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| Question | |
| **Energy doses for pediatric defibrillation during resuscitation** | |
| **Population:** | Infants and children (excluding newborn children) who are in ventricular fibrillation or pulseless ventricular tachycardia during out-of-hospital or in-hospital cardiac arrest |
| **Intervention:** | Initial defibrillation dose approximating 2J/kg (1.5-2.5 J/kg) |
| **Comparison:** | Compared with initial defibrillation dose of >2.5J/kg, <1.5J/kg or any other specified dose |
| **Main outcomes:** | Any clinical outcome including but not limited to:   * survival to hospital discharge with good neurologic outcome * survival to hospital discharge * survival to hospital admission * return of circulation (ROC)   The PLS TF prefers outcomes defined in the P-COSCA publication1 |
| **Setting:** | in cardiac arrest |
| **Perspective:** |  |
| **Background:** |  |
| **Conflict of interests:** |  |

# Assessment

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| Problem Is the problem a priority? | | |
| Judgement | Research evidence | Additional considerations |
| ○ No ○ Probably no ○ Probably yes ● Yes ○ Varies ○ Don't know | Shockable ventricular arrhythmias (VF, pVT) are less frequently recorded in pediatric cardiac arrest but are associated with a higher survival rate than non-shockable rhythms (asystole, PEA). Early defibrillation is the foundation of treatment but optimal energy doses for initial and subsequent shocks remain controversial.  Differences remain in the first shock dose recommended by ILCOR member councils, with the ERC and ANZCOR recommending 4J/kg for the first and all subsequent shocks and the AHA recommending an initial dose of 2-4 J/kg (for ease of teaching, a dose of 2 J/kg is used in algorithms and training materials). For refractory VF, the AHA guidelines recommend increasing the defibrillation dose to 4 J/kg, suggesting that subsequent energy doses should be at least 4 J/kg and noting that higher levels may be considered, not to exceed 10 J/kg.  Current ILCOR treatment recommendations2 suggest the routine use of an initial dose of 2 to 4 J/kg of monophasic or biphasic defibrillation waveforms for infants or children in VF or pVT cardiac arrest. They recognized that there was insufficient evidence from which to base a recommendation for second and subsequent defibrillation dosages. | A systematic review3 failed to show a significant benefit of one dosing regimen over another but was hampered by small sample sizes and study heterogeneity.  The more recent large pediatric in-hospital registry study4 provided support for a 2 J/kg dose for initial defibrillation but did not provide guidance for subsequent doses.  The current systematic review aims to review all available evidence that may support or change the current recommendations. |
| Desirable Effects How substantial are the desirable anticipated effects? | | |
| Judgement | Research evidence | Additional considerations |
| ● Trivial ○ Small ○ Moderate ○ Large ○ Varies ○ Don't know | Overall, based on current evidence the systematic review results suggest with very low certainty (downgraded for imprecision and risk of bias) that neither defibrillation doses <2 J/kg nor defibrillation doses >2 J/kg are superior to defibrillation doses approximating 2 J/kg for treatment of shockable rhythms in cardiac arrest in children for the critically important outcomes of survival to hospital discharge (SHD) and return of spontaneous circulation (ROSC) and the important outcome of termination of the shockable rhythm (VF or pVT).  Very low certainty data from 4 cohort studies, involving 266 patients showed no significant difference to ROSC associated with defibrillation dose <2 J/kg compared to that approximating 2 J/kg (51 more survivors per 1,000 resuscitations; CI 95%: 42 fewer to 152 more). Very low certainty data from 2 cohort studies involving 225 patients also showed no significant difference to SHD associated with defibrillation dose <2 J/kg compared to that approximating 2 J/kg (29 more survivors per 1,000 resuscitations; CI 95%: 96 fewer to 192 more).  Additional very low certainty evidence from two observational studies of 265 children found no significant effect on termination of VF/pVT associated with defibrillation dose <2 J/kg compared to that approximating 2 J/kg (179 fewer per 1,000; CI 95%: 415 fewer to 888 more).  Very low certainty data from 6 cohort studies, involving 596 patients showed no significant difference to ROSC associated with defibrillation dose >2 J/kg compared to that approximating 2 J/kg (29 fewer survivors per 1,000 resuscitations; CI 95%: 133 fewer to 98 more). Very low certainty data from 2 cohort studies involving 225 patients also showed no significant difference to SHD associated with defibrillation dose >2 J/kg compared to that approximating 2 J/kg (82 more survivors per 1,000 resuscitations; CI 95%: 253 fewer to 1000 more).  Additional very low certainty evidence from two observational studies of 265 children found no significant effect on termination of VF/pVT associated with defibrillation dose >2 J/kg compared to that approximating 2 J/kg (22 fewer per 1,000; CI 95%: 99 fewer to 77 more). |  |
| Undesirable Effects How substantial are the undesirable anticipated effects? | | |
| Judgement | Research evidence | Additional considerations |
| ● Trivial ○ Small ○ Moderate ○ Large ○ Varies ○ Don't know | Specific undesirable effects (outside of the lack of ROSC/SHD) were not consistently reported in the studies identified eg. myocardial damage.  None of these outcomes were proposed *a priori* as important or critical by the PLS Task Force. |  |
