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| Question | |
| **Should A clinical decision rule be used to diagnose termination of resuscitation in patients with in-hospital cardiac arrest?** | |
| **Population:** | patients with in-hospital cardiac arrest |
| **Intervention:** | A clinical decision rule |
| **Purpose of the test:** | Predict death following in-hospital cardiac arrest |
| **Role of the test:** | Facilitate reliable prehospital termination of resuscitation decisions |
| **Linked treatments:** | None |
| **Anticipated outcomes:** | Prediction of death before hospital discharge |
| **Setting:** | In-hospital cardiac arrest |
| **Perspective:** | Clinicians resuscitating patients from in-hospital cardiac arrest |
| **Background:** | About half of all in-hospital resuscitation attempts are terminated because of no return of spontaneous circulation. Deciding when to terminate resuscitation is therefore a very important clinical issue. |
| **Subgroups:** | Adults and children |
| **Conflict of interests:** | None |

# 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 | There are no current ILCOR recommendations on clinical decision rules to terminate resuscitation during in-hospital cardiac arrest. | About half of all in-hospital resuscitation attempts are terminated without return of spontaneous circulation. Knowing when to terminate resuscitation is, therefore, an important clinical question in everyday practice. |
| Test accuracy How accurate is the test? | | |
| Judgement | Research evidence | Additional considerations |
| ○ Very inaccurate ● Inaccurate ○ Accurate ○ Very accurate ○ Varies ○ Don't know | We identified 3 studies using the UN10 rule (unwitnessed arrest, non-shockable rhythm, and no return of spontaneous circulation after 10 minutes of resuscitation) to measure prediction of survival to hospital discharge {Van Walraven 1999 129; Van Walraven 2001 1602; Petek 2019 e194941} .  Reported positive predictive values were 100% (95% CI: 97.1-100%) {Van Walraven 1999 129} 98.9% (95% CI: 96.5%-99.7%) {Van Walraven 2001 1602} and 93.7% (95% CI: 93.3%-94.0%) {Petek 2019 e194941}.  Reported specificities were 100% (95% CI: 97.1%-100%) {Van Walraven 1999 129}, 99.1% (95% CI: 97.1%-99.8%) {Van Walraven 2001 1602}, and 94.6% (95% CI: 94.3%-94.9%) {Petek 2019 e194941}.  Reported sensitivities were: 12.2% (95% CI: 10.3%-14.4%) {Van Walraven 1999 129} 14.4% (95% CI: 12.4%-16.0%) {Van Walraven 2001 1602}, and 19.1% (95% CI: 18.8%-19.3%) {Petek 2019 e194941}.  Reported negative predictive values were 10.8% (95% CI: 8.9-12.8%) {Van Walraven 1999 129}, 17.0% (95% CI: 15.3-18.7) {Van Walraven 2001 1602}, and 22.0% (95% CI: 21.9%-22.0%) {Petek 2019 e194941}.  We identified one observational study {Petek 2019 e194941} investigating the UN10 rule to predict survival with unfavorable neurological outcome. The study reported a positive predictive value of 95.2% (95% CI: 94.9%-95.6%), a specificity of 95.3% (95% CI: 95.0%-95.6%), a sensitivity of 18.8% (95% CI: 18.5%-19.0%), and a negative predictive value of 19.1% (95% CI: 18.8%-19.3%) {Petek 2019 e194941}.  We identified no studies investigating prediction of no return of spontaneous circulation or death within 30 days. | Positive predictive value may be over-estimated as treatment and survival rate has improved over the last 15 years. The studies by Van Walraven and Cooper include data from the 1990's and 1980's of which some of the patients might have survived if arresting in the modern era. |
| Desirable Effects How substantial are the desirable anticipated effects? | | |
| Judgement | Research evidence | Additional considerations |
| ○ Trivial ○ Small ○ Moderate ● Large ○ Varies ○ Don't know | No evidence exist on the desirable effects of using a clinical decision rule. | Hospitals that continue resuscitation efforts for longer times have higher survival rates compared to hospitals where resuscitation is terminated sooner. Use of a clinical decision rule for termination could therefore ensure that resuscitation is not terminated premature (given a perfect positive predictive value of the decision rule). |
| Undesirable Effects How substantial are the undesirable anticipated effects? | | |
| Judgement | Research evidence | Additional considerations |
| ● Large ○ Moderate ○ Small ○ Trivial ○ Varies ○ Don't know | No evidence exist on the desirable effects of using a clinical decision rule. | If a clinical decision rule does not have a positive predictive value of 100% it could mean that resuscitation is terminated too soon and some patients may not be guaranteed the best possible chance of survival. |
