic reviews performed as new published evidence warrants them or when the ILCOR Pediatric Task Force prioritizes a topic. The AHA science experts then review the evidence and update the AHA's guidelines as needed, typically on an annual basis. A description of the evidence review process is available in the 2017 CoSTR summary.³

The ILCOR systematic review process uses the Grading of Recommendations Assessment, Development, and Evaluation methodology and its associated nomenclature to determine the quality of evidence and strength of recommendations for the CoSTR. The expert writing group for this 2018 PALS guidelines focused update reviewed the studies and analysis of the 2018 CoSTR summary² and carefully considered the ILCOR Pediatric Task Force consensus recommendations in light of the structure and resources of the out-of-hospital and in-hospital resuscitation systems and providers who use AHA guidelines. In addition, the writing group determined the Classes of Recommendation and Levels of Evidence according to the recommendations of the American College of Cardiology/AHA Task Force on Clinical Practice Guidelines⁴ (Table) by using the process detailed in the "2015 American Heart Association Guidelines Update for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care."⁵

It is important to note that this 2018 PALS guidelines focused update reevaluates only the recommendations for the use of antiarrhythmic drugs during ventricular fibrillation (VF)/pulseless ventricular tachycardia (pVT) cardiac arrest. All other recommendations and algorithms published in "Part 12: Pediatric Advanced Life Support" in the 2015 guidelines update⁶ and "Part 14: Pediatric Advanced Life Support" in the "2010 American Heart Association Guidelines for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care"⁷ remain the official recommendations of the AHA ECC

Science Subcommittee and writing groups. The recommendations contained in the "2017 American Heart Association Focused Update on Pediatric Basic Life Support and Cardiopulmonary Resuscitation Quality: An Update to the American Heart Association Guidelines for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care" continue to apply to CPR delivered to pediatric patients in cardiac arrest.⁸

BACKGROUND

Shock-refractory VF/pVT refers to VF or pVT that persists or recurs after ≥ 1 shocks. Two antiarrhythmic medications are currently discussed in the AHA guidelines: lidocaine, a fast sodium channel blocker (Class IB) that acts in part by accelerating repolarization, and amiodarone, a multiple ion channel blocker (Class III) that is believed to act predominantly by prolonging repolarization. An antiarrhythmic drug alone is unlikely to pharmacologically convert VF/pVT to an organized perfusing rhythm. Rather, the primary objective of antiarrhythmic drug therapy in shock-refractory VF/pVT is to facilitate successful defibrillation and to reduce the risk of recurrent arrhythmias. In concert with shock delivery, antiarrhythmic drugs can facilitate the restoration and maintenance of a spontaneous perfusing rhythm. Some antiarrhythmic drugs have been associated with increased rates of return of spontaneous circulation (ROSC) and survival to hospital admission,^{9,10} but none have yet been demonstrated to increase long-term survival or survival with good neurological outcome. Thus, establishing vascular access to enable drug administration should not compromise the quality of CPR or delay timely defibrillation, both of which are associated with improved long-term survival. The optimal sequence of PALS interventions, including administration of antiarrhythmic drugs during resuscitation, and the preferred manner and timing of drug administration in relation to shock delivery are still not known.

The 2018 ILCOR Pediatric Task Force review addressed the use of antiarrhythmic drugs during pediatric cardiac arrest (in infants, children, and adolescents <18 years of age) with a shockable rhythm in any setting (in hospital and out of hospital), during CPR or immediately after ROSC. This review was triggered by the publication of 2 adult studies examining the use of antiarrhythmic medications in adult cardiac arrest.^{11,12} However, unlike previous ILCOR reviews and several earlier AHA PALS guidelines, the ILCOR Pediatric Task Force review and this 2018 PALS guidelines focused update are based only on pediatric studies and did not consider evidence extrapolated from adult studies. The writing group agreed that pediatric patients with VF/pVT cardiac arrest differ substantially from adult patients in ways that could influence presentation, treatment, and response to antiarrhythmic drugs. We did not address the use of antiarrhythmic medications after ROSC.

