

## QUESTION

Should [intervention] vs. [comparison] be used for [health problem and/or population]?

<b>POPULATION:</b>	Patients with return of spontaneous circulation (ROSC) after cardiac arrest
<b>INTERVENTION:</b>	Any specific neuroprotective drug therapy administered after ROSC
<b>COMPARISON:</b>	Placebo or another drug
<b>MAIN OUTCOMES:</b>	Mortality at 30-days, hospital discharge or 180 days Functional outcome at 30-days, hospital discharge or 180 days
<b>SETTING:</b>	Out-of-hospital or in-hospital cardiac arrest
<b>PERSPECTIVE:</b>	
<b>BACKGROUND:</b>	Brain injury after cardiac arrest is a major problem. No treatment exists at the moment.
<b>CONFLICT OF INTERESTS:</b>	None

## ASSESSMENT

<b>Problem</b> Is the problem a priority?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<input type="radio"/> No <input type="radio"/> Probably no <input type="radio"/> Probably yes <input checked="" type="radio"/> Yes <input type="radio"/> Varies <input type="radio"/> Don't know	Cardiac arrest is a major health problem and many patients die in the intensive care unit or in the hospital with hypoxic brain injury. Currently there are no specific treatments available that alleviates brain injury and care is largely supportive. A treatment that alleviates brain injury would be of great importance.	
<b>Desirable Effects</b> How substantial are the desirable anticipated effects?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<input type="radio"/> Trivial <input checked="" type="radio"/> Small <input type="radio"/> Moderate <input type="radio"/> Large <input type="radio"/> Varies <input type="radio"/> Don't know	According to the evidence no pharmacological treatment has been shown to have any beneficial effect on neither survival nor functional outcome in patients after cardiac arrest. The conducted trials are fairly small and rule out fairly large effects. But the conducted trial sequential analyses have not identified any clear need to for larger trials on drugs such as steroids, coenzyme-Q10 and thiamine.	
<b>Undesirable Effects</b> How substantial are the undesirable anticipated effects?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<input type="radio"/> Trivial <input checked="" type="radio"/> Small <input type="radio"/> Moderate <input type="radio"/> Large <input type="radio"/> Varies <input type="radio"/> Don't know	Thus far the conducted trials are small so whether these drugs have important side-effects are unknown. It is also possible that a drug that saves lives in a patient with severe brain injury can lead to the survival of patients with a poor functional outcome. Whether this is true is not possible to know given the current available evidence.	
<b>Certainty of evidence</b> What is the overall certainty of the evidence of effects?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<input checked="" type="radio"/> Very low <input type="radio"/> Low <input type="radio"/> Moderate <input type="radio"/> High <input type="radio"/> No included studies	Most conducted studies are small and single center decreasing the certainty of evidence.	
<b>Values</b> Is there important uncertainty about or variability in how much people value the main outcomes?		

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<input type="radio"/> Important uncertainty or variability <input checked="" type="radio"/> Possibly important uncertainty or variability <input type="radio"/> Probably no important uncertainty or variability <input type="radio"/> No important uncertainty or variability	<p>As the current evidence suggest no effect there is probably no clear difference in how people value these results. This is especially true for coenzyme-Q10 which is currently not used routinely in ICUs. With regards to steroids and thiamine the situation is different, these drugs are commonly used and these are cheap drugs. Therefore one could argue that why not use these even based on very limited evidence, if there is limited risk of harm. However, the risk of harm is possible with both steroids and thiamine and therefore probably most clinicians would favor not using these drugs routinely without better evidence.</p>	

### Balance of effects

Does the balance between desirable and undesirable effects favor the intervention or the comparison?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<input checked="" type="radio"/> Favors the comparison <input type="radio"/> Probably favors the comparison <input type="radio"/> Does not favor either the intervention or the comparison <input type="radio"/> Probably favors the intervention <input type="radio"/> Favors the intervention <input type="radio"/> Varies <input type="radio"/> Don't know	<p>The evidence does not suggest the beneficial effect of any neuroprotective drug on outcome in patients with ROSC after cardiac arrest. As these drugs are not routinely used in other critically ill patients, there is the possibility of harm most clinicians probably would favor the comparison i.e. not giving these drugs.</p>	

### Resources required

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<input type="radio"/> Large costs <input type="radio"/> Moderate costs <input type="radio"/> Negligible costs and savings <input type="radio"/> Moderate savings <input type="radio"/> Large savings <input type="radio"/> Varies <input checked="" type="radio"/> Don't know	<p>Poor neurologic recovery is costly after cardiac arrest. Most neuroprotective drugs included in the review are cheap and probably easy to administer favoring their use. But as side-effects and poor recovery is possible we do not know about the resources required.</p>	

