Systematic review of paediatric track and trigger systems for hospitalised children

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Abstract

Context: Early and accurate recognition of the deteriorating hospitalised child is complex. Paediatric track and trigger systems (PTTS) support clinical decision-making by 'tracking' the child's condition through monitoring of clinical signs and 'triggering' a request for an appropriate review when pre-determined criteria are breeched.

Objective: To describe the number and nature of published PTTS and appraise the evidence on their validity, calibration, and effect on important patient outcomes (death, cardiac and/or respiratory arrest, unplanned transfer to intensive/high dependency care, immediate/urgent request for review, rapid response system activation).

Method: GRADE methodology. Papers identified through Electronic database and citation searching.

Results

Thirty-three PTTS were identified from 55 studies. There was considerable variety in the number and type of parameters, although all contained one or more vital signs. The evidence to support PTTS implementation was very low and the majority of outcomes did not achieve statistical significance. When PTTS was implemented as part of a rapid response system, the evidence was moderate to low but there was some evidence of a statistically significant improvement in outcome.

Conclusion

There is now some limited evidence for the validity and clinical utility of PTTS scores. The high (and increasing) number of systems is a significant confounder. Further research is needed particularly around the thresholds for the vital signs and the reliability, accuracy and calibration of PTTS in different settings.

Background

Effective management of clinical deterioration in hospitalised children is a priority for healthcare professionals, patients and carers alike. Optimal care for a deteriorating child is complex.[1] It requires that: signs and symptoms of deterioration are recognised by ward staff; staff are empowered to call for assistance promptly; the assistance is readily available and appropriately skilled; and the interventions arising from this response improve outcomes. The first 'link' in this chain is early, accurate recognition of clinical deterioration. This is frequently inadequate.[2-4]

A number of tools are available to help staff identify deteriorating children. These 'early warning systems' prompt calls for senior assistance with changes in vital signs or other parameters.[5] In 2005 21.5% of UK paediatric centres reported using an 'early warning system';[6] this rose to 85% by 2013.[7] Many different systems are in use but they appear in two main forms: 'score' and 'trigger'-based systems. Score-based systems assign values to vital signs, and other clinical indicators, representing the extent of deviation from 'normal.' These component values are combined to generate an overall score. Higher scores should represent an increased risk of deterioration, prompting review by senior clinicians. Trigger-based systems contain a number of pre-defined thresholds. When one or more thresholds are breeched, this 'triggers' a pre-determined response. Unlike score-based systems, trigger-based systems result in a dichotomous 'all or nothing' response. This typically means activation of a rapid response system (RRS) (also known as 'critical care outreach', 'rapid response' or 'medical emergency' teams). Although there are differences between these types of tools, they share two common characteristics: the ability to 'track' the child's condition through ongoing monitoring and the facility to 'trigger' a request for an appropriate clinical review. Therefore, for the purpose of this review, score and trigger-based systems will be collectively referred to as paediatric track and trigger systems (PTTS).

The ideal PTTS utilises routinely monitored clinical signs, is simple to use and acceptable to users with robust validation in a relevant population.[5] As with all clinical prediction tools, there is an important trade-off between sensitivity and specificity. The overall predictive performance of a tool is most commonly summarised by the area under the receiver operator characteristic (AUROC) curve, with values greater than 0.7 regarded as useful. Score-based systems should also have acceptable calibration, and accurately classify children into low, medium and high risk categories.[8] As score-based PTTS are generally used with an action/escalation plan, calibration indicates the appropriateness of the response to each PTTS score in light of the degree of risk.

We conducted a systematic review of PTTS performance in 2009 and reported that the evidence on validity, calibration, reliability and utility was weak, and adoption of PTTS into clinical practice could not be recommended (findings summarised in supplemental data Table A).[5] Since this work there has been widespread implementation of PTTS and an increase in the literature describing their predictive performance. This updated systematic review is necessary to reconsider these recommendations.

Objectives

This review was undertaken to examine the key characteristics of PTTS and to appraise the evidence on their validity, calibration and clinical utility.

Methods

Paediatric track and trigger systems were defined to be any system which attempts to identify hospitalised children who are at risk of, or suffering from, critical deterioration through ongoing monitoring of clinical signs. Children in critical care, emergency room and theatres were excluded as they have differing staffing and monitoring strategies.

The review protocol rigorously adhered to the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) approach.[9] The review was framed using the PICO criteria (Table 1). Quality of evidence was assessed as high, moderate, low or very low using the GRADE approach where randomised controlled trials start as high quality evidence, and observational studies as low level. Five factors can lead to evidence being downgraded and three factors may result in evidence upgrade. Results are presented as an evidence profile, a detailed assessment of the quality of the evidence together with a summary of the findings for each outcome. Where sufficient detail was provided, the risk ratio (RR) and 95% confidence intervals (CI) for each outcome were calculated. Results were separated into studies examining the introduction of a PTTS alone and those introducing a PTTS as part of a package of interventions, such as a RRS. Predictive validity was also summarised. There were no amendments to the protocol during the study.

Inclusion criteria

- Randomised controlled trials and observational studies describing the effect of PTTS (either alone or as part of a package of interventions) on ward in-patient outcomes (listed in Table 2).
- Observational studies describing the performance of PTTS in detecting these outcomes or its use in clinical practice

Exclusion Criteria

- Studies set in the emergency department, operating theatre or critical care unit
- Studies concerning both adult and paediatric patients unless the paediatric data could be adequately separated.

Primary outcomes:

In accordance with GRADE, outcomes were identified and ranked in terms of their importance to patients (Table 2).

Search strategy

The following databases were searched: AMED, CINAHL, Cochrane Library, EMBASE, and OVID Pubmed (Supplemental data Table B). A broad search strategy was adopted, informed by the previous systematic review[5] with Medical Subject Headings (MeSH) and free text searching using keywords in the title or abstract. Results were limited to papers from 1990 relating to children. Google scholar was searched using the terms paediatric early warning system/score and paediatric rapid response/medical emergency team. Abstracts from the annual conferences of the Royal College of Paediatrics and Child Health (RCPCH), European Society of Paediatric and Neonatal Intensive Care (ESPNIC) and European Society of Intensive Care Medicine (ESCIM), together with the bi-annual World Congress in Paediatric Intensive Care were hand-searched from 2000 onwards.

After removal of duplicates, the title and abstract of records were independently screened by two researchers (SC and JW). The full-text of 155 papers were reviewed. Eligible studies underwent manual searching of references and citation searching on the Web of Science database. Uncertainty regarding inclusion of a paper was resolved through discussion within the research team.

Data extraction:

Three data extraction forms were developed based on the initial systematic review.[5] Separate forms were developed for randomised control trials, observational studies and studies of diagnostic accuracy (Supplemental Data C). Extracted data were entered into Microsoft Excel for Mac 2011 (version 14.4.7).

Evidence appraisal and analysis.

PTTS were firstly categorised as '*scoring'* or '*trigger'* systems. Systems were then classified as being either '*age-independent'* (a single system applied regardless of age) or '*age-dependent'* (multiple systems with differing age-related thresholds).

Risk of bias for diagnostic accuracy studies was assessed using QUADAS 2 (Supplemental data Table D).[10] Remaining quantitative studies were assessed against criteria in the GRADE handbook (Supplemental data Table E).[11] The risk of bias of qualitative studies was not assessed. Pooled risk ratio and 95% confidence intervals for each outcome were calculated using Vasser stats.[12] The overall quality of evidence for each patient-important outcome was ranked following the GRADE approach. Evidence profiles were formulated in GRADE Pro GDT.[13]

Results

Search results

The search was conducted on 27th May 2016 (Figure 1, Supplemental data Table B). Thirty-three PTTS were identified from 55 papers. Different PTTS with the same name were numbered in order of publication to distinguish between them.

Main characteristics of Patient Track and Trigger Systems

Table 3 summarises the included studies, PTTS characteristics and quality rating. Many systems were minor modifications of previously published systems. Twenty-one were classified as 'scoring systems', and 12 as 'trigger systems'. Fourteen were 'age-dependent' and 19 'age-independent'. Three papers[50,66,67] reported use of a PTTS to activate a paediatric RRS but did not describe its characteristics.

There was wide variation in the number and type of parameters within PTTS. Median parameters per system was 6 (range 3 – 19). Some broader parameters shared the same name (such as 'respiratory' or 'cardiovascular') but were constituted from differing component parts or had differing thresholds for scoring/triggering (Table 3).

All PTTS included one or more vital signs. Some PTTS parameters combined vital signs with other clinical indicators such as skin colour. Thresholds and age-bandings varied (Table 4), although many differences were minor. Systems providing additional guidance on 'normal' vital sign values are seen in Supplemental data Table F.

Seven studies evaluated PTTS as a single intervention (4 studies examined PTTS introduction into hospitals with established RRS[29,49,54,64] and 3 without[15,27,41]). Results are shown in Table 5. A further 12 studies examined the impact of PTTS as part of a package of interventions,[15,18,32,36,37,52,61-63,66-68] mainly RRS implementation (Table 6). Eighteen studies reported diagnostic accuracy[14,16,17,19,21-24,26,28,30,31,34,42,46,51,55,59] (Table 7). No randomised controlled trials were identified.

