

BMJ Open Performance of universal early warning scores in different patient subgroups and clinical settings: a systematic review

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ABSTRACT

Objective To assess predictive performance of universal early warning scores (EWS) in disease subgroups and clinical settings.

Design Systematic review.

Data sources Medline, CINAHL, Embase and Cochrane database of systematic reviews from 1997 to 2019.

Inclusion criteria Randomised trials and observational studies of internal or external validation of EWS to predict deterioration (mortality, intensive care unit (ICU) transfer and cardiac arrest) in disease subgroups or clinical settings.

Results We identified 770 studies, of which 103 were included. Study designs and methods were inconsistent, with significant risk of bias (high: n=16 and unclear: n=64 and low risk: n=28). There were only two randomised trials. There was a high degree of heterogeneity in all subgroups and in national early warning score ($I^2=72\%$ – 99%). Predictive accuracy (mean area under the curve; 95% CI) was highest in medical (0.74; 0.74 to 0.75) and surgical (0.77; 0.75 to 0.80) settings and respiratory diseases (0.77; 0.75 to 0.80). Few studies evaluated EWS in specific diseases, for example, cardiology (n=1) and respiratory (n=7). Mortality and ICU transfer were most frequently studied outcomes, and cardiac arrest was least examined (n=8). Integration with electronic health records was uncommon (n=9).

Conclusion Methodology and quality of validation studies of EWS are insufficient to recommend their use in all diseases and all clinical settings despite good performance of EWS in some subgroups. There is urgent need for consistency in methods and study design, following consensus guidelines for predictive risk scores. Further research should consider specific diseases and settings, using electronic health record data, prior to large-scale implementation.

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INTRODUCTION

Across diseases, patient deterioration can range from critical care review and sepsis to cardiorespiratory arrest and death.^{1,2} Delays or failures in timely detection of deterioration adversely affect prognosis, morbidity, mortality and healthcare utilisation.³ For example, the 20 000 in-hospital cardiac arrests

Strengths and limitations of this study

- The first systematic review to investigate the performance of early warning scores (EWS) in different patient disease subgroups and clinical settings.
- Meta-analysis was performed for different EWS and national EWS validation studies in different disease and clinical setting subgroups.
- This study is limited to specific diseases and settings and does not consider the use of EWS in the general population.
- Analysis of predictive accuracy of EWS is based on area under the curve, not other validation measures.
- During the study period 1997–2019, approaches to EWS and their validation have changed.

per year in England are associated with costs of £50 million for resuscitation and postarrest care.⁴ Around the world, earlier recognition and prevention of deterioration in unwell patients has far-reaching implications for reduction in mortality and morbidity, reduction in the cost of healthcare and allocation of scarce high dependency and critical care resources. Preventive interventions are needed to overcome these challenges.⁵

Specific characteristics have long been known to be associated with deteriorating patient health,^{2,5–8} including physiological parameters, such as heart rate and blood pressure.^{5,9–12} Early warning scores (EWS), widely used in high-income countries, were borne out of the need for early detection of patient deterioration. EWS are tools derived from prediction models that assess patient characteristics and physiological parameters to stratify the risk of developing a worsening event or need for medical attention.¹³ The algorithms underlying EWS can be ‘aggregate-weighted’ to sum up a set of parameters to produce a score or use more advanced statistical modelling.¹⁴ EWS inform clinical decision making, enabling escalation of attention and care when required. Universal tools, such

Box 1 Definitions

- Universal early warning scores (EWS): EWS that are globally adopted and applicable in every setting and for any disease subgroup.
- Standardised EWS: EWS model with a set of parameters used in a unified approach to predict deterioration in any patient subgroup.^{8 23}
- External validation: evaluation of the model's predictive accuracy with data different than the one used for model development.²⁷
- Internal validation: evaluation of a model's predictive accuracy with the same data set used for the development or in a population in which the model is intended for use.²⁷
- Discrimination: the ability of a model to distinguish between the patients who will develop an outcome of interest and the ones who will not.²⁶
- Calibration: the accuracy of risk estimates in relation to the observed number of events.⁷³

as the modified early warning score (MEWS),¹⁵ were developed for use across different hospital settings, but specialised, non-standard EWS are also designed for particular subgroups, for example, Rapid Emergency Medicine Score¹⁶ and Quick Sequential Organ Failure Assessment (qSOFA)¹⁷ for patients with infections. In recognising different settings, EWS may have compromised simplicity and timeliness of assessment.¹³ For example, a number of EWS rely on parameters that do not exist in the first hours of assessment, such as blood investigations and imaging.^{1 18 19}

From fragmented implementation and inadequate early assessment via specialised tools, EWS have shifted back to universal prediction models, particularly, the national early warning score (NEWS),²⁰ followed by NEWS2.²¹ NEWS was designed to produce a universal assessment of acute illness severity across the National Health Service (NHS).²² While showing good discrimination compared with other EWS, especially in predicting mortality, there was a need to accommodate additional clinical parameters in the score. The updated NEWS2, emphasising appropriate scoring for type 2 respiratory failure, confusion and severe sepsis,²¹ was formally endorsed by NHS England²³ to be the EWS used in acute care. However, there have been concerns regarding excessive calls to clinicians, administrative workload and variable symptoms across diseases and settings.²⁴ The effectiveness of the universal EWS (box 1) with standardised use across all settings is not clear in specific disease populations²⁵ and requires validation to estimate discrimination and calibration, like other clinical prediction models.²⁶ While internal validation is useful, generalisability and reproducibility needs external validation.²⁷

Systematic reviews have evaluated EWS in prehospital, intensive care unit (ICU) and general settings,^{3 28 29} and sepsis,¹⁵ with narrow inclusion criteria and inadequate assessment of study quality. A recent systematic review evaluated development and validation of EWS in general

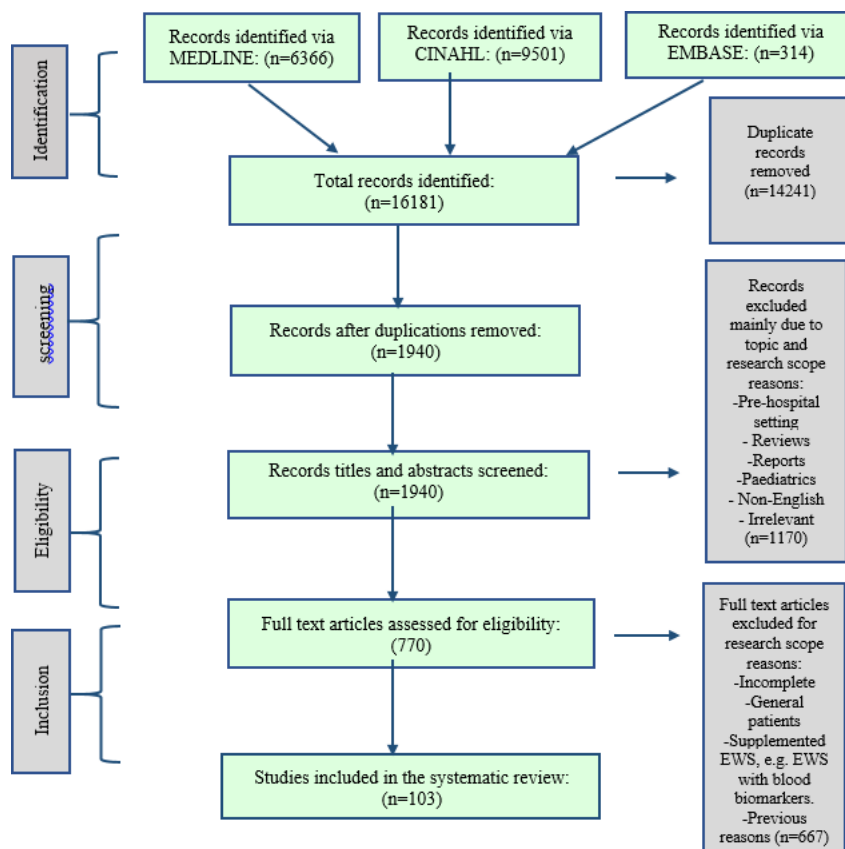


Figure 1 Search strategy and included studies regarding universal early warning scores (EWS) in different disease subgroups and clinical settings.

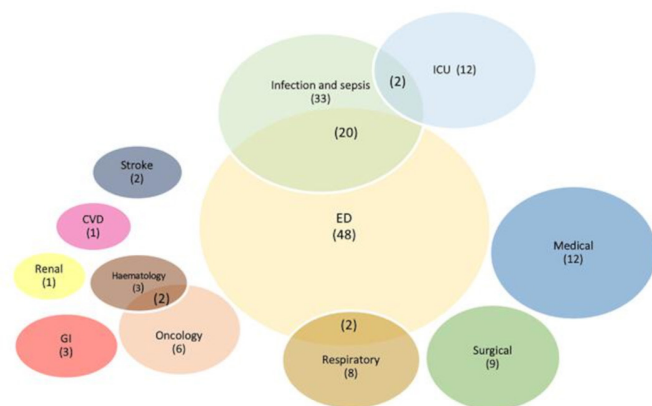


Figure 2 Number of studies regarding performance of early warning scores in different disease subgroups and clinical settings. Each bubble represents the disease subgroup and/or setting where different early warning scores were examined. The size of the bubble represents the number of studies (n), and overlapping bubbles show studies where disease subgroup and settings overlap. CVD, cardiovascular diseases; ED, emergency department; GI, gastrointestinal diseases; ICU, intensive care unit.

patients but did not include studies in specific disease subgroups or settings.³⁰

OBJECTIVE

In a systematic review, we will assess performance of universal EWS in particular diseases and clinical settings in predicting mortality, transfer to ICU and cardiac arrest.

