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| Question | |
| **Should termination of resuscitation rules be used to diagnose no chance of survival in adults and children with out-of-hospital cardiac arrest?** | |
| **Population:** | adults and children with out-of-hospital cardiac arrest |
| **Intervention:** | termination of resuscitation rules |
| **Purpose of the test:** | Predict survival outcomes |
| **Role of the test:** | Facilitate reliable prehospital termination of resuscitation decisions |
| **Linked treatments:** | None |
| **Anticipated outcomes:** | Termination of resuscitation on scene without transporting to hospital |
| **Setting:** | Prehospital setting |
| **Perspective:** | Patient, clinician and EMS system perspective |
| **Background:** | This was systematically reviewed by ILCOR in 2020 identifying very-low certainty evidence for a conditional recommendation to use termination of resuscitation rules. In 2024, an updated systematic review was published based on the 2020 ILCOR review (Termination of Resuscitation Rules and Survival Among Patients With Out-of-Hospital Cardiac Arrest: A Systematic Review and Meta-Analysis. Smyth MA, Gunson I, Coppola A, Johnson S, Greif R, Lauridsen KG, Taylor-Philips S, Perkins GD. JAMA Netw Open 2024;7:e2420040. doi: 10.1001/jamanetworkopen.2024.20040.  In the present review, we have conducted an adolopment of the 2024 review by Smyth et al. and searched for additional studies. |
| **Subgroups:** | We consider adults and pediatric patients as separate subgroups. |
| **Conflict of interests:** | Kasper G. Lauridsen was a co-author on the Smyth 2024 review for which an adolopment was performed. |

