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| Question | |
| **Should coma score be assessed vs. none for predicting good neurological outcomes in children after cardiac arrest?** | |
| **Population:** | Children (<18 years) who achieve a return of spontaneous or mechanical circulation (ROC) after resuscitation from in-hospital cardiac arrest (IHCA) and out-of-hospital (OHCA), from any cause. |
| **Intervention:** | coma score assessed within 10 days after cardiac arrest. |
| **Comparison:** | none |
| **Main outcomes:** | Prediction of survival with good neurological outcome: defined as a Pediatric Cerebral Performance Category (PCPC) score of 1, 2 or 3, or Vineland Adaptive Behavioural scale-II ≥ 70. PCPC score ranges 1 (normal), 2 (mild disability), 3 (moderate disability), 4 (severe disability), 5 (coma), and 6 (brain death). We will also separately report studies defining good neurological outcomes with other assessment tools, or as a PCPC score 1 or 2, or change in PCPC score from baseline ≤2. |
| **Study DESIGN** | Randomized controlled trials (RCTs) and non-randomized studies (non-randomized controlled trials, interrupted time series, controlled before-and-after studies, cohort studies) were eligible for inclusion. Unpublished studies (e.g., conference abstracts, trial protocols\*) and animal studies were excluded. We selected studies where the sensitivity and false-positive rate (FPR) of the prognostic (index) test are reported and a 2s2 contingency table could be created. |
| **TIMEFRAME** | All years and all languages were included as long as there was an English abstract; unpublished studies (e.g., conference abstracts, trial protocols) were excluded. Literature search updated to Feb 17th 2022. |

