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| **Vasopressors during adult cardiac arrest – Vasopressin or vasopressin plus epinephrine compared to epinephrine**  |
| **Population:** | Adult individuals with cardiac arrest in any setting (our-of-hospital or in-hospital). |
| **Intervention:** | Vasopressor or a combination of vasopressors provided intravenously or intraosseously during cardiopulmonary resuscitation. |
| **Comparison:** | No vasopressor, a different vasopressor, a different combination of vasopressors, a different vasopressor dose, or a different timing of vasopressors provided intravenously or intraosseously during cardiopulmonary resuscitation. |
| **Main outcomes:** | Clinical outcome including survival, favorable neurological outcome, and health-related quality of life at hospital discharge, 30 days, 90 days, 180 days, and 1 year. |

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| ProblemIs the problem a priority? |
| Judgement | Research evidence | Additional considerations |
| ○ No○ Probably no○ Probably yes● Yes○ Varies○ Don't know | Cardiac arrest, both in the out-of-hospital and in-hospital setting, is relatively common and carries a very high morbidity and mortality. |  |
| Desirable EffectsHow substantial are the desirable anticipated effects? |
| Judgement | Research evidence | Additional considerations |
| ○ Trivial○ Small○ Moderate○ Large○ Varies● Don't know | For both the vasopressin vs epinephrine and the vasopressin plus epinephrine vs epinephrine only comparisons, no study found a significant difference in any outcomes between groups. | Studies were underpowered preventing definitive conclusions from being drawn from results. |
| Undesirable EffectsHow substantial are the undesirable anticipated effects? |
| Judgement | Research evidence | Additional considerations |
| ○ Trivial○ Small○ Moderate○ Large○ Varies● Don't know | One potential undesirable effect is an increasing complexity in the cardiac arrest treatment algorithm, which may not be warranted if there are no differences in outcomes. |  |
| Certainty of evidenceWhat is the overall certainty of the evidence of effects? |
| Judgement | Research evidence | Additional considerations |
| ● Very low○ Low○ Moderate○ High○ No included studies | The certainty of evidence varies but is low or very low for all outcomes.

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| **Comparison (OHCA)** | **Outcome** |
| **Return of spontaneous circulation** | **Survival at hospital discharge** | **Favorable neurological outcome at hospital discharge** |
| Initial vasopressin compared to initial epinephrine | ⨁⨁◯◯Low | ⨁◯◯◯Very low | Not applicable |
| Initial epinephrine plus vasopressin compared to epinephrine only | ⨁◯◯◯Very low | ⨁◯◯◯Very low | ⨁⨁◯◯Low |

 | The low to very low certainty of evidence is due largely to inadequate sample sizes and inconsistency of results across trials. |
| ValuesIs 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 | A study suggests that patients value survival with favorable neurological outcome most highly.1 | The importance of neurological intact survival is generally agreed upon with recognition that survival without neurological recovery is an undesirable outcome for most patients. |
| Balance of effectsDoes 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 | Given the neutral results and the presumed benefit of keeping the recommendations for treating cardiac arrest as simple as possible, the balance of favorable and unfavorable effects slightly favors epinephrine.  | As the studies on these comparisons are likely underpowered, even when pooled, further research should not be precluded in this area. |
| Resources required |
| Judgement | Research evidence | Additional considerations |
| ○ Large costs○ Moderate costs● Negligible costs and savings○ Moderate savings○ Large savings○ Varies○ Don't know |  |  |
| Certainty of evidence of required resourcesWhat is the certainty of the evidence of resource requirements (costs)? |
| Judgement | Research evidence | Additional considerations |
| ○ Very low○ Low○ Moderate○ High● No included studies |  |  |
| Cost effectivenessDoes 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 |  |  |
| EquityWhat 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 |  |  |
| AcceptabilityIs the intervention acceptable to key stakeholders? |
| Judgement | Research evidence | Additional considerations |
| ○ No● Probably no○ Probably yes○ Yes○ Varies○ Don't know | We have not identified any research that assessed acceptability. However, the provision of vasopressin is currently not the standard of care and would likely not be acceptable. | The provision of vasopressin is not currently part of the algorithm for treatment of cardiac arrest internationally, so the education and associated cost of introducing this change would likely not be acceptable, given the neutral results of available studies. |
| FeasibilityIs the intervention feasible to implement? |
| Judgement | Research evidence | Additional considerations |
| ○ No○ Probably no● Probably yes○ Yes○ Varies○ Don't know | Vasopressin was previously used more broadly during cardiopulmonary resuscitation but is currently not the standard of care. | Implementing the addition of vasopressin to the treatment algorithm would require some cost for both medication and training, which might be burdensome for some healthcare systems. |

|  | **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 |

# Conclusions

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| Recommendation |
| We suggest against the administration of vasopressin in place of epinephrine during cardiopulmonary resuscitation (weak recommendation, very low certainty of evidence).We suggest against the addition of vasopressin to epinephrine during cardiopulmonary resuscitation (weak recommendation, very low certainty of evidence). |
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| Justification |
| In suggesting that vasopressin not be used in place for or in addition to epinephrine, we are placing value on keeping the cardiac arrest treatment algorithm simpler when there is no evidence to support increasing complexity by adding additional medication options. |

# References

1. Haywood K, Whitehead L, Nadkarni VM, Achana F, Beesems S, Böttiger BW, Brooks A, Castrén M, Ong ME, Hazinski MF, et al. COSCA (Core Outcome Set for Cardiac Arrest) in Adults: An Advisory Statement From the International Liaison Committee on Resuscitation. *Circulation*. 2018;137:e783-e801. doi: 10.1161/CIR.0000000000000562