Table. ACC/AHA Recommendation System: Applying Class of Recommendation and Level of Evidence to Clinical Strategies, Interventions, Treatments, or Diagnostic Testing in Patient Care* (Updated August 2015)

CLASS (STRENGTH) OF RECOMMENDATION	LEVEL (QUALITY) OF EVIDENCE†‡
CLASS I (STRONG) Benefit >>> Risk Suggested phrases for writing recommendations: <ul style="list-style-type: none"> ■ Is recommended ■ Is indicated/useful/effective/beneficial ■ Should be performed/administered/other ■ Comparative-Effectiveness Phrases†: <ul style="list-style-type: none"> ○ Treatment/strategy A is recommended/indicated in preference to treatment B ○ Treatment A should be chosen over treatment B 	LEVEL A <ul style="list-style-type: none"> ■ High-quality evidence‡ from more than 1 RCT ■ Meta-analyses of high-quality RCTs ■ One or more RCTs corroborated by high-quality registry studies
CLASS IIa (MODERATE) Benefit >> Risk Suggested phrases for writing recommendations: <ul style="list-style-type: none"> ■ Is reasonable ■ Can be useful/effective/beneficial ■ Comparative-Effectiveness Phrases†: <ul style="list-style-type: none"> ○ Treatment/strategy A is probably recommended/indicated in preference to treatment B ○ It is reasonable to choose treatment A over treatment B 	LEVEL B-R (Randomized) <ul style="list-style-type: none"> ■ Moderate-quality evidence‡ from 1 or more RCTs ■ Meta-analyses of moderate-quality RCTs
CLASS IIb (WEAK) Benefit ≥ Risk Suggested phrases for writing recommendations: <ul style="list-style-type: none"> ■ May/might be reasonable ■ May/might be considered ■ Usefulness/effectiveness is unknown/unclear/uncertain or not well established 	LEVEL B-NR (Nonrandomized) <ul style="list-style-type: none"> ■ Moderate-quality evidence‡ from 1 or more well-designed, well-executed nonrandomized studies, observational studies, or registry studies ■ Meta-analyses of such studies
CLASS III: No Benefit (MODERATE) Benefit = Risk <i>(Generally, LOE A or B use only)</i> Suggested phrases for writing recommendations: <ul style="list-style-type: none"> ■ Is not recommended ■ Is not indicated/useful/effective/beneficial ■ Should not be performed/administered/other 	LEVEL C-LD (Limited Data) <ul style="list-style-type: none"> ■ Randomized or nonrandomized observational or registry studies with limitations of design or execution ■ Meta-analyses of such studies ■ Physiological or mechanistic studies in human subjects
CLASS III: Harm (STRONG) Risk > Benefit Suggested phrases for writing recommendations: <ul style="list-style-type: none"> ■ Potentially harmful ■ Causes harm ■ Associated with excess morbidity/mortality ■ Should not be performed/administered/other 	LEVEL C-EO (Expert Opinion) Consensus of expert opinion based on clinical experience

COR and LOE are determined independently (any COR may be paired with any LOE).
 A recommendation with LOE C does not imply that the recommendation is weak. Many important clinical questions addressed in guidelines do not lend themselves to clinical trials. Although RCTs are unavailable, there may be a very clear clinical consensus that a particular test or therapy is useful or effective.
 * The outcome or result of the intervention should be specified (an improved clinical outcome or increased diagnostic accuracy or incremental prognostic information).
 † For comparative-effectiveness recommendations (COR I and IIa; LOE A and B only), studies that support the use of comparator verbs should involve direct comparisons of the treatments or strategies being evaluated.
 ‡ The method of assessing quality is evolving, including the application of standardized, widely used, and preferably validated evidence grading tools; and for systematic reviews, the incorporation of an Evidence Review Committee.
 COR indicates Class of Recommendation; EO, expert opinion; LD, limited data; LOE, Level of Evidence; NR, nonrandomized; R, randomized; and RCT, randomized controlled trial.

USE OF ANTIARRHYTHMIC DRUGS DURING RESUSCITATION FROM PEDIATRIC VF/pVT CARDIAC ARREST

2018 Evidence Summary

Amiodarone and Lidocaine

Only 1 pediatric study was identified in the 2018 ILCOR systematic review of the literature.¹³ This same pediatric

study was included in the 2015 guidelines update but was reviewed to determine whether any modification of AHA guidelines was warranted. The observational study is derived from the AHA Get With The Guidelines–Resuscitation registry. It evaluated a cohort of children enrolled from 2000 to 2008 who had an in-hospital cardiac arrest requiring CPR for at least 2 minutes, with a rhythm of VF/pVT at any time during the cardiac arrest.¹³ Of the 9280 eligible patients with cardiac arrest, 1099

(12%) had VF/pVT documented at some time during the cardiac arrest; after those who received prearrest lidocaine or amiodarone were excluded, 889 patients were available for evaluation. Patients receiving lidocaine had statistically higher rates of ROSC compared with patients receiving amiodarone or no antiarrhythmic medication. There was no significant difference in ROSC for patients receiving amiodarone compared with those receiving no antiarrhythmic medication. There was no difference in survival to hospital discharge across the 3 groups. On multivariate analysis, lidocaine was independently associated with ROSC (odds ratio, 2.02; 95% CI, 1.36–3.00). Neither lidocaine nor amiodarone was found to have a significant independent association with survival to hospital discharge.