# 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 | Cardiac arrest is uncommon in children; however, has a low rate of survival and high chance of neurological injury. Prediction of good or poor neurological outcome is a key skill for clinicians to guide appropriate treatment and realistic expectation with parents and legal guardians. |  |
| Desirable Effects How substantial are the desirable anticipated effects? | | |
| Judgement | Research evidence | Additional considerations |
| ● Trivial ○ Small ○ Moderate ○ Large ○ Varies ○ Don't know | The relationship between coma assessment using the Glasgow Coma Score (GCS) motor score alone, or total GCS and good neurological outcome at intensive care unit or hospital discharge and 6 months, were evaluated in 3 studies [Nishisaki 2007 10, Lin 2013 285, Lin 2020 534] in 296 patients. In one study, GCS motor score ≥4 within 1 hour and at 4-6 hours post ROC, for predicting good neurological outcome at 6 months, had a sensitivity of 17 and 50% with a corresponding FPR of 6 and 7%, respectively [Lin 2020 534]. Using total GCS measured at resuscitation or within 1 hour, a score of ≥5 predicted good neurological outcome with a low sensitivity of 30% and a FPR of 14% [Lin 2013 285]. Whereas, using a total GCS score ≥8 had a slightly higher sensitivity of 31% with a low FPR of 6% [Nishisaki 2007 10]. However, only one study was available to assess each test using total GCS or GCS motor score cut off, or at each testing time point. | High risk of confounding with sedation and medication. Not blinded. Not always clear on inclusion and denominator values (eg could they be fully assessed, or under sedation, NMB etc). |
| Undesirable Effects How substantial are the undesirable anticipated effects? | | |
| Judgement | Research evidence | Additional considerations |
| ○ Large ○ Moderate ● Small ○ Trivial ○ Varies ○ Don't know | A false positive prediction of a good outcome and continued treatment based on comas score may lead to inappropriate treatment in a patient with a poor neurological outcome. This is possible to occur given the variability of cut offs for sensitivity and specificity and the potential for confounding from medication, sedation and neuro-muscular blocking drugs, impairing coma assessment. |  |
| 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 | The certainty of evidence from coma score is very low because of the risk of bias, especially risk of confounding from concurrent medication (sedative drug) use and risk for self-fulfilling prophecy. |  |
| 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 | Neurological outcome is a critical outcome after cardiac arrest (P-COSCA: Topjian, et al Circulation 2020; 142). However, tools and definitions to measure good neurological outcome in our studies were the PCPC 1 to 2 and 1 to 3, or <1 change in PCPC and the VABS II >70. Change from baseline neurodevelopmental status may be more important than the neurodevelopmental level, especially in infants and children with pre-existing neurological impairment.  We defined good neurological outcome prediction as imprecise when the false positive rate (FPR) was above 30%. However, there is no universal consensus on what the acceptable limits for imprecision should be in prediction for infants and children after cardiac arrest.  A low false positive rate means that a low proportion of patients, predicted to have a good outcome will have a *falsely optimistic prediction* (test predicted a good outcome, but patient went on to have a bad outcome). The task force felt that when focused on accuracy of predicting a good outcome - a low false positive rate (e.g. <30%) is more desirable to avoid falsely optimistic prediction than a high sensitivity. The cut off of 30% FPR (equivalent to 70% specificity) was chosen as the consequences of false optimism were felt by the task force to be less critical than false pessimism. False optimism may result in continued life sustaining therapy in a patient who will eventually have a poor outcome. This will involve increased resources and treatment; however, may also allow more time for further prognostic evaluation. Also, reasons for not achieving a very low false positive rate may be non-neurological causes of poor outcome or death, not attributable to the index test assessment.  A high sensitivity means the majority of patients, who have a good outcome, tested positive and therefore a corresponding low proportion will have a *falsely pessimistic prediction* (test predicted a poor outcome, but patient went on to have a good outcome). When considering the accuracy of predicting a poor outcome (compared to predicting a good outcome), then a low rate of falsely pessimistic predictions is very important. Our cut off threshold for considering precise sensitivity was therefore higher (>95%), as the consequences of inaccurate poor outcome prediction (e.g. false pessimism) may lead to a decision to limit or withdraw life sustaining therapies in a patient who could have a good neurological outcome. . |  |
| 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 | Considering the sensitivity of coma score prediction, relatively low false positive rate at all time points, but limited studies examining each predictive testing threshold, timepoint and score, the balance of effects neither favors for or against the use of coma scores as a predictive test for good neurological outcome. |  |
| Resources required How 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 | Costs for the assessment of coma are negligible. However, no study assessed savings from prognostication based on coma score have been included in our review. |  |
| 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 | We did not identify any studies assessing cost assessing coma score. |  |
| 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 | We did not identify any studies addressing cost-effectiveness. |  |
| 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 | Considering the negligible costs of coma score, a problem of inequity is unlikely. |  |
| Acceptability Is 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 study assessing acceptability, but acceptability is likely. |  |
| Feasibility Is the intervention feasible to implement? | | |
| Judgement | Research evidence | Additional considerations |
| ○ No ○ Probably no ● Probably yes ○ Yes ○ Varies ○ Don't know | Although feasibility was not specifically addressed in any of the studies included in this review, the assessment of coma score requires basic training of clinical neurological examination. No additional equipment is required and is therefore feasible in resource limited settings. |  |

# 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** | 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 |
| **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 |
| **We cannot make a recommendation for or against using total GCS, GCS motor score after ROC for predicting good neurological outcome in children after cardiac arrest (weak recommendation, very-low-certainty evidence).** |
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| Justification |
| For coma score, limited evidence suggests that the specificity for prediction of good neurological outcome is similar across all assessment time points (<1 hour to 4-6hours) after cardiac arrest, although the FPR ranges from 6-14%.    Inconsistency in specificity across timepoints raises concern about the heterogenity of studies, patient inclusion and accuracy of this prognostic test. This may be partly due to confounding from the effect of sedatives used for delivery of neuroprotective interventions ( e.g. targeted temperature management) or to facilitate ventilation.    No studies reported any assessment of the confounding influence of medication on coma score. No studies included blinding of test results from treating clinicians and no study had blinded outcome assessment.  None of the included studies specifically excluded the presence of residual sedation at the time coma score was assessed. Lack of blinding is a major limitation of coma score, even if WLST based on coma score only has not been documented in any of the studies included in our review.  Despite its limitations, given the ease of assessment and no requirement for additional equipment required, (the balance between the costs and benefits may favours benefits). |

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| Subgroup considerations |
| None. |

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| Implementation considerations |
| Coma score is an easy clinical assessment; however, the examiner requires knowledge of basic neurological examination. |

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| Monitoring and evaluation |
| None |

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| Research priorities |
| Use of coma score, including GCS motor score and other reported scores (eg FOUR score), require assessment in the paediatric population. |

# References Summary