Effect of Patient Track and Trigger Systems as a single intervention on patient important outcomes

Death – Very low evidence.

The 2 observational studies[29,41] had small sample sizes and low event rates. The studies demonstrated that death on intensive care following unplanned admission from the ward had a relative risk of 1.28 (95% CI 0.66-2.52), however results were not significant[41]. Relative risk of unexpected death on the ward could not be calculated as there was only 1 death in the study population[29].

Cardiac arrest – Very low evidence.

Three studies examined cardiac arrest.[27,49,54] Two studies were severely limited by methodological concerns.[49,54] The relative risk of cardiac arrest on the ward demonstrated an increase after PTTS implementation (1.32, 0.33-5.26), although this was not statistically significant[27].

Respiratory arrest – No evidence

No studies examined the effect of PTTS implementation on respiratory arrest in hospitalised children.

Unplanned transfer to intensive care – Very low evidence.

Of the 4 studies[15,27,29,41] examining unplanned admission to intensive care, 1 also included admissions to the high dependency unit (HDU)[29] and a further study reported transfers to a specialist hospital with intensive care facilities, although it is not known if these children received intensive care.[15] Results were mixed, with PTTS introduction reported as either increasing or decreasing the risk of transfer.

Surrogate measures of illness severity included the requirement for inotropes and ventilation, PIM2 score and length of intensive care stay. Only the change in the rate of invasive ventilation after unplanned transfer was statistically significant,[41] with a relative risk of 0.83 (0.72-0.97). This was predicted to result in 128 fewer patients requiring invasive ventilation per 1000 PICU transfers.

Call for emergency assistance – Very low evidence.

Emergency assistance was defined as activation of the code blue or cardiac arrest team. A single study reported a reduction in calls after a PTTS was introduced, but relative risk could not be calculated as neither the number of calls nor the denominator were reported.[64]

Call for Urgent assistance – Very low evidence.

Four studies examined urgent calls for assistance.[15,29,49,64] A single study[15] reported a statistically significant reduction in calls to paediatricians (0.23, 0.11-0.47) and respiratory therapists (0.36, 0.14-0.96).

Length of hospital stay – Very low evidence

A single study reported a decreased length of hospital stay post PTTS implementation (1.5 days/patient versus 1.6 days/patient) but the relative risk could not be calculated.[64]

<u>Patient Track and Trigger Systems as part of a package of intervention</u>.

Ten observational studies described the introduction of PTTS as part of instigating a RRS.[18,32,36,37,57,61-63,66,67] A further study[52] in a hospital with an established RRS examined a package of interventions designed to increase situational awareness.

Death – Moderate evidence

Nine studies reported impact on mortality.[18,32,36,37,57,61-63,66] Pooled results indicated a statistically significant reduction in the risk for death in hospital of 0.64 (0.59-0.69), with 27 fewer deaths predicted per 10,000 admissions. Relative risk of death on PICU following unplanned transfer from the ward was reduced at 0.70 (0.59-0.83), equating to 171 (97 – 234) fewer predicted deaths per 10,000 PICU patients. There was also a significant reduction in unexpected deaths on the ward (relative risk 0.26, 0.13-0.50), with 2 fewer predicted deaths per 10,000 admissions after RRS and PTTS implementation. These are rare events and hence the absolute effect size is small.

Cardiac arrest – Low evidence

Five studies[18,36,37,61,66] reported the impact of an RRS with an embedded PTTS on the rate of cardiac arrest. Ward cardiac arrests per 10,000 non-PICU admissions were significantly reduced (relative risk 0.60, 0.37-0.97). Unsurprisingly given the low event rates, the predicted absolute reductions are very small, with 1 fewer predicted death per 10,000 non-PICU ward admissions. Notably when the relative risk of arrest was calculated per 10,000 non-PICU patient days, the result was not statistically significant (0.85, 0.52-1.39).

Respiratory arrest – Low evidence

Bag-valve-mask ventilation and intubation on the ward were considered under the outcome of respiratory arrest. The 3 studies[18,36,61] all utilised different metrics. There was a statistically significant reduction in the risk of ward intubation of 0.27 for events both per 1000 patient days[36] (0.08-0.98) and per 1000 discharges[61] (0.71-0.98). Again the absolute effect was small, with 2 fewer predicted ward intubations per 10,000 patient days (0 fewer to 2 fewer) and 11 fewer per 10,000 discharges (0 fewer to 13 fewer).

Cardiac and/or respiratory arrest – Moderate evidence

Six studies combined the reporting of cardiac and respiratory arrests for three metrics.[36,57,61-63,67] All results were statistically significant. The relative risk of ward arrest per 10,000 non-PICU admissions was 0.69 (0.53-0.89) or 6 fewer predicted arrests. When reported against patient discharges, a predicted reduction of 23 ward arrests per 10,000 discharges was estimated (relative risk 0.61, 0.46-0.80). The relative risk of arrest per 10,000 patient days was also reduced (0.36, 0.22-0.59) with an estimated reduction of 2 arrests per 10,000 patient days.

Request for emergency assistance – Low level evidence

Calls for emergency assistance were reported by 3 studies[18,61,62] using 3 metrics. No metric achieved statistical significance.

Unplanned transfer to Intensive Care –Very low level evidence

Five studies[18,32,52,61,62] described 10 different metrics relating to the risk of unplanned transfer to PICU. The relative risk of unplanned transfer requiring vasopressors in the first hour was 0.36 (0.21-0.65), with an absolute rate of 30 fewer patients per 1000 unplanned PICU admission.[18] The remaining results did not achieve statistical significance.

Diagnostic accuracy of PTTS

Eighteen studies[14,16,17,19,21-23,26,28,30,31,34,42,46,51,55,59,69] examined the diagnostic accuracy of 14 PTTS to predict patient important outcomes (Table 6). One study[22] reported inaccurate values for sensitivity and specificity and the methodology did not permit accurate calculation[70]. The results were therefore removed from the table. The majority were retrospective studies, which increased the risk of bias. PTTS systems were examined across a variety and combinations of outcomes. Diagnostic accuracy studies have been included as this is an important consideration when selecting a PTTS for implementation.

Death in hospital – very low evidence

A single study of the *In-patient Triage and Treatment* (ITAT) system,[31] set in a resource-limited environment was examined for the ability to predict death in hospital. The study suffered from data collection concerns as a significant proportion of children were excluded due to missing data. AUROC of 0.76 demonstrated reasonable ability to identify children at risk of death within 2 days.

Cardiac arrest – very low evidence

Three case controlled studies were identified,[17,55,59] of which 1 compared the validity of 3 differing PTTS.[17] Similar levels of sensitivity were seen across the differing systems, but specificity varied. AUROC values ranged from 0.73 to 0.91. Trigger-based system[17] appeared to perform less well than the score-base systems.[17,59]

Respiratory arrest – no evidence

No studies evaluated respiratory arrest as a stand-alone outcome.

Unplanned transfer to intensive care – very low evidence

Unplanned transfer to PICU was evaluated by 9 studies.[14,16,19,21,24,28,30,42,51] One study examined children readmitted to the PICU within 48 hours,[30] one included urgent RRS call or death on ward[21] and another excluded patients who had received a code blue call prior to transfer.[14] AUROC ranged from 0.71 (95%CI not reported) to 0.96 (0.93-0.98).

Unplanned transfer to PICU or HDU – very low evidence

Four studies[23,26,34,46] examined the composite outcome of transfer to PICU or HDU. Three studies[26,34,46] used the same data set to validate prospectively and evaluate retrospectively the ability to predict unplanned transfer, cardiac/respiratory arrest and/or death. However no arrests or deaths occurred so the outcome was limited to unplanned transfer. AUROC ranged from 0.79 (0.73-0.84) to 0.86 (0.82-0.91).

Calibration - No evidence

No studies assessed calibration.

Discussion

PTTS are now an established part of care for children in hospital. Most paediatric centres report using them.[7] There is striking diversity in the components, thresholds and efficacy of the systems. The *Paediatric Early Warning System Score I*[59] remains the most complex, with nineteen parameters. By contrast, the *Paediatric Early Warning Score I*[48,49] and its derivatives[42,51,55,58,60,64] has far fewer parameters. However, these 'simpler' systems are constituted from parameters which have three to four sub-parts requiring assessment. For example, the 'cardiovascular' parameter in the *Paediatric Early Warning Score I* requires assessment of skin colour, capillary refill time and heart rate, whilst the 'respiratory' parameter combines respiratory rate, oxygen therapy, tracheal tug and other signs of respiratory effort. Within these 'simpler' systems clinicians often had to make independent judgments of the 'normal' values for heart rate and respiratory rate. It is also unclear what score they should assign if the clinical features identified were spread across two or more 'sub-scores'. Therefore it may be that the superficially more complex systems containing objective and unambiguous scoring frameworks may be simpler for clinicians to use.

The evidence to support the clinical utility of PTTS is variable. Implemented without a RRS, PTTS did not demonstrate statistically significant relative reduction in cardiac or respiratory arrest, or mortality. A single study in a specialist children's hospital demonstrated a reduction in the rate of invasive ventilation after unplanned admission to PICU (RR 0.83,0.72 – 0.97). The study predicted that PTTS implementation would result in 128 fewer patients requiring ventilation per 1000 unplanned ward to PICU transfers. A separate study[15] set in a community hospital reported a relative reduction in risk of urgent calls to both physician and respiratory therapists, with a predicted absolute reduction of 17 and 6 fewer calls per 1000 patient days respectively. However it is unclear whether low rates of urgent calls is a desirable outcome that ultimately benefits patients.