The raw data were used to calculate a relative risk of each outcome. There was a statistically significant improvement in ROSC in patients who received lidocaine compared with amiodarone (64% versus 44%; $P=0.004$; relative risk, 1.46; 95% CI, 1.13–1.88). There was no statistical difference in survival to hospital discharge in patients who received lidocaine compared with those receiving amiodarone (25% versus 17%; $P=NS$; relative risk, 1.50; 95% CI, 0.90–2.52) or when those who received lidocaine, amiodarone, or no antiarrhythmic medication were compared.

The results of this study were not reported by year of cardiac arrest. The study did not report adverse events, making it impossible to balance the risk and benefit of administration of antiarrhythmic medication in this population.

2018 Recommendation

Amiodarone and Lidocaine—Unchanged

- 1. For shock-refractory VF/pVT, either amiodarone or lidocaine may be used (Class IIb; Level of Evidence C-LD). This is unchanged from the 2015 recommendation.⁶**

The Pediatric Cardiac Arrest Algorithm—2018 Update (Figure) is unchanged in the depiction of sequences and therapies from the version published in 2015.⁶ To clarify the use of antiarrhythmic medications for shock-refractory VF/pVT, under Drug Therapy in the box on the right, the doses of amiodarone and lidocaine are clearly separated with the word “or.” The writing group also took the opportunity to review the complete text of the algorithm and to eliminate minor wording differences between the adult and pediatric cardiac arrest algorithms. Under Asystole/PEA (pulseless electrical activity), in Box 10, the writing group added the word “capnography” to the last bullet after “Consider advanced airway” and made minor edits to Box 12, eliminating the bulleted phrase “Organized rhythm→check pulse.” In the CPR Qual-

ity box on the right, in the fourth bullet, the word “rotate” was changed to “change.” These changes will make the wording identical to that in the boxes located in the same position in the Adult Cardiac Arrest Algorithm—2018 Update. All other parts of the Pediatric Cardiac Arrest Algorithm are unchanged.

Discussion

Past ILCOR pediatric evidence reviews, CoSTRs, and AHA PALS guidelines on the topic of antiarrhythmic therapy in pediatric cardiac arrest have incorporated data extrapolated from adult studies. For this update, the consensus of the ILCOR Pediatric Task Force was to consider only pediatric studies because the experts agreed that the pediatric cardiac arrest population differs significantly from the adult cardiac arrest population. The most recent adult studies examining the effect of antiarrhythmic medication for shock-refractory VF/pVT had an average patient age of >60 years and specifically excluded patients <18 years of age.^{11,12,14} Pediatric cardiac arrests typically occur in patients with progressive respiratory failure or shock, and most are preceded by a period of hypoxia and hypotension, with a terminal rhythm of bradycardia or asystole. Ventricular arrhythmias are more common in certain subpopulations, such as children with congenital heart disease or channelopathies. However, in general, VF/pVT is uncommon, occurring as the first documented rhythm in 10% to 14% of pediatric in-hospital cardiac arrests^{13,15–18} and in 7% of pediatric out-of-hospital cardiac arrests.^{19,20} Subsequent VF/pVT (ie, VF/pVT that develops during resuscitation from an arrest with a non-VF/pVT initial arrest rhythm such as pulseless electrical activity or asystole) occurs in 15% of pediatric in-hospital cardiac arrests.¹⁵ In the Valdes et al¹³ study, subsequent VF/pVT was associated with lower rates of ROSC and survival to hospital discharge than initial VF/pVT was; this outcome is consistent with other pediatric^{16,17} and adult²¹ reports.

Unlike pediatric cardiopulmonary arrest, cardiac arrest in adults is often secondary to a sudden ventricular arrhythmia. Coronary occlusion with subsequent myocardial ischemia serves as a common trigger for these arrhythmias, typically with no preceding hypoxia or hypotension. The most common arrest rhythm in adult cardiac arrest is VF/pVT, present in up to 44% of adult cardiac arrests.^{21,22} Because it is unclear how differences between pediatric and adult cardiac arrest may influence the effect of antiarrhythmic therapy, the writing group agreed with the ILCOR Pediatric Task Force to analyze evidence from only pediatric cardiac arrest studies.