METHODS

Search strategy

The protocol adhered to Preferred Reporting Items for Systematic Review and Meta-Analysis Protocols guidelines.³¹ Published articles were identified in MEDLINE, CINAHL and Embase, between 1997 (initial development of EWS) and 2019. The Cochrane database was searched for systematic reviews (CDSR) and trials (CENTRAL). For grey literature, Google Scholar was searched. During the screening procedure, studies were added from references in review articles and studies. Search strategies were developed by two authors (BA and AB) and reviewed by a third author (TB). Terms used for searching databases include terms for early warning or track and trigger scores and acronyms, identified subgroups and settings (eg, Medical Subject Heading (MeSH)) and free-text search terms (figure 1; online supplemental methods).

Inclusion and exclusion criteria

Patient subgroups were identified according to disease categories and clinical settings (online supplemental methods). Studies were included if: (1) validation of a universal EWS with standardised prediction model in adult patients; (2) EWS validation was in a specific setting or disease; (3) the performance of the EWS, or the impact on mortality, transfer to ITU and cardiac arrest, was

examined; and (4) they were prospective or retrospective cohort, cross-sectional, case-control design or trials.

Studies were excluded if: (1) patients were less than 16 years of age; (2) EWS performance was only examined in derivation, not validation; (3) non-universal EWS was developed for a specific subgroup, for example, obstetric early warning score for obstetric patients or qSOFA for patients with infections; or (4) EWS validation was performed in a general patient dataset or setting, for example, validation in a general hospital without consideration of hospital subgroups.

Data extraction

Articles were screened by title and abstract by one author (BA), then full-text screening was by two reviewers (BA and AB). Data were extracted independently by two reviewers (BA and AB) using a standardised and piloted data form. A third reviewer (TB) resolved any disagreements. Items for extraction for studies examining predictive accuracy were based on the CHARMS³² checklist, except for tool derivation, which was excluded.

Quality assessment

Risk of biases in validation studies was assessed using Prediction model Risk Of Bias ASsessment Tool (PROBAST),³³ which classifies studies as low, unclear or high risk of bias in four aspects: participant selection, predictors, outcomes and analysis within the overall risk of bias and the study applicability domains.

Evidence synthesis

We conducted the analysis using MS Excel and R programs. We summarised the results using descriptive statistics and graphical plots. Meta-analysis was performed, in different subgroups, using area under the curve (AUC) for identified universal EWS and for NEWS in studies. Fisher-Z transformation for correlation coefficients was conducted for AUC into normally distributed Z with 95% CI to evaluate the effect size and test for the heterogeneity. Where applicable, narrative synthesis was conducted.

Patient and public involvement

Patients or the public were not involved in the design, or conduct, or reporting, or dissemination plans of our research.

RESULTS

Study characteristics

Of the 16181 articles identified by our search, we screened 1355 articles by title and abstract, assessing 770 articles in full for eligibility. We included 103 studies, published between 2006 and 2019, in the final stage. These studies were predominantly observational (retrospective=65, prospective=36 and RCT=2). Emergency department (ED) (n=48) was the most common clinical setting, followed by medical (n=12), ICU (n=12) and surgical (n=9) settings. Sepsis (n=33) was the most common disease subgroup. Other subgroups ranged

Table 1 Studysetting and design for included studies of predictive performance for early warning scores in patient subgroups and settings

Author, year	Country	Subgroups										Settings				Study design				Case- control patients
		CVD	GI	Haematology	Renal	Stroke	Oncology	Respiratory	Infection/ sepsis	ICU	ED	Surgical	Medical	Retrospective	Prospective	RCT				
Kellet, 2012 ⁴⁶	Canada	●	○	○	●	●	●	○	○	●	●	●	●	○	○	○	10007			
Kim, 2017	Korea	○	●	○	○	○	○	○	○	○	○	○	●	○	○	○	2172			
Bozkurt, 2015	Turkey	○	●	○	○	○	○	○	○	○	○	○	○	●	○	○	202			
Seak, 2017	Taiwan	○	●	○	○	○	○	○	○	○	○	○	●	○	○	○	66			
Hu, 2016 ⁶⁶	USA	○	○	●	○	○	●	○	○	○	○	○	●	○	○	○	565			
Lijehult, 2016 ⁵³	Denmark	○	○	○	○	●	○	○	○	○	○	○	●	○	○	○	274			
Mulligan,2010 ⁶⁰	UK	○	○	●	○	○	○	○	○	○	○	○	○	●	○	○	71			
Cooksley, 2012 ⁶¹	UK	○	○	○	○	○	●	○	○	○	○	○	●	○	○	○	840			
Vaughn, 2018 ³⁹	USA	○	○	○	○	○	●	○	○	○	○	○	●	○	○	○	504			
Young, 2014	USA	○	○	●	○	○	●	○	○	○	○	○	●	○	○	○	61			
Von, 2007	UK	○	○	○	○	○	●	○	○	○	○	○	●	○	○	○	43			
Pedersen, 2018	Denmark	○	○	○	○	○	○	●	○	○	○	○	●	○	○	○	11266			
Forster, 2018	UK	○	○	○	○	○	○	●	○	○	○	○	●	○	○	○	8812			
Pimentel, 2018 ⁴¹	UK	○	○	○	○	○	○	●	○	○	○	○	●	○	○	○	1394			
Sbiti-Rohr, 2016 ⁵²	Switzerland	○	○	○	○	○	○	●	○	○	○	○	○	○	○	●	925			
Brabrand, 2017	Denmark	○	○	○	○	○	○	●	○	○	○	●	○	●	○	○	570			
Jo, 2016	Korea	○	○	○	○	○	○	●	○	○	○	○	●	○	○	○	553			
Barlow, 2007	UK	○	○	○	○	○	○	●	○	○	○	○	○	●	○	○	419			
Bilben, 2016 ⁵⁵	Norway	○	○	○	○	○	○	●	○	○	○	○	○	●	○	○	246			
Delahanty, 2019	USA	○	○	○	○	○	○	○	●	○	○	○	●	○	○	○	920026			
Redfern, 2018	UK	○	○	○	○	○	○	○	●	○	○	○	●	○	○	○	241996			
Churpek, 2017 ³⁵	USA	○	○	○	○	○	○	○	●	○	○	○	○	●	○	○	53849			
Faisal, 2019	UK	○	○	○	○	○	○	○	●	○	○	○	●	○	○	○	36161			
Churpek,2017 ³⁵	USA	○	○	○	○	○	○	○	●	○	○	○	○	●	○	○	18523			
Henry, 2015 ⁴⁰	USA	○	○	○	○	○	○	○	●	○	○	○	●	○	○	○	13014			
Brink,2019 ⁵⁴	TheNetherlands	○	○	○	○	○	○	○	●	○	○	○	●	○	○	○	8204			
De groot, 2017	TheNetherlands	○	○	○	○	○	○	○	○	○	○	○	○	○	○	○	2280			
Corfield, 2014	UK	○	○	○	○	○	○	○	○	○	○	○	○	○	○	○	2003			
Goulden, 2018 ⁵⁶	UK	○	○	○	○	○	○	○	○	○	○	○	○	○	○	○	1818			
Khwannimit, 2019 ³⁸	Thailand	○	○	○	○	○	○	○	○	○	○	○	○	○	○	○	1589			
Ghanem-oubi, 2011 ⁶³	Israel	○	○	○	○	○	○	○	○	○	○	○	○	○	○	○	1072			

Continued

Table 1 Continued

Author, year	Country	Subgroups							Settings				Study design				Case-control patients	
		CVD	GI	Haematology	Renal	Stroke	Oncology	Respiratory	Infection/sepsis	ICU	ED	Surgical	Medical	Retrospective	Prospective	RCT		
Saeed, 2019	UK, France, Italy, Sweden & Spain	○	○	○	○	○	○	○	●	○	●	○	○	●	○	○	○	1058
Innocenti, 2018 ⁶⁵	Italy	○	○	○	○	○	○	○	●	○	○	○	○	●	○	○	○	742
Camm, 2018	UK	○	○	○	○	○	○	○	●	○	●	○	○	●	○	○	○	533
Tirotta, 2017	Italy	○	○	○	○	○	○	○	●	○	○	○	○	○	●	○	○	526
Pong, 2019	Malaysia	○	○	○	○	○	○	○	●	○	●	○	○	●	○	○	○	364
Prabhakar, 2019	Malaysia	○	○	○	○	○	○	○	●	○	●	○	○	●	○	○	○	343
Martino, 2018	Italy	○	○	○	○	○	○	○	●	○	●	○	○	●	○	○	○	310
Vorwerk, 2009 ¹⁹	UK	○	○	○	○	○	○	○	●	○	●	○	○	●	○	○	○	308
Qin, 2017 ⁵¹	China	○	○	○	○	○	○	○	●	○	●	○	○	●	○	○	○	292
Schmedding, 2019	Gabon	○	○	○	○	○	○	○	●	○	●	○	○	○	●	○	○	277
Albur, 2016 ⁶⁴	UK	○	○	○	○	○	○	○	●	○	○	○	○	○	●	○	○	245
çildir, 2013 ³⁶	Turkey	○	○	○	○	○	○	○	●	○	●	○	○	○	●	○	○	230
Chiew, 2019 ⁵⁴	Malaysia	○	○	○	○	○	○	○	●	○	●	○	○	●	○	○	○	214
Samsudin, 2018	Malaysia	○	○	○	○	○	○	○	●	○	●	○	○	●	○	○	○	214
Chang, 2018	China	○	○	○	○	○	○	○	●	○	●	○	○	●	○	○	○	152
Geier, 2013	Germany	○	○	○	○	○	○	○	●	○	●	○	○	○	●	○	○	151
Asimwe, 2015	Uganda	○	○	○	○	○	○	○	●	○	○	○	○	○	●	○	○	150
Hung, 2017	Taiwan	○	○	○	○	○	○	○	●	○	●	○	○	●	○	○	○	114
Garcea, 2006	UK	○	○	○	○	○	○	○	●	○	○	○	○	●	○	○	○	110
Yoo, 2015	Korea	○	○	○	○	○	○	○	●	○	○	○	○	●	○	○	○	100
Siddiqui, 2017 ³⁷	Malaysia	○	○	○	○	○	○	○	●	●	○	○	○	●	○	○	○	58

