**OUT-OF-HOPSITAL TERMINATION OF RESUSCITATION (TOR) RULES**

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| Question | |
| **Do prehospital termination of resuscitation (TOR) rules reliably predict in-hospital outcome following out-of-hospital cardiac arrest?** | |
| **Population:** | Adults and children with out-of-hospital cardiac arrest |
| **Intervention:** | Prehospital application of a termination of resuscitation rule (TOR) |
| **Purpose of the test:** | Predict in-hospital outcome |
| **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:** | out-of-hospital, non-disaster response |
| **Perspective:** | Patient, clinician and EMS system perspective |
| **Background:** | The strongest predictor of favorable outcome following out-of-hospital cardiac arrest is return of spontaneous circulation (ROSC) in the prehospital phase. Several studies have reported that quality of cardiopulmonary resuscitation (CPR) is reduced during transport suggesting that rescuers should remain on scene providing resuscitation rather than expediting transport to hospital. In addition, transporting patients with active CPR increases risk for the ambulance crew due to being unrestrained in the back of a moving ambulance.  However, many resuscitation attempts fail to achieve ROSC and ambulance crews may be required to make a decision to either cease resuscitation or continue resuscitation on route to hospital. Termination of resuscitation rules have been developed to assist clinicians when making a decision to cease resuscitation. |
| **Subgroups:** | Adults and children |
| **Conflict of interests:** | MAS & GDP funded by NIHR (UK) to develop an updated prehospital termination of resuscitation guideline for use by UK ambulance clinicians |