The indication for the use of amiodarone or lidocaine in this 2018 PALS guidelines focused update is shock-refractory VF/pVT, defined as VF or pVT that per-

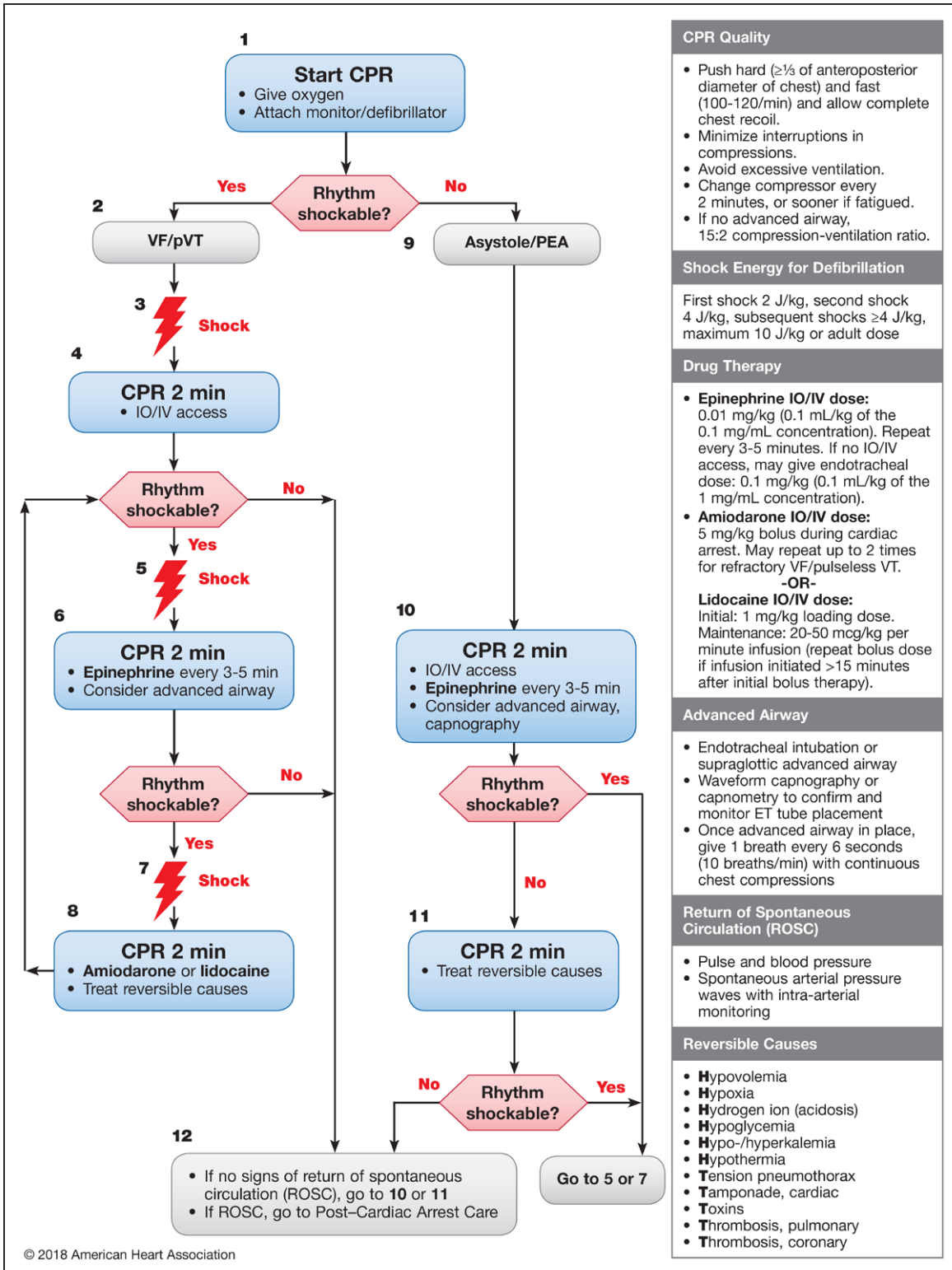


Figure. Pediatric Cardiac Arrest Algorithm—2018 Update.

CPR indicates cardiopulmonary resuscitation; ET, endotracheal; IO, intraosseous; IV, intravenous; PEA, pulseless electrical activity; pVT, pulseless ventricular tachycardia; ROSC, return of spontaneous circulation; VF, ventricular fibrillation; and VT, ventricular tachycardia.

sists or recurs after the delivery of at least 1 shock. In the Valdes et al¹³ study, the mean number of shocks administered is 3, but the number of subjects who required >1 shock is not reported, so it is impossible to

determine with certainty how many of the patients in the study had shock-refractory VF/pVT. In the absence of evidence to the contrary, the writing group assumed that enrolled patients received at least 1 shock before

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antiarrhythmic therapy and could therefore be considered to have shock-refractory VF/pVT.

