Available online at www.sciencedirect.com

Resuscitation Plus

journal homepage: www.elsevier.com/locate/resuscitation-plus

Review

Do paediatric early warning systems reduce mortality and critical deterioration events among children? A systematic review and meta-analysis

Shu-Ling Chong[a,b,], Mark Sen Liang Goh[c], Gene Yong-Kwang Ong[a,b], Jason Acworth[d,e], Rehena Sultana[f], Sarah Hui Wen Yao[a], Kee Chong Ng[a,b], for the International Liaison Committee on Resuscitation (ILCOR) and ILCOR Pediatric Life Support Task Force, Barney Scholefield[g], Richard Aickin[h], Ian Maconochie[g], Dianne Atkins[i], Thomaz Bittencourt Couto[j], Anne-Marie Guerguerian[k], Monica Kleinman[i], David Kloeck[l], Vinay Nadkarni[i], Gabrielle Nuthall[h], Amelia Reis[j], Antonio Rodriguez-Nunez[m], Steve Schexnayder[i], Janice Tijssen[k], Patrick Van de Voorde[n], Peter Morley[o]*

Abstract

Aim: We conducted a systematic review and meta-analysis to answer the question: Does the implementation of Paediatric Early Warning Systems (PEWS) in the hospital setting reduce mortality, cardiopulmonary arrests, unplanned codes and critical deterioration events among children, as compared to usual care without PEWS?

Methods: We conducted a comprehensive search using Medline, EMBASE, Cochrane Central Register of Controlled Trials, Cumulative Index to Nursing and Allied Health Literature and Web of Science. We included studies published between January 2006 and April 2022 on children <18 years old performed in inpatient units and emergency departments, and compared patient populations with PEWS to those without PEWS. We excluded studies without a comparator, case control studies, systematic reviews, and studies published in non-English languages. We employed a random effects meta-analysis and synthesised the risk and rate ratios from individual studies. We used the Scottish Intercollegiate Guidelines Network (SIGN) to appraise the risk of bias.

Results: Among 911 articles screened, 15 were included for descriptive analysis. Fourteen of the 15 studies were pre- versus post-implementation studies and one was a multi-centre cluster randomised controlled trial (RCT). Among 10 studies (580,604 hospital admissions) analysed for mortality, we found an increased risk (pooled RR 1.18, 95% CI 1.01–1.38, $p = 0.036$) in the group without PEWS compared to the group with PEWS. The sensitivity analysis performed without the RCT (436,065 hospital admissions) showed a non-significant relationship (pooled RR 1.17, 95% CI 0.98–1.40, $p = 0.087$). Among four studies (168,544 hospital admissions) analysed for unplanned code events, there was an increased risk in the group without PEWS (pooled RR 1.73, 95%CI 1.01–2.96, $p = 0.046$) There were no differences in the rate of cardiopulmonary arrests or critical deterioration events between groups. Our findings were limited by potential confounders and imprecision among included studies.

Conclusions: Healthcare systems that implemented PEWS were associated with reduced mortality and code rates. We recognise that these gains vary depending on resource availability and efferent response systems.

PROSPERO registration: CRD42021269579.

Keywords: Child, Early Warning Scores, Mortality, Resuscitation

* Corresponding author at: Department of Emergency Medicine, KK Women's and Children's Hospital, 100 Bukit Timah Road, Singapore 229899, Singapore.

E-mail addresses: Chong.Shu-Ling@kkh.com.sg (S.-L. Chong), mark.goh@mohh.com.sg (M.S.L. Goh), geneong@yahoo.com (G.Y.-K. Ong), jason.acworth@health.qld.gov.au (J. Acworth), rehena.sultana@duke-nus.edu.sg (R. Sultana), ng.kee.chong@singhealth.com.sg (K.C. Ng).

https://doi.org/10.1016/j.resplu.2022.100262

Received 3 May 2022; Received in revised form 2 June 2022; Accepted 5 June 2022

Contents

Introduction . . . 2
Methods . . . 2
Eligibility criteria . . . 3
Information sources . . . 3
Search strategy . . . 3
Study selection . . . 3
Data collection process and data items . . . 3
Risk of bias in individual studies . . . 3
Summary measures and synthesis of results . . . 3
Risk of bias across studies . . . 4
Certainty of evidence . . . 4
Results . . . 4
Study selection and study characteristics . . . 4
Risk of bias within studies . . . 5
Results of individual studies and synthesis of results . . . 5
Risk of bias across studies . . . 9
Certainty of evidence . . . 9
Discussion . . . 9
Limitations . . . 10
Conclusion . . . 10
Conflicts of Interest . . . 10
Funding . . . 10
Data sharing statement . . . 10
CRediT authorship contribution statement . . . 10
Appendix A. Supplementary material . . . 10
References . . . 10

Introduction

Paediatric Early Warning Systems (PEWS) were derived to meet the need for early and accurate identification of children at risk of clinical deterioration.[1] Published PEWS use a constellation of physiological criteria (including vital signs), clinical assessment findings, pre-existing medical conditions, and clinician or parental concerns.[2,3] Elevated scores are an early surrogate for cardiopulmonary collapse, and PEWS are reported to forewarn by up to 11 hours before actual deterioration.[3,4]

Intuitively, implementation of PEWS creates a formalised structure within healthcare systems that may detect early changes in clinical status. PEWS are a component of the "afferent" arm of a Rapid Response System that then informs and facilitates interventions performed by a rapid response team (RRT) or a paediatric medical emergency team (MET) (the "efferent" arm). Elevated PEWS were found to correlate with the severity of illness.[5] Adding PEWS to existing emergency department (ED) systems improved triage in 5 diverse EDs across 4 European countries.[6,7] Others reported that PEWS implementation resulted in good data capture and staff satisfaction.[8,9]

Others have questioned the true value of PEWS implementation for patient care. In a large validation study in the Netherlands, they found that none of the PEWS had high sensitivity and specificity.[10] Although elevated scores were associated with increased likelihood of paediatric intensive care unit (PICU) readmission, thresholds were not sufficiently sensitive nor specific to be clinically useful.[11] The Effect of a Pediatric Early Warning System on All-Cause Mortality in Hospitalized Pediatric Patients (EPOCH) Randomized Clinical Trial across 21 hospitals in 7 countries showed that implementing PEWS did not decrease all-cause mortality.[12]

The literature on effectiveness of PEWS varies in the location of PEWS implementation (general paediatric units, specific specialist wards or EDs), study populations (general paediatric versus specific subpopulations), associated interventions, as well as the choice of outcome measures.[13–15] The impact of PEWS on clinically-important patient-centric outcomes may be confounded by the presence of co-interventions present in many before-after study designs.[16] In addition, mortality as a critical outcome is rare, especially in resource-rich healthcare facilities. Assessment of PEWS effectiveness based on mortality may underestimate the benefits of PEWS in the overall care of acutely ill children.

In view of the above contention, we therefore sought to perform an updated systematic review and meta-analysis, from January 2006 to April 2022 to answer the question: Does the implementation of PEWS (with or without RRT/PMET) in the hospital setting reduce mortality, cardiopulmonary arrests, unplanned codes and critical deterioration events among children, as compared to usual care without PEWS?