Implemented as part of a RRS, PTTS demonstrated more positive results and the evidence overall was of moderate quality. There was a statistically significant reduction in the relative and absolute risk of death in hospital, on the ward and following PICU transfer. Childhood mortality remains a rare but devastating event. The contributing factors are complex, but the failure to recognise serious illness and correctly interpret physical signs correctly has been cited as a significant factor.[71] This review demonstrates the potential of PTTS and associated interventions to reduce the number of in-hospital deaths by an estimated 31 cases per 10,000 hospital admissions. Given the rarity of childhood death, this is a significant improvement.

PTTS as part of a package of interventions also had a positive impact on cardiac and respiratory arrests on the ward. When examined separately the quality of evidence was low, however studies of all arrests were of moderate quality. Again, the events are relatively rare and although a significant reduction was seen in the relative risk, predicted absolute effect was low, with only 1 fewer predicted cardiac arrest on the ward per 10,000 non-PICU admissions, and 11 fewer ward intubations per 10,000 discharges. Studies have demonstrated the significant short-term financial cost of paediatric arrests, estimated in 2009 at £3884 and £3569 per event for cardiac and respiratory events respectively.[72] The emotional cost, particularly for children and their families, is harder to quantify but cannot be underestimated.

Unplanned transfer to the PICU generally demonstrated an increase post-RRS implementation, but studies did not achieve statistical significance. Only the metric of unplanned PICU transfers requiring vasopressors within the first hour was statistically significant, however the effect was not sustained. 12 hours post-transfer, there was no difference between the groups.

Many of the metrics used to assess the outcomes did not achieve statistical significance. The relatively low incidence of these events means that many years of data are required to achieve studies with sufficient statistical power, prompting calls for valid, yet pragmatic measures to be adopted.[40]

There is low evidence of the predictive validity of PTTS in detecting children at risk of cardiopulmonary arrest or admission to a higher level of care. There remains very low evidence on the ability to predict mortality. The evidence arises from the single centre study in a resource limited setting. This may simply reflect the study power issue with relatively low rates of unexpected deaths in hospital in developed countries.

Scoring systems are generally used with a decision-algorithm, indicating the appropriate action for each PTTS score. This facilitates a graded response, where low scores prompt review by the nurse in charge and high scores require referral to a senior clinician. However, effective use requires appropriate assessment of the degree of risk indicated for each score. To date, no studies have analysed the calibration of score-based PTTS, therefore it is unclear whether current decision-algorithms are appropriate for the degree of risk.

Limitation of the systematic review

This updated systematic review was restricted to published PTTS and it is highly likely that there are many more unpublished systems in clinical practice. There is a potential risk of bias through non-publication of studies with equivocal or negative results,[73] particularly for locally developed PTTS.

Most studies have been conducted in specialist children's hospitals and the results may have limited applicability to secondary care settings due to the different mix of patients and staffing.

Implications for practice

Our previous systematic review highlighted the lack of evidence to support PTTS. Validity, utility and reliability were largely unknown. More robust research was called for before more widespread adoption.[5] The situation has improved somewhat in the intervening years. The evidence is stronger for PTTS as part of a package of interventions. This may reflect the complexities of healthcare delivery. Management of complex conditions is rarely resolved by a single intervention, and this may explain the popularity of packages of interventions or 'care bundles'.

There is no consensus on what type of PTTS should be implemented, or on the constituent parameters. Score-based systems may have benefits over trigger systems. They offer the opportunity to implement a graded response, which may be a better use of resources and expertise. This may be most relevant in centres without a RRS. Score-based systems have also had more extensive evaluation and demonstrated better sensitivity. Currently the *Bedside PEWS* has been the most intensively evaluated. This score was developed and tested in a single tertiary centre, but has undergone several further evaluations in other settings and is currently subject to a multi-centre, international cluster-randomised trial in 22 hospitals.[74]

Implications for research

Further validation studies of existing PTTS are needed to determine their predictive performance in at-risk populations of differing ages and severity of illness. In particularly, testing is needed in a range of settings particularly those outside of specialist children's hospitals. Calibration of score-based PTTS is urgently needed to determine the most appropriate decision-algorithms for the PTTS.

Further studies on the most appropriate threshold for vital signs are needed. The recently proposed centile curves and reference ranges for heart rate and respiratory rate[75] in hospitalised children have not, as yet, undergone any multi-centre validation, nor have they been utilised and evaluated within any PTTS system. As these represent the first evidence-based reference ranges for hospitalised children, they have the potential to improve the predictive validity of PTTS.

The wide variety of metrics to measure outcomes hinders comparison of differing PTTS scores in diverse settings and prevents benchmarking analysis. Cardiopulmonary arrest and death remain rare in hospitalised children. Meta-analysis may facilitate statistically significant findings but is currently limited by the heterogeneity of outcome measures. Pragmatic outcome measures are needed to facilitate clinical research.[40] National and international recommendations for the monitoring, reporting and conduct of research, in a similar fashion to those for adult RRS,[76] and paediatric critical care[77] would facilitate comparative analysis.

Conclusion

Although there remains low levels evidence on the effect of PTTS as a single intervention, there is moderate evidence of its impact on mortality and cardiac and respiratory arrests when delivered as a care package. The high (and increasing) number of systems, outcomes and metrics is a significant confounder. Further research is needed on the optimal characteristics, diagnostic accuracy and calibration of PTTS in different settings.

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Table 1: Systematic review PICO criteria

Participants	Hospitalised children (0-18 years) on paediatric wards excluding critical care, theatre, accident and emergency
Intervention	Development, use or evaluation of an early warning system to detect clinical deterioration
Comparison	Not applicable
Outcome	Any patient important outcome including (but not restricted to) death, cardiac and/or respiratory arrest, admission to intensive care or high dependency unit, immediate or urgent request for review, RRS activation.

Table 2: Patient important outcomes

Importance and rank		Direct outcomes	Surrogate outcomes
Critical for decision making	9	Death	
	8	Cardiac arrest Respiratory arrest	CPR (chest compressions and/or bag-valve-mask) Call for immediate assistance Code Blue
	7	PICU admission	Severity of illness scores (e.g. PiM2) Severity of illness markers (e.g. pH, lactate) Treatment markers (e.g. days of ventilation, length of PICU stay)
Important, but not critical for decision making	6	HDU admission	Severity of illness scores (e.g. PiM2) Severity of illness markers (e.g. pH, lactate) Treatment markers (e.g. days of non-invasive ventilation, length of HDU stay)
	5	Length of hospital stay	RRS call Urgent call to healthcare profesional
	4		
Low importance for decision making	3		
	2		
	1		

Abbreviations: CPR: Cardiopulmonary resuscitation; **HDU:** High Dependency Unit; P**IM2:** Pediatric Index of Mortality 2; **PICU:** Paediatric Intensive Care Unit; **RRS:** Rapid Response System

Table 3: Overview of included studies, PTTS key characteristics and parameters

System	Paper (First author, year)	Country	Setting*	Score or trigger	Age categories (n)	Parameters (n)	Parameters																				Overall risk of bias
							O2 sats	Heart rate	Respiratory rate	Systolic BP	CRT	Temperature	Staff concern	Parent concern	Respiratory	Behaviour	Cardiovascular	Consciousness	Seizure	Resp distress	Vomiting post-surgery	Airway threat	GCS	5m nebulisers	Oxygen therapy	Other parameters	
Bedside PEW system	Parshuram 2009[14] Parsharam 2011a[15] Parsharam 2011b[16] Robson 2013[17] Bonafide 2014[18] Fuijkschot 2014[19] Kaul 2014[20] Gawronski 2016[21]	Canada Canada Canada (3) & UK (1) USA USA Netherlands USA Italy	CH CCH CH (4) CH CH CH CH CH	S	5	7	✓	✓	✓	✓	✓									✓					✓		H H L H L H S H
Bristol PEW tool.	Haines 2006[22] Tume 2007[23] Robson 2013[17] McLellan 2014[24]	UK UK USA USA	CH CH CH CH	T	5	14	✓[£]	✓	✓				✓						✓				✓[i]			Apnoea ±bradycardia; DKA; clinically tiring or complete airway obstruction; hyperkalaemia; nebulised adrenaline; signs of shock (e.g. prolonged CRT (3s), poor perfusion, ± low BP); suspected meningococcus; Unresponsive or reponding only to pain[i]	H H H H
Burns Centre PEWS	Rahman 2016[25]	USA	CH	S	1	7		✓	✓			✓				✓										Intake; Output; Skin	H
Cardiff and Vale PEW system	Edwards 2009[26]	UK	UH	S	5	8	✓[i]	✓	✓	✓			✓		✓			✓				✓			✓[i]		L
C-CHEWS	McLellan 2013[27] McLellan 2014[24] Agulnik, 2016[28]	USA USA USA	CH CH CH	S	1	5							✓	✓[i]	✓	✓	✓									Family absent[i]	H H H
CHEW	McLellan 2013[27]	USA	CH	S	1	5							✓	✓[i]	✓	✓	✓									Family absent[i]	H
Children's Early Warning Tool	McKay 2013[29]	Australia	UH	S	4	9	✓	✓	✓	✓	✓	✓						✓		✓					✓		H