Another potential limitation of the Valdes et al¹³ study is the period during which patients were enrolled in the study. The study included patients who had in-hospital cardiac arrest between 2000 and 2008, spanning the years during which the “2005 American Heart Association Guidelines for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care” were introduced.²³ These 2005 guidelines emphasized the importance of high-quality CPR, including emphasis on minimizing interruptions in chest compressions by using a new compression-to-ventilation ratio and a new defibrillation sequence (1 shock followed by immediate resumption of CPR instead of 3 “stacked” shocks). Because recommended resuscitation sequences and interventions differed substantially before and after the implementation of the 2005 guidelines, the Valdes et al study was downgraded in the ILCOR systematic review for indirectness (ie, many patients in the study were treated in a manner inconsistent with current resuscitation practice). This issue highlights a challenge of resuscitation research: As guidelines are updated, research protocols become outdated and comparisons challenging. In the future, authors are encouraged to provide subgroup analyses of patients enrolled in studies after major guideline changes.

SUMMARY

A review of the peer-reviewed publications on antiarrhythmic therapy in pediatric shock-refractory VF/pVT cardiac arrest resulted in no change in PALS guideline recommendations but has identified several gaps in our knowledge. As noted in the 2010 guidelines,⁷ high-quality CPR and defibrillation are the only therapies proven to increase survival in patients with VF/pVT. The optimal sequence of PALS interventions

for VF/pVT cardiac arrest, including administration of a vasopressor or antiarrhythmic medication, and the timing of medication administration in relation to shock delivery are not known. The sequence of interventions recommended in the current PALS algorithm should consider the individual patient and the environment of care.

Future updates will address new research such as targeted temperature management after ROSC²⁴ and hemodynamic monitoring to guide CPR quality^{25–27} to integrate new published evidence into resuscitation recommendations.

ARTICLE INFORMATION

The American Heart Association makes every effort to avoid any actual or potential conflicts of interest that may arise as a result of an outside relationship or a personal, professional, or business interest of a member of the writing panel. Specifically, all members of the writing group are required to complete and submit a Disclosure Questionnaire showing all such relationships that might be perceived as real or potential conflicts of interest.

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Disclosures

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Robert M. Sutton	The Children's Hospital of Philadelphia, University of Pennsylvania School of Medicine	NHLBI (PI of multicenter trial investigating blood pressure-directed CPR, post-cardiac arrest debriefings)†	None	None	Roberts and Durkee*; Donahue, Durham, and Noonan*; Lewis and Gellen*	None	Zoll Medical Speaker Honoraria* 	None
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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.