### Certainty of evidence of required resources

What is the certainty of the evidence of resource requirements (costs)?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<input type="radio"/> Very low <input type="radio"/> Low <input type="radio"/> Moderate <input type="radio"/> High <input checked="" type="radio"/> No included studies	<p>No studies have assessed costs.</p>	

### Cost effectiveness

Does the cost-effectiveness of the intervention favor the intervention or the comparison?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS

<input type="radio"/> Favors the comparison <input type="radio"/> Probably favors the comparison <input type="radio"/> Does not favor either the intervention or the comparison <input type="radio"/> Probably favors the intervention <input type="radio"/> Favors the intervention <input type="radio"/> Varies <input checked="" type="radio"/> No included studies	No studies have assessed cost-effectiveness.	
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### Equity

What would be the impact on health equity?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<input type="radio"/> Reduced <input type="radio"/> Probably reduced <input type="radio"/> Probably no impact <input type="radio"/> Probably increased <input type="radio"/> Increased <input type="radio"/> Varies <input checked="" type="radio"/> Don't know	We do not know as we have not identified any drug that improves outcome.	

### Acceptability

Is the intervention acceptable to key stakeholders?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<input type="radio"/> No <input type="radio"/> Probably no <input type="radio"/> Probably yes <input type="radio"/> Yes <input type="radio"/> Varies <input checked="" type="radio"/> Don't know	We do not know as we do not know if these drugs work.	

### Feasibility

Is the intervention feasible to implement?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<input type="radio"/> No <input type="radio"/> Probably no <input checked="" type="radio"/> Probably yes <input type="radio"/> Yes <input type="radio"/> Varies <input type="radio"/> Don't know	Most studies interventions involve the administration of intravenous drugs. It is likely that this therapy would be feasible in most settings.	

## SUMMARY OF JUDGEMENTS

PROBLEM	JUDGEMENT						
	No	Probably no	Probably yes	Yes		Varies	Don't know
DESIRABLE EFFECTS	Trivial	<b>Small</b>	Moderate	Large		Varies	Don't know
UNDESIRABLE EFFECTS	Trivial	<b>Small</b>	Moderate	Large		Varies	Don't know
CERTAINTY OF EVIDENCE	<b>Very low</b>	Low	Moderate	High			No included studies
VALUES	Important uncertainty or variability	<b>Possibly important uncertainty or variability</b>	Probably no important uncertainty or variability	No important uncertainty or variability			

<b>BALANCE OF EFFECTS</b>	<b>Favors the comparison</b>	Probably favors the comparison	Does not favor either the intervention or the comparison	Probably favors the intervention	Favors the intervention	Varies	Don't know
<b>RESOURCES REQUIRED</b>	Large costs	Moderate costs	Negligible costs and savings	Moderate savings	Large savings	Varies	<b>Don't know</b>
<b>CERTAINTY OF EVIDENCE OF REQUIRED RESOURCES</b>	Very low	Low	Moderate	High			<b>No included studies</b>
<b>COST EFFECTIVENESS</b>	Favors the comparison	Probably favors the comparison	Does not favor either the intervention or the comparison	Probably favors the intervention	Favors the intervention	Varies	<b>No included studies</b>
<b>EQUITY</b>	Reduced	Probably reduced	Probably no impact	Probably increased	Increased	Varies	<b>Don't know</b>
<b>ACCEPTABILITY</b>	No	Probably no	Probably yes	Yes		Varies	<b>Don't know</b>
<b>FEASIBILITY</b>	No	Probably no	<b>Probably yes</b>	Yes		Varies	Don't know

## TYPE OF RECOMMENDATION

Strong recommendation against the intervention ○	<b>Conditional recommendation against the intervention</b> ●	Conditional recommendation for either the intervention or the comparison ○	Conditional recommendation for the intervention ○	Strong recommendation for the intervention ○
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## CONCLUSIONS

### Recommendation

There is insufficient evidence to recommend the use of any specific drug therapy for comatose survivors of cardiac arrest.

### Justification

Our systematic review of the evidence has not identified any drug that improves outcome in patients after cardiac arrest.

### Subgroup considerations

We have not identified any sub-group differences.

### Implementation considerations

We have not identified any drug therapy that works and therefore we cannot evaluate implementation. But the administration of intravenous drugs is common practice and is likely to be easy to implement.

### Monitoring and evaluation

### Research priorities

There is a need for larger multicentre trial evaluating the effect of various drugs on outcome in patients with return of spontaneous circulation after cardiac arrest.

## REFERENCES SUMMARY