# QUESTION

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| **Should Early/ prophylactic antibiotics vs. Delayed/ clinically-driven administration be used for Adult patients following return of spontaneous circulation from cardiac arrest?** | |
| **POPULATION: INTERVENTION: COMPARISON:**  **MAIN OUTCOMES:**  **SETTING: PERSPECTIVE: BACKGROUND:**  **CONFLICT OF INTERESTS:** | Adult patients following return of spontaneous circulation from cardiac arrest |
| Early/ prophylactic antibiotics |
| Delayed/ clinically-driven administration |
| Survival with good neurological outcome- last recorded time point (up to day 30)- randomised controlled trials; Survival with good neurological outcome- last recorded time point (up to day 30)- observational studies; Survival- last recorded timepoint (up to 30-days)- randomised controlled trials; Survival- last recorded timepoint (up to day 30)- observational studies; Pneumonia- randomised controlled trials; Pneumonia- observational studies; Critical care length of stay- randomised controlled trials; Critical care length of stay- observational studies; Duration of mechanical ventilation- randomised controlled trials; Duration of mechanical ventilation- observational studies; Antibiotic duration- randomised controlled trials; Antibiotic duration- observational studies; |
| Any setting (in-hospital and out-of-hospital) |
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| Keith Couper and Joyce Yeung were first and last author of the systematic review that forms the starting point for this Adolopment process. |

**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 | Infective complications are common in patients admitted to intensive care units. Such complications are associated with increased length of stay.  In patients admitted following cardiac arrest, pneumonia has been reported in 50-60% of patients. In part, this reflects the risk of aspiration during the cardiac arrest events. In this patient group, a key challenge is early and accurate identification of infection. Standard criteria for identifying infection are affected by patient treatment (i.e. targeted temperature management) and pathophysiology following cardiac arrest (i.e. systemic inflammatory response as part of the post-cardiac arrest syndrome). The decision to treat infection is further complicated by the need for prudent antibiotic prescribing in all health settings driven by the international challenge of antibiotic resistance.  However, in patients that die on the intensive care unit following cardiac arrest, cause of death is typically attributed to multi-organ failure or neurological failure, rather than an infective complication. |  |
| **Desirable Effects**  How substantial are the desirable anticipated effects ? | | |
| **JUDGEMENT** | **RESEARCH EVIDENCE** | **ADDITIONAL CONSIDERATIONS** |
| * Trivial * Small * Moderate * Large * Varies * Don't know | Infective complications are common in patients admitted to intensive care units. Such complications are associated with increased length of stay.  However, in patients that die on the intensive care unit following cardiac arrest, cause of death is typically attributed to multi-organ failure or neurological failure, rather than an infective complication. |  |
| **Undesirable Effects**  How substantial are the undesirable anticipated effects ? | | |
| **JUDGEMENT** | **RESEARCH EVIDENCE** | **ADDITIONAL CONSIDERATIONS** |
| * Large * Moderate * Small * Trivial * Varies * Don't know | Our meta-analyses of observational studies and randomised controlled trials did not find any statistically significant evidence of harm in relation to the intervention for any important or critical outcome.  We did not include any outcomes that specifically address potential complications of antibiotic use, such as gastrointestinal effects or development of resistant organisms. |  |
|  | An additional issue is the potential for antibiotics to lead to the generation of anti-biotic resistant organisms at a population level. |
| **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 | Across all outcomes, evidence certainty was recorded as low or very low. |  |

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| **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 | There is possible important uncertainty in how clinicians value the outcome of incidence of pneumonia.  Some may take the view that the purpose of prophylactic antibiotics is to reduce infective complications, such that the incidence of pneumonia is the most important outcome even if this does not translate in to improved survival or reduced critical care length of stay.  Others may take the view that the expressed international need for prudent use of antibiotics and the potential side-effects of antibiotics means that antibiotic prophylaxis should not be used unless it is shown to have an effect on key clinical outcomes . |  |
| **Balance of effects**  Does the balance between desirable and undesirable effects favor the intervention or the comparis on? | | |
| **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 | There is important uncertainty as to benefit of the intervention. Our review did not explicitly examine harms of the intervention.  There may be different clinical approaches regarding antibiotic use in patients with evidence of gastric aspiration. These patients were excluded from randomised controlled trials, and management of this patient was not addressed in any observational study. There is a need for further research in this area. |  |
| * Varies * Don't know |  |
| **Acceptability**  Is the intervention acceptable to key stakeholders? | | |
| **JUDGEMENT** | **RESEARCH EVIDENCE** | **ADDITIONAL CONSIDERATIONS** |
| * No * Probably no * Probably yes * Yes | At an individual level, the intervention is likely to be acceptable to clinicians and patients. Antibiotics do have adverse effects including allergic reaction, gastrointestinal effects and increas ed individual antibiotic resistance. The financial cost of antibiotics is likely acceptable. |  |
| * Varies | At a societal level, antimicrobial resistance is identified by the World Health |

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| * Don't know | Organisation as a key global health concern. The clinically appropriate use of  antibiotics is a key factor in limiting the development of antimicrobial resistance. |  |
| **Feasibility**  Is the intervention feasible to implement? | | |
| **JUDGEMENT** | **RESEARCH EVIDENCE** | **ADDITIONAL CONSIDERATIONS** |
| * No * Probably no * Probably yes * Yes | Antibiotics are commonly used drugs. The intervention is feasible to implement. |  |
| * Varies * Don't know |  |

**SUMMARY OF JUDGEMENTS**

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|  | **JUDGEMENT** | | | | | | |
| **PROBLEM** | No | Probably no | **Probably yes** | Yes |  | Varies | Don't know |
| **DESIRABLE EFFECTS** | Trivial | Small | Moderate | Large |  | Varies | **Don't know** |
| **UNDESIRABLE EFFECTS** | Large | Moderate | Small | Trivial |  | 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** |
| **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 | | | Conditional recommendation for the intervention | | Strong recommendation for the intervention | |
| ○ | | **●** | | comparison  ○ | ○ | | ○ | |

**CONCLUSIONS**

## Recommendation

We suggest against the use of prophylactic antibiotics in patients following return of spontaneous circulation.

## Justification

In our review of the evidence, we found that the use of prophylactic antibiotics did not affect key clinical outcomes, although we acknowledge the overall low certainty of evidence. Furthermore, we note international concerns regarding antimicrobial resistance and the need for prudent use of antibiotics.

We note the results of a recent high-quality randomised controlled trial which reported a reduced incidence of pneumonia in patients treated with prophylactic antibiotics. However, this study not detect any difference in other key outcomes such as critical care length of stay, although we acknowledge that the study was not powered to detect such a difference.

## Subgroup considerations

N/A

## Implementation considerations

This recommendation explicitly refers to the use of prophylactic antibiotics.

Randomised controlled trials excluded patients with presumed infection at baseline. Cardiac arrest patients with clinical evidence of infection should continue to be treated in line with current hospital guidelines.

## Monitoring and evaluation

N/A

**Research priorities**

* Randomised controlled trials powered to reliably evaluate the effect of antibiotic prophylaxis on outcomes such as critical care length of stay or duration of invasive mechanical ventilation.
* Development of guidelines to inform the decision to prescribe antibiotics following cardiac arrest, particularly where there is gastric aspiration.