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REFERENCES

- Atkins DL, Aickin RP, Bingham R, Couper K, Couto TB, de Caen AR, Guerguerian AM, Hazinski MF, Lavonas E, Meaney P, Nadkarni VM, Ng KC, Nuthall GA, Ohshimo S, Ong GYK, Reis AG, Schexnayder SM, Scholefield BR, Shimizu NS, Tijssen JA, Van de Voorde P, Maconochie IK. Antiarrhythmic drugs for cardiac arrest in adults and children: consensus on science and treatment recommendations. Brussels, Belgium: International Liaison Committee on Resuscitation (ILCOR) Pediatric Life Support Task Force. 2018. <https://costr.ilcor.org/document/antiarrhythmic-drugs-for-cardiac-arrest-pediatric>. Accessed July 30, 2018.
- Soar J, Donnino MW, Maconochie I, Aickin R, Atkins DL, Andersen LW, Berg KM, Bingham R, Böttiger BW, Callaway CW, Couper K, Couto TB, de Caen AR, Deakin CD, Drennan IR, Guerguerian A-M, Lavonas EJ, Meaney PA, Nadkarni VM, Neumar RW, Ng K-C, Nicholson TC, Nuthall GA, Ohshimo S, O'Neil BJ, Ong GY-K, Paiva EF, Parr MJ, Reis AG, Reynolds JC, Ristagno G, Sandroni C, Schexnayder SM, Scholefield BR, Shimizu N, Tijssen JA, Van de Voorde P, Wang T-L, Welsford M, Hazinski MF, Nolan JP, Morley PT, on behalf of the ILCOR Collaborators. 2018 International Consensus on Cardiopulmonary Resuscitation and Emergency Cardiovascular Care Science With Treatment Recommendations summary. *Circulation*. 2018;138:XXX-XXX. doi: 10.1161/CIR.0000000000000611
- Olasveengen TM, de Caen AR, Mancini ME, Maconochie IK, Aickin R, Atkins DL, Berg RA, Bingham RM, Brooks SC, Castrén M, Chung SP, Considine J, Couto TB, Escalante R, Gazmuri RJ, Guerguerian AM, Hatanaka T, Koster RW, Kudenchuk PJ, Lang E, Lim SH, Løfgren B, Meaney PA, Montgomery WH, Morley PT, Morrison LJ, Nation KJ, Ng KC, Nadkarni VM, Nishiyama C, Nuthall G, Ong GY, Perkins GD, Reis AG, Ristagno G, Sakamoto T, Sayre MR, Schexnayder SM, Sierra AF, Singletary EM, Shimizu N, Smyth MA, Stanton D, Tijssen JA, Travers A, Vaillancourt C, Van de Voorde P, Hazinski MF, Nolan JP, on behalf of the ILCOR Collaborators. 2017 International Consensus on Cardiopulmonary Resuscitation and Emergency Cardiovascular Care Science With Treatment Recommendations summary [published correction appears in *Circulation*. 2017;136:e468]. *Circulation*. 2017;136:e424-e440. doi: 10.1161/CIR.0000000000000541
- Halperin JL, Levine GN, Al-Khatib SM, Birtcher KK, Bozkurt B, Brindis RG, Cigarroa JE, Curtis LH, Fleisher LA, Gentile F, Gidding S, Hlatky MA, Ikonomidis J, Joglar J, Pressler SJ, Wijeyesundera DN. Further evolution of the ACC/AHA clinical practice guideline recommendation classification system: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. *Circulation*. 2016;133:1426-1428. doi: 10.1161/CIR.0000000000000312
- Morrison LJ, Gent LM, Lang E, Nunnally ME, Parker MJ, Callaway CW, Nadkarni VM, Fernandez AR, Billi JE, Egan JR, Griffin RE, Shuster M, Hazinski MF. Part 2: evidence evaluation and management of conflicts of interest: 2015 American Heart Association guidelines update for cardiopulmonary resuscitation and emergency cardiovascular care. *Circulation*. 2015;132(suppl 2):S368-S382. doi: 10.1161/CIR.0000000000000253
- de Caen AR, Berg MD, Chameides L, Gooden CK, Hickey RW, Scott HF, Sutton RM, Tijssen JA, Topjian A, van der Jagt EW, Schexnayder SM, Samson RA. Part 12: pediatric advanced life support: 2015 American Heart Association guidelines update for cardiopulmonary resuscitation and emergency cardiovascular care. *Circulation*. 2015;132(suppl 2):S526-S542. doi: 10.1161/CIR.0000000000000266
- Kleinman ME, Chameides L, Schexnayder SM, Samson RA, Hazinski MF, Atkins DL, Berg MD, de Caen AR, Fink EL, Freid EB, Hickey RW, Marino BS, Nadkarni VM, Proctor LT, Qureshi FA, Sartorelli K, Topjian A, van der Jagt EW, Zaritsky AL. Part 14: pediatric advanced life support: 2010 American Heart Association guidelines for cardiopulmonary resuscitation and emergency cardiovascular care. *Circulation*. 2010;122(suppl 3):S876-S908. doi: 10.1161/CIRCULATIONAHA.110.971101
- Atkins DL, de Caen AR, Berger S, Samson RA, Schexnayder SM, Joyner BL Jr, Bigham BL, Niles DE, Duff JP, Hunt EA, Meaney PA. 2017 American Heart Association focused update on pediatric basic life support and cardiopulmonary resuscitation quality: an update to the American Heart Association guidelines for cardiopulmonary resuscitation and emergency cardiovascular care. *Circulation*. 2018;137:e1-e6. doi: 10.1161/CIR.0000000000000540
- Kudenchuk PJ, Cobb LA, Copass MK, Cummins RO, Doherty AM, Fahrenbruch CE, Hallstrom AP, Murray WA, Olsufka M, Walsh T. Amiodarone for resuscitation after out-of-hospital cardiac arrest due to ventricular fibrillation. *N Engl J Med*. 1999;341:871-878. doi: 10.1056/NEJM199909163411203
- Dorian P, Cass D, Schwartz B, Cooper R, Gelaznikas R, Barr A. Amiodarone as compared with lidocaine for shock-resistant ventricular fibrillation. *N Engl J Med*. 2002;346:884-890. doi: 10.1056/NEJMoa013029