| Certainty of evidence What is the overall certainty of the evidence of effects? | | |
| Judgement | Research evidence | Additional considerations |
| ● Very low ○ Low ○ Moderate ○ High ○ No included studies | Seven studies4-10 were included in the systematic review. None of these provided clinical trial data. The 7 identified studies were all cohort studies and provided very low certainty evidence (downgraded for imprecision and risk of bias) for the comparisons with the important and critical outcomes described. | The task force also recognised that most of the studies were conducted in sites where either 2 J/kg or 4 J/kg doses were recommended for initial defibrillation. The variability of dosing was largely attributable to the limited number of energy dose settings on defibrillators. So, although no specific energy dose was found superior, energy selections would generally have been approximating either 2 or 4 J/kg. |
| Values Is there important uncertainty about or variability in how much people value the main outcomes? | | |
| Judgement | Research evidence | Additional considerations |
| ○ Important uncertainty or variability ○ Possibly important uncertainty or variability ● Probably no important uncertainty or variability ○ No important uncertainty or variability | The ILCOR P-COSCA initiative developed a core outcome set specific for pediatric cardiac arrest studies. The design and methods of the initiative included use of a Delphi process to develop consensus on a core domain set.1  Survival to hospital discharge (SHD), a P-COSCA outcome, and return of spontaneous circulation (ROSC) were chosen as critical outcomes for this review and are highly valued. Termination of the shockable rhythm (VF/pVT) was considered an important measurable outcome.  We have not identified any studies that specifically addressed how patients valued the different outcomes. |  |
| Balance of effects Does the balance between desirable and undesirable effects favor the intervention or the comparison? | | |
| Judgement | Research evidence | Additional considerations |
| ○ Favors the comparison ○ Probably favors the comparison ● Does not favor either the intervention or the comparison ○ Probably favors the intervention ○ Favors the intervention ○ Varies ○ Don't know | Acknowledging the very low level of certainty, the current available data suggest that the critical (SHD, ROSC) and important (termination of VF/pVT) outcomes are not significantly better or worse when initial defibrillation doses of <2 J/kg or >2 J/kg are used for children in cardiac arrest with a shockable rhythm (VF or pVT) compared with initial doses approximating 2 J/kg. |  |
| Resources required | | |
| Judgement | Research evidence | Additional considerations |
| ○ Large costs ○ Moderate costs ● Negligible costs and savings ○ Moderate savings ○ Large savings ○ Varies ○ Don't know | While no studies evaluated this specifically (including cost effectiveness) there should be no difference in resources/costs involved in delivering different defibrillation doses. |  |
| Certainty of evidence of required resources What is the certainty of the evidence of resource requirements (costs)? | | |
| Judgement | Research evidence | Additional considerations |
| ○ Very low ○ Low ○ Moderate ○ High ● No included studies | No studies regarding resource requirements were included in this systematic review. |  |
| Cost effectiveness Does the cost-effectiveness of the intervention favor the intervention or the comparison? | | |
| Judgement | Research evidence | Additional considerations |
| ○ Favors the comparison ○ Probably favors the comparison ○ Does not favor either the intervention or the comparison ○ Probably favors the intervention ○ Favors the intervention ○ Varies ● No included studies | Cost effectiveness data was not identified in this systematic review. |  |
| Equity What would be the impact on health equity? | | |
| Judgement | Research evidence | Additional considerations |
| ○ Reduced ○ Probably reduced ● Probably no impact ○ Probably increased ○ Increased ○ Varies ○ Don't know |  | Defibrillation interventions are currently offered in hospitals and in EMS systems with ALS capability. This varies by country and region and may not be readily available in all areas in the developing world.  Paediatric defibrillation requires a moderate investment in equipment and a significant investment in training, skills maintenance, and quality control programs to be successful. While defibrillation is supported in essentially all hospital settings in the developed world, advanced life (ALS) support-capable emergency medical services agencies and IHCA teams will need to maintain this capability as well. |
| Acceptability Is the intervention acceptable to key stakeholders? | | |
| Judgement | Research evidence | Additional considerations |
| ○ No ○ Probably no ○ Probably yes ○ Yes ● Varies ○ Don't know | The systematic review search strategy used did not identify any studies that addressed how patients or clinicians valued different outcomes. | Essentially all hospital resuscitation teams and all ALS-based emergency medical services (EMS) systems already provide defibrillation.  Guidelines for pediatric defibrillation dosing vary between different resuscitation councils around the world with some recommending an initial dose of 2J/kg and others recommending 4 J/kg. It is likely that local guidance will stay in place unless there is clear evidence to change. |
| Feasibility Is the intervention feasible to implement? | | |
| Judgement | Research evidence | Additional considerations |
| ○ No ○ Probably no ○ Probably yes ● Yes ○ Varies ○ Don't know |  | A change in recommended initial dosing for pediatric defibrillation would be readily implementable. |