System	Paper (First author, year)	Country	Setting*	Score or trigger	Age categories (n)	Parameters (n)	Parameters: O2 sats	Heart rate	Respiratory rate	Systolic BP	CRT	Temperature	Staff concern	Parent concern	Respiratory	Behaviour	Cardiovascular	Consciousness	Seizure	Resp distress	Vomiting post-surgery	Airway threat	GCS	5m nebulisers	Oxygen therapy	Other parameters	Overall risk of bias
CH LA PEWS	Mandell 2015[30]	USA	CH	S	1	5									√	√	√									Medical History	H
ITAT	Olson 2013[31]	Malawi	RH	S	5	4	√	√	√			√															H
MET activation criteria I	Tibballs 2005[32] Tume 2007[23] Kinney 2008[33] Edwards 2011[34] Krmpotic 2013[35]	Australia UK Australia UK Canada	CH CH CH UH CH	T	5	9	√[£]	√	√	√			√					√[i]	√[i]	√ [ii]		√				Cardiac or respiratory arrest; apnoea or cyanosis[ii]	H H H L H
MET activation criteria II	Brilli 2007[36]	USA	CH	T	1	4	√[i]						√	√				√		√[i]					√[i]	[i] *and* worsening retractions or cyanosis	L
MET activation criteria III	Tibballs 2009[37] Azzopardi 2011[38] Lobos 2014[39]	Australia Australia Canada	CH CH CH	T	5	9	√[£]	√	√	√			√[i]	√ [i]				√[ii]	√[ii]	√ [iii3]		√				Cardiac or respiratory arrest; apnoea or cyanosis[iii]	H S H
MET activation criteria IV	Bonafide 2012[40]	USA	CH	T	1	6							√	√	√	√	√									Early warning score in red zone	L
Modified Bristol PEW system	Sefton 2014[41]	UK	CH	T	5	16	√[£]	√[$]	√				√						√				√[i]			Apnoea ±bradycardia; Clinically tiring or impending complete airway obstruction; children scored by AVPU reponding only to pain or unresponsive[i]; Hyperkalaemia; Marked increased work of breathing; Nebulised adrenaline or no improvement after nebulised adrenaline; pH <7.2, Poor perfusion, prolonged CRT (≥3s), ± low BP, large central/peripheral temp gradient; Unresolved pain on current anagesia therapy	H
MPEWS I	Skaletzky 2012[42]	USA	CH	S	1	3									√	√	√										H

System	Paper (First author, year)	Country	Setting*	Score or trigger	Age categories (n)	Parameters (n)	O2 sats	Heart rate	Respiratory rate	Systolic BP	CRT	Temperature	Staff concern	Parent concern	Respiratory	Behaviour	Cardiovascular	Consciousness	Seizure	Resp distress	Vomiting post-surgery	Airway threat	GCS	5m nebulisers	Oxygen therapy	Other parameters	Overall risk of bias
MPEWS II	Bonafide 2013[43] Roberts 2014[44]	USA USA	CH CH	S	5	18	✓	✓	✓	✓	✓	✓						✓		✓					✓	Abnormal airway or positive pressure ventilation; Active acquired or congenital heart disease or history of heart surgery; Baseline supplemental FiO_2 requirement; CVL; IV bolus fluid or blood product within past 4 hours; Pre/post any transplant; Presence of gastrostomy or jejunostomy tube; Previous ICU admission; Severe developmental, neurological or neuromuscular disease	Q Q
MPEWS III	Fuijkschot 2014[19]	Netherlands	CH	S	5	8	✓	✓	✓	✓	✓	✓								✓					✓		H
NHSI PEWS	Ennis 2014[45] Mason 2016[46]	Ireland UK	UH UH	S	4	7	✓	✓	✓				✓[i]	✓[i]				✓		✓						Stridor, apnoea	H L
PERT activation criteria	Van Voorhis 2009[47]	USA	CH	T	1	5	✓[i]	✓[i]	✓[i]	✓[i]			✓					✓	✓							Pain or agitation that is difficult to control	H
PEW score I	Monaghan 2005[48] Randhawa 2011[49] Watson 2014[50]	UK USA USA	CH CH CH	S	1	4									✓	✓	✓				✓[i]			✓[i]			H H H
PEW score II	Tucker 2009[51] Brady 2013[52] Brady 2014[53] McLellan 2014[24]	USA USA USA USA	CH CH CH CH	S	1	4									✓	✓	✓				✓[i]			✓[i]			H L Q H
PEW score III	Demmel 2010[54]	USA	CH	S	1	4								✓	✓	✓	✓										H
PEW score IV	Akre 2010[55]	USA	CH	S	1	4									✓	✓	✓				✓[i]			✓[i]			H

System	Paper (First author, year)	Country	Setting*	Score or trigger	Age categories (n)	Parameters (n)	O2 sats	Heart rate	Respiratory rate	Systolic BP	CRT	Temperature	Staff concern	Parent concern	Respiratory	Behaviour	Cardiovascular	Consciousness	Seizure	Resp distress	Vomiting post-surgery	Airway threat	GCS	15m nebulisers	Oxygen therapy	Other parameters	Overall risk of bias
PEW score V	Henderson 2012[56]	UK	Remote rural	S	4	6	✓	✓	✓	✓		✓						✓									H
PEW signs	Anwar-ul-Haque 2010[57]	Pakistan	UH	T	1	8	✓	✓	✓	✓			✓					✓	✓	✓							H
PEW system	Skaletzky 2009[58]	USA	CH	S	1	3									✓	✓	✓										H
PEW system score I	Duncan 2006[59] Robson 2011[17]	Canada UK	CH CH	S	5	19	✓	✓	✓	✓	✓	✓											✓		✓	>3 medical specialities involved in care; abnormal airway (not tracheostomy); bolus fluid; CVL in situ; gastrostomy; home oxygen; medication score; previous admission to ICU; pulses; severe cerebal palsy; transplant recipient	H H
PEW system score II	Panesar 2014[60]	USA	CH	S	1	3									✓	✓	✓										H
PMET triggers I	Hunt 2008[61]	USA	CH	T	1	12	✓						✓	✓				✓	✓	✓						Abnormal/worsening respiratory symptoms; progressive lethargy; circulatory compromise/acute shock syndrome; SVT/other dysrhythmia; respiratory arrest; cardiac arrest	H
PMET triggers II	Kotsakis 2011[62]	Canada (4)	CH (4)	T	5	7	✓	✓	✓	✓			✓[i]	✓[i]					✓				✓				L
RRT activation criteria	Sharek 2007[63]	USA	CH	T	1	6	✓	✓	✓	✓			✓					✓									L
TCH PAWS	Bell 2013[64]	USA	CH	S	1	5									✓	✓	✓				✓[i]					Every hour respiratory treatments[i]	H
THCS MET calling criteria	Kukreti 2014[65]	Canada	CH	T	1	7	✓	✓	✓	✓[i]	✓[i]		✓					✓[ii]	✓[ii]	✓		✓	✓[ii]			Poor peripheral pulses, mottled extremities[1]	S

System	Paper (First author, year)	Country	Setting*	Score or trigger	Age categories (n)	Parameters (n)	Parameters																				Overall risk of bias
							O2 sats	Heart rate	Respiratory rate	Systolic BP	CRT	Temperature	Staff concern	Parent concern	Respiratory	Behaviour	Cardiovascular	Consciousness	Seizure	Resp distress	Vomiting post-surgery	Airway threat	GCS	5m nebulisers	Oxygen therapy	Other parameters	
PTTS parameters not specified	Hanson 2010[66]	USA	CH	NS	NS	NS																					L
	Zenker 2007[67]	USA	CH																								H

Key: *All studies are single centre unless otherwise stated.
[i,ii,iii:] indicators that are combined within a single parameter; [£] seperate parameters for children with and without cyanotic heart disease; [a] in preceding 72 hours; [$] following one bolus of 10mls/kg fluid;

Overall risk of bias: L: Low; **H:** High; **Q:** Qualitative study (not assessed); **S:** Survey (not assessed)

Abbreviations: BP: blood pressure; **C-CHEWS:** Cardiac Children's Hospital Early Warning Score; **CCH:** Children's community hospital; **CH:** Children's hospital; **CRT:** capillary refill time; **CVL:** Central venous line; **DKA**: Diabetic ketoacidosis; **GCS:** Glasgow Coma Score; **ICU:** Intensive Care Unit; **ITAT:** Inpatient triage, assessment and treatment score; **LA:** Los Angeles; **MET:** Medical Emergency Team; **MPEWS:** Modified Pediatric Early Warning Score; **NHSI:** NHS Institute; **NS:** Not specified; **O_2 sats:** oxygen saturation; **PAWS:** Pediatric Advanced Warning Score; **PERT:** Pediatric Early Response Team; **PEW:** Paediatric/Pediatric Early Warning; PMET: Pediatric Medical Emergency Team; **RH:** Referral hospital; **RRT:** Rapid Response Team; **TCH:** Texas Children's Hospital; **THSC:** Toronto Hospital for Sick Children; **UH:** University Hospital