- Kudenchuk PJ, Leroux BG, Daya M, Rea T, Vaillancourt C, Morrison LJ, Callaway CW, Christenson J, Ornato JP, Dunford JV, Wittwer L, Weisfeldt ML, Aufderheide TP, Vilke GM, Idris AH, Stiell IG, Colella MR, Kaye T, Egan D, Desvigne-Nickens P, Gray P, Gray R, Straight R, Dorian P; and the Resuscitation Outcomes Consortium Investigators. Antiarrhythmic drugs for non-shockable-turned-shockable out-of-hospital cardiac arrest: the ALPS study (Amiodarone, Lidocaine, or Placebo). *Circulation*. 2017;136:2119-2131. doi: 10.1161/CIRCULATIONAHA.117.028624
- Kudenchuk PJ, Brown SP, Daya M, Rea T, Nichol G, Morrison LJ, Leroux B, Vaillancourt C, Wittwer L, Callaway CW, Christenson J, Egan D, Ornato JP, Weisfeldt ML, Stiell IG, Idris AH, Aufderheide TP, Dunford JV, Colella MR, Vilke GM, Brienza AM, Desvigne-Nickens P, Gray PC, Gray R, Seals N, Straight R, Dorian P; on behalf of the Resuscitation Outcomes Consortium Investigators. Amiodarone, lidocaine, or placebo in out-of-hospital cardiac arrest. *N Engl J Med*. 2016;374:1711-1722. doi: 10.1056/NEJMoa1514204
- Valdes SO, Donoghue AJ, Hoyme DB, Hammond R, Berg MD, Berg RA, Samson RA; on behalf of the American Heart Association Get With The Guidelines-Resuscitation Investigators. Outcomes associated with amiodarone and lidocaine in the treatment of in-hospital pediatric cardiac arrest with pulseless ventricular tachycardia or ventricular fibrillation. *Resuscitation*. 2014;85:381-386. doi: 10.1016/j.resuscitation.2013.12.008
- Amino M, Yoshioka K, Opthof T, Morita S, Uemura S, Tamura K, Fukushima T, Higami S, Otsuka H, Akieda K, Shima M, Fujibayashi D, Hashida T, Inokuchi S, Kodama I, Tanabe T. Comparative study of nifekalant versus amiodarone for shock-resistant ventricular fibrillation in out-of-hospital cardiopulmonary arrest patients. *J Cardiovasc Pharmacol*. 2010;55:391-398. doi: 10.1097/FJC.0b013e3181d3d3cc7
- Samson RA, Nadkarni VM, Meaney PA, Carey SM, Berg MD, Berg RA; on behalf of the American Heart Association National Registry of CPR Investigators. Outcomes of in-hospital ventricular fibrillation in children. *N Engl J Med*. 2006;354:2328-2339. doi: 10.1056/NEJMoa052917
- Nadkarni VM, Larkin GL, Peberdy MA, Carey SM, Kaye W, Mancini ME, Nichol G, Lane-Truitt T, Potts J, Ornato JP, Berg RA; on behalf of the National Registry of Cardiopulmonary Resuscitation Investigators. First documented rhythm and clinical outcome from in-hospital cardiac arrest among children and adults. *JAMA*. 2006;295:50-57. doi: 10.1001/jama.295.1.50
- Meert KL, Donaldson A, Nadkarni V, Tieves KS, Schleien CL, Brill RJ, Clark RS, Shaffner DH, Levy F, Statler K, Dalton HJ, van der Jagt EW, Hackbarth R, Pretzlaff R, Hernan L, Dean JM, Moler FW; on behalf of the Pediatric Emergency Care Applied Research Network. Multicenter cohort study of in-hospital pediatric cardiac arrest. *Pediatr Crit Care Med*. 2009;10:544-553. doi: 10.1097/PCC.0b013e3181a7045c
- Moler FW, Meert K, Donaldson AE, Nadkarni V, Brill RJ, Dalton HJ, Clark RS, Shaffner DH, Schleien CL, Statler K, Tieves KS, Hackbarth R, Pretzlaff R, van der Jagt EW, Levy F, Hernan L, Silverstein FS, Dean JM; on behalf of the Pediatric Emergency Care Applied Research Network. In-hospital versus out-of-hospital pediatric cardiac arrest: a multicenter cohort study. *Crit Care Med*. 2009;37:2259-2267. doi: 10.1097/CCM.0b013e3181a00a6a
- Atkins DL, Everson-Stewart S, Sears GK, Daya M, Osmond MH, Warden CR, Berg RA; and the Resuscitation Outcomes Consortium Investigators. Epidemiology and outcomes from out-of-hospital cardiac arrest in children: the Resuscitation Outcomes Consortium Epistry-Cardiac Arrest. *Circulation*. 2009;119:1484-1491. doi: 10.1161/CIRCULATIONAHA.108.802678
- McNally B, Robb R, Mehta M, Vellano K, Valderrama AL, Yoon PW, Sasson C, Crouch A, Perez AB, Merritt R, Kellermann A. Out-of-hospital cardiac arrest surveillance: Cardiac Arrest Registry to Enhance Survival (CARES), United States, October 1, 2005-December 31, 2010. *MMWR Surveill Summ*. 2011;60:1-19.
- Meaney PA, Nadkarni VM, Kern KB, Indik JH, Halperin HR, Berg RA. Rhythms and outcomes of adult in-hospital cardiac arrest. *Crit Care Med*. 2010;38:101-108. doi: 10.1097/CCM.0b013e3181b43282
- Daya RM, Schmicker RH, Zive DM, Rea TD, Nichol G, Buick JE, Brooks S, Christenson J, MacPhee R, Craig A, Rittenberger JC, Davis DP, May S, Wigginton J, Wang H; on behalf of the Resuscitation Outcomes Consortium Investigators. Out-of-hospital cardiac arrest survival improving over time: results from the Resuscitation Outcomes Consortium (ROC). *Resuscitation*. 2015;91:108-115. doi: 10.1016/j.resuscitation.2015.02.003
- Part 12: pediatric advanced life support: 2005 American Heart Association guidelines for cardiopulmonary resuscitation and emergency