# Summary of judgements

|  | **Judgement** | | | | | | |
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| **Problem** | No | Probably no | Probably yes | **Yes** |  | Varies | Don't know |
| **Desirable Effects** | **Trivial** | Small | Moderate | Large |  | Varies | Don't know |
| **Undesirable Effects** | **Trivial** | Small | Moderate | Large |  | Varies | Don't know |
| **Certainty of evidence** | **Very low** | Low | Moderate | High |  |  | No included studies |
| **Values** | Important uncertainty or variability | Possibly important uncertainty or variability | **Probably no important uncertainty or variability** | No important uncertainty or variability |  |  |  |
| **Balance of effects** | Favors the comparison | Probably favors the comparison | **Does not favor either the intervention or the comparison** | Probably favors the intervention | Favors the intervention | Varies | Don't know |
| **Resources required** | Large costs | Moderate costs | **Negligible costs and savings** | Moderate savings | Large savings | Varies | Don't know |
| **Certainty of evidence of required resources** | Very low | Low | Moderate | High |  |  | **No included studies** |
| **Cost effectiveness** | Favors the comparison | Probably favors the comparison | Does not favor either the intervention or the comparison | Probably favors the intervention | Favors the intervention | Varies | **No included studies** |
| **Equity** | Reduced | Probably reduced | **Probably no impact** | Probably increased | Increased | Varies | Don't know |
| **Acceptability** | No | Probably no | Probably yes | Yes |  | **Varies** | Don't know |
| **Feasibility** | No | Probably no | Probably yes | **Yes** |  | Varies | Don't know |

# Type of recommendation

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| Strong recommendation against the intervention | Conditional recommendation against the intervention | **Conditional recommendation for either the intervention or the comparison** | Conditional recommendation for the intervention | Strong recommendation for the intervention |
| ○ | ○ | **●** | ○ | ○ |

# Conclusions

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| Recommendation |
| In the absence of evidence to demonstrate a clear preference for any particular energy dose, we continue to suggest the use of an initial defibrillation dose of 2 to 4 J/kg for infants or children in VF or pVT cardiac arrest [weak recommendation, very low quality evidence].  This review did not investigate the evidence for second and subsequent defibrillation dosages. |
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| Justification |
| There is currently no supporting evidence that any particular defibrillation dose for initial management of VF/pVT in pediatric cardiac arrest improves ROSC or survival to hospital discharge. |

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| Subgroup considerations |
| The benefit or harm associated with different defibrillation dosing strategies in paediatric resuscitation may differ across settings. Importantly, the available data do not inform the questions of whether better outcomes might be achieved by different energy dosing strategies in in-hospital compared to out-of-hospital arrest settings, for primary of secondary shockable rhythms or when monophasic or biphasic defibrillator waveforms are used. When AEDs are utilized in pediatric arrest it is more likely that higher defibrillation doses (J/kg) will be used. |
| Implementation considerations |
| It is likely that a change in recommended defibrillation dosing would be acceptable to key stakeholders. |

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| Monitoring and evaluation |
| See below |
| Research priorities |
| Shockable ventricular arrhythmias (VF, pVT) are less frequently recorded in pediatric cardiac arrest compared to adult populations. Prehospital and in-hospital studies, ideally comparing existing different dosing strategies with planned subgroup analyses based on patient age and type of shockable rhythm (primary vs secondary) are ethical, necessary, and critically important to help guide clinicians in making these complex decisions. As different resuscitation councils recommend either 2 or 4 J/kg as an initial defibrillation dose, this may provide an opportunity for an international comparative study.  Further examination of the potential adverse effects of higher defibrillation doses when fixed energy doses are provided (AEDs) would also be helpful.  Future studies would benefit from including outcome measures consistent with the P-COSCA recommendations. |

# References Summary

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