# 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 | Routine transport of all prehospital cardiac cases is becoming increasingly unacceptable in many parts of the world. The reasons for this are multifactorial but include:  • Increasingly limited healthcare resources at hospital  • Increased risk to rescuers during emergent transport  • Recognition that failure to achieve prehospital ROSC is the strongest predictor of poor clinical outcome  • Recognition that interruptions to CPR when transferring a patient from scene to the ambulance are likely to adversely impact patient outcome  • Evidence suggesting quality of CPR may be affected during emergent ambulance transport.  These influences have led to the development and implementation of TOR rules however there has been little study of the impact of these rules in clinical practice |  |
| Test accuracy How accurate is the test? | | |
| Judgement | Research evidence | Additional considerations |
| ● Very inaccurate ○ Inaccurate ○ Accurate ○ Very accurate ○ Varies ○ Don't know | Many TOR studies report on either the derivation and internal validation of a rule or external validation through historical cohorts. However, these TOR rules generally lack clinical implementation and clinical testing. Only 1 study (Morrison 2014) reported a validation of a TOR in clinical practice by ambulance clinicians.  Due to heterogeneity across studies it was not possible to perform a meta-analysis in 2020 and the additional studies identified in this review did not change that. The estimated number of false positive cases (number of cases recommended for termination who survived) varies significantly across studies and TOR rules. Smyth et al. reported pooled specificities of external validation studies of TOR rules varying from 0.81-0.98 as point estimates indicating the inability to correctly classify all survivors. The varying accuracy for the TOR rules across studies indicates that the performance of a TOR rule depends on the setting, the population, and the survival outcomes in that population. | We prioritized high specificity (i.e. a low number of missed survivors) and in accordance with previous reviews we consider at least 1% of missed survivors as inappropriate. Therefore, we prioritized specificity and positive predictive values with confidence intervals of at least 0.99. |
| Desirable Effects How substantial are the desirable anticipated effects? | | |
| Judgement | Research evidence | Additional considerations |
| ○ Trivial ○ Small ○ Moderate ● Large ○ Varies ○ Don't know | Maximizing patient clinical outcomes while reducing risk faced by  ambulance clinicians during emergent transport, and preserving  limited Emergency Department (ED) resources is highly desirable in  all health care environments. Included studies indicated that TOR rules are cost-efficient. |  |
| Undesirable Effects How substantial are the undesirable anticipated effects? | | |
| Judgement | Research evidence | Additional considerations |
| ○ Trivial ○ Small ○ Moderate ● Large ○ Varies ○ Don't know | There is a lack of evidence reporting the use of TOR in  clinical practice.  Smyth et al. reported pooled specificities of external validation studies of TOR rules varying from 0.81-0.98 as point estimates indicating the inability to correctly classify all survivors. Several studies report only few missed survivors while some reported a substantial amount. Although the  proportions are small (often below the 1% medical futility  threshold) such a scenario is likely to be unacceptable to society  as a whole. The number of missed survivors for the TOR rules varies significantly across studies indicating that the performance of a TOR rule depends on the setting, the population, and the survival outcomes. |  |
| 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 evidence derives from observational studies, mostly historical cohorts, downgraded due to risk of bias, indirectness, imprecision, inconsistency and significant heterogeneity across patient and clinician populations. | Patient selection and lower survival outcomes in the cohorts examined may represent a major driver for the accuracy of the TOR rules and limit the application to clinical practice. |
| 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 | There remains to be only 1 clinical application study of a TOR rule in 954 patients (Morrison 2014) reporting a sensitivity of 0.64 (95%CI  0.61 to 0.68) and specificity of 1.00 (95%CI 0.92 to 1.00).  Several external validation studies of TOR rules report patients  being misclassified as non-survivors even though they did survive (Smyth 2024). |  |
| 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 | We found one prospective study applying a TOR rule during out-of-hospital  resuscitation (Morrison 2014). In this study  non-compliance was high with 198/954 (20.7%) cases eligible for  TOR transported to hospital. |  |
| 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 | It is unclear if other prehospital clinicians would have similarly high non-compliance rates. It is unclear if other prehospital clinicians would have similarly high non-compliance rates. |  |
| 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 | Only one prospective study applying a TOR rule during out-of-hospital  resuscitation was identified (Morrison 2014). It is unclear if findings would be similar for other prehospital clinician groups. |  |
| 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 | TOR rules to accurately discriminate between which patients will  and will not survive are a research priority for many healthcare  professionals and EMS Systems. However, in many cultures it  may be impossible for non-physicians to terminate resuscitation  due to legal constraints. In others, it may be socially  unacceptable not to avail the patient of all possible resources  (including hospital) before any decision is made to discontinue  resuscitation. |  |
| 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 performance of TOR rules seems to vary significantly among different studies in different settings. Khan et al. 2024 and Nazeha et al. 2024 investigated cost-effectiveness of TOR rules finding varying cost-effectiveness for different TOR rules. Nazeha et al. estimated that If TOR is exercised for every eligible case, it could expect to save approximately $400,440 per QALY loss compared to no TOR. |  |
| Resources required | | |
| Judgement | Research evidence | Additional considerations |
| ○ Large costs ○ Moderate costs ○ Negligible costs and savings ○ Moderate savings ○ Large savings ● Varies ○ Don't know | Khan et al. estimated quality-adjusted life years for survivors based on data from a systematic review applied on OHCA in the United Kingdom and identified that the most cost-effective strategies were the ERC TOR rule (incremental cost-effectiveness ratio (ICER) of £8,111), the Korean Cardiac Arrest Research Consortium 2 (KOC 2) TOR rule (ICER of £17,548), and the universal Basic Life Support (BLS) TOR rule (ICER of £19,498,216).14 The KOC 2 TOR rule was cost-effective at the established cost-effectiveness threshold of £20,000–£30,000 per QALY. Nazeha et al. investigated the cost-effectiveness following implementation of TOR rules in Singapore based on cases that were terminated in the field and all cases applicable for TOR although clinicians decided transport to hospital. They found that terminating CPR on all patients eligible for the TOR rule would result in 31 additional deaths per 10,000 patients compared to No TOR. If TOR is exercised for every eligible case, it could expect to save approximately $400,440 per QALY loss compared to no TOR. |  |
| 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 | Only two studies investigated cost-effectiveness based on historical cohort data and various assumptions. The evidence was downgraded for risk of bias, indirectness, and imprecision. |  |
| 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 | Khan et al. estimated quality-adjusted life years for survivors based on data from a systematic review applied on OHCA in the United Kingdom and identified that the most cost-effective strategies were the ERC TOR rule (incremental cost-effectiveness ratio (ICER) of £8,111), the Korean Cardiac Arrest Research Consortium 2 (KOC 2) TOR rule (ICER of £17,548), and the universal Basic Life Support (BLS) TOR rule (ICER of £19,498,216).14 The KOC 2 TOR rule was cost-effective at the established cost-effectiveness threshold of £20,000–£30,000 per QALY. Nazeha et al. investigated the cost-effectiveness following implementation of TOR rules in Singapore based on cases that were terminated in the field and all cases applicable for TOR although clinicians decided transport to hospital. They found that terminating CPR on all patients eligible for the TOR rule would result in 31 additional deaths per 10,000 patients compared to No TOR. If TOR is exercised for every eligible case, it could expect to save approximately $400,440 per QALY loss compared to no TOR. | The performance of the TOR rule depends on the setting, population, and survival outcomes. Thus, the cost-effectiveness would likely differ significantly based on the setting. |
| 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 identified studies |  |
| Acceptability Is the intervention acceptable to key stakeholders? | | |
| Judgement | Research evidence | Additional considerations |
| ○ No ○ Probably no ○ Probably yes ○ Yes ● Varies ○ Don't know | In countries where prehospital termination of resuscitation is established practice studies suggest it is acceptable to prehospital clinicians, Emergency Department physicians and the families of non-survivors of cardiac arrest.(Anderson 2017; Anderson 2018; Anderson 2018; Delbridge 1996; Edwardsen, 2002; Schmidt 1995)  Only one study suggesting prehospital TOR is acceptable for clinicians and ED physicians was identified (Morrison 2014) | Internationally there may be cultural and legal barriers to prehospital termination of resuscitation.  A TOR that misclassifies a patient as a non-survivor (i.e. an avoidable death) is unlikely to be acceptable to stake holders. |
| Feasibility Is the intervention feasible to implement? | | |
| Judgement | Research evidence | Additional considerations |
| ○ No ○ Probably no ○ Probably yes ○ Yes ● Varies ○ Don't know | Only one clinical study was identified. | Likely to be feasible in mature EMS systems with effective governance arrangements and where legislation does not prohibit non-physicians making termination of resuscitation decisions. |