Table 4: Vital sign thresholds within trigger and score-based PTTS

System	Age range	Heart Rate		Respiratory Rate		Systolic BP		CRT	Oxygen saturation	Temperature
Trigger systems (values stated prompt triggering)										
Bristol PEW tool[17,22-24]	>6 m	≤95	≥150		≥70			3s	≥92% in oxygen ≥75% in oxygen (CHD)	
	6-12 m	≤95	≥150		≥60					
	1-5 y	≤95	≥150		≥40					
	5-12 y		≥120		≥25					
	>12 y		≥100		≥25					
MET activation criteria I[23,32-34] MET activation criteria III[37,38]	Term-3 m	<100	>180		>60	<50			<90% in oxygen <60% in oxygen (CHD)	
	4-12 m	<100	>180		>50	<60				
	1-4 y	<90	>160		>40	<70				
	5-12 y	<80	>140		>30	<80				
	>12 y	<60	>130		>30	<90				
MET activation criteria II[36]	All								<90% in oxygen	
Modified Bristol PEW system[41]	<3 m	≤95	≥150	<20	≥70			≥3s	≤92% in oxygen ≤75% in oxygen (CHD)	
	3-6 m	≤95	≥150	Half lower value for age (not specified)	≥70					
	6-12 m	≤95	≥150		≥60					
	1-5 y	≤95	≥150		≥40					
	5-12 y		≥120		≥25					
	>12 y		≥100		≥25					
PERT activation criteria[47] RRT activation criteria[63]	All	Acute change		Acute change		Acute change			Acute change	
PEW signs[57]	All	Acute change		Acute change		Acute change			Acute change <90%	
PMET triggers I[61]	All								Decrease despite 1st-line interventions	
PMET triggers II[62] THCS MET calling criteria[65]	Term-3m	<100	>180		>60	<50			<90% in oxygen <60% in oxygen (CHD)	
	4-12m	<100	>180		>50	<60				
	1-4y	<90	>160		>40	<70				
	5-12y	<80	>140		>40	<80				
	>12y	<60	>130		>30	<90				

System	Age range	Heart Rate		Respiratory Rate		Systolic BP		CRT	Oxygen saturation	Temperature	
Score systems (values stated score 1 or more)											
Bedside PEW system[14-17,20,21]	0 - <3 m	≤110	≥150	≤29	≥61	≤60	≥80	≥3 s	≤94%		
	3 - <12m	≤100	≥150	≤24	≥51	≤80	≥100				
	1-4y	≤90	≥120	≤19	≥41	≤90	≥110				
	> 4-12y	≤70	≥110	≤19	≥31	≤90	≥120				
	>12y	≤60	≥100	≤11	≥17	≤100	≥130				
Burns Centre PEWS[25]	All			> 10 above normal parameter				≥2s	>95% with supplemental oxygen	<36.5	>38.4
Cardiff and Vale PEW system[26]	<1 y	<90	>160	<20	>50	<70	>90		Requiring oxygen to keep above 90%		
	1-2 y	<80	>150	<15	>45	<80	>95				
	2-5 y	<75	>140	<15	>40	<80	>100				
	5-12 y	<60	>120	<10	>35	<90	>110				
	>12 y	<55	>100	<10	>30	<100	>120				
C-CHEWS[24,27,28]	All	Mild tachycardia (≥10% for age)		Mild tachypnoea (≥10% for age)				≥3 s	Mild desaturations below baseline		
Childrens Early Warning Tool[29]	<1y	≤100	>160	≤20	>45	≤75	>150	>2s	≤93%	<35.5	>38.0
	1-4y	≤90	>140	≤15	>35	≤80	>150				
	5-11y	≤80	>130	≤15	>30	≤85	>150				
	>12y	≤60	>120	≤15	>25	≤95	>150				
Children's Hospital LA PEWS[30]	All	20 above normal rate		10 above normal parameter				≥3 s	Requiring oxygen to maintain normal saturations		
ITAT[31]	<3 m	<110	>150	<30	>60				≤95%	<36	>37.4
	3-12m	<100	>150	<25	>50						
	1-4y	<90	>120	<20	>40						
	4-12y	<70	>110	<20	>30						
	>12y	<60	>100	<12	>15						
MPEWS I[42] PEW score I[48-50] PEW score II[24,51-53] PEW score III[54] PEW score IV[55] PEW system score II[60]	All	20 above normal rate		> 10 above normal parameter				≥3 s			
MPEWS II[43,44]	<3 m	<110	>160	<30	>60	<60	>90	≥ 2s	<95	<36	>38.4
	3-<12 m	<100	>150	<25	>50	<80	>110				
	1-<4 y	<90	>130	<20	>40	<90	>120				
	4-<12 y	<70	>120	<20	>30	<90	>120				
	>/=12 y	<60	>110	<12	>16	<100	>130				

System	Age range	Heart Rate		Respiratory Rate		Systolic BP		CRT	Oxygen saturation	Temperature	
Score systems (values stated score 1 or more)											
MPEWS III[19]	0 - <3 m	≤110	≥150	≤29	≥61	≤60	≥80	≥3 s	≤94%	<36.5	>37.5
	3 - <12m	≤100	≥150	≤24	≥51	≤80	≥100				
	1-4y	≤90	≥120	≤19	≥41	≤90	≥110				
	> 4-12y	≤70	≥110	≤19	≥31	≤90	≥120				
	>12y	≤60	≥100	≤11	≥17	≤100	≥130				
NHSI PEWS[45,46]	0-11m	<90	>160	<30	>60						
	1-4y	<90	>140	<20	>40						
	5-12y	<70	>120	<20	>30						
	13-18y	<60	>100	<10	>20						
PEW system score I[17,59]	<3 m	<110	>150	<30	>60	<60	>80	≥ 2s	≤95	<36	>38.5
	3-12 m	<100	>150	<25	>50	<80	>100				
	1-4 y	<90	>120	<20	>40	<90	>110				
	4-12 y	<70	>110	<20	>30	<90	>120				
	>12 y	<60	>100	<12	>16	<100	>130				
TCH PAWS[64]	All	≥20 above baseline		≥10 above baseline				≥3 s	5 points below baseline		

Abbreviation: **BP:** Blood pressure; **C-CHEWS**: Cardiac Children's Hospital Early Warning Score; **CH**: Children's Hospital; **CHD:** cyanotic heart disease; **CRT:** Capillary refill time; **GCS:** Glasgow Coma Score; **ITAT**: Inpatient triage, assessment and treatment score; **LA:** Los Angeles; **PAWS**: Pediatric Advanced Warning Score; **PERT**: Pediatric Early Response Team; **PEW**: Paediatric/Pediatric Early Warning; **MET**: Medical Emergency Team; **MPEWS**: Modified Pediatric Early Warning Score; **PMET**: Pediatric Medical Emergency Team; **RRT**: Rapid Response Team; **TCH**: Texas Children's Hospital; **THSC:** Toronto Hospital for Sick Children

Table 5: Evidence profile for PTTS implementation

		Quality assessment							Events (n/1000)		Effect		Quality
Outcome Importance	**Metric**	**Number of studies, PTTS**	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**PTTS**	**No PTTS**	**Relative (95% CI)**	**Absolute (95% CI)**	
Death **CRITICAL**	Death after PICU admission from ward/PICU admissions from ward	1 Modified Bristol PEW system[41]	observational studies	not serious	not serious	not serious	very serious[a]	publication bias strongly suspected[b]	17/157 (10.8)	14/166 (8.4)	**RR 1.28** (0.66 to 2.52)	**24 more per 1000** (from 29 fewer to 128 more)	⊕◯◯◯ VERY LOW
	Unexpected death on ward/ward patients	1 CEWT[29]	observational studies	not serious	not serious	not serious	very serious[a]	publication bias strongly suspected[b]	0/899 (0.0)	1/1059 (0.1)	not estimable	not estimable	⊕◯◯◯ VERY LOW
Cardiac arrest **CRITICAL**	Ward arrests/1000 patient days	1 C-CHEWS[27]	observational studies	not serious	not serious	not serious	serious[d]	publication bias strongly suspected[b]	6/12344 (0.5)	3/8115 (0.4)	**RR 1.32** (0.33 to 5.26)	**1 more per 1000** (from 2 fewer to 16 more)	⊕◯◯◯ VERY LOW
	Ward arrests/1000 patient days	1 PEW score I[49]	observational studies	serious[c]	not serious	not serious	serious[d]	publication bias strongly suspected[b]	0.12	0.61	not estimable	not estimable	⊕◯◯◯ VERY LOW
	Days between ward cardiac arrests	1 PEW score III[54]	observational studies	very serious[e]	not serious	not serious	serious[d]	publication bias strongly suspected[b]	1053	299	not estimable	not estimable	⊕◯◯◯ VERY LOW
Unplanned transfer to PICU **CRITICAL**	Invasive ventilation after unplanned PICU transfer/ Unplanned PICU transfers	1 Modified Bristol PEW system[41]	observational studies	not serious	not serious	not serious	very serious[a]	publication bias strongly suspected[b]	104/166 (62.7)	118/157 (75.2)	**RR 0.83** (0.72 to 0.97)	**128 fewer per 1000** (from 23 fewer to 210 fewer)	⊕◯◯◯ VERY LOW
	Unplanned transfer from ward to PICU/10,000 patient days	1 C-CHEWS[27]	observational studies	not serious	not serious	not serious	serious[d]	publication bias strongly suspected[b]	102/12344 (8.3)	66/8115 (8.1)	**RR 1.02** (0.75 to 1.38)	**1 more per 10,000** (from 3 fewer to 16 more)	⊕◯◯◯ VERY LOW
	Median days of invasive ventilation	1 Modified Bristol PEW system[41]	observational studies	not serious	not serious	not serious	not serious	publication bias strongly suspected[b]	2	4	not estimable	not estimable	⊕◯◯◯ VERY LOW