Methods

This systematic review was registered with PROSPERO (CRD42021269579). We extended the duration of included studies,

initially from January 2011 to December 2020, to 2006 to April 2022 to present a comprehensive and updated review of the literature. All items were reported in accordance with the Preferred Reporting Items for Systematic Review and Meta-Analyses (PRISMA) guidelines.[17]

Eligibility criteria

We included all studies with children <18 years old performed in the inpatient units and EDs of paediatric hospitals but excluded outpatient clinics. We included studies published between January 2006 and April 2022 on the general paediatric population as well as those that focused on specific populations (e.g. oncology or cardiology units). We excluded patients >18 years and preterm infants. We compared patient populations among whom PEWS were implemented (intervention) to those among whom PEWS were *not* implemented (comparator). The implemented PEWS could include any formalised set of criteria to alert clinicians to potential deterioration. We excluded all studies that did not have a comparator group (no PEWS). For outcomes, we included: (1) mortality; (2) cardiopulmonary arrest; (3) unplanned code events; and (4) critical deterioration. We chose the specific outcomes of cardiopulmonary arrests and unplanned codes because these were individually measured and accounted for in the literature. Under critical deterioration, we included the following composite definition of significant clinical deterioration: (a) Unplanned/crash tracheal intubation; (b) Unanticipated fluid resuscitation and inotropic/vasopressor use; (c) Cardiopulmonary resuscitation (CPR) or Extracorporeal Membrane Oxygenation (ECMO); and (d) Death in patients (all-cause mortality) without a Do Not Resuscitate (DNR) order.[18] We also included unplanned or emergency admissions to Paediatric Intensive Care Unit (PICU) as these reflected the utilisation of critical care resources. For study designs, we included randomised controlled trials (RCTs) and non-randomised studies including before- and after- implementation studies. Case series, case control, systematic reviews, unpublished studies and studies published in non-English languages, were excluded.

Information sources

We included the following electronic databases: Medline, EMBASE, Cochrane Central Register of Controlled Trials, CINAHL (Cumulative Index to Nursing and Allied Health Literature) and Web of Science. To understand if there were concurrent similar systematic reviews being carried out, we searched the following: PROSPERO, ClinicalTrials.gov, International Standard Randomised Controlled Trial Number registry, WHO International Clinical Trials Registry Platform and EU Clinical Trials Register.

Search strategy

We drew up a comprehensive search strategy with inputs from a medical librarian as well as our clinical team. We used and exploded the Medical Subject Headings (MeSH) terms for Medline and Cochrane, and Emtree terms for EMBASE as appropriate for each term's tree. Their synonyms were included in the title, abstract and keyword searches. We performed the search on 26th June 2021 and updated the search on 18th May 2022. We provided the search terms for each electronic database (Supplementary Table 1). We hand-searched the bibliography of systematic reviews, as well as publications that we included, to ensure that our literature search was comprehensive.

Study selection

We uploaded the studies from the search strategy to Covidence, an internet-based software that facilitates collaboration between study team members during the study selection process.[19] SLC, MGSL, GOYG, JA, SYHW, and KCN performed screening in both phases. In the first phase, we screened the studies' titles and abstracts for relevance. In the second phase, we applied the eligibility criteria (as detailed above). At both stages, two reviewers independently screened the articles. Any conflicts were resolved by a third independent reviewer. The study team was not blinded to the study authors nor the institutions where the research was performed. For the meta-analysis, we included all studies that provided quantitative measures of the prior mentioned outcomes in both the intervention arm (PEWS) and the comparator arm (no PEWS). We excluded studies with an unacceptable risk of bias (refer Risk of Bias in individual studies) from the meta-analysis.

Data collection process and data items

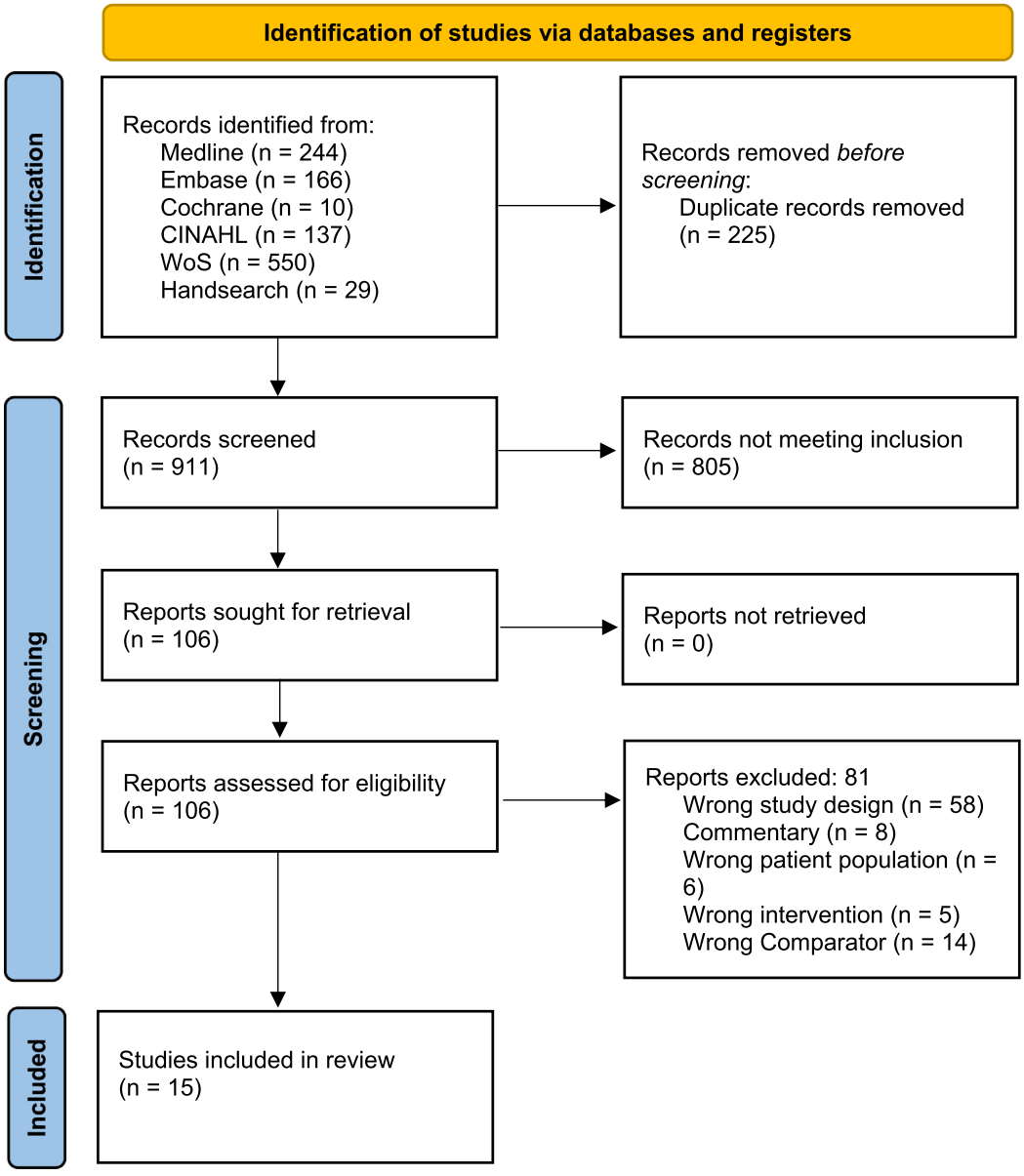
Two independent reviewers extracted the data independently using a Microsoft Excel form, with variables determined a priori. SLC and MGSL piloted the data collection form first and refined the variables before SLC, MGSL, GOYG, JA, SYHW and KCN performed the extraction. We extracted the following: Study title, first author, year of publication, number of centres, country/countries involved, study design, and the study population. We also specified the PEWS used in the study, activation criteria, and the response arm (e.g. RRT or MET). For outcomes, we collected data on mortality, cardiopulmonary arrest, unplanned code events, and critical deterioration. Critical deterioration was a composite outcome that included significant clinical deterioration events (refer Eligibility criteria),[18] emergency or unplanned PICU admissions as defined by the authors. Where there was insufficient information, we aimed to contact the original study investigators for the required data, and follow-up in two weeks with another email for non-responders. If there was still no response after four weeks, we considered them un-contactable.