Studies are ranked according to sample size from largest to smallest in each subgroup.

Note: black dots in the subgroup column represent the disease or the settings where the sample was studied and brown dots in the study by Kellet (2012) represent different samples for each subgroup. CVD, cardiovascular disease; ED, emergency department; GI, gastrointestinal diseases; ICU, intensive care unit.

from respiratory (n=8) to renal (n=1) (figures 1 and 2). Mortality was the main studied outcome. Cardiac arrest was infrequently studied (n=8).

Quality assessment

There was a significant risk of bias found in majority of studies (high risk=16; unclear risk=64) and low risk in only 28 studies. In terms of applicability, narrow inclusion of conditions in a certain disease group was commonly related to risk of bias, while in general settings, biases were often due to low sample size or unspecified timing of EWS assessment. There was a wide variation in sample size (median: 551 and range: 43–920 029). There was variation in defining study population by number of patients, hospital admissions or not specifying the particular study sample. Almost half of the studies (n=49; 48%) validated in <500 patients with either multiple observations or a single observation set (tables 1–4). External validation was more common (n=83) than internal validation (n=18), and two studies included internal and external validations (online supplemental table S1).

EWS validation in patient subgroups

Subgroups and EWS

In the studies validating EWS, there was heterogeneity in subgroup definitions, models and methods of predictive accuracy. There was overlap between diseases and settings commonly between studies of patients with infections receiving care in ED^{34–36} and patients with sepsis admitted to ICU.^{37 38} EWS models that were integrated with electronic health records (EHRs) were examined in recent studies (n=9). Research on datasets using EWS-embedded EHRs had larger sample sizes, ranging from 504³⁹ to 13 014 patients⁴⁰ (tables 1–4), with moderate to high predictive ability (AUC: 0.65–0.85). Several studies included comparison between different EWS in the same cohort (n=21)^{35 38 41} (online supplemental table S2).

Methodology

There was significant heterogeneity in methods across studies. The majority of studies were observational. Evaluation of predictive accuracy of different EWS in the same study was common.^{22 42–44} To measure accuracy of EWS, AUC was most commonly used (n=94), especially when comparing different EWS in the same study.^{22 45} Presentation of results was variable; for example, confidence intervals were missing in many studies. Other measures, such as analysing sensitivity and specificity, prognostic index and ORs, were found in only eight studies (tables 1–4). Consequently, it was only feasible to analyse predictive accuracy in studies where AUC was the selected measure.

Timing from EWS assessment to endpoints was variable. Many studies included (n=43) AUC within 24–48 hours,

while 11 studies had endpoints more than 48 hours after EWS. However, the majority (n=65; 63%) did not specify time horizon or in-hospital outcome.

Predictive performance of EWS

Outcomes were most commonly mortality, transfer to ICU, developing sepsis (in patients with infections) and cardiac arrest. Few studies examined other outcomes, for example, respiratory arrest (n=1) and organ failure (n=4). Mortality, ICU admission and cardiac arrest were best predicted in medical (AUC mean: 0.74, 0.75 and 0.74)^{46–48} and surgical settings (0.80, 0.79 and 0.75),^{49 50} and respiratory diseases (0.75, 0.80 and 0.75), respectively. EWS prediction of sepsis had reasonable predictive performance in all subgroups (AUC: 0.71–0.79) and infectious diseases in particular (AUC: 0.79). Certain outcomes related to specific disease groups were not studied, for example, cardiac arrest was not studied in cardiac patients²²; respiratory arrest was not tested in respiratory patients.^{46–52}

The best predictive performance was found in studies examining cardiac,⁴⁶ stroke^{46 53} and renal⁴⁶ diseases (AUC: 0.93, 0.88 and 0.87, respectively). In emergency settings, predictive accuracy was variable (AUC: 0.56–0.91).^{54–58} In haematology and oncology diseases, EWS predictive accuracy was suboptimal in mortality (online supplemental figure S1), cardiac arrest and ICU transfer (AUC: 0.52–0.69; figures 3 and 4).^{59–61} EWS prediction of ICU transfer was reasonable in ED,^{57 62} infectious diseases,^{63 64} and where both groups overlap,^{42 65} but not in gastroenterology and haematology (AUC: 0.64 and 0.60)^{60 66} (online supplemental figure S2). Cardiac arrest was the least examined outcome among the three endpoints (n=8) and unstudied in cardiac diseases (figures 3 and 4, online supplemental figure S3).

For mortality prediction, meta-analysis of included EWS showed high degree of statistical heterogeneity across all subgroups ($I^2=72\%$ – 99%) (figure 5). In validation studies of NEWS in different disease subgroups, there was also significant heterogeneity ($I^2=99\%$; figure 6).

DISCUSSION

In this comprehensive review of universal EWS across all diseases and settings, we had three main findings. First, EWS studies in different diseases and clinical settings were heterogeneous in methodology, predictive performance measures and number of studies in each subgroup. Second, validation of EWS is limited in specialised settings, including cardiac disease. Third, despite widespread EHR and EWS integration, few studies have explored EHR-based EWS.

Inconsistency in evaluation and the lack of high-quality validation make the evidence of validity questionable, ultimately affects how EWS can and should be used in clinical practice as a risk score for deterioration prediction. Heterogeneity across studies in all subgroups challenges implementation of EWS in all diseases and all settings.

Table 2 Early warning scores, predictive measures and outcomes for included studies in patient subgroups and settings

Author, year	EHR	EWS										Predictive measure	Outcomes studied				
		VIEWS	MEWS	EWS	NEWS	NEWS2	SOS	Worthing	HOTEL	TREWS	HEWS		Mortality	ICU	CA	RA	Sepsis
Kellett, 2012 ⁴⁶	X	●	○	○	○	○	○	○	○	○	○	AUC	✓	X	X	X	X
Kim, 2017	✓	●	○	○	○	○	○	○	○	○	○	AUC	X	✓	X	X	X
Bozkurt 2015	X	○	●	○	○	○	○	○	○	○	○	AUC	✓	X	X	X	X
Seak, 2017	X	○	●	○	○	○	○	○	○	○	○	AUC	✓	✓	X	X	X
Hu, 2016 ⁴⁸	✓	○	○	●	○	○	○	○	○	○	○	AUC	✓	✓	✓	X	X
Lijehult, 2016 ⁵³	X	○	○	●	○	○	○	○	○	○	○	AUC	✓	X	X	X	X
Mulligan, 2010 ⁶⁰	X	○	○	●	○	○	○	○	○	○	○	AUC	✓	✓	X	X	X
Cooksley, 2012 ⁶¹	X	○	●	○	●	○	○	○	○	○	○	AUC	✓	✓	✓	X	X
Vaughn, 2018 ³⁹	✓	○	●	○	○	○	○	○	○	○	○	AUC	✓	✓	X	X	X
Young, 2014	X	○	●	○	○	○	○	○	○	○	○	Sens & Spec	✓	X	X	X	X
Von, 2007	X	○	●	○	○	○	○	○	○	○	○	AUC	✓	X	X	X	X
Pedersen, 2018	✓	○	○	○	●	○	○	○	○	○	○	AUC	✓	X	X	X	X
Forster, 2018	✓	○	○	○	●	○	○	○	○	○	○	Sens & Spec	✓	X	X	X	X
Pimentel 2018 ⁴¹	✓	○	○	○	●	●	○	○	○	○	○	AUC	✓	✓	✓	X	X
Sbiti-Rohr, 2016 ⁵²	X	○	○	○	●	○	○	○	○	○	○	AUC	✓	X	X	X	X
Brabrand, 2017	X	○	○	○	●	○	○	○	○	○	○	AUC	✓	X	X	X	X
Jo, 2016	X	○	○	○	●	○	○	○	○	○	○	AUC	✓	X	X	X	X
Barlow, 2007	X	○	○	●	○	○	○	○	○	○	○	AUC	✓	X	X	X	X
Bilben, 2016 ⁵⁵	X	○	○	○	●	○	○	○	○	○	○	AUC	✓	X	X	X	X
Delahanty <i>et al</i> , 2019	X	○	●	○	●	○	○	○	○	○	○	AUC	✓	X	X	X	✓
Redfern, 2018	X	○	○	○	●	○	○	○	○	○	○	AUC	✓	✓	X	X	X
Churpek, 2017 ³⁵	X	○	●	○	●	○	○	○	○	○	○	AUC	✓	✓	X	X	X
Faisal, 2019	X	○	○	○	●	○	○	○	○	○	○	AUC	X	X	X	X	✓
Churpek, 2017	X	○	●	○	●	○	○	○	○	○	○	AUC	✓	X	X	X	X
Henry, 2015 ⁴⁰	✓	○	●	○	○	○	○	○	○	○	○	AUC	✓	X	X	X	X
Brink, 2019 ³⁴	X	○	○	○	●	○	○	○	○	○	○	AUC	✓	X	X	X	X
de Groot, 2017 ⁴³	X	○	●	○	●	○	○	○	○	○	○	AUC	✓	✓	X	X	X
Corfield, 2014	X	○	○	○	●	○	○	○	○	○	○	AUC	✓	X	X	X	X
Goulden, 2018 ⁵⁶	✓	○	○	○	●	○	○	○	○	○	○	AUC	✓	✓	X	X	X
Khwannimit, 2019 ³⁸	X	○	●	○	●	○	○	○	○	○	○	AUC	✓	X	X	X	X
Ghanem-Zoubi, 2011 ⁶³	X	○	●	○	○	○	○	○	○	○	○	AUC	✓	X	X	X	X
Saeed, 2019	X	○	○	○	○	○	○	○	○	○	○	AUC	✓	✓	X	X	X