		Quality assessment							Events (n/1000)		Effect		Quality
Outcome Importance	Metric	Number of studies, PTTS	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	PTTS	No PTTS	Relative (95% CI)	Absolute (95% CI)	
	Inotropes after unplanned PICU transfer/Unplanned PICU transfers	1 Modified Bristol PEW system[41]	observational studies	not serious	not serious	not serious	very serious[a]	publication bias strongly suspected[b]	40/166 (24.1)	50/157 (31.8)	**RR 0.76** (0.53 to 1.08)	**76 fewer per 1000** (from 25 more to 150 fewer)	⊕◯◯◯ VERY LOW
	Median days of inotropes	1 Modified Bristol PEW system[41]	observational studies	not serious	not serious	not serious	very serious[a]	publication bias strongly suspected[b]	0	0	not estimable	not estimable	⊕◯◯◯ VERY LOW
	Median days of PICU stay	1 Modified Bristol PEW system[41]	observational studies	not serious	not serious	not serious	very serious[a]	publication bias strongly suspected[b]	3	5	not estimable	not estimable	⊕◯◯◯ VERY LOW
	Transfer to centre with PICU facilities* or death on ward /1000 patient days	1 Bedside PEW system[15]	observational studies	not serious	not serious	serious[f]	serious[d]	none	1/2350 (0.4)	2/842 (2.4)	**RR 0.18** (0.02 to 1.98)	**2 fewer per 1000** (from 2 fewer to 2 more)	⊕◯◯◯ VERY LOW
	Transfer to centre with PICU facilities* or death on ward /1000 patient days	1 Bedside PEW system[15]	observational studies	not serious	not serious	serious[f]	serious[d]	none	19/2350 (8.1)	5/842 (5.9)	**RR 1.36** (0.51 to 3.64)	**2 more per 1000** (from 3 fewer to 16 more)	⊕◯◯◯ VERY LOW
	Median PIM2 score	1 Modified Bristol PEW system[41]	observational studies	not serious	not serious	serious[g]	not serious	publication bias strongly suspected[b]	0.04	0.06	not estimable	not estimable	⊕◯◯◯ VERY LOW
Requirement for PICU and /or HDU **CRITICAL**	Unplanned transfer from ward to PICU or HDU/ward patients	1 CEWT[29]	observational studies	not serious	not serious	serious[f]	not serious	publication bias strongly suspected[b]	24/899 (2.7)	40/1059 (3.8)	**RR 0.71** (0.43 to 1.16)	**11 fewer per 1000** (from 3 fewer to 16 more)	⊕◯◯◯ VERY LOW
Call for emergency assistance **CRITICAL**	Code blue events/1000 patient days	1 TCH PAWS[64]	observational studies	very serious[c]	not serious	serious[h]	not serious	publication bias strongly suspected[b]	0.256	0.293	not estimable	not estimable	⊕◯◯◯ VERY LOW

		Quality assessment							Events (n/1000)		Effect		Quality
Outcome Importance	Metric	Number of studies, PTTS	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	PTTS	No PTTS	Relative (95% CI)	Absolute (95% CI)	
Call for urgent assistance **IMPORTANT**	Urgent call to paediatrician/ 1000 patient days	1 Bedside PEW system[15]	observational studies	not serious	not serious	serious[h]	serious[d]	none	12/2350 (5.1)	19/842 (22.6)	**RR 0.23** (0.11 to 0.47)	**17 fewer per 1000** (from 12 fewer to 20 fewer)	⊕◯◯◯ VERY LOW
	Urgent call to respiratory therapist/1000 patient days	1 Bedside PEW system[15]	observational studies	not serious	not serious	serious[h]	serious[d]	none	8/2350 (3.4)	8/842 (9.5)	**RR 0.36** (0.14 to 0.96)	**6 fewer per 1000** (from 0 fewer to 8 fewer)	⊕◯◯◯ VERY LOW
	RRS call /1000 patient days	1 TCH PAWS[64]	observational studies	very serious[c]	serious[i]	serious[h]	not serious	publication bias strongly suspected[b]	5.85	4.88	not estimable	not estimable	⊕◯◯◯ VERY LOW
	Call to RRS/ward patients	1 CEWT[29]	observational studies	not serious	serious[i]	serious[h]	not serious	publication bias strongly suspected[b]	5/899 (0.6)	4/1059 (0.4)	**RR 1.47** (0.40 to 5.47)	**2 more per 1000** (from 2 fewer to 17 more)	⊕◯◯◯ VERY LOW
	Call to RRS	1 PEW score I[49]	observational studies	serious[c]	serious[i]	serious[h]	very serious[a]	publication bias strongly suspected[b]	19.4% reduction in RRS activation after PTTS implementation				⊕◯◯◯ VERY LOW
Length of hospital stay **IMPORTANT**	Mean days in hospital	1 TCH PAWS[64]	observational studies	not serious	not serious	serious[k]	not serious	publication bias strongly suspected[b]	1.5	1.6	not estimable	not estimable	⊕◯◯◯ VERY LOW

Other considerations include risk of publication bias, dose-response gradient and large magnitude of effect.
Outcomes in shading are statistically significant.

*Transfer following invasive ventilation, > 60ml/kg fluid resuscitation, inotropes, CPR

Abbreviations: C-CHEWS: Cardiac Children's Hospital Early Warning Score; **CEWT:** Children's Early Warning Tool; **HDU** – High Dependency Unit; **PAWS**: Pediatric Advanced Warning Score; **PEW**: Paediatric/Pediatric Early Warning; **MET**: Medical Emergency Team; **MPEWS**: Modified Pediatric Early Warning Score; **PMET**: Pediatric Medical Emergency Team; **RRT**: Rapid Response Team; **TCH**: Texas Children's Hospital; **THSC:** Toronto Hospital for Sick Children; **PICU** – Paediatric Intensive Care Unit; **RR** – relative risk; **RRS** – Rapid Response System

a. Very low number of events and small sample size therefore results uncertain. Downgraded by 2
b. Single study of small sample size. Considering that PTTS are widely used, the possibility of publication bias is strongly suspected. Downgraded by 1.
c. Implementation study with retrospective data collection, poor definitions of outcome, and inadequate control and reporting of confounding. Downgraded by 1.
d. Low number of events and limited sample size, therefore results uncertain. Downgrade by 1
e. Implementation study with poor definition of outcomes, inadequate control of confounding measures and poor description of outcome measurement. Downgraded by 1.
f. Threshold to transfer to higher level of care can be influenced by numerous factors including capacity, physician preference, parental concern and nurse staffing on ward/ PICU. Therefore indirect measure of patient outcome but only warrants downgrading by 1.
g. Well validated surrogate outcome which is widely used to assess risk of death in PICU, therefore only downgraded by 1.
h. Urgent call to individual or emergency team can be influenced by many factors including nurse staffing levels, nurse skill mix and experience, ward culture, previous experience of emergency situations and training and education. Downgraded by 1.
i. Studies describing RRS calls demonstrated differing results with some demonstrating increasing calls and others decreasing calls. Downgraded by 1.
j. No statistical analysis or CI presented so high degree of uncertainty about the results. Downgraded by 2.
k. Length of stay can be influenced by non-patient factors such as nurse staffing, capacity, parental ability, and clinician subjective assessment. Therefore downgraded by 1.