| Certainty of the evidence of test accuracy What is the overall certainty of the evidence of test accuracy? | | |
| Judgement | Research evidence | Additional considerations |
| ● Very low ○ Low ○ Moderate ○ High ○ No included studies | The certainty of the evidence regarding the accuracy of the clinical decision rules for termination of resuscitation was inconsistent across studies and the certainty of evidence for test accuracy was very-low. The two studies showing the highest negative predictive values were based on data from the 1980s and 1990s that may differ from today with regards to resuscitation efficacy and survival outcomes. |  |
| Certainty of the evidence of test's effects What is the overall certainty of the evidence for any critical or important direct benefits, adverse effects or burden of the test? | | |
| Judgement | Research evidence | Additional considerations |
| ● Very low ○ Low ○ Moderate ○ High ○ No included studies | We found no prospective studies applying a clinical decision rule during in-hospital resuscitations and no direct evidence of the effects on patient outcomes and duration of resuscitation attempts. The studies did report patients being misclassified as non-survivors even though they did survive. This may result in lower survival rates if applied to clinical practice. |  |
| Certainty of the evidence of management's effects What is the overall certainty of the evidence of effects of the management that is guided by the test results? | | |
| Judgement | Research evidence | Additional considerations |
| ● Very low ○ Low ○ Moderate ○ High ○ No included studies | There are no studies on the management’s effects. |  |
| Certainty of the evidence of test result/management How certain is the link between test results and management decisions? | | |
| Judgement | Research evidence | Additional considerations |
| ○ Very low ○ Low ● Moderate ○ High ○ No included studies | There are no studies on the test result/ management. | Clinicians will terminate resuscitation attempts if known that the patient has no, or almost no, chance of surviving the resuscitation attempt. |
| Certainty of effects What is the overall certainty of the evidence of effects of the test? | | |
| Judgement | Research evidence | Additional considerations |
| ○ Very low ● Low ○ Moderate ○ High ○ No included studies | No prospective studies and no randomized studies were identified. Available studies show that the UN10 rule is unable to identify patients during resuscitation that have no chance of surviving the resuscitation attempt. |  |
| 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 | No included research examining patient values or provider values. |  |
| 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 | The clinical decision rules misclassified several patients as non-survivors even though they survived with positive predictive values as low as 93% meaning that resuscitation would be terminated, and patients would die if implementing the decision rule. | The EIT Task Force values a very high positive predictive value over the negative predictive value as the most important thing would be not to terminate resuscitation too early and thereby decrease survival rates. |
| 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 | No studies evaluated the cost associated with implementing a clinical decision rule. | Correct use of the clinical decision rule may require training of all healthcare providers of unknown duration and frequency. Application of the rule in clinical practice is not believed to increase costs or resource requirements. |
| 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 | No studies evaluated cost and/or resource requirements. |  |
| 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 | No studies evaluated cost and/or resource requirements. |  |
| 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 | No included studies examined health equity. |  |
| Acceptability Is the intervention acceptable to key stakeholders? | | |
| Judgement | Research evidence | Additional considerations |
| ○ No ● Probably no ○ Probably yes ○ Yes ○ Varies ○ Don't know | No studies investigated acceptability. | Implementing a clinical decision rule with a high likelihood of misidentifying patients as non-survivors will likely not be accepted by stake holders. |
| Feasibility Is the intervention feasible to implement? | | |
| Judgement | Research evidence | Additional considerations |
| ○ No ○ Probably no ● Probably yes ○ Yes ○ Varies ○ Don't know | No studies investigated implementation or feasibility of learning to use a clinical decision rule. |  |