Risk of bias in individual studies

We used the Scottish Intercollegiate Guidelines Network (SIGN) to appraise the risk of bias in each study. [20] We assessed for risk of bias at both the study and the outcome level. Checklists were used depending on the study design (e.g. cohort or randomised controlled trial). Overall assessment ranged from unacceptable (0) to high quality (++). Two independent reviewers (GOYK and JA) assessed each article and differences were resolved by consensus.

Summary measures and synthesis of results

Extracted data were combined in a two-stage meta-analysis approach. In the first step, incidence rate rations (IRR) with their 95% confidence intervals (CI) were estimated from individual studies reporting patient-days such as number of deaths per 1000 patient-days. Likewise, risk ratios (RR) with 95% CI were estimated from individual studies reporting binary outcome data such as number of cardiac arrests in a hospital during a specific time period. In the second stage, a restricted Maximum Likelihood (REML) random effects meta-analysis was employed to combine RRs and IRRs from individual studies. Pooled results were reported as RR with 95% CI. Statistical heterogeneity was quantified using the I^2 statistic for analyses.[21] I^2 values >75% was considered as considerable amount of heterogeneity. We performed a sensitivity analysis by study design, pooling



CINAHL = Cumulative Index to Nursing and Allied Health Literature, WoS = Web of Science

Fig. 1 – Flowchart of studies selected for analysis.

all studies at first regardless of study design and then only for the observational studies (thereby excluding the RCT). Meta-analysis results were presented in forest plot.

Risk of bias across studies

Publication bias was explored using visual inspection of the funnel plot, and Begg & Mazumdar's test was carried out to check the statistical symmetry of the funnel plot.[22]

Certainty of evidence

We performed the certainty assessment using GRADE. This assessment was based on the study design, risk of bias, inconsistency, indirectness, imprecision and other considerations.[23]

All analyses were conducted using Comprehensive Meta Analysis V5 and SAS 9.4 software.

Results

Study selection and study characteristics

Among a total of 911 articles screened, 106 articles were assessed for eligibility and 15 were included for descriptive analysis.[12,18,32–36,24–31] (Fig. 1) Articles were published between 2007 and 2018, mostly in the United States (7/15), followed by Australia (2/15) and Canada (2/15) (Table 1). Fourteen of the 15 studies were pre- versus post-implementation studies with either prospective or retrospective controls, and one study was a multi-centre cluster randomised trial in multiple countries (Belgium, Canada, England, Ireland, Italy, New Zealand and Netherlands).[12] The other multi-centre study of four sites in Canada compared post-implementation of PEWS to historical controls.[30] The majority of the studies were performed in the general paediatric population,

Table 1 – Description of studies included in the Systematic Review.

First Author	No. of sites	Country (s)	Study Design	Study Population
Brilli, 2007	1	United States	Cohort study (prospective post-implementation data compared with historical controls)	General
Sharek, 2007	1	United States	Cohort study (prospective post-implementation data compared with historical controls)	General
Hunt, 2008	1	United States	Prospective cohort study pre- and post-implementation	General
Tibballs, 2009	1	Australia	Cohort study (prospective post-implementation data compared with historical controls)	General
Anwar-ul-Haque, 2010	1	Pakistan	Retrospective cohort study pre- and post-implementation	General
Hanson, 2010	1	United States	Interrupted time series with historical controls	General
Kotsakis, 2011	4	Canada	Cohort study (prospective post-implementation data compared with historical controls)	General
Parshuram, 2011	1	Canada	Prospective cohort study pre- and post-implementation	General
McKay, 2013	1	Australia	Prospective cohort study pre- and post-implementation	General
Bonafide, 2014	1	United States	Interrupted time series with historical controls	General
Sefton, 2014	1	United Kingdom	Cohort study (Clinical audit/Evaluation of prospectively collected data)	General
Douglas, 2016	1	United States	Retrospective cohort study pre- and post-implementation	General
Agulnik, 2017	1	Guatemala	Retrospective cohort study pre- and post-implementation	Oncology
Kroeger, 2018	1	United States	Retrospective chart review pre- and post- implementation of pre-transfer PEWS score (prior to transfer out of ICU)	Cardiology
Parshuram, 2018	21	Belgium, Canada, England, Ireland, Italy, New Zealand, Netherlands	Multi-centre cluster randomized trial	General

with one in a paediatric cardiology unit and one in a paediatric oncology hospital (Table 1).

Studies used a wide range of PEWS and modified PEWS that spanned vital signs, clinical deterioration signs, biochemical abnormalities, and staff or parental concerns (Table 2). While most studies involved an efferent arm consisting of either a RRT or MET in response to trigger criteria, others reported implementing staff training and modified escalation as part of their centres' PEWS-related interventions. In the only RCT included in this systematic review, the efferent arm remained status quo as per the existing system in each hospital.[12]

Risk of bias within studies

We had methodological concerns regarding the comparability between the groups with PEWS versus no PEWS being investigated in pre- and post- implementation designs. Efforts to minimise bias and confounding were mostly absent, with some studies recognising potential confounding from concurrent quality improvement initiatives and co-interventions.[18,25–27,29,30,32,33,35] There was no effort to blind the investigators who evaluated outcome data from the exposure (PEWS versus no PEWS), although there was recognition that knowledge of exposure status could have influenced the assessment of outcome.[27] The single RCT was not blinded.[12] The observational studies assumed patients in each arm had complete outcome data. Of the 15 studies, three studies were assigned an unacceptable risk of bias (RoB 0) and were excluded from the subsequent synthesis of results (Supplementary Table 2).

Results of individual studies and synthesis of results

Among 10 studies (580,604 hospital admissions) analysed for mortality, the group without PEWS was associated with a higher risk of mortality, compared to the group with PEWS (pooled RR 1.18, 95% CI 1.01–1.38, $p = 0.036$) (Fig. 2) There was significant heterogeneity across studies ($I^2 = 63.5\%$). The sensitivity analysis performed after removing the single RCT (436,065 hospital admissions) showed a non-significant relationship (pooled RR 1.17, 95% CI 0.98–1.40, $p = 0.087$, $I^2 = 67.5\%$) (Fig. 3).