Table 6: Evidence profile for PTTS as part of a package of interventions

		Quality assessment							Events (n/10,000)		Effect		Quality
Outcome, Importance	**Metric**	**№ of studies, PTTS**	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**PTTS as part of RRS**	**No RRS**	**Relative (95% CI)**	**Absolute (95% CI)**	
Death CRITICAL	Death on PICU following unplanned transfer from ward/all PICU patients	1 MET AC III[37]	observational studies	not serious	not serious	not serious	not serious	very strong association[b]	228/5753 (4.0)	266/4666 (5.7)	**RR 0.70** (0.59 to 0.83)	**171 fewer per 10,000** (from 97 fewer to 234 fewer)	⊕⊕⊕⊕ HIGH
	Death in hospital/10,000 admissions	4 NS[66] PMET triggers II[62] MET AC III[37] RRT AC [63]	observational studies	not serious	not serious	not serious	not serious	strong association[a]	1136/218970 (5.2)	1661/224736 (7.4)	**RR 0.64** (0.59 to 0.69)	**27 fewer per 10,000** (from 23 fewer to 30 fewer)	⊕⊕⊕◯ MODERATE
	Unexpected death on ward/10,000 admissions	3 MET AC II[36] NS[66] MET AC III[37]	observational studies	not serious	not serious	not serious	not serious	none	11/151327 (0.1)	37/129679 (0.3)	**RR 0.26** (0.13 to 0.50)	**2 fewer per 10,000** (from 1 fewer to 2 fewer)	⊕⊕◯◯ LOW
	Death within 24 hours of arrest/arrested patients	2 PMET triggers I[61] MET AC III[37]	observational studies	not serious	not serious	not serious	very serious[c]	none	2/12 (16.7)	18/36 (50.0)	**RR 0.50** (0.33 to 1.00)	**250 fewer per 1000** (from 0 fewer to 335 fewer)	⊕◯◯◯ VERY LOW
	Death in PICU following unplanned transfer from ward/PICU transfers from ward	4 PEW signs[57] MET AC I[32] Bedside PEW System[18] PMET triggers II[62]	observational studies	not serious	not serious	not serious	not serious	none	137/2146 (6.4)	210/2479 (8.5)	**RR 0.83** (0.68 to 1.02)	**144 fewer per 10,000** (from 17 more to 271 fewer)	⊕⊕◯◯ LOW

		Quality assessment							Events (n/10,000)		Effect		Quality
Outcome, Importance	**Metric**	**№ of studies, PTTS**	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**PTTS as part of RRS**	**No RRS**	**Relative (95% CI)**	**Absolute (95% CI)**	
	Death following PICU readmission within 48 hours/10,000 hospitals admissions	1 PMET triggers II[62]	observational studies	not serious	not serious	not serious	not serious	none	7/55963 (0.1)	16/55469 (0.3)	**RR 0.43** (0.18 to 1.05)	**2 fewer per 10,000** (from 0 fewer to 2 fewer)	⊕⊕◯◯ LOW
	Death during ward emergency or code/10,000 patient days	2 Bedside PEW System[18] MET AC II[36]	observational studies	not serious	not serious	not serious	not serious	none	2/230645 (0.0)	9/284541(0.0)	not estimable	not estimable	⊕⊕◯◯ LOW
Cardiac arrest CRITICAL	Cardiac arrest on ward/10,000 non-ICU admissions	3 MET AC II[36] NS[66] MET AC III[37]	observational studies	not serious	not serious	not serious	not serious	none	28/145574 (0.2)	40/125013 (0.3)	**RR 0.60** (0.37 to 0.97)	**1 fewer per 10,000** (from 0 fewer to 2 fewer)	⊕⊕◯◯ LOW
	Cardiac arrest on ward/10,000 non-ICU patient days	3 MET AC II[36] PMET triggers I[61] Bedside PEW System[18]	observational studies	not serious	not serious	not serious	not serious	none	9/280233 (0.0)	20/332934 (0.1)	**RR 0.85** (0.52 to 1.39)	**0 fewer per 10,000** (from 0 more to 0 fewer)	⊕⊕◯◯ LOW
	Cardiac arrest (ward and PICU)/10,000 hospital admissions	1 NS[66]	observational studies	not serious	not serious	not serious	not serious	none	15/5471 (2.7)	43/10576 (4.1)	**RR 0.67** (0.38 to 1.21)	**13 fewer per 10,000** (from 9 more to 25 fewer)	⊕⊕◯◯ LOW
Respiratory arrest CRITICAL	Ward intubation/10,000 patient days	1 PMET triggers I[61]	observational studies	not serious	not serious	not serious	not serious	none	3/49588 (0.1)	11/48393 (0.2)	**RR 0.27** (0.08 to 0.98)	**2 fewer per 10,000** (from 0 fewer to 2 fewer)	⊕⊕◯◯ LOW

		Quality assessment							Events (n/10,000)		Effect		Quality
Outcome, Importance	**Metric**	**№ of studies, PTTS**	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**PTTS as part of RRS**	**No RRS**	**Relative (95% CI)**	**Absolute (95% CI)**	
	Ward intubation/10,000 patient discharges	1 PMET triggers I[61]	observational studies	not serious	not serious	not serious	none	none	3/7503 (0.4)	11/7504 (1.5)	**RR 0.27** (0.71 to 0.98)	**11 fewer per 10,000** (from 0 fewer to 13 fewer)	⨁◯◯◯ VERY LOW
	Respiratory arrest on ward/10,000 patient days	1 MET AC II[36]	observational studies	not serious	not serious	not serious	not serious	none	4/52494 (0.1)	16/92188 (0.2)	**RR 0.44** (0.15 to 1.31)	**1 fewer per 10,000** (from 1 fewer to 1 more)	⨁⨁◯◯ LOW
	Ward intubation/10,000 non-ICU patient days	1 Bedside PEW System[18]	observational studies	not serious	not serious	not serious	not serious	none	0.12	0.09	not estimable	not estimable	⨁⨁◯◯ LOW
Cardiac and/or respiratory arrest CRITICAL	Arrest on ward/1000 non-ICU admissions	4 PEW signs[57] MET AC II[36] RRT AC[63] PMET triggers II[62]	observational studies	not serious	not serious	not serious	not serious	strong association[a]	89/68701 (1.3)	173/91644 (1.9)	**RR 0.69** (0.53 to 0.89)	**6 fewer per 10,000** (from 2 fewer to 9 fewer)	⨁⨁⨁◯ MODERATE
	Arrest on ward/10,000 discharges	2 PMET triggers I [61]NS [67]	observational studies	serious[d]	not serious	not serious	not serious	strong association[a]	68/19185 (3.5)	176/30065 (5.9)	**RR 0.61** (0.46 to 0.80)	**23 fewer per 10,000** (from 12 fewer to 32 fewer)	⨁⨁⨁◯ MODERATE
	Arrest on ward/10,000 patient days	3 MET AC II[36] PMET triggers I [61] RRT AC[63]	observational studies	not serious	not serious	not serious	not serious	none	19/136502 (0.1)	94/243118 (0.4)	**RR 0.36** (0.22 to 0.59)	**2 fewer per 10,000** (from 2 fewer to 3 fewer)	⨁⨁◯◯ LOW
Request for emergency assistance	Code blue call on ward/10,000 non-ICU patient days	1 Bedside PEW System[18]	observational studies	not serious	not serious	not serious	not serious	none	115/178151 (0.6)	102/192353 (0.5)	**RR 1.22** (0.93 to 1.59)	**1 more per 10,000** (from 0 fewer to 3 more)	⨁⨁◯◯ LOW

		Quality assessment							Events (n/10,000)		Effect		Quality
Outcome, Importance	**Metric**	**№ of studies, PTTS**	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**PTTS as part of RRS**	**No RRS**	**Relative (95% CI)**	**Absolute (95% CI)**	
CRITICAL Bonafide Kotsakis hunt	Code blue call on ward/10,000 hospital admissions	1 PMET triggers II[62]	observational studies	not serious	not serious	not serious	not serious	none	210/55469 (3.8)	150/55963 (2.7)	**RR 1.41** (1.15 to 1.74)	**11 more per 10,000** (from 4 fewer to 20 more)	⊕⊕◯◯ LOW
	Code blue call on ward/10,000 patient days	1 PMET triggers I[61]	observational studies	very serious[e]	not serious	not serious	not serious	none	88/49588 (1.8)	51/48393 (1.1)	**RR 1.68** (1.19 to 2.38)	**7 more per 10,000** (from 2 more to 15 more)	⊕◯◯◯ VERY LOW
Unplanned transfer to PICU CRITICAL	Unplanned transfers requiring vasopressors in first 1 hour/unplanned PICU admissions	1 Bedside PEW system[18]	observational studies	not serious	not serious	not serious	none	none	16/936 (1.7%)	41/874 (4.7%)	**RR 0.36** (0.21 to 0.65)	**30 fewer per 1000** (from 16 fewer to 37 fewer)	⊕◯◯◯ VERY LOW
	Unplanned ward transfers/ 10,000 admissions	2 PMET triggers II[62] MET AC I[32]	observational studies	not serious	not serious	not serious	not serious	none	1178/91855 (12.8)	1560/160249 (9.7)	**RR 1.32** (1.22 to 1.42)	**31 more per 10,000** (from 21 more to 41 more)	⊕⊕◯◯ LOW
	Unplanned ward transfers/10,000 non-PICU patient days	1 Bedside PEW system[18]	observational studies	not serious	not serious	not serious	not serious	none	936/178151 (5.3)	874/192353 (4.5)	**RR 1.16** (1.05 to 1.27)	**7 more per 10,000** (from 2 more to 12 more)	⊕⊕◯◯ LOW
	Unplanned readmissions from ward /10,000 admissions	1 PMET triggers II[62]	observational studies	not serious	not serious	not serious	not serious	none	200/55469 (3.6)	163/55963 (2.9)	**RR 1.24** (1.01 to 1.52)	**7 more per 10,000** (from 0 fewer to 15 more)	⊕⊕◯◯ LOW
	Critical deterioration events/10,000 non-PICU patient days)	1 Bedside PEW System[18]	observational studies	not serious	not serious	not serious	not serious	none	281/178151 (1.6)	260/192353 (1.4)	**RR 1.17** (0.99 to 1.38)	**2 fewer per 10,000** (from 0 fewer to 5 more)	⊕⊕◯◯ LOW
	Median PRISM III-12 score on admission	1 Bedside PEW System[18]	observational studies	not serious	not serious	not serious	not serious	none	0	2	not estimable	not estimable	⊕⊕◯◯ LOW