Continued

Table 2 Continued

Author, year	EWS										Predictive measure	Outcomes studied				
	EHR	IEWS	MEWS	EWS	NEWS	NEWS2	SOS	Worthing	HOTEL	TREWS	HEWS	Mortality	ICU	CA	RA	Sepsis
Innocenti, 2018 ⁶⁵	X	○	●	○	●	○	○	○	○	○	○	✓	X	X	X	X
Camm, 2018	X	○	○	○	●	○	○	○	○	○	○	✓	✓	X	X	X
Tirotta, 2017	X	○	●	○	●	○	○	○	○	○	○	✓	X	X	X	X
Pong, 2019	X	○	●	○	●	○	○	○	○	○	○	✓	X	X	X	X
Prabhakar, 2019	X	○	●	○	●	○	○	○	○	○	○	✓	X	X	X	X
Martino, 2018	X	○	●	○	○	○	○	○	○	○	○	✓	✓	X	X	X
Vorwerk, 2009 ¹⁹	X	○	●	○	○	○	○	○	○	○	○	✓	X	X	X	X
Qin, 2017 ⁵¹	X	○	●	○	○	○	○	○	○	○	○	✓	X	X	X	X
Schmedding, 2019	X	○	●	○	○	○	○	○	○	○	○	✓	X	X	X	X
Albur, 2016 ⁶⁴	X	○	○	●	○	○	○	○	○	○	○	✓	X	X	X	X
Cildir, 2013 ³⁶	X	○	●	○	○	○	○	○	○	○	○	✓	X	X	X	X
Chiew, 2019 ⁵⁴	X	○	●	○	●	○	○	○	○	○	○	✓	X	X	X	X
Samsudin, 2018	X	○	●	○	●	○	○	○	○	○	○	✓	✓	X	X	X
Chang, 2018	X	○	●	○	○	○	○	○	○	○	○	✓	X	X	X	X
Geier, 2013	X	○	●	○	○	○	○	○	○	○	○	✓	X	X	X	✓
Asimwe, 2015	X	○	●	○	○	○	○	○	○	○	○	✓	X	X	X	X
Hung, 2017	X	○	●	○	○	○	○	○	○	○	○	✓	X	X	X	X
Garcea, 2006	X	○	○	●	○	○	○	○	○	○	○	✓	✓	X	X	X
Yoo, 2015	X	○	●	○	○	○	○	○	○	○	○	✓	✓	X	X	X
Siddiqui, 2017 ³⁷	X	○	○	●	○	○	○	○	○	○	○	✓	X	X	X	X

Studies are ranked according to sample size from largest to smallest in each subgroup.

AUC, area under the curve; CA, cardiac arrest; EHR, electronic health records; EWS, early warning score; HEWS, Hamilton early warning score; HOTEL, Hypotension, Oxygen saturation, Temperature, ECG abnormality, Loss of independence score; ICU, intensive care unit; MEWS, modified early warning score; NEWS, national early warning score; RA, respiratory arrest; Sens & Spec, sensitivity and specificity; SOS, search out severity score; TREWS, triage in emergency department early warning score; VIEWS, vitalpac early warning score; Worthing, worthing physiological scoring system.

Table 3 Study design and setting for included studies of predictive performance for early warning scores in clinical settings

Author, year	Country	Settings				Study design				Number of patients
		ICU	ED	Surgical	Medical	Retrospective	Prospective	RCT	Case-control	
Calvert, 2016	Israel	●	○	○	○	●	○	○	○	29 083
Awad, 2017	UK	●	○	○	○	●	○	○	○	11 722
Reini, 2012	Sweden	●	○	○	○	○	●	○	○	518
Chen, 2019	Taiwan	●	○	○	○	●	○	○	○	370
Baker, 2015	Tanzania	●	○	○	○	○	●	○	○	269
Gök, 2019	Turkey	●	○	○	○	●	○	○	○	250
Moseson, 2014	USA	●	○	○	○	○	●	○	○	227
Jo, 2013	South Korea	●	○	○	○	●	○	○	○	151
Kwon, 2018	Korea	○	●	○	○	●	○	○	○	1 986 334
Usman, 2019	USA	○	●	○	○	●	○	○	○	115 734
Jang, 2019	Korea	○	●	○	○	●	○	○	○	56 368
Wei, 2019	China	○	●	○	○	●	○	○	○	39 977
Lee, 2019	Korea	○	●	○	○	●	○	○	○	27 173
Singer, 2017	USA	○	●	○	○	●	○	○	○	22 530
Eick, 2015	Germany	○	●	○	○	○	●	○	○	5730
Bulut, 2014 ⁵⁸	Turkey	○	●	○	○	○	●	○	○	2000
Kivipuro, 2018	Finland	○	●	○	○	○	●	○	○	1354
Eckart, 2019 ⁶²	USA	○	●	○	○	●	○	○	○	1303
Ho, 2013	Malaysia	○	●	○	○	●	○	○	○	1024
Skitch, 2018	Canada	○	●	○	○	●	○	○	○	845
Liu, 2014	Malaysia	○	●	○	○	○	●	○	○	702
Dundar, 2016 ⁵⁷	Turkey	○	●	○	○	○	●	○	○	671
Yuan, 2018	China	○	●	○	○	○	●	○	○	621
Naidoo, 2014	South Africa	○	●	○	○	●	○	○	○	590
Liu, 2015	China	○	●	○	○	○	●	○	○	551
So, 2015	China	○	●	○	○	○	●	○	○	544
Dundar, 2019	Turkey	○	●	○	○	●	○	○	○	455
Lam, 2006	China	○	●	○	○	○	●	○	○	425
Xie, 2018	China	○	●	○	○	○	●	○	○	383
Cattermole, 2009	China	○	●	○	○	○	●	○	○	330
Heitz, 2010	USA	○	●	○	○	●	○	○	○	280

Continued

Table 3 Continued

Author, year	Country	Settings				Study design				Number of patients
		ICU	ED	Surgical	Medical	Retrospective	Prospective	RCT	Case-control	
Sirivilaithon, 2019	Thailand	○	●	○	○	○	○	○	●	250
Cattermole, 2014	China	○	●	○	○	○	●	○	○	230
Najafi, 2018	Iran	○	●	○	○	○	●	○	○	185
Bartkowiak, 2019 ⁵⁰	USA	○	○	●	○	●	○	○	○	32 537
Kovacs, 2016	UK	○	○	●	●	●	○	○	○	20 626
Plate, 2018	The Netherlands	○	○	●	○	○	●	○	○	1782
Sarani, 2012	The Netherlands	○	○	●	○	○	●	○	○	572
Hollis, 2016	USA	○	○	●	○	●	○	○	○	522
Gardner-Thorpe 2006	UK	○	○	●	○	○	●	○	○	334
Garcea, 2010	UK	○	○	●	○	●	○	○	○	280
Cuthbertson, 2007 ⁴⁹	UK	○	○	●	○	●	○	○	○	136
Prytherch, 2010	UK	○	○	○	●	●	○	○	○	35 585
Smith, 2013 ²²	UK	○	○	○	●	●	○	○	○	35 585
Rasmussen, 2018	Denmark	○	○	○	●	●	○	○	○	17 312
Ghosh, 2018	USA	○	○	○	●	●	○	○	○	2097
Duckitt, 2007 ⁴⁷	UK	○	○	○	●	○	●	○	○	1102
Colombo, 2017	Italy	○	○	○	●	●	○	○	○	471
Abbot, 2016 ⁴⁸	UK	○	○	○	●	○	●	○	○	322
Wheeler, 2013	Malawi	○	○	○	●	○	●	○	○	302
Graziadio, 2019	UK	○	○	○	●	○	●	○	○	292

Studies are ranked according to sample size from largest to smallest in each subgroup.