One of the 10 studies reported a significantly increased risk of mortality in the group without PEWS, compared to the group with PEWS (RR 1.52, 95% 1.33–1.74, $p < 0.001$).[27] This study utilised paediatric MET trigger criteria that were adapted from adult criteria with the addition of age-related abnormal readings (Table 2). Along with activation criteria, this study introduced a MET service after three months of extensive training for doctors and nurses.

Among six studies (413,370 hospital admissions) that reported the outcome of cardiopulmonary arrests, none of the studies demonstrated a significant difference with the introduction of PEWS. Overall, the risk of cardiopulmonary arrest without the implementation of PEWS was similar to the group with PEWS (pooled RR 1.22, 95% CI 0.93–1.59, $p = 0.153$, $I^2 = 0.0\%$) (Fig. 4).

For the outcome of unplanned code events reported in four studies (168,544 hospital admissions), there was a significant increase in the risk of codes in the group without PEWS compared to the group with PEWS (pooled RR 1.73, 95%CI 1.01–2.96, $p = 0.046$, I^2 51.5%) (Supplementary Fig. 1). Two studies reported an increased risk without PEWS. One study reported an increased risk of hospital-wide

Table 2 – Paediatric Early Warning Scores and presence of rapid response team (RRT) or Medical Emergency Team (MET).

First Author	Name the PEWS used in the study (self-derived vs validated tool)	Activation criteria	Describe the Intervention	If RRT/PMET: Composition of RRT/PMET
Brilli, 2007	Self-derived MET trigger criteria	Vital signs, increased work of breathing, agitation or decreased consciousness, staff or parental concern	MET	PICU fellow, PICU nurse, senior paediatric resident, respiratory therapist, manager of patient services
Sharek, 2007	Criteria to activate the RRT were similar to Tibballs et al. [38] and Brilli et al.	Vital signs, acute change in level of consciousness, staff concern	RRT	Physician (paediatric ICU attending physician or fellow), experienced paediatric ICU or cardiovascular ICU nurse, an ICU-trained respiratory therapist, and a nursing supervisor
Hunt, 2008	Self-derived MET trigger criteria	Vital signs, respiratory distress, seizures with apnoea, change in mental status, dysrhythmias, cardiopulmonary arrest, staff or parental concern	MET	PICU fellow, PICU nurse, PICU respiratory therapist, nursing shift coordinator, senior assistant resident, junior assistant resident, intern, paediatric pharmacist, security officer and hospital chaplain
Tibballs, 2009	Pediatric MET calling criteria were adapted from adult MET calling criteria with the addition of age-related abnormal readings	Vital signs, cardiopulmonary arrest, seizures, staff or parental concerns	MET	Initially: ICU Physician (consultant/ registrar), nurse, ED doctor and nurse + medical registrar; subsequently after 6 months ED nurse withdrew
Anwar-ul-Haque, 2010	PEWS	Vital signs, laboured breathing, decrease in consciousness, seizures, staff concerns	RRT	PICU physicians and primary team
Hanson, 2010	Published antecedents and antecedents identified in chart reviews of local cardiac arrests were used to develop activation criteria	Vital signs, changes in respiratory pattern or mental status, repeat or prolonged seizures, staff concerns	MET	Paediatric critical care fellow, resident, critical care nurse and respiratory therapist
Kotsakis, 2011	Paediatric MET Triggers published by Tibballs et al. [38]	Vital signs, acute drop in GCS by more than 2 points, seizures, staff or parental concerns	MET	PICU physician (PICU attending and fellow/resident during the day and a PICU fellow/resident overnight with attending backup), critical care nurse, and a respiratory therapist.
Parshuram, 2011	Bedside PEWS	Vital signs	Staff re-training	
McKay, 2013	PEWS were age-specific scores adapted from the scoring system used at Great Ormond Street Hospital, London (based on PEWS from -Morgan R, Williams F, Wright M. An early warning scoring system for detecting developing critical illness. Clin. Intensive Care 1997; 8: 100.))	Vital signs	Newly designed ward observation chart, staff training, escalation to senior	2 tier response: First for bedside nurse to contact child's primary admitting team to review child. Failure to respond to escalate seniority of MO contacted; MET system continued to be the other formal medical response
Bonafide, 2014	Parshuram and colleagues' Bedside PEWS (Pashuram 2011)	Vital signs	MET	(1) a fellow, attending, or nurse practitioner, (2) a nurse (3) a respiratory therapist

Table 2 (continued)

First Author	Name the PEWS used in the study (self-derived vs validated tool)	Activation criteria	Describe the Intervention	If RRT/PMET: Composition of RRT/PMET
Sefton, 2014	Modified Bristol Paediatric Early Warning	Vital signs, biochemistry, unresolved pain staff concerns	Primary/on-call medical/surgical team with a target response of 'within 10 minutes' for airway trigger and 'within 30 minutes' for all other triggers	Existing medical/surgical teams and on call team, ICU consultant as needed
Douglas, 2016	Adaptation of the Brighton PEWS by Akre et al	Vitals, lethargy or confusion, staff or parental concern	RRT	PICU Registered Nurse, Respiratory therapist, PICU resident or Nursing Practitioner
Agulnik, 2017	Modified PEWS adapted from Boston Children's Hospital tool and algorithm	Vitals, neurological deterioration, cardiac dysrhythmia	Staff training + modified escalation	Floor oncologist and PICU physician (same as prior to PEWS implementation)
Kroeger, 2018	Modified Vanderbilt Children's Hospital Pediatric Early Warning core (modified from the validated Brighton score)	Vital signs, neurological deterioration	Nursing PEWS - PEWS score is recorded by the ward nursing staff on arrival to the acute care floor	N/A - used front line staff
Parshuram, 2018	Bedside PEWS	Vital signs	Escalation for immediate review	(If available) Part of existing system in each hospital

