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| Question |
| **Should a higher MAP target (>71 mmHg) vs. a lower MAP target (65-70 mmHg) be used for patients treated in the intensive care unit after cardiac arrest (out-of-hospital or in-hospital)?** |
| **Population:** | Patients treated in the intensive care unit after cardiac arrest (out-of-hospital or in-hospital) |
| **Intervention:** | A higher MAP target (>71 mmHg) |
| **Comparison:** | A lower MAP target (65-70 mmHg) |
| **Main outcomes:** | 180-day mortality; Good functional outcome at 180-days; ICU mortality; Severe arrhythmia or cardiac arrest in the ICU; |
| **Setting:** | Any setting |
| **Perspective:** |  |
| **Background:** |  |
| **Conflict of interests:** |  |

# Assessment

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| ProblemIs the problem a priority? |
| Judgement | Research evidence | Additional considerations |
| ○ No○ Probably no○ Probably yes● Yes○ Varies○ Don't know | Most death in those admitted to an intensive care unit after cardiac arrest are due to circulatory failure, multiorgan failure or hypoxic brain injury. Monitoring and treatment of blood pressure is an integral part of management in the ICU for all types of patients. Vasopressors such as noradrenaline are very commonly used and provide the opportunity to increase the mean arterial blood pressure (MAP) easily. A higher MAP could improve cerebral and coronary blood flow and decrease the risk of ischaemia, but whether this influences patient outcome is unclear.  |  |
| Desirable EffectsHow substantial are the desirable anticipated effects? |
| Judgement | Research evidence | Additional considerations |
| ○ Trivial● Small○ Moderate○ Large○ Varies○ Don't know | It would be very desirable if MAP augmentation could improve outcome in patients after cardiac arrest. The use of vasopressors to increase MAP is a very common and simple intervention that is likely to be available in most settings. Using a higher MAP target would need minimal resources compared to current practice. The current evidence rules out larger relative treatment effects than 25%. If the baseline outcome rate is 50% this would equal a difference of 12.5% (a number needed to treat of 8). It is likely that a smaller treatment effect would also be considered desirable.  |  |
| Undesirable EffectsHow substantial are the undesirable anticipated effects? |
| Judgement | Research evidence | Additional considerations |
| ○ Trivial● Small○ Moderate○ Large○ Varies○ Don't know | The use of vasopressors to target a higher MAP could have undesirable effects such as the onset of cardiac arrhythmias, worsening cardiac function due to an increase in cardiac oxygen consumption and recurrent cardiac arrest. Observational studies in cardiac arrest patients and general ICU patients suggest that an increase in vasopressor load may be associated with poor outcome. However, the results of this systematic review do not suggest that targeting a higher MAP results in more cardiac arrhythmias or recurrent cardiac arrests.  |  |
| 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 level of evidence for targeting a MAP of higher than 65 mmHg compared to a higher target is judged to be moderate to low. There is some imprecision with regards to the true effect of the intervention. There is also some inconsistency between the effect seen in the included studies. There is also indirectness as mainly patients who have experienced an out-of-hospital cardiac arrest due to a cardiac cause have been included. No study thus far has included in-hospital cardiac arrest patients.  |  |
| 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 | Most people will value the patient centered outcomes of good functional recovery and death very highly. There may be more variability with regards to the value of the secondary outcomes such as cardiac arrhythmias and recurrent cardiac arrest.  |  |
| 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 | The point estimate favors the comparison (MAP > 65 mmHg) rather than a higher MAP (MAP>70 mmHg) but the differences are not significant and very small.  | Given the lack of evidence for a higher MAP, the balance of effects probably favors using a similar threshold for MAP as is used for other critical illness states such as septic shock. |
| Resources requiredHow large are the resource requirements (costs)?" |
| Judgement | Research evidence | Additional considerations |
| ○ Large costs○ Moderate costs● Negligible costs and savings○ Moderate savings○ Large savings○ Varies○ Don't know | Thus far the effect of a higher MAP compared to a lower MAP is unclear. By not suggesting a higher MAP target, vasopressor requirements may be lower, which could lead to modest cost savings. |  |
| 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 | No study including a cost analysis was identified. There may also be some variability in the price of vasopressors between different countries. In some settings the use of noradrenaline may mandate the use of a central venous cannula and the insertion of such may increase costs. However, it is likely that targeting a lower MAP will result in the use of fewer central venous cannulas.  |  |
| 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 | No studies assessing cost effectiveness were identified.  | We assume that costs would not play any major role as the difference in cost would likely only be due to the different amount of vasopressor used and that is likely to be minimal. |
| 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 | Given the lack of evidence to support a benefit from targeting a higher MAP, we do not think the intervention would have any effect on equity. Vasopressors, while relatively inexpensive compared to other critical care interventions, are still limited in some lower-resource setting, so an intervention requiring more vasopressors without benefitting the patients could place financial stress on some settings and thus decrease equity.  |  |
| AcceptabilityIs the intervention acceptable to key stakeholders? |
| Judgement | Research evidence | Additional considerations |
| ○ No○ Probably no○ Probably yes○ Yes○ Varies● Don't know | If the evidence showed a clear benefit from a higher MAP target, the intervention would probably be acceptable to stakeholders. There is however still uncertainty about the overall effect of a higher MAP on outcome after cardiac arrest. Therefore, it is difficult to assess the acceptability.  |  |
| FeasibilityIs the intervention feasible to implement? |
| Judgement | Research evidence | Additional considerations |
| ○ No○ Probably no● Probably yes○ Yes○ Varies○ Don't know | Using vasopressors to target a lower or higher MAP goal is likely to be feasible to implement worldwide.  |  |