		Quality assessment						Events (n/10,000)		Effect		Quality
Outcome, Importance	**Metric**	**№ of studies, PTTS**	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**PTTS as part of RRS**	**No RRS**	**Relative (95% CI)**	**Absolute (95% CI)**	
	Unsafe transfer (intubation, vasoactive drugs or >3 fluid bolus prior to or within first hour in PICU)/10,000 non-PICU inpatient days	1 PEW score II[52]	observational studies	not serious	not serious	not serious	not serious	none	2.4	4.4	not estimable	not estimable	⨁⨁◯◯ LOW
	Unplanned transfers requiring vasopressors in first 12 hours/unplanned PICU admissions	1 Bedside PEW System[18]	observational studies	not serious	not serious	not serious	serious[f]	none	57/936 (6.1%)	71/874 (8.1%)	**RR 0.75** (0.54 to 1.05)	**20 fewer per 1000** (from 4 more to 37 fewer)	⨁◯◯◯ VERY LOW
	Unplanned ward transfers requiring mechanical ventilation in first 1 hour/unplanned PICU transfers	1 Bedside PEW System [18]	observational studies	not serious	not serious	not serious	serious[f]	none	42/936 (4.5%)	45/874 (5.1%)	**RR 0.87** (0.58 to 1.31)	**9 fewer per 1000** (from 13 more to 23 fewer)	⨁◯◯◯ VERY LOW
	Unplanned ward transfers requiring mechanical ventilation in first 12 hours/ unplanned PICU transfers	1 Bedside PEW System [18]	observational studies	not serious	not serious	not serious	serious[f]	none	103/936 (11.0%)	112/874 (12.8%)	**RR 0.86** (0.67 to 1.10)	**18 fewer per 1000** (from 13 more to 42 fewer)	⨁◯◯◯ VERY LOW

Abbreviations: AC: Activation criteria; **C-CHEWS:** Cardiac Children's Hospital Early Warning Score; **MET:** Medical Emergency Team; **MPEWS:** Modified Pediatric Early Warning Score; **NHSI:** NHS Institute; **NS:** Not specified; **PAWS:** Pediatric Advanced Warning Score; **PERT:** Pediatric Early Response Team; **PEW:** Paediatric/Pediatric Early Warning; **PICU** – Paediatric Intensive Care Unit, **PMET**: Pediatric Medical Emergency Team; **RR: R**elative risk; **RRT:** Rapid Response Team; **TCH:** Texas Children's Hospital; **THSC:** Toronto Hospital for Sick Children
Outcomes in shading are statistically significant

a. Large effect of relatively rare outcome. Upgraded by 1.
b. Very large effect of relatively rare outcome. Upgraded by 2.
c. Extremely small sample size. Downgraded by 1.
d. One study poorly reported the definition of arrest and both studies inadequately described the risk of confounding. Downgraded by 1.
e. Inadequate definition of code blue call, retrospective data collection, inadequate description of risk of confounding. Downgraded by 2
f. Small sample size. Downgraded by 1.

Table 7: Studies reporting predictive validity of PEWS

Paper	Design	Patients	Outcome measures	System	Score	Sensitivity % (95% CI)	Specificity % (95% CI)	AUROC (95% CI)
Olson[31]	Prospective nested case-control	54 cases, 161 controls	Death within 2 days	ITAT	≥ 4	44.0 *(31.3-58.5)*	86.0 *(79.1-90.5)*	0.76
Robson[17]	Retrospective case-controlled evaluation of 3 systems	96 cases, 96 controls	Actual or impending cardiopulmonary arrest (code blue)	Bedside PEW system	≥8	43.8 *(33.8-54.2)*	85.4 *(76.4-91.5)*	0.73
				Bristol PEW tool	≥1	76.3 *(66.0-83.9)*	61.5 *(50.9-71.1)*	0.75
				PEW system score I	≥5	86.6 *(77.6-92.3)*	72.9 *(62.7-81.2)*	0.85
Duncan[59]	Retrospective case control	87 cases 128 controls	Actual or impending cardiopulmonary arrest (code blue)	PEW system score I	≥5	78.0 *(67.8-86.0)*	95.0 *(88.6-97.6)*	0.9
Akre[55]	Retrospective, descriptive	186 cases	Code blue and/or RRS activation	PEW score IV	≥ 4	85.5 *(79.4-90.1)*		
Mandell[30]	Retrospective case-controlled	38 cases, 151 controls	Unplanned PICU readmission within 48 hours	CH LA PEWS	≥2	76	56	0.71
Parsharum 2011[16]	Prospective international multi-centre case-controlled	686 cases 1388 controls	Urgent PICU admission and/or immediate call to resuscitation team	Bedside PEW system	≥8	57.4 *(53.6-61.2)*	94.7 *(93.3-95.8)*	0.87 (0.85-0.89)
McLellan 2014a[24]	Retrospective cohort	64 cases (10 arrests, 54 PICU transfers), 248 controls	Unplanned PICU transfer or cardiopulmonary arrest	C-CHEWS	≥ 3	95.3	76.2	0.92
				PEW I	≥ 3	54.7 *(41.7-67.2)*	86.3 *(81.4-90.3)*	0.79
Fuijschot[19]	Retrospective cohort	24 cases	Unplanned PICU admission	Bedside PEWS	≥7	64	91	
				MPEWS III	≥8	67	88	
Skaletzky[42]	Retrospective case-controlled	100 cases, 250 controls	PICU admission	MPEWS I	2.5	62.0 *(51.7-71.4)*	89.2 *(84.5-92.6)*	0.81 (0.75-0.86)
Tucker[51]	Prospective, cohort	2979	PICU admission	PEW score II	≥3	90.2 *(77.8-96.3)*	74.4 *(72.8-75.9)*	0.89 (0.84-0.94)
Parshuram 2009[14]	Prospective case-controlled validation	60 case, 120 controls	Urgent PICU admission without code blue	Bedside PEW system	≥8	82 *(69.1-90.1)*	93 *(86.9-96.9)*	0.91 (0.86-0.96)
Agulnik[28]	Retrospective case-controlled	110 cases 220 controls	Unplanned admission to PICU	C-CHEWS	≥ 3	93.6 *(86.9-97.2)*	88.2 *(83.0-92.0)*	0.96 (0.93-0.98)
Gawronski[21]	Retrospective case-controlled	19 cases 80 controls	Unplanned PICU transfer, Urgent RRS consult or unexpected death on ward	Bedside PEW system	≥8	73.7 *(48.6-89.9)*	98.8 *(92.3-99.9)*	0.87
Tume 2007[23]	Retrospective cohort	33 cases (PICU) 32 cases (HDU)	Unplanned admission to PICU or HDU	Bristol PEW tool	≥ 1 (HDU)	84.4 *(66.5-94.1)*		
					≥ 1 (PICU)	87.9 *(70.9-96.0)*		

Paper	Design	Patients	Outcome measures	System	Score	Sensitivity % (95% CI)	Specificity % (95% CI)	AUROC (95% CI)
				MET activation criteria I	≥ 1 (HDU)	87.5 *(70.1-96.0)*		
					≥ 1 (PICU)	87.9 *(70.9-96.0)*		
Edwards 2009[26]	Prospective cohort	1000[1]	Adverse outcome (PICU/PHDU admission; respiratory/cardiac arrest*; death*)	Cardiff and Vale PEW system	≥2	*68.7 (41.5-87.9)*	*89.9 (87.9-91.7)*	0.86 (0.82-0.91)
Edwards 2011[34]	Retrospective cohort study	1000[1]	Adverse outcome (PICU/PHDU admission; death*)	MET activation criteria I	≥1	*68.3 (57.7-77.3)*	*83.2 (83.1-83.2)*	0.79 (0.73-0.84)
Mason [46]	Retrospective cohort study	1000[1]	Adverse outcome (PICU/PHDU admission; death*)	NHSI PEW system	≥2	*62.5 (35.9-83.7)*	*42.0 (38.9-45.1)*	0.83 (0.77-0.88)

One study[22] reported incorrect values for sensitivity and specificity and these have been eliminated from analysis.

Values in italics were not reported in the paper and have been calcuated using available data;.

[1]Published values were calculated based on the number of observations taken, rather than the number of patients and have re-calculated;

Key: * No respiratory/cardiac arrests or deaths occurred

Abbreviations: AUROC: Area Under Receiver Operating Characteristic Curve; **C-CHEWS**: Cardiac Children's Hospital Early Warning Score; **CI:** Confidence interval; **ITAT**: Inpatient triage, assessment and treatment score; **NHSI:** National Health Service Institute; **MET**: Medical Emergency Team; **MPEWS**: Modified Pediatric Early Warning Score; **PEW**: Paediatric/Pediatric Early Warning; **PHDU:** Paediatric High Dependency Unit; **PICU:** Paediatric Intensive Care Unit; **PMET**: Pediatric Medical Emergency Team **PPV:** positive predictive value; **QR**: Quality rating**; RRS:** Rapid Response System

Figure 1: Flow diagram