# Summary of judgements

|  | **Judgement** | | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **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** | Trivial | Small | Moderate | **Large** |  | 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 |
| For adult out-of-hospital cardiac arrest, we suggest that emergency medical service systems may implement termination of resuscitation (TOR) rules to assist clinicians in deciding wehter to discontinue resuscitation efforts at the scene or to transport to hospital with ongoing CPR. We suggest that TOR rules may only be implemented following local validation of the TOR rule with acceptable specificity considering local culture, values, and setting (conditional recommendation, very-low certainty evidence).  For pediatric out-of-hospital cardiac arrest we suggest not to use TOR rules to decide whether to terminate resuscitation efforts or not due to insufficient evidence (conditional recommendation, very-low certainty evidence). |
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| Justification |
| The task force made a conditional recommendation for the use of termination of resuscitation (TOR) rules for adult OHCA in line with the last CoSTR on termination of resuscitation. The values in making this recommendation remain largely unchanged. In making this recommendation, we recognize variation in patient values, resources available, and performance of TOR rules in different settings.  We note that the certainty of evidence is very low and limited by a lack of clinical validation studies. The task force recognizes that application of TOR rules may result in missed survivors but has the potential to reduce variation in practice associated with clinician judgement and prevent premature terminations by clinicians.  We recognize that termination of resuscitation rules are already implemented in some EMS systems. In settings where EMS personnel will transport all patients to the hospital, the use of TOR rules may be associated with reduced costs. In contrast, the potential economic benefit in EMS systems with physician-staffed ambulances competent of terminating CPR may be absent. The task force recognizes that the performance of TOR rules varies depending on the EMS system, the setting, and the survival rate in the population. TOR rules should not be implemented without assessing the local validity of a TOR rule and the validity should be reassessed as survival outcomes change over time.  We considered pediatric OHCA as a separate population, and we value that missed survivors in this population may be valued differently from the adult population. Several missed survivors were seen when applying adult TOR rules to the pediatric population and the two TOR rules derived specifically for the pediatric population remains to be externally validated. |

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| Subgroup considerations |
| We considered insufficient evidence for use of TOR rules for pediatric patients. |

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| Implementation considerations |
| We suggest that implementation should be preceded by local validation of the performance of the TOR rule. |

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| Monitoring and evaluation |
| We suggest that survival rates should be monitored when implementing TOR rules and the performance and appropriateness of TOR rules should be reconsidered as survival rates increase. |

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| Research priorities |
| There is a paucity of evidence addressing use of TOR rules in clinical practice. Studies are required to address:  · Accuracy of TOR rules in clinical practice  · Compliance with OOH-TOR rules  · Implementation strategies of TOR rules for EMS based on evidence  · Societal perceptions and acceptability of TOR rules  · Validation of TOR rules specific for children  · Impact of TOR rules on non-heart-beating organ donation  · Risk associated with emergent transport of futile cases with ongoing resuscitation |