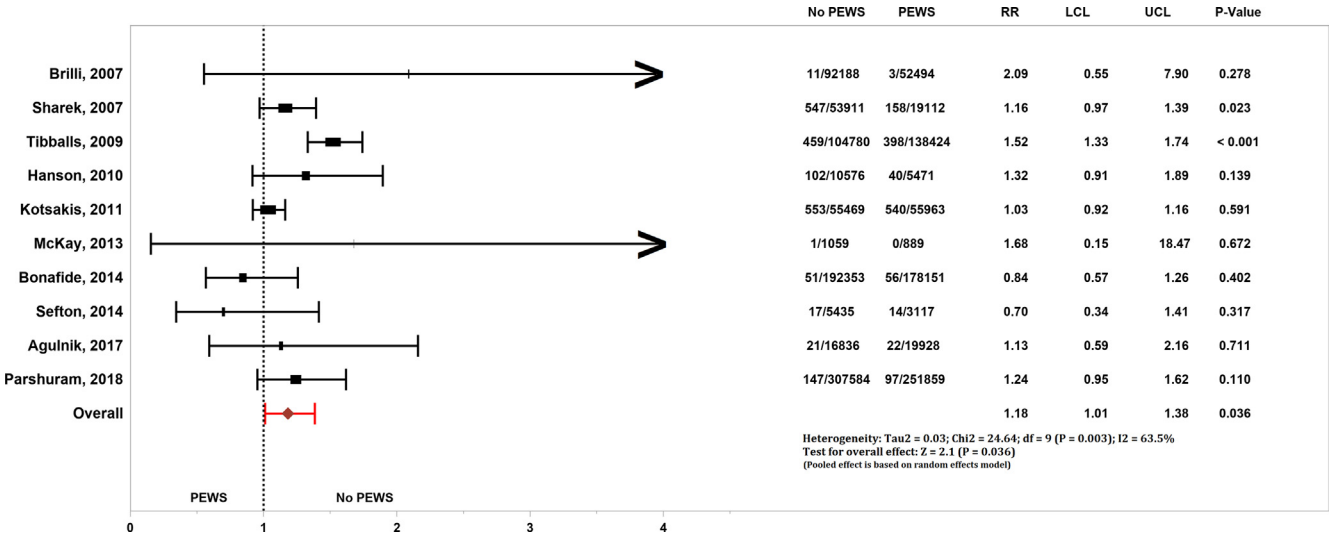


Fig. 2 – Analysis for outcome of Mortality (all included studies).

code rates without PEWS (RR 3.56, 95% CI 1.43–8.84, $p = 0.006$) that decreased after introducing PEWS and RRT.[25] The other study introduced activation criteria as part of a rapid response system, and found increased likelihood of codes without PEWS, but no increased risk of mortality or actual cardiopulmonary arrests.[30]

Among six studies (156,031 hospital admissions) analysed for critical deterioration, there was no significant increased risk among those without PEWS compared to those with PEWS (pooled RR 1.21, 95% CI 0.90–1.62, $p = 0.199$, $I^2 = 84.2\%$) (Fig. 5). The sensitivity analysis performed after the RCT was removed (11,492 hospital admissions) similarly yielded no significant relationship (Supplementary Fig. 2). Two studies reported an increased risk of critical deterioration in the group without PEWS compared to the group with PEWS. The first was a study performed in a resource-limited paediatric oncology hospital in Guatemala and reported increased risk of deterioration events resulting in unplanned PICU admissions for the group without PEWS (RR 1.43, 95% CI 1.13–1.82, $p = 0.003$). After the successful implementation of PEWS, the authors went on to find that PICU utilisation for inpatient transfers decreased significantly.[35] The second was a multi-centre cluster RCT across multiple countries that found a significantly higher risk of clinical deterioration in the group without PEWS compared to the group with PEWS (RR 1.67, 95% CI 1.34–2.08, $p < 0.001$). Each participating hospital kept their existing practice of RRT or MET.

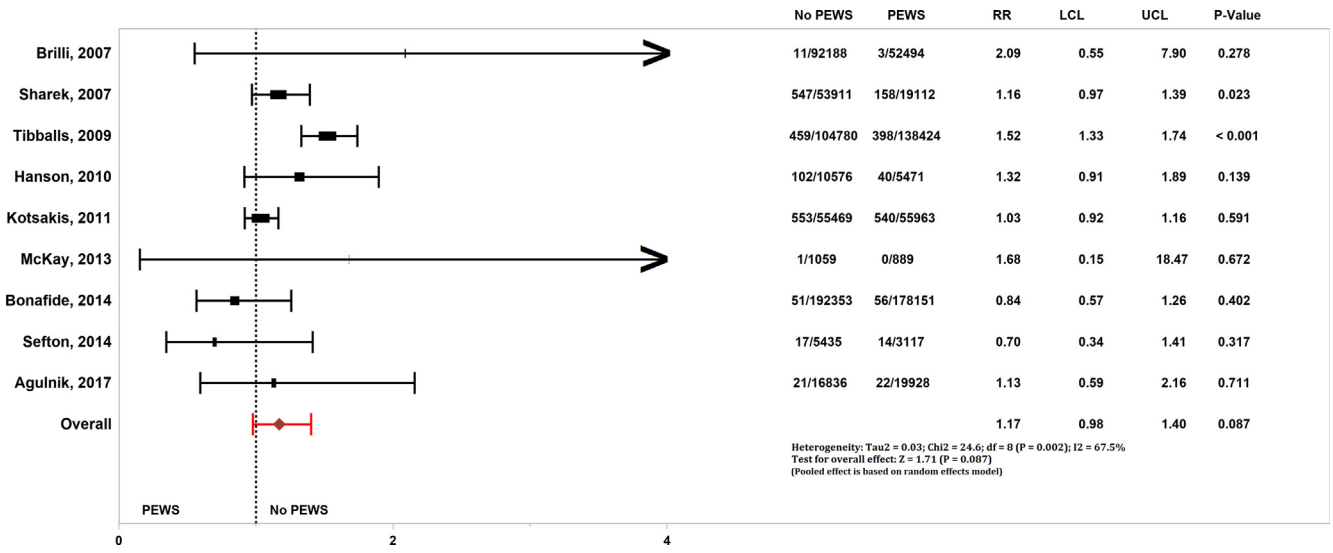


Fig. 3 – Sensitivity Analysis for outcome of Mortality (observational studies only).

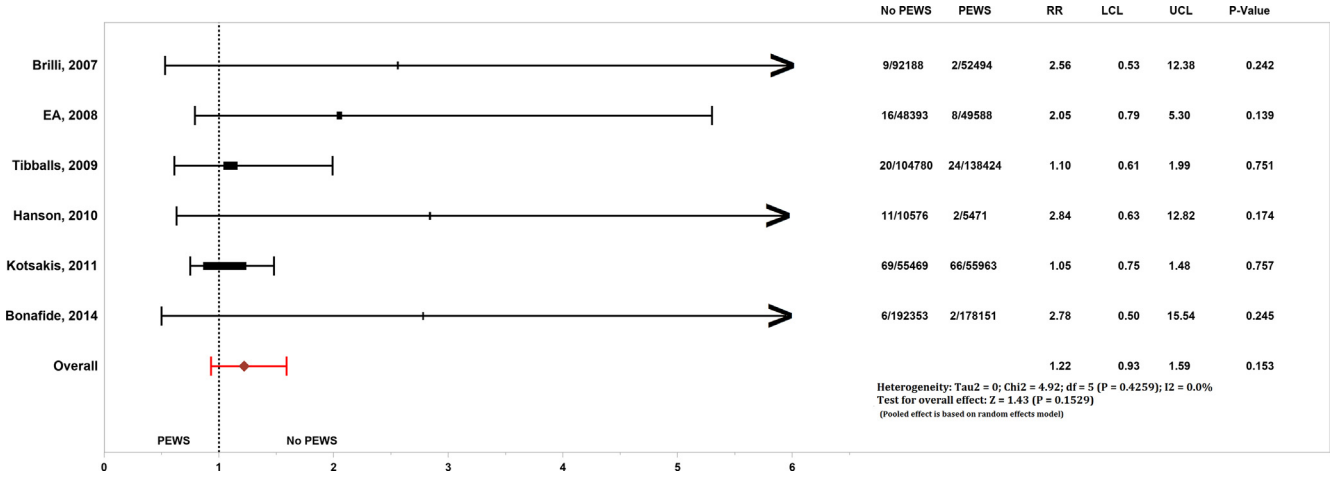


Fig. 4 – Analysis for outcome of Cardiopulmonary Arrest.