- cardiovascular care. *Circulation*. 2005;112(suppl):IV-167–IV-187. doi: 10.1161/circulationaha.105.166573
24. Moler FW, Silverstein FS, Holubkov R, Slomine BS, Christensen JR, Nadkarni VM, Meert KL, Browning B, Pemberton VL, Page K, Gildea MR, Scholefield BR, Shankaran S, Hutchison JS, Berger JT, Ofori-Amanfo G, Newth CJ, Topjian A, Bennett KS, Koch JD, Pham N, Chanani NK, Pineda JA, Harrison R, Dalton HJ, Alten J, Schleien CL, Goodman DM, Zimmerman JJ, Bhalala US, Schwarz AJ, Porter MB, Shah S, Fink EL, McQuillen P, Wu T, Skellett S, Thomas NJ, Nowak JE, Baines PB, Pappachan J, Mathur M, Lloyd E, van der Jagt EW, Dobyns EL, Meyer MT, Sanders RC Jr, Clark AE, Dean JM; on behalf of the THAPCA Trial Investigators. Therapeutic hypothermia after in-hospital cardiac arrest in children. *N Engl J Med*. 2017;376:318–329. doi: 10.1056/NEJMoa1610493
 25. Berg RA, Sutton RM, Reeder RW, Berger JT, Newth CJ, Carcillo JA, McQuillen PS, Meert KL, Yates AR, Harrison RE, Moler FW, Pollack MM, Carpenter TC, Wessel DL, Jenkins TL, Notterman DA, Holubkov R, Tamburro RF, Dean JM, Nadkarni VM; on behalf of the Eunice Kennedy Shriver National Institute of Child Health and Human Development Collaborative Pediatric Critical Care Research Network (CPCCRN) PICqCPR (Pediatric Intensive Care Quality of Cardio-Pulmonary Resuscitation) Investigators. Association between diastolic blood pressure during pediatric in-hospital cardiopulmonary resuscitation and survival. *Circulation*. 2018;137:1784–1795. doi: 10.1161/CIRCULATIONAHA.117.032270
 26. Morgan RW, Kilbaugh TJ, Shoap W, Bratinov G, Lin Y, Hsieh TC, Nadkarni VM, Berg RA, Sutton RM; on behalf of the Pediatric Cardiac Arrest Survival Outcomes (PICASO) Laboratory Investigators. A hemodynamic-directed approach to pediatric cardiopulmonary resuscitation (HD-CPR) improves survival. *Resuscitation*. 2017;111:41–47. doi: 10.1016/j.resuscitation.2016.11.018
 27. Sutton RM, Friess SH, Naim MY, Lampe JW, Bratinov G, Weiland TR 3rd, Garuccio M, Nadkarni VM, Becker LB, Berg RA. Patient-centric blood pressure-targeted cardiopulmonary resuscitation improves survival from cardiac arrest. *Am J Respir Crit Care Med*. 2014;190:1255–1262. doi: 10.1164/rccm.201407-1343OC