Black dots in the subgroup column represent the disease or the settings where the sample was studied, and brown dots in the study by Kellet represent different samples for each subgroup.

CVD, cardiovascular disease; ED, emergency department; GI, gastrointestinal diseases; ICU, intensive care unit.

Table 4 Early warning scores, predictive measures and outcomes for included studies of predictive performance for early warning scores in clinical settings

Author, year	EHR	EWS										Outcomes studied					
		IEWS	MEWS	EWS	NEWS	NEWS2	SOS	Worthing	HOTEL	TREWS	HEWS	Predictive measure	Mortality	ICU	CA	RA	Sepsis
Calvert, 2016	X	o	●	o	o	o	o	o	o	o	o	AUC	X	X	X	X	✓
Awad, 2017	X	o	o	o	●	o	o	o	o	o	o	AUC	✓	X	X	X	X
Reini, 2012	X	o	●	o	o	o	o	o	o	o	o	AUC	✓	X	X	X	X
Chen, 2019	X	o	o	o	●	o	o	o	o	o	o	AUC	X	X	X	✓	X
Baker, 2015	X	o	o	o	●	o	o	o	o	o	o	AUC	✓	X	X	X	X
Gök, 2019	X	o	●	o	o	o	o	o	o	o	o	AUC	X	X	X	X	✓
Moseson, 2014	X	o	●	o	o	o	o	o	o	o	o	AUC	✓	X	X	X	X
Jo, 2013	X	●	●	o	o	o	o	o	●	o	o	AUC	✓	X	X	X	X
Kown, 2018	X	o	●	o	o	o	o	o	o	o	o	AUC	✓	✓	X	X	X
Usman, 2019	X	o	●	o	●	o	o	o	o	o	o	AUC	✓	X	X	X	✓
Jang, 2019	X	o	●	o	o	o	o	o	o	o	o	AUC	X	X	✓	X	X
Wei, 2019	X	o	●	o	o	o	o	o	o	o	o	AUC	✓	X	X	X	X
Lee, 2019	X	o	●	o	●	o	o	o	o	●	o	AUC	✓	X	X	X	X
Singer, 2017	X	o	●	o	o	o	o	o	o	o	o	AUC	✓	✓	X	X	X
Eick, 2015	X	o	●	o	o	o	o	o	o	o	o	AUC	✓	X	X	X	X
Bulut, 2014 ⁵⁸	X	o	●	o	o	o	o	o	o	o	o	AUC	✓	X	X	X	X
Kivipuro, 2018	X	o	o	o	●	o	o	o	o	o	o	AUC	✓	X	X	X	X
Eckart, 2019 ⁶²	X	o	o	o	●	o	o	o	o	o	o	AUC	✓	✓	X	X	X
, 2013	X	o	●	o	o	o	o	o	o	o	o	AUC	X	✓	X	X	X
Skitch, 2018	X	o	o	o	●	o	o	o	o	o	●	AUC	X	X	X	X	✓
Liu, 2014	X	o	●	o	o	o	o	o	o	o	o	AUC	✓	X	✓	X	X
Dundar, 2016 ⁵⁷	X	●	●	o	o	o	o	o	o	o	o	AUC	✓	✓	X	X	X
Yuan, 2018	X	o	●	o	●	o	o	o	o	o	o	AUC	✓	✓	X	X	X
Naidoo, 2014	X	o	o	o	o	o	o	o	o	●	o	Sens & Spec	✓	X	X	X	X
Liu, 2015	X	o	●	o	●	o	o	o	o	o	o	AUC	✓	X	X	X	X
So, 2015	X	o	●	o	o	o	o	o	o	o	o	Sens & Spec	✓	X	X	X	X
Dundar, 2019	X	o	o	o	●	o	o	o	o	o	o	AUC	✓	X	X	X	X
Lam, 2006	X	o	●	o	o	o	o	o	o	o	o	AUC	✓	✓	X	X	X
Xie, 2018	X	o	●	o	o	o	o	o	o	o	o	AUC	✓	✓	X	X	X
Cattermole, 2009	X	o	●	o	o	o	o	o	o	o	o	AUC	✓	X	X	X	X
Heltz, 2010	X	o	●	o	o	o	o	o	o	o	o	AUC	✓	X	X	X	X
Sirivilathon, 2019	X	o	o	o	●	o	o	o	o	o	o	AUC	X	X	X	X	X
Cattermole, 2014	X	o	●	o	●	o	o	●	o	o	o	AUC	✓	X	X	X	X

Continued

Table 4 Continued

Author, year	EHR	EWS										Predictive measure	Outcomes studied			
		IEWS	MEWS	EWS	NEWS	NEWS2	SOS	Worthing	HOTEL	TREWS	HEWS		Mortality	ICU	CA	RA
Najafi, 2018	X	○	○	○	●	○	○	○	○	○	○	AUC	✓	X	X	X
Bartkowiak, 2019 ⁵⁰	X	○	●	○	●	○	○	○	○	○	○	AUC	✓	✓	✓	X
Kovacs, 2016	X	○	○	○	●	○	○	○	○	○	○	AUC	✓	✓	✓	X
Plate, 2018	X	●	○	○	○	○	○	○	○	○	○	AUC	✓	✓	X	X
Sarani, 2012	X	○	●	○	○	○	○	○	○	○	○	Sens & Spec	✓	✓	X	X
Hollis, 2016	X	○	○	●	○	○	○	○	○	○	○	AUC	✓	✓	X	X
Gardner-Thorpe, 2006	X	○	●	○	○	○	○	○	○	○	○	Sens & Spec	✓	✓	X	X
Garcea <i>et al.</i> , 2010	X	○	○	●	○	○	○	○	○	○	○	AUC	✓	X	X	X
Cuthbertson, 2007 ⁴⁹	X	○	●	○	○	○	○	○	○	○	○	AUC	X	✓	X	X
Prytherch, 2010	X	●	○	○	○	○	○	○	○	○	○	AUC	✓	X	X	X
Smith, 2013 ²²	X	○	○	○	●	○	○	○	○	○	○	AUC	✓	✓	✓	X
Rasmussen, 2018	X	○	○	○	●	○	○	○	○	○	○	AUC	✓	X	X	X
Ghosh, 2018	✓	○	●	○	●	○	○	○	○	○	○	AUC	✓	X	X	X
Duckitt, 2007 ⁴⁷	X	○	○	●	○	○	○	●	○	○	○	AUC	✓	✓	X	X
Colombo, 2017	X	○	●	○	○	○	○	○	○	○	○	AUC	✓	X	X	X
Abbot, 2016 ⁴⁸	X	○	○	○	●	○	○	○	○	○	○	AUC	✓	X	X	X
Wheeler, 2013	X	○	●	○	○	○	○	○	●	○	○	AUC	✓	X	X	X
Graziadio, 2019	X	○	○	○	●	○	○	○	○	○	○	AUC	✓	✓	X	X

Studies are ranked according to sample size from largest to smallest in each subgroup.

AUC, area under the curve; CA, cardiac arrest; EHR, electronic health records; EWS, early warning score; HEWS, Hamilton early warning score; HOTEL, Hypotension, Oxygen saturation, Temperature, ECG abnormality, Loss of independence score; MEWS, modified early warning score; NEWS, national early warning score; RA, respiratory arrest; Sens and Spec, sensitivity and specificity; SOS, search out severity score; TREWS, triage in emergency department early warning score; VIEWS, vitalpac early warning score; Worthing, worthing physiological scoring system.

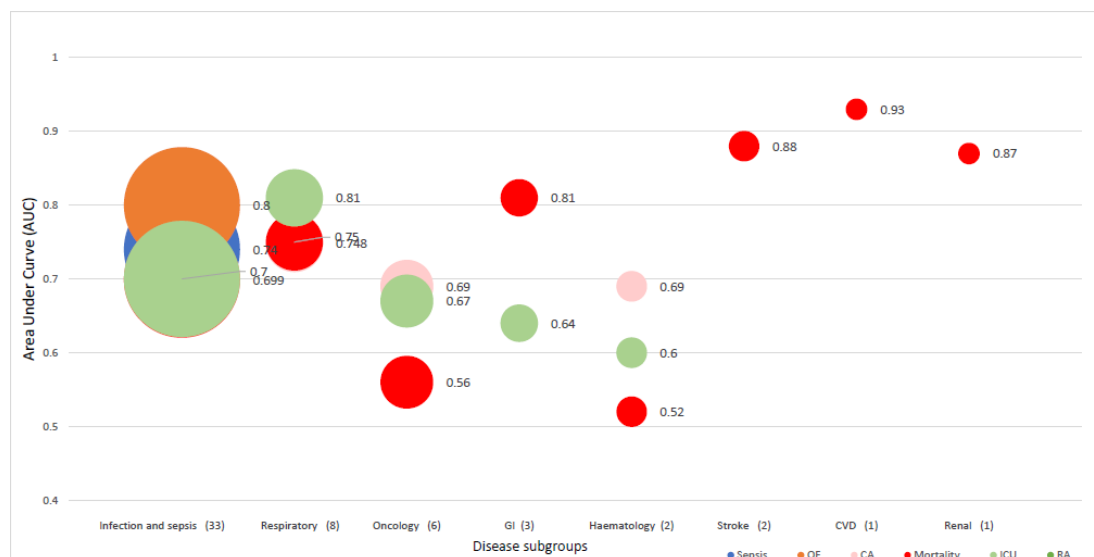


Figure 3 Early warning score performance in different disease subgroups. Each bubble represents critical events predicted by early warning scores for each disease subgroup with average AUC of studies beside each event type. The size of the bubble represents the number of studies in each subgroup. CA, cardiac arrest; CVD, cardiovascular diseases; GI, gastrointestinal diseases; ICU, intensive care unit; OF, organ failure; RA, respiratory arrest.