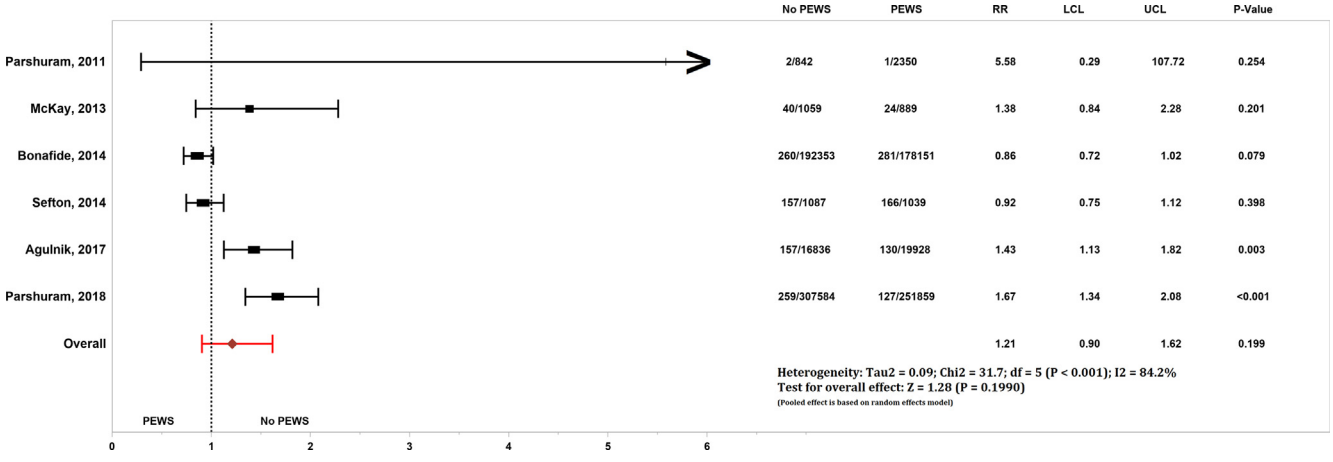


Fig. 5 – Analysis for outcome of Critical Deterioration.

Risk of bias across studies

We did not detect evidence of significant publication bias in the 4 outcome measures using funnel plots, and Begg and Mazumdar's test (Supplementary Figs. 3–6).

Certainty of evidence

We found the certainty of evidence to be very low for all four outcomes chosen, given the serious risk of bias and imprecision for the cohort studies included in this systematic review and meta-analysis (Supplementary Table 3).

Discussion

We performed a systematic review and meta-analysis to compare clinical outcomes between patient populations with PEWS compared to those without. In populations without PEWS, we found an increased risk of mortality (pooled RR 1.18, 95% CI 1.01–1.38, p = 0.036) and unplanned code events (pooled RR 1.73, 95% CI 1.01–2.96, p = 0.046). The finding of increased mortality in the group without PEWS was not consistent when we performed a sensitivity analysis on cohort studies alone. Implementation of PEWS was not associated with a change in the rate or proportion of cardiopulmonary arrests (pooled RR 1.22, 95% CI 0.93–1.59, p = 0.153) or critical deterioration events (pooled RR 1.21, 95%CI 0.90–1.62, p = 0.199).

An earlier systematic review published in 2017 looked at the effectiveness of PEWS for detecting clinical deterioration, effectiveness of PEWS response mechanisms and evidence for PEWS implementation strategies.[37] They found gains in early clinical interventions and potential improvements in patient safety through multidisciplinary coordination and teamwork but reported a lack of standardised outcomes to enable robust comparison between studies.[37] The authors also concluded that diversity in these scoring systems (with different weightage to physiological parameters, clinical findings and thresholds for action) made it difficult to compare the performance of PEWS between studies. We recognise that these differences in PEWS components and thresholds will continue to exist as various PEWS are derived from different patient populations, and between countries and centres with different human and technology resource availability. Therefore, we sought to perform a pragmatic systematic review to understand if the incorporation of PEWS with or without RRT/MET improved clinical outcomes irrespective of healthcare resource availability.

Most studies on PEWS have focused on validation of each respective tool, and a recent systematic review highlighted that some paediatric track and trigger tools (PTTT) have good diagnostic accuracy, primarily in the prediction of PICU transfers.[13] The same authors reported methodological concerns precluding recommendations on effectiveness of PEWS. They included studies that involved inpatients 0–18 years old, with outcome measures of mortality, critical events including unplanned admission to a higher level of care, cardiac arrest, respiratory arrest, medical emergencies requiring immediate assistance, acuity at PICU admission and PICU outcomes. In contrast, we chose to narrow our search to include only studies that actually implemented PEWS in their healthcare settings and had a comparator arm ("No PEWS"). We also limited the outcomes to those of mortality, cardiopulmonary arrest, unplanned code events and critical deterioration. These specifications allowed us to focus on the impact of PEWS within systems that had already implemented PEWS and allowed us to study commonly-used outcomes that improved comparability.

We recognise that the difference in outcomes reported among studies could firstly be attributed to variation in patient population. Sharek et al reported a reduction in both mortality and code rates in a quaternary care children's hospital setting.[25] The authors recognised that their hospital serves children at high-risk for codes due to a high case mix, and demonstrated higher pre-intervention code rates compared to other centres.[25] Conversely, others with a relatively low rate of paediatric cardiac arrest postulate that the low incidence might itself lend to difficulty demonstrating a significant reduction of such events.[38]

Secondly, various PEWS differ in composition of physiological criteria and trigger thresholds.[39] Many of these are either locally derived and internally validated, or modified from the published literature with external validation.[40] The concept of a universally-generalisable PEWS is challenged by the fact that data-driven models reporting good accuracy are site-specific.[41] This means that each healthcare setting that seeks to implement PEWS must first and foremost have the capability for robust validation of these scores within their own populations.[40] Given the complexity of PEWS implementation, resource-limited settings may modify scores to ensure compliance and sustainability.[42] Some predictive scores are specialty-specific scores, which may have better performance within those patient populations compared to PEWS derived from the generic paediatric population.[43] These variations could have accounted for the heterogeneity seen in our study.

We propose that the robustness and timeliness of the RRT/MET response is another important contributory factor to the heterogeneity seen. An accurate PEWS can facilitate early interventions provided there are successful implementation strategies in place. These should ensure that resuscitation occurs when the patients are clinically unstable but not yet pulseless, resulting in downstream gains. Tibballs et al demonstrated not only a reduction in preventable cardiac arrest, but also in survival from unexpected cardiac arrest on the wards, after the introduction of a MET service.[27] In another study, despite no significant reduction in mortality, the introduction of PEWS paired with a clinical response system resulted in a reduction in invasive ventilation among PICU admissions and shorter PICU stay.[33]

In view of the low incidence of death and cardiopulmonary arrests, proximal outcomes like that of significant clinical deterioration events have been used to surrogate for late PICU admissions. Nevertheless, in the multi-centre RCT that found a significant decrease in significant clinical deterioration events, they did not find any impact on rates of cardiac arrest, urgent ICU admission, mortality after urgent ICU admission, risk-adjusted ICU mortality, or PICU resource use.[12] The authors recognised that late PICU admissions may constitute a minor proportion of overall PICU admissions and that such savings may not modify overall mortality or PICU resource use.