# 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 |
| There is insufficient scientific evidence to recommend a specific blood pressure goal after cardiac arrest. Therefore, we suggest a mean arterial blood pressure of at least 60-65mmHg in patients after out-of-hospital (moderate to low certainty of evidence) and in-hospital cardiac arrest (low to very low certainty of evidence). |
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| Justification |
| ● The prior treatment recommendation read as follows: “We suggest haemodynamic goals (eg, mean arterial pressure, systolic blood pressure) be considered during postresuscitation care and as part of any bundle of postresuscitation interventions (weak recommendation, low-certainty evidence). There is insufficient evidence to recommend specific haemodynamic goals; such goals should be considered on an individual patient basis and are likely to be influenced by post-cardiac arrest status and preexisting comorbidities”. The four RCTs conducted since that recommendation was formulated provide significant new evidence but have not yet identified an optimal blood pressure strategy.● While no specific mean arterial blood pressure strategy has been found to be beneficial in cardiac arrest trials, the task force thought it was important to provide more specific guidance than had been provided previously. The threshold of 65mmHg was agreed upon as it is the standard in other forms of critical illness and there is no evidence to deviate from that practice in post-arrest patients. Observational data (Bro Jeppesen 2015, Laurikkala 2015, McGuigan 2023) suggest that the lowest MAP not associated with worse outcome after cardiac arrest is around 60-70 mmHg, and the Surviving Sepsis Guidelines recommend targeting a MAP of higher 65 mmHg in patients with septic shock (Rhodes 2017)● We observed no statistically significant benefit from targeting a higher MAP for any critical outcome● We observed no statistically significant harm, in relation to the occurrence of a new cardiac arrest or an arrhythmia resulting in haemodynamic compromise, from targeting a higher MAP● All RCT studies conducted thus far have focused on patients with a likely cardiac cause of the arrest and a high likelihood of a favorable outcome ● Whether a higher MAP target, such as 80-100mmHg, may be beneficial for some patients has not been determined by trials to-date. The task force acknowledged that this is part of clinical practice at some cardiac arrest centers. The current treatment recommendation purposefully does not proscribe an upper limit for MAP targets as one is not clearly superior to the other.  |

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| Subgroup considerations |
| Sub-group analyses performed based on patient age (higher or lower than 65), presence of chronic hypertension as a comorbidity (based on the use of medication for chronic hypertension), non-shockable compared to shockable initial rhythm and the temperature target (33 or 36 degrees) did not show any significant subgroup effects. There was an interaction between treatment group in the sub-group of patients based on time to return of spontaneous circulation (ROSC). It appeared that in patients with a time to ROSC longer than 25 minutes targeting a higher MAP resulted in worse outcome.  |

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| Implementation considerations |
| It is likely that the implementation of a lower or higher MAP goal in cardiac arrest patient would be feasible in most settings. Different MAP goals are common in ICU patients, and we may assume that having different MAP goals in cardiac arrest patients would be feasible.  |

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| Monitoring and evaluation |
| All performed cardiac arrest studies have included fairly homogenous samples of patients. We do not know the effect or the safety profile of targeting a higher or lower MAP in other types of cardiac arrest patients.  |

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| Research priorities |
| All conducted studies have focused on patients with a probable cardiac cause of the cardiac arrest. There is limited evidence as to the optimal MAP in patients not meeting these criteria. Data on MAP targets after in-hospital cardiac arrest are lacking.Data on MAP targets in the pre-hospital setting are lacking.The current evidence can exclude a relative positive or negative treatment effect of targeting a higher MAP of more than 25% but not lower. This difference may unrealistic and there may be a need for larger trials Whether the effect of MAP on outcome could be different in certain sub-groups of patients, such as those with chronic hypertension, is currently unknown. Targeting a higher blood pressure could be beneficial in patients with deranged autoregulation but to date there are limited data on how this could be done in the early hours of care in the ICU which would be needed for it to be used for individualization of the MAP targetThere are limited data on whether increasing MAP influences cerebral or coronary blood flowThere are limited data on whether MAP as opposed to some other proxy for organ perfusion (lactate clearance, urinary output, capillary refill) is the optimal bed-side targetThe optimal strategy to achieve a target MAP following cardiac arrest is uncertain. This may include use of intravenous fluids (fluid type and volume), specific vasopressors or combinations of vasopressors, and use of mechanical support.  |

# References Summary