In methodology, observations selections method, time horizon between EWS score and event and the metric used in assessment were inconsistent. Choosing multiple observations or a single observation prior the outcome may not significantly affect the ranking of EWS.⁶⁷ Yet, selecting a single observation is generally associated with high AUC compared with multiple observations,^{46 67} supporting the use of multiple observations for each episode. Moreover, AUC, the most commonly used measure of predictive performance, has limitations and other metrics, including positive predictive value, should also be assessed.⁶⁸ Recording observations at an agreed

threshold point before events in a standardised method is necessary to evaluate EWS effectively.

The universal EWS with standardised models were primarily designed for general patient populations in wards and EDs and remain undervalued in specific diseases and settings. In medical and ED contexts, EWS perform well, suggesting the role of EWS in general settings, or at the early stage of clinical assessment. Our positive findings in respiratory disease may indicate the emphasis of several EWS, such as NEWS2, on respiratory changes when patients are deteriorating. Specific disease areas may show unique alarm signs when critical events

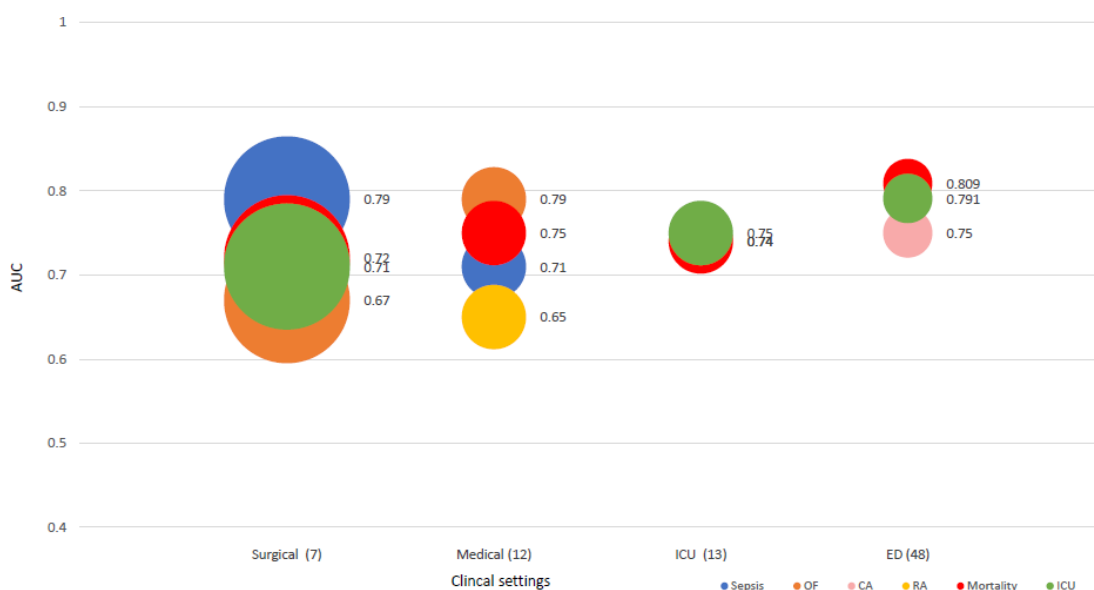


Figure 4 Early warning score performance in different clinical settings. Each bubble represents critical events predicted by early warning scores for each disease subgroup with average AUC of studies beside each event type. The size of the bubble represents the number of studies in each subgroup. CA, cardiac arrest; ED, emergency department; ICU, intensive care units; OF, organ failure; RA, respiratory arrest.

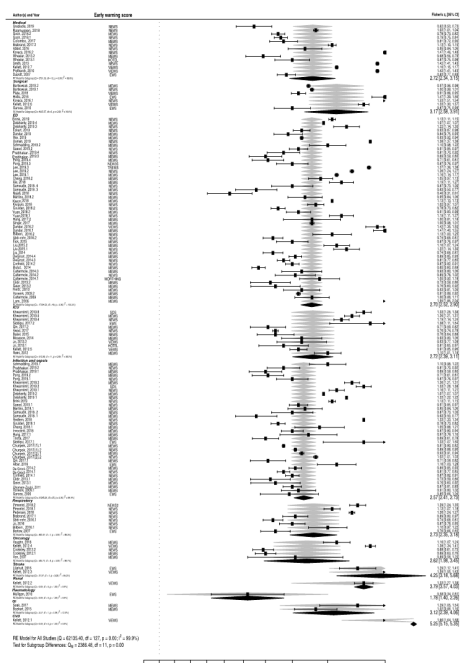
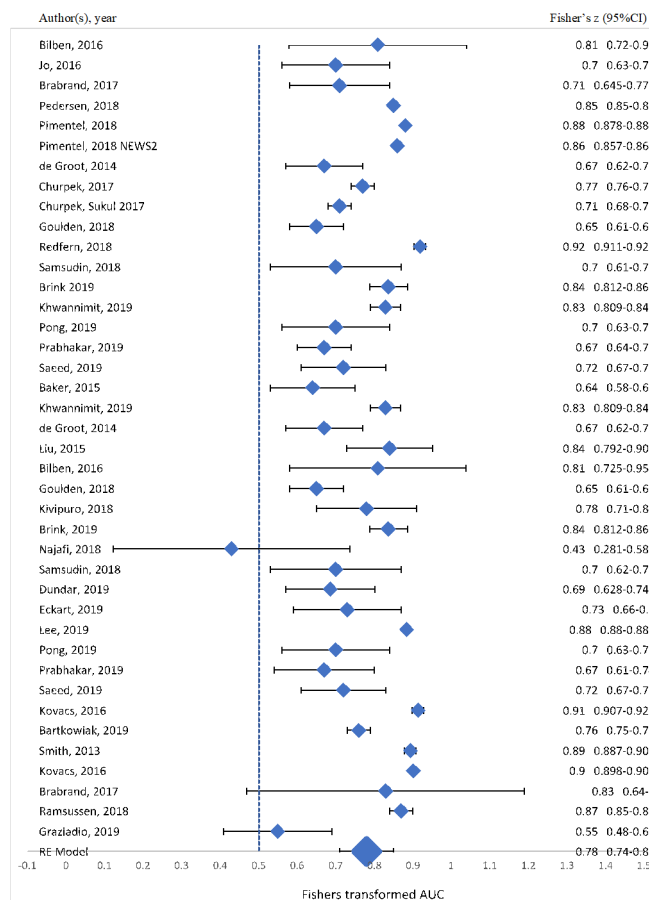


Figure 5 Forest plot of predictive accuracy of universal early warning scores (EWS) for mortality in different disease subgroups and clinical settings. CVD, cardiovascular diseases; ED, emergency department; GI, gastrointestinal diseases; Hem, haematological diseases; ICU, intensive care units; Infec, infectious diseases; Med, medical settings; Onco, oncology diseases; Renal, renal diseases; renal diseases; Resp, respiratory diseases; stroke, patients who had a stroke; Surg, surgical settings. Note: number following author(s) and year indicate more than one EWS evaluated in the study.

are anticipated, which may not be captured by universal EWS, such as NEWS2, where prediction of deterioration is based on predefined thresholds in all patients.²³ Critical events are commonly associated with CVD. With CVD being a leading cause of mortality globally, and the significant impact of morbidity on health and social care, early detection of deterioration is necessary.⁶⁹ However, EWS are poorly validated in CVD, some of the parameters may not be applicable and EWS may be unrepresentative.²⁵ A recent study of NEWS2 in patients with COVID-19 infection found poor performance in severity prediction,⁷⁰ despite pre-existing conditions being common and predictive in patients with severe outcomes. EWS may need to take account of disease-specific risk factors and comorbidities.

Widespread uptake of EHR and digitisation of patient observations are expected to contribute to efficient use of EWS by reducing human errors in documentation and calculation, as well as delays in escalation of care. However, relatively few studies have considered EHR-based EWS, and those studies have not analysed whether predictive performance of EWS is related to EHR use, diseases or settings. Investigating implementation and adoption of EWS is necessary to understand the application and performance of EWS. Predictive algorithms derived by machine learning have been successfully used



RE model for all studies: $Q(df=39)=37566.8345$, $p\text{-val} < .0001$, $I^2=99.87\%$

Figure 6 Forest plot of predictive accuracy of NEWS for mortality. AUC, area under the curve; NEWS, national early warning score.

in developing and validating EWS^{41 71} but will require robust evaluation. Studying the implementation process of EWS within EHR will provide opportunities for qualitative and quantitative insights into escalation of care, as well as facilitators and barriers to use of EWS in routine practice.