# 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 is no current ILCOR recommendation addressing prehospital termination of resuscitation (TOR) rules following out-of-hospital cardiac arrest.  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 only the derivation and internal validation of a rule. As such these TOR rules have not been tested clinically in any way. A significant number of studies report external validation of TOR rules providing an indication of the optimal performance of the TOR that may over-estimate its performance in clinical practice. Only 1 study (Morrison 2014, 486) reported a validation of a TOR in clinical practice by ambulance clinicians.  Due to heterogeneity across studies it was not possible to perform meta-analysis, however where multiple studies address accuracy of a singular TOR, we estimated performance of the TOR per 1000 patients tested using the range of sensitivities, specificities and prevalences reported in the studies.  The estimated number of false positive cases (number of cases recommended for termination who survived) per 1000 patients tested ranged from 0 to 149. Similarly, for prediction of poor neurologic outcome, the number of false positive cases (number of cases predicted to have poor neurologic outcome who survived with favourable neurologic outcome) per 1000 patients tested ranged from 0 to 6.  Where several papers report the performance of a single TOR we calculated diagnostic odds ratios (DOR) for each included study. The diagnostic odds ratio (DOR) describes the odds of a positive test (TOR predicts death) in those with disease (patients who die in hospital) relative to the odds of a positive test (TOR predicts death) in those without disease (patients survives to discharge). Unlike positive or negative predictive values, the DOR is independent of disease prevalence.  For prediction of death the DOR ranged from 0.1 (95%CI 0.04 to 0.4) (Yates 2018, 21) to 499.3 (95%CI 31.1 to 8010.6) (Morrison 2007 , 266). For prediction of poor neurologic outcome the DOR ranged from 5.7 (95%CI 2.6 to 12.6) (Kashiura 2016, 49 ) to 170.1 (95%CI 10.5 to 2766.1) (Cheong 2016, 623). | We adopted prediction of death (or poor neurologic outcome) to be the true positive as per recommendations by Morrison (2019, 199). In the scenario where the true positive is death, specificity reports the ability of the test to identify potential survivors. A specificity of 1.0 indicates all survivors are identified, whereas any specificity below 1.0 indicates potential survivors may be missed and avoidable deaths may occur.  Similarly, sensitivity reports the ability of the TOR to identify patients who will die. A sensitivity of 1.0 indicates all non-survivors are identified, whereas any sensitivity below 1.0 indicates non-survivors may be missed and avoidable transports may occur.  From an ethical/moral perspective, perfect specificity should therefore be favoured over high sensitivity. In other words studies with perfect specificity and moderate sensitivity prioritise transporting patients with even a small chance of survival. |
| Desirable Effects How substantial are the desirable anticipated effects? | | |
| Judgement | Research evidence | Additional considerations |
| ○ Trivial ○ Small ○ Moderate ● Large ○ Varies ○ Don't know | Maximising 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. | SFDFsf |
| Undesirable Effects How substantial are the undesirable anticipated effects? | | |
| Judgement | Research evidence | Additional considerations |
| ● Large ○ Moderate ○ Small ○ Trivial ○ Varies ○ Don't know | There is a paucity of evidence reporting the use of TOR in clinical practice.  Many studies report cases where application of a TOR misses a potential survivor (potentially avoidable death). 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. | A reduction in the proportion of patients transported with CPR in progress may adversely impact non-heart-beating organ donation.  Growing body of epidemiologic evidence to suggest resuscitation should continue for around 45 minutes so ensure potential survivors are not missed. (Goto 2014, 192; Nagao 2016, 1386). |
| 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 downgraded due to risk of bias, indirectness, imprecision, inconsistency and significant heterogeneity across patient and clinician populations. The majority of identified studies comprised derivation and internal validations studies or external validation studies undertaken with retrospective data samples.  The majority of studies report sensitivity and specificity, and fail to report positive predictive values or positive likelihood ratios. Diagnostic odds ratios were calculated. | Sensitivity and specificity provide population level data that do not take into account false positive (TOR indicates will die but patient survives – avoidable death) and false negative cases (TOR indicates patient will survive but dies – unnecessary transport).  Predictive values and likelihood values may not provide an accurate assessment of performance where the incidence of non-survival significantly outweighs the incidence survival |
| 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 one prospective study (n-953) applying a TOR rule during out-of-hospital resuscitation 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) (Morrison 2014, 486). External validation studies applying the same rule to a dataset identified sensitivity ranging from 0.51 (95%CI 0.50 to 0.53)(Morrison 2007, 266) to 0.91 (95% CI 0.91 to 0.91) (Goto 2019, 240). Reported specificity ranged from 0.62 (95%CI 0.60 to 0.63)(Goto 2019, 240) to 1.0 (95%CI 0.99 to 1.0)(Morrison 2007, 266).  Several external validation studies of TOR rules report patients being misclassified as non-survivors even though they did survive (Cheong 2016, 623; Chiang 2015, 318; Fukuda 2014, 144; Goto 2019, 240; Kajino 2013, 54; Kashiura 2016, 49; Kim 2015, 104; Lee 2019, e134; Ong 2007, 244; Sasson 2008, 1432; SOS Kanto 2017, 345; Yoon 2019, 73; Drennan 2014, 1488; Grunau 2017, 374; Jordan 2017, 75; Skrifvars 2010, 679; Yates 2018, 21; Diskin 2014, 910). 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 | We found one prospective study applying a TOR rule during out-of-hospital resuscitation by EMT’s (Morrison 2014, 486). 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 | We found one prospective study applying a TOR rule during out-of-hospital resuscitation by EMT’s (Morrison 2014, 486). In this study non-compliance was high with 198/953 (20.7%) cases eligible for TOR transported to hospital. 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 by EMT’s was identified (Morrison 2014, 486). It is unclear if findings would be similar for other non-EMT 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 | Several external validation studies of TOR rules report patients being misclassified as non-survivors even though they did survive (Cheong 2016, 623; Chiang 2015, 318; Fukuda 2014, 144; Goto 2018, 240; Kajino 2013, 54; Kashiura 2016, 49; Kim 2015, 104; Lee 2019, e134; Ong 2007, 244; Sasson 2008, 1432; SOS Kanto 2017, 345; Yoon 2019, 73; Drennan 2014, 1488; Grunau 2017, 374; Jordan 2017, 75; Skrifvars 2010, 679; Yates 2018, 21; Diskin 2014, 910). | Most studies report high specificity (infrequently miss a potential survivor) however any misclassification of a potential survivor as appropriate to terminate resuscitation may be societally unacceptable. |
| 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 exist examining costs for implementation of TOR rules were identified.  No studies addressing the costs of training prehospital clinicians to implement prehospital TOR rules were identified.  No studies addressing the governance costs associated with implementation of a prehospital TOR were identified. |  |
| 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 examining the resources required to implement a TOR rule were identified. |  |
| 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 examining the cost effectiveness of a TOR rule were identified. | The annual hospital cost for futile prehospital resuscitation has previously been estimated to cost $500 million in the USA (Gray 1991, 1393). Bonnin et al (1993, 1457) estimated that transporting a patient to be pronounced dead on arrival would cost between $2000 and $95,000 (US) per patient depending upon the extent of ED resuscitative efforts. It has further been reported that futile resuscitation attempts account for $58 million (US) of Medicare reimbursement (Suchard 1999, 801) . Although these data are old and may not be generalisable they suggest that transport of futile cardiac arrest cases may be associated with significant cost. |
| 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 studies reporting impact on health equity were identified. | Implementation of a prehospital TOR will reduce emergent transports, this may be construed by some as reducing health equity by reducing cardiac arrest victims exposure to advanced health care resources at hospital. |
| 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; 80; Anderson 2018, 62; Anderson 2018, 208; Delbridge 1996, 649; Edwardsen, 2002, 440; Schmidt 1995, 513)  Only one study suggesting prehospital TOR is acceptable for clinicians and ED physicians was identified (Morrison 2014, 486) | 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 | Several studies indicate the variables needed to make a termination of resuscitation decision are readily available to prehospital clinicians.    Very limited data exist to evaluate implementation of a TOR by prehospital clinicians | 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** | | | | | | |
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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 |