Aside from the outcomes chosen in our study, other benefits of PEWS implementation must be considered. These include improved communication between healthcare workers and changes to safety culture.[24,43] Adoption and maintenance of PEWS within the larger inter-disciplinary context provides opportunity to iteratively improve processes and upscale health technologies.[44,45] The implementation of a standardised system may also serve to eliminate variations in care, streamline interventions and provide opportunities to investigate "missed" cases of deterioration that are potentially actionable.[46] The PUMA (Paediatric early warning system Utilisation and Morbidity Avoidance) Programme is one such framework that pro-

vides not only the PEWS tools but also guidance on implementation to support improvement initiatives.[47]

We recognise that while we did not demonstrate a clear superiority among systems that implemented PEWS in reducing death, cardiopulmonary arrest or critical deterioration events, the absence of a demonstrable effect does not necessarily preclude the implementation of PEWS as part of a clinical response system that will enhance early recognition and intervention in the deteriorating child. Future research should focus on prospective evaluation of PEWS with clear documentation of the efferent arm interventions for patients at risk of decompensation from specific aetiologies including primary respiratory, circulatory or neurologic causes.[48]

Limitations

We recognise that there are inherent limitations to the study designs employed by most of the studies. Regardless of prospective or historical controls, a pre- and post-implementation comparison is fraught by confounding, not least by the impact of improved quality of care with the passage of time. Therefore, it was not possible to establish causality between the implementation of PEWS and improved outcomes in many of these studies. Moreover, the introduction of PEWS would have resulted in hospital-wide education of physicians, nurses and allied health staff, and it was not possible to measure improvements in outcomes attributed to each of these factors.[27] Implementation of PEWS is complex, requiring adherence to protocols, effective communication and, overall, a motivated culture. We were unable to account for these in our systematic review. Finally, we acknowledge that not all cardiopulmonary arrests are the same, and that within this group some are more preventable than others.[26] By grouping all the cardiopulmonary arrest outcomes together, we potentially diluted the impact that PEWS implementation would have on these events.

Conclusion

We detected reductions in mortality and code rates among healthcare systems that implemented PEWS. We recognise that gains in clinical outcomes are dependent on healthcare setting, resource availability, and presence of robust efferent response systems.

Conflicts of Interest

There are no known conflicts of interest.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Data sharing statement

Data are available on reasonable request, directed to the Corresponding author.

We would also like to thank Ms Peggy Fong Bih Yuh from KK Women's and Children's Hospital library for her assistance in the literature search.

CRediT authorship contribution statement

Shu-Ling Chong: Conceptualization, Methodology, Investigation, Data curation, Validation, Writing – original draft, Writing – review & editing. **Mark Goh Sen Liang:** Conceptualization, Methodology, Investigation, Data curation, Validation, Writing – review & editing. **Gene Ong Yong-Kwang:** Conceptualization, Methodology, Data curation, Validation, Writing – review & editing. **Jason Acworth:** Conceptualization, Methodology, Data curation, Validation, Writing – review & editing. **Rehena Sultana:** Conceptualization, Formal analysis, Writing – review & editing. **Sarah Yao Hui Wen:** Conceptualization, Methodology, Data curation, Writing – review & editing. **Kee Chong Ng:** Conceptualization, Methodology, Data curation, Validation, Writing – review & editing, Supervision. **Barney Scholefield:** . **Richard Aickin:** . **Ian Maconochie:** . **Dianne Atkins:** . **Thomaz Bittencourt Couto:** . **Anne-Marie Guerguerian:** . **Monica Kleinman:** . **David Kloeck:** . **Vinay Nadkarni:** . **Gabrielle Nuthall:** . **Amelia Reis:** . **Antonio Rodriguez-Nunez:** . **Steve Schexnayder:** . **Janice Tijssen:** . **Patrick Van de Voorde:** . **Peter Morley:** .

Appendix A. Supplementary material

Supplementary data to this article can be found online at https://doi.org/10.1016/j.resplu.2022.100262.

Author details

for the International Liaison Committee on Resuscitation (ILCOR) and ILCOR Pediatric Life Support Task Force [a]*Department of Emergency Medicine, KK Women's and Children's Hospital, Singapore 100, Bukit Timah Road, Singapore 229899, Singapore* [b]*Duke-NUS Medical School, Singapore 8 College Road, Singapore 169857, Singapore* [c]*Department of Internal Medicine, National University Hospital System, Singapore 5 Lower Kent Ridge Road, Singapore 119074, Singapore*[d]*Emergency Department, Queensland Children's Hospital, Australia 501 Stanley St, South Brisbane, QLD 4101, Australia* [e]*Faculty of Medicine, University of Queensland, St Lucia, QLD 4072, Australia* [f]*Centre of Quantitative Medicine, Duke-NUS Medical School, Singapore 8 College Road, Singapore 169857, Singapore* [g]*United Kingdom* [h]*New Zealand* [i]*United States* [j]*Brazil* [k]*Canada* [l]*South Africa* [m]*Spain* [n]*Belgium* [o]*Australia*

REFERENCES

1. Roland D. Paediatric early warning scores: Holy Grail and Achilles' heel. Arch Dis Child Educ Pract Ed 2012;97:208–15.
2. Sandell JM, Maconochie IK. Paediatric early warning systems (PEWS) in the ED. Emerg Med J 2016;33:754–5.
3. Solevåg AL, Eggen EH, Schröder J, Nakstad B. Use of a modified pediatric early warning score in a department of pediatric and adolescent medicine. PLoS One 2013;8:e72534.