There are several limitations in this review and in included studies. We aimed for a comprehensive investigation of all EWS developing since 1997, but this long study period may lead to bias in comparing studies with old and new validation approaches statistically and technically. We excluded EWS specifically derived and validated for particular disease populations or settings and excluded studies considering a general patient population. Meta-analysis was only done for studies using AUC, excluding other methods for assessing performance of EWS. The distinction between general patient settings and specific disease or patient subgroups is dependent on hospital, healthcare system and country, and there is inevitably overlap between patients and settings at different stages in patient pathways. It was only feasible to include studies with a clear disease or setting identified to avoid confusion.

Validation of EWS in disease subgroups should consider similarities and differences across diseases, sample size

and include measures of model discrimination and calibration. Further research should adhere to established guidelines on clinical outcomes and predictive clinical scoring for decision making, such as the PROGRESS framework.⁷²

CONCLUSION

Universal EWS in specific disease subgroups and settings require further validation of their performance in detecting worsening outcomes. Despite good performance in respiratory patients and medical and surgical settings in studies to date, the predictive accuracy of EWS in all disease subgroups and all clinical settings remains unknown. The current evidence base does not necessarily support use of standard EWS in all patients in all settings. Future research should include validation of EWS in particular patient subgroups and settings, with standardised methodology following established guidelines. Going towards the utilisation of EHR for EWS development, validation and implementation within EHR should be considered for improved EWS systems.

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The performance of early warning scores in different patient subgroups and clinical settings: A systematic review.

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Supplementary methods: Search strategy for MEDLINE

- 1- EWS OR early warning score* OR EARLY WARNING SYSTEM* OR RAPID RESPONSE SYSTEM* OR MEWS OR MODIFIED EARLY WARNING SCORE* OR MODIFIED EARLY WARNING SYSTEM* OR news OR national early warning score OR news2 OR national early warning score 2 OR (track and trigger system*)
- 2- (MH "Intensive Care Units")
- 3- ICU OR intensive care unit* OR CRITICAL CARE UNIT* OR CRITICAL CARE
- 4- 2 OR 3
- 5- 1 AND 4
- 6- (MH "Nervous System Diseases")
- 7- neurological disorder* OR neurological disease OR neurological condition*
- 8- 6 OR 7
- 9- 1 AND 8
- 10- MH "Cardiovascular Diseases") OR (MH "Cardiology")
- 11- (MH "Thoracic Surgery")
- 12- cardiovascular disease* OR cardiovascular disorder* OR heart disease* OR cardiology* OR cardiac surgery OR thoracic surgery
- 13- 10 OR 11 OR 12
- 14- 1 AND 13
- 15- (MH "Musculoskeletal Diseases") OR (MH "Orthopedics")
- 16- orthopedic disease* OR orthopedic surgery
- 17- 15 OR 16
- 18- 1 AND 17
- 19- (MH "Kidney Diseases, Cystic") OR (MH "Kidney Failure, Chronic") OR (MH "Polycystic Kidney Diseases") OR (MH "Renal Insufficiency, Chronic")
- 20- renal disease* OR renal failure OR kidney disease*
- 21- 19 OR 20
- 22- 1 AND 21
- 23- (MH "Hematologic Diseases")
- 24- hematologic disorder* OR hematologic disease* OR hematology
- 25- 23 OR 24
- 26- 1 AND 25
- 27- (MH "Respiratory Tract Diseases")
- 28- respiratory disease* OR respiratory disorder*
- 29- 27 OR 28
- 30- 1 AND 29
- 31- (MH "Gastroenterology")
- 32- gastrointestinal disorder* OR gastrointestinal disease* OR gastroenterology OR hepatology
- 33- 31 OR 32
- 34- 1 AND 33
- 35- (MH "Medical Oncology") OR (MH "Surgical Oncology")
- 36- oncology OR cancer OR chemotherapy
- 37- 35 OR 36
- 38- 1 AND 37
- 39- (MH "Wounds and Injuries") OR (MH "Emergency Medicine")
- 40- emergency department* OR emergency OR emergency room* OR trauma*
- 41- 39 OR 40
- 42- 1 AND 41
- 43- (MH "Sepsis") OR (MH "Infection")
- 44- INFECTION* OR INFECTIOUS DISEASE* OR SEPSIS
- 45- 43 OR 44
- 46- 1 AND 45
- 47- (MH "Obstetrics")
- 48- (obstetrics and gynecology) OR OBSTETRIC*
- 49- 47 OR 48
- 50- 1 AND 49
- 51- (MH "Allergy and Immunology")
- 52- immunological disease* OR immunological disorder*

53- 51 OR 52
54- 1 AND 53
55- (MH "Internal Medicine")
56- medical ward*
57- 55 OR 56
58- 1 AND 57
59- (MH "General Surgery")
60- surgical ward*
61- 59 OR 60
62- 1 AND 61
63- 5 OR 9 OR 14 OR 18 OR 22 OR 26 OR 30 OR 34 OR 38 OR 42 OR 46 OR 50 OR 54 OR 58 OR 62

Supplementary methods: Search strategy for CINAHL

- 1- EWS OR early warning score* OR EARLY WARNING SYSTEM* OR RAPID RESPONSE SYSTEM* OR MEWS OR MODIFIED EARLY WARNING SCORE* OR MODIFIED EARLY WARNING SYSTEM* OR news OR national early warning score OR news2 OR national early warning score 2 OR (track and trigger system*)
- 2- (MH "Intensive Care Units")
- 3- ICU OR intensive care unit* OR CRITICAL CARE UNIT* OR CRITICAL CARE
- 4- 2 OR 3
- 5- 1 AND 4
- 6- (MH "Nervous System Diseases")
- 7- neurological disorder* OR neurological disease OR neurological condition*
- 8- 6 OR 7
- 9- 1 AND 8
- 10- (MH "Heart Diseases") OR (MH "Cardiovascular Diseases")
- 11- (MH "Heart Surgery")
- 12- cardiovascular disease* OR cardiovascular disorder* OR heart disease* OR cardiology* OR cardiac surgery OR thoracic surgery
- 13- 10 OR 11 OR 12
- 14- 1 AND 13
- 15- (MH "Orthopedic Surgery") OR (MH "Musculoskeletal Diseases")
- 16- orthopedic disease* OR orthopedic surgery
- 17- 15 OR 16
- 18- 1 AND 17
- 19- (MH "Kidney, Cystic") OR (MH "Kidney Diseases")
- 20- renal disease* OR renal failure OR kidney disease*
- 21- 19 OR 20
- 22- 1 AND 21
- 23- (MH "Hematologic Diseases")
- 24- (MH "Lymphatic Diseases")
- 25- hematologic disorder* OR hematologic disease* OR hematology
- 26- 23 OR 24 OR 25
- 27- 1 AND 26
- 28- (MH "Respiratory Tract Diseases")
- 29- respiratory disease* OR respiratory disorder*
- 30- 28 OR 29
- 31- 1 AND 30
- 32- (MH "Digestive System Diseases")
- 33- gastrointestinal disorder* OR gastrointestinal disease* OR gastroenterology OR hepatology
- 34- 32 OR 33
- 35- 1 AND 34
- 36- (MH "Cancer Patients") OR (MH "Oncology")
- 37- oncology OR cancer OR chemotherapy
- 38- 36 OR 37
- 39- 1 AND 38
- 40- (MH "Wounds and Injuries") OR (MH "Trauma")
- 41- emergency department* OR emergency OR emergency room* OR trauma*
- 42- 40 OR 41
- 43- 1 AND 42
- 44- (MH "Infection")
- 45- INFECTION* OR INFECTIOUS DISEASE* OR SEPSIS
- 46- 44 OR 45
- 47- 1 AND 46
- 48- (MH "Obstetric Emergencies") OR (MH "Obstetric Patients")
- 49- (obstetrics and gynecology) OR OBSTETRIC*
- 50- 48 OR 49
- 51- 1 AND 50
- 52- (MH "Internal Medicine")
- 53- (MH "Allergy and Immunology")

54- medical ward
55- immunological disease* OR immunological disorder*
56- 52 OR 53 OR 54 OR 55
57- 1 AND 56
58- (MH "Surgical Patients")
59- surgical ward*
60- 58 OR 59
61- 1 AND 60
62- 5 OR 9 OR 14 OR 18 OR 22 OR 27 OR 31 OR 35 OR 39 OR 43 OR OR 47 OR 51 OR 57 OR 61

Supplementary methods: Patients' subgroups

- 1- Cardiology patients
- 2- Neurology patients
- 3- Orthopaedic patients
- 4- Renal patients
- 5- Haematology patients
- 6- Respiratory patients
- 7- Gastroenterology patients
- 8- Oncology patients
- 9- Emergency patients
- 10- Infection patients
- 11- Medical patients
- 12- Surgical patients
- 13- Intensive care patients

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Table S1. Risk of bias assessment results