# 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 conditionally suggest for the use of termination of resuscitation (TOR) rules to assist clinicans in deciding whether to discontinue resuscitation efforts or to transport to hospital with ongoing CPR **(conditional recommendation / very-low certainty evidence)**. |
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| Justification |
| The Task Force recognises that the majority of studies identified describe either the derivation and internal validation of individual termination of resuscitation rules, or the external validation of previously published termination of resuscitation rules. We found only one study addressing clinical validation (the use of a termination of resuscitation rule in clinical practice) of a TOR rule by emergency medical technicians (EMT’s) with defibrillators. Robust evidence to support the widespread implementation of termination of resuscitation (TOR) rules in clinical practice is therefore weak. Despite several studies reporting a specificity of 1.0, the Task Force acknowledges that implementation of a TOR rule may result in missed survivors. However, inclusion of a TOR within a termination guideline has the potential to reduce variation in practice associated with clinician judgement, and improve termination decisions more generally.  In making a conditional recommendation the Task Force recognises that termination of resuscitation is common practice in many EMS systems. We support the principle of discontinuing resuscitation when treatment is futile as it preserves the dignity of the recently deceased, reduces risk for EMS providers and protects scarce healthcare resources. However, the Task Force also acknowledges that identification of futile cases is challenging and is often informed by both clinical guidelines and clinician insight.    The task force advocates for the adoption of termination of resuscitation guidelines that take into account the patients prior wishes and / or expectations, consideration of patient pre-existing co-morbidities and quality of life both before and after the cardiac arrest event. Such termination of resuscitation guidelines may be informed by the inclusion of an evidence based TOR rule, however the Task Force believes a TOR rule should not be the sole determinant of when to discontinue resuscitation.  In those EMS systems that do implement prehospital termination of resuscitation, the EMS system must ensure there is no conflict with legislation prohibiting non-physicians from discontinuing resuscitation and have appropriate governance arrangements to monitor practice. Where an evidence based TOR rule is included to inform practice, the EMS system should consider the generalizability of the TOR rule in question to their health care system. In some health care systems it may be appropriate for EMS systems to communicate with organ donation teams prior to implementing change.  The Task Force acknowledge that prehospital termination of resuscitation may not be feasible in some instances. In some locations the legal infrastructure may require ambulance clinicians to provide resuscitation in all but a very limited number of circumstances (e.g. in the presence of rigor mortis). In other areas, it may not be culturally acceptable for non-physicians to make a clinical decision to stop resuscitation in the prehospital environment. Where this is the case, or where clinical governance arrangements are insufficient to monitor practice we suggest transport to hospital with ongoing CPR may be preferable. |

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| Subgroup considerations |
| No evidence addressing implementation of TOR rules in the paediatric population was identified. |

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| Implementation considerations |
| * When considering adoption of an evidence based TOR rule, EMS systems must consider if their system is comparable to the EMS systems involved in the study. Where EMS systems differ it may not be appropriate to adopt that particular TOR rule * EMS systems must ensure they are compliant with legislation * EMS systems should consult the community they serve ensure prehospital termination is socially acceptable * EMS systems must train ambulance personnel in the use of any TOR rule * EMS systems should provide appropriate bereavement training for ambulance personnel * EMS systems should consider the impact on non-heart-beating organ donation when implementing a TOR rule |

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| Monitoring and evaluation |
| * Any TOR should be implemented with the context of a robust clinical governance framework * Compliance with the TOR should be audited on a regular basis |

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| Research priorities |
| There is a paucity of evidence addressing use of TOR in clinical practice. Studies are required to address:   * Accuracy of TOR rules in clinical practice * EMS compliance with TOR rules * Health economic implications of TOR rule implementation * Societal perceptions of TOR rules * TOR rules specific for children * Impact of TOR rules on non-heart-beating organ donation |

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