4. Akre M, Finkelstein M, Erickson M, Liu M, Vanderbilt L, Billman G. Sensitivity of the pediatric early warning score to identify patient deterioration. Pediatrics 2010;125:e763–9.
5. Brown SR, Martinez Garcia D, Agulnik A. Scoping Review of Pediatric Early Warning Systems (PEWS) in Resource-Limited and Humanitarian Settings. Front Pediatr 2018;6:410.
6. Zachariasse JM, Espina PR, Borensztajn DM, et al. Improving triage for children with comorbidity using the ED-PEWS: an observational study. Arch Dis Child 2021. https://doi.org/10.1136/archdischild-2021-322068.
7. Zachariasse JM, Nieboer D, Maconochie IK, et al. Development and validation of a Paediatric Early Warning Score for use in the emergency department: a multicentre study. Lancet Child Adolesc Heal 2020;4:583–91.
8. Gold DL, Mihalov LK, Cohen DM. Evaluating the Pediatric Early Warning Score (PEWS) system for admitted patients in the pediatric emergency department. Acad Emerg Med Off J Soc Acad Emerg Med 2014;21:1249–56.
9. McElroy T, Swartz EN, Hassani K, et al. Implementation study of a 5-component pediatric early warning system (PEWS) in an emergency department in British Columbia, Canada, to inform provincial scale up. BMC Emerg Med 2019;19:74.
10. Seiger N, Maconochie I, Oostenbrink R, Moll HA. Validity of different pediatric early warning scores in the emergency department. Pediatrics 2013;132:e841–50.
11. Mandell IM, Bynum F, Marshall L, Bart R, Gold JI, Rubin S. Pediatric Early Warning Score and unplanned readmission to the pediatric intensive care unit. J Crit Care 2015;30:1090–5.
12. Parshuram CS, Dryden-Palmer K, Farrell C, et al. Effect of a pediatric early warning system on all-cause mortality in Hospitalized pediatric patients: The epoch randomized clinical trial. JAMA – J Am Med Assoc 2018;319:1002–12.
13. Trubey R, Huang C, Lugg-Widger FV, et al. Validity and effectiveness of paediatric early warning systems and track and trigger tools for identifying and reducing clinical deterioration in hospitalised children: A systematic review. BMJ Open 2019;9:e022105.
14. Chapman SM, Wray J, Oulton K, Pagel C, Ray S, Peters MJ. "The Score Matters": wide variations in predictive performance of 18 paediatric track and trigger systems. Arch Dis Child 2017;102:487–95.
15. Wee BYH, Lee JH, Mok YH, Chong S-L. A narrative review of heart rate and variability in sepsis. Ann Transl Med 2020;8:768.
16. Joffe AR, Anton NR, Burkholder SC. Reduction in hospital mortality over time in a hospital without a pediatric medical emergency team: Limitations of before-and-after study designs. Arch Pediatr Adolesc Med 2011;165:419–23.
17. Moher D, Liberati A, Tetzlaff J, Altman DG. Preferred reporting items for systematic reviews and meta-analyses: The PRISMA statement. BMJ 2009;339:b2535.
18. Parshuram CS, Bayliss A, Reimer J, Middaugh K, Blanchard N. Implementing the Bedside Paediatric Early Warning System in a community hospital: A prospective observational study. Paediatr Child Health 2011;16:e18–22.
19. Veritas Health Innovation. Covidence systematic review software. Covidence. www.covidence.org. Published 2019.
20. Scottish Intercollegiate Guidelines Network. SIGN Checklists. https://www.sign.ac.uk/what-we-do/methodology/checklists/. Accessed November 1, 2021.
21. Higgins JPT, Thompson SG. Quantifying heterogeneity in a meta-analysis. Stat Med 2002;21:1539–58.
22. Begg CB, Mazumdar M. Operating characteristics of a rank correlation test for publication bias. Biometrics 1994;50:1088–101.
23. Schunermann H, Brozek J, Guyatt G, Oxman A. GRADE Handbook. https://gdt.gradepro.org/app/handbook/handbook.html. Published 2013.
24. Brilli RJ, Gibson R, Luria JW, et al. Implementation of a medical emergency team in a large pediatric teaching hospital prevents respiratory and cardiopulmonary arrests outside the intensive care unit. Pediatr Crit Care Med 2007;8:236–46.
25. Sharek PJ, Parast LM, Leong K, et al. Effect of a rapid response team on hospital-wide mortality and code rates outside the ICU in a Children's Hospital. JAMA 2007;298:2267–74.
26. Hunt EA, Zimmer KP, Rinke ML, et al. Transition from a traditional code team to a medical emergency team and categorization of cardiopulmonary arrests in a children's center. Arch Pediatr Adolesc Med 2008;162:117–22.
27. Tibballs J, Kinney S. Reduction of hospital mortality and of preventable cardiac arrest and death on introduction of a pediatric medical emergency team. Pediatr Crit Care Med 2009;10:306–12.
28. Anwar-ul-Haque SAF, Zaidi S, Haider SR. Experience of pediatric rapid response team in a tertiary care hospital in Pakistan. Indian J Pediatr 2010;77:273–6.
29. Hanson CC, Randolph GD, Erickson JA, et al. A reduction in cardiac arrests and duration of clinical instability after implementation of a paediatric rapid response system. Postgrad Med J 2010;86:314–8.
30. Kotsakis A, Lobos A-T, Parshuram C, et al. Implementation of a multicenter rapid response system in pediatric academic hospitals is effective. Pediatrics 2011;128:72–8.
31. McKay H, Mitchell IA, Sinn K, et al. Effect of a multifaceted intervention on documentation of vital signs and staff communication regarding deteriorating paediatric patients. J Paediatr Child Health 2013;49:48–56.
32. Bonafide CP, Localio AR, Roberts KE, Nadkarni VM, Weirich CM, Keren R. Impact of rapid response system implementation on critical deterioration events in children. JAMA Pediatr 2014;168:25–33.
33. Sefton G, McGrath C, Tume L, Lane S, Lisboa PJG, Carrol ED. What impact did a Paediatric Early Warning system have on emergency admissions to the paediatric intensive care unit? An observational cohort study. Intensive Crit Care Nurs 2015;31:91–9.
34. Douglas K, Collado JC, Keller S. Implementation of a Pediatric Early Warning Scoring System at an Academic Medical Center. Crit Care Nurs Q 2016;39:363–70.
35. Agulnik A, Mora Robles LN, Forbes PW, et al. Improved outcomes after successful implementation of a pediatric early warning system (PEWS) in a resource-limited pediatric oncology hospital. Cancer 2017;123:2965–74.
36. Kroeger AR, Morrison J, Smith AH. Predicting unplanned readmissions to a pediatric cardiac intensive care unit using predischarge Pediatric Early Warning Scores. Congenit Heart Dis 2018;13:98–104.
37. Lambert V, Matthews A, MacDonell R, Fitzsimons J. Paediatric early warning systems for detecting and responding to clinical deterioration in children: a systematic review. BMJ Open 2017;7:e014497.
38. Tibballs J, Kinney S, Duke T, Oakley E, Hennessy M. Reduction of paediatric in-patient cardiac arrest and death with a medical emergency team: preliminary results. Arch Dis Child 2005;90:1148–52.
39. Chapman SM, Maconochie IK. Early warning scores in paediatrics: an overview. Arch Dis Child 2019;104:395–9.
40. van Sambeeck SJ, Fuijkschot J, Kramer BW, Vos GD. Pediatric Early Warning System Scores: Lessons to be Learned. J Pediatr intensive care 2018;7:27–32.
41. Fu L-H, Schwartz J, Moy A, et al. Development and validation of early warning score system: A systematic literature review. J Biomed Inform 2020;105:103410.
42. Rosman SL, Karangwa V, Law M, Monuteaux MC, Briscoe CD, McCall N. Provisional Validation of a Pediatric Early Warning Score for Resource-Limited Settings. Pediatrics 2019;143:e20183657.
43. Downey CL, Tahir W, Randell R, Brown JM, Jayne DG. Strengths and limitations of early warning scores: A systematic review and narrative synthesis. Int J Nurs Stud 2017;76:106–19.
44. Duncan H, Hudson AP. Implementation of a paediatric early warning system as a complex health technology intervention. Arch Dis Child 2021;106:215–8.