TOOL	Study	Validation	Quality	
			Risk of bias	Applicability
PROBAST	Kellett, 2012 (S1)	External	low	low
	Kim, 2017 (S2)	External	Unclear	unclear
	Bozkurt, 2015 (S3)	External	High	high
	Seak, 2017 (S4)	External	High	high
	Hu, 2016 (S5)	Internal	Unclear	high
	Liljehult, 2016 (S6)	External	Unclear	high
	Mulligan, 2010 (S7)	External	High	high
	Cooksley, 2012 (S8)	External	Unclear	unclear
	Vaughn, 2018 (S9)	External	High	high
	Young, 2014 (S10)	External	High	high
	von Lilienfeld-Toal, 2007 (S11)	External	Unclear	high
	Pedersen, 2018 (S12)	External and Internal	low	low
	Forster, 2018 (S13)	External	low	low
	Pimentel, 2018 (S14)	External	low	unclear
	Sbiti-rohr, 2016 (S15)		Unclear	high
	Brabrand, 2017 (S16)	External	Unclear	unclear
	Jo, 2016 (S17)	External	High	high
	Barlow, 2007 (S18)	External	low	unclear
	Bilben, 2016 (S19)	External	Unclear	unclear
	Delahanty, 2019 (S20)	Internal	low	low
	Redfern, 2018 (S21)	External	low	low
	Churpek, 2017 (S22)	External	High	high
	Faisal, 2019 (S23)	External	low	low
	Churpek 2017 (S24)	External	low	low
	Henry, 2015 (S25)	Internal	low	low
	Brink 2019 (S26)	External	Unclear	unclear
	de Groot, 2014 (S27)	External	Unclear	unclear
	Corfield, 2014 (S28)	External	low	low
	Goulden, 2018 (S29)	External	Unclear	unclear
	Khwannimit, 2019 (S30)	External	Unclear	unclear
	Ghanem-Zoubi, 2011 (S31)	External	Unclear	unclear
	Saeed, 2019 (S32)	Internal	Unclear	unclear
	Innocenti, 2018 (S33)	External	Unclear	unclear
	Camm, 2018 (S34)	External	Unclear	unclear
	Tirotta, 2017 (S35)	External	Unclear	unclear
	Pong, 2019 (S36)	Internal	Unclear	unclear
	Prabhakar, 2019 (S37)	Internal	Unclear	unclear
	Martino, 2018 (S38)	External	Unclear	unclear
	Vorwerk, 2009 (S39)	External	Unclear	unclear
	Qin, 2017 (S40)	External	Unclear	unclear
	Schmedding, 2019 (S41)	External	Unclear	unclear
	Albur, 2016 (S42)	External	Unclear	unclear
	Cildir, 2013 (S43)	External	Unclear	unclear
	Chiew, 2019 (S44)	External	Unclear	unclear

Samsudin, 2018 (S45)	Internal	Unclear	unclear
Chang, 2018 (S46)	External	Unclear	high
Geier, 2013 (S47)	External	Unclear	unclear
Asiimwe, 2015 (S48)	Internal	Unclear	unclear
Hung, 2017 (S49)	External	Unclear	high
Garcea, 2006 (S50)	External	Unclear	high
Yoo, 2015 (S51)	External	Unclear	unclear
Siddiqui, 2017 (S52)	External	Unclear	unclear
Calvert, 2016 (S53)	Internal	low	unclear
Awad, 2017 (S54)	Internal	low	low
Reini, 2012 (S55)	External	Unclear	unclear
Chen, 2019 (S56)	External	Unclear	high
Baker, 2015 (S57)	External	Unclear	unclear
Gök, 2019 (S58)	External	low	unclear
Moseson, 2014 (S59)	External	Unclear	unclear
Jo, 2013 (S60)	External	Unclear	unclear
Kwon, 2018 (S61)	External and Internal	Unclear	unclear
Usman, 2019 (S62)	External	High	high
Jang, 2019 (S63)	Internal	low	low
Wei, 2019 (S64)	External	High	high
Lee, 2019 (S65)	Internal	low	low
Singer, 2017 (S66)	External	Unclear	unclear
Eick, 2015 (S67)	External	Unclear	unclear
Bulut, 2014 (S68)	External	Unclear	unclear
Kivipuro, 2018 (S69)	External	Unclear	unclear
Eckart, 2019 (S70)	External	Unclear	unclear
Ho, 2013 (S71)	External	Unclear	unclear
Skitch, 2018 (S72)	External	Unclear	unclear
Liu, 2014 (S73)	Internal	low	unclear
Dundar, 2016 (S74)	External	Unclear	high
Yuan, 2018 (S75)	External	Unclear	high
Naidoo, 2014 (S76)	External	Unclear	unclear
Liu, 2015 (S77)	External	low	unclear
So, 2015 (S78)	External	Unclear	unclear
Dundar, 2019 (S79)	External	Unclear	high
Lam, 2006 (S80)	External	Unclear	unclear
Xie, 2018 (S81)	External	Unclear	unclear
Cattermole, 2009 (S82)	Internal	Unclear	unclear
Heitz, 2010 (S83)	External	High	unclear
Srivilaithon, 2019 (S84)	Internal	Unclear	unclear
Cattermole, 2014 (S85)	External	Unclear	unclear
Najafi, 2018 (S86)	External	Unclear	high
Bartkowiak, 2019 (S87)	External	Unclear	unclear
Kovacs, 2016 (S88)	External	low	low
Plate, 2018 (S89)	External	low	low
Sarani, 2012 (S90)	External	low	low
Hollis, 2016 (S91)	External	Unclear	unclear

Gardner-Thorpe 2006 (S92)	External	Unclear	unclear
Garcea, 2010 (S93)	External	High	high
Cuthbertson, 2007 (S94)	External	High	unclear
Prytherch, 2010 (S95)	Internal	low	low
Smith, 2013 (S96)	External	low	low
Ramsussen, 2018 (S97)	External	Unclear	unclear
Ghosh, 2018 (S98)	Internal	low	low
Duckitt, 2007 (S99)	Internal	low	low
Colombo, 2017 (S100)	External	High	high
Abbot, 2016 (S101)	External	High	high
Wheeler, 2013 (S102)	External	Unclear	unclear
Graziadio, 2019 (S103)	External	Unclear	unclear

Table S2. Early warning scores used in studies of patients' sub-populations and settings

		HR	SBP	RR	Temp	APVU/ LOC	O2 Sat	Supp O2	Urine OP	Other
Kellett, 2012 (S1)	VIEWS	✓	✓	✓	✓	X	✓	✓	X	X
Seak, 2017 (S4)	MEWS	✓	✓	✓	✓	✓	X	X	X	X
Bozkurt, 2015 (S3)	MEWS	✓	✓	✓	✓	✓	X	X	X	X
Kim, 2017 (S2)	NEWS	✓	✓	✓	✓	✓	✓	✓	X	X
Hu, 2016 (S5)	VIEWS	✓	✓	✓	✓	✓	✓	✓	X	X
Mulligan, 2010 (S7)	EWS	✓	✓	✓	✓	✓	X	X	X	X
Liljehult, 2016 (S6)	EWS	✓	✓	✓	✓	✓	✓	✓	X	X
Cooksley, 2012 (S8)	MEWS	✓	✓	✓	✓	✓	✓	X	✓	X
Cooksley, 2012 (S8)	NEWS	✓	✓	✓	✓	✓	✓	✓	X	X
Vaughn, 2018 (S9)	MEWS	✓	✓	✓	✓	✓	X	X	X	X
Von Lilienfeld-Toal, 2007 (S11)	MEWS	✓	✓	✓	✓	✓	X	X	X	X
Young, 2014 (S10)	MEWS	✓	✓	✓	✓	X	X	X	X	✓
Barlow, 2007 (S18)	EWS	✓	✓	✓	✓	✓	✓	X	✓	X
Bilben, 2016 (S19)	NEWS	✓	✓	✓	✓	✓	✓	✓	X	X
Brabrand, 2017 (S16)	NEWS	✓	✓	✓	✓	✓	✓	✓	X	X
Forster, 2018 (S13)	NEWS	✓	✓	✓	✓	✓	✓	✓	✓	X
Jo, 2016 (S16)	NEWS	✓	✓	✓	✓	✓	✓	✓	X	X
Pedersen, 2018 (S12)	NEWS	✓	✓	✓	✓	✓	✓	✓	X	X
Pimentel, 2018 (S14)	NEWS	✓	✓	✓	✓	✓	✓	✓	X	X
Pimentel, 2018 (S14)	NEWS2	✓	✓	✓	✓	✓	✓	✓	X	✓
Sbiti-rohr, 2016 (S15)	NEWS	✓	✓	✓	✓	✓	✓	✓	X	X
Henry, 2015 (S25)	MEWS	✓	✓	✓	✓	✓	X	X	X	X
Innocenti, 2018 (S33)	MEWS	✓	✓	✓	✓	✓	X	X	X	X
Garcea, 2006 (S50)	EWS	✓	✓	✓	✓	✓	X	X	✓	X
Qin, 2017 (S40)	MEWS	✓	✓	✓	✓	✓	X	X	X	X
Albur, 2016 (S42)	EWS	✓	✓	✓	✓	✓	✓	X	X	X
Asimwe, 2015 (S48)	MEWS	✓	✓	✓	✓	✓	X	X	X	X
Brink 2019 (S26)	NEWS	✓	✓	✓	✓	✓	✓	✓	X	X
Camm, 2018 (S34)	NEWS	✓	✓	✓	✓	✓	✓	✓	X	X
Chang, 2018 (S46)	MEWS	✓	✓	✓	✓	✓	X	X	X	X
Chiew, 2019 (S44)	MEWS	✓	✓	✓	✓	✓	X	X	X	X
Chiew, 2019 (S44)	NEWS	✓	✓	✓	✓	✓	✓	✓	X	X
Churpek, 2017 (S22)	NEWS	✓	✓	✓	✓	✓	✓	✓	X	X
Churpek, 2017 (S22)	MEWS	✓	✓	✓	✓	✓	X	X	X	