# Summary of judgements

|  | **Judgement** | | | | | | |
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| **Problem** | No | Probably no | **Probably yes** | Yes |  | Varies | Don't know |
| **Test accuracy** | Very inaccurate | **Inaccurate** | Accurate | Very accurate |  | 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 the evidence of test accuracy** | **Very low** | Low | Moderate | High |  |  | No included studies |
| **Certainty of the evidence of test's effects** | **Very low** | Low | Moderate | High |  |  | No included studies |
| **Certainty of the evidence of management's effects** | **Very low** | Low | Moderate | High |  |  | No included studies |
| **Certainty of the evidence of test result/management** | Very low | Low | **Moderate** | High |  |  | No included studies |
| **Certainty of effects** | 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 did not identify any clinical decision rule that was able to reliably predict death following in-hospital cardiac arrest.  We recommend against use of the UN10 rule as a sole strategy to terminate in-hospital resuscitation (strong recommendation, very low quality of evidence). |
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| Justification |
| In making this recommendation, the EIT task force considered the following:  Several other scores have been developed aiming at predicting the chance of surviving based on pre-arrest factors only including the GO-FAR score {Ebell 2013 1872} and comorbidity scores {Ebell 1997 171}. While these scores may be suitable to trigger do-not -resuscitate discussions, they are not aimed at deciding when to terminate resuscitation during a resuscitation attempt and were therefore not included in this review.  We identified the Resuscitation Predictor Scoring Scale {Cooper 2003 6} aiming to identify patients with low likelihood of surviving a cardiac arrest after 15 minutes of resuscitation. This score was not included in the review as the score aimed at identifying patients with low likelihood but not patients with no likelihood of surviving the cardiac arrest.  Several studies (primarily pre-hospital) have looked at other factors such as end-tidal CO2 and echocardiographic findings to terminate resuscitation. These have been included in reviews by the ILCOR advanced life support task force, and end-tidal CO2 and echocardiographic findings may be considered together with other factors to decide when to terminate in-hospital resuscitation.  All identified studies were based on historical cohorts and carry a risk of a self-fulfilling prophesy bias as clinicians may have terminated resuscitation on patients who potentially had a chance of surviving in the observed studies. Prospective studies are needed in order to reliably assess the effect of such clinical decision rules.  Two of the included studies {Van Walraven 1999 129} and {Van Walraven 2001 1602} included patients resuscitated in the 1980’s and 1990’s, where resuscitation practices differed from present time and where reported survival rates were lower compared to present time {Benjamin 2018 e67}. The third study {Petek 2019 e194941} included patients resuscitated between 2000 and 2016 but a large percentage of the arrests occurred before 2010. As previously stated, survival rates are now higher than previous decades.  The task force prioritized a perfect positive predictive value (no survivors predicted to be dead) for any clinical prediction rule due to the risk of terminating resuscitation on a patient who could have survived.  The task force discussed that it is reasonable not to terminate resuscitation as long as the patient has a shockable rhythm. No single clinical factor or no single decision rule has been identified as sufficient to terminate resuscitation. Therefore, the EIT task force members suggested that a decision to terminate IHCA resuscitation should continue to be based on a combination of factors that are known to be associated with a low chance of survival, e.g. end-tidal CO2, cardiac stand-still on echocardiography, duration of resuscitation, patient age, and patient comorbidities. |

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| Subgroup considerations |
| No evidence addressing implementation of clinical prediction rules in the pediatric population was identified. |

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| Implementation considerations |
| We found no clinical evaluation of any clinical prediction rule for termination of resuscitation. |

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| Monitoring and evaluation |
| It is important to measure compliance and survival rates and continuously reassess the criteria if considering implementation of any clinical prediction rule. |

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| Research priorities |
| We identified several knowledge gaps in the published literature.  There are no clinical decision tools to predict the absence of return of spontaneous circulation during in-hospital resuscitation.  There are clinical decision tools that combine existing decision tool elements such as resuscitation duration and cardiac arrest rhythm with e.g. end-tidal CO2 and/ or findings on cardiac ultrasound.  No studies were found on the use of clinical decision tool to terminate resuscitation for pediatric in-hospital cardiac arrest.  There is a lack of prospective clinical validation studies and randomized trials investigating the use of a clinical decision tool to terminate resuscitation during in-hospital cardiac arrest.  It is unknown how the use of a clinical decision tool affects resuscitation practices, cost-benefit, or how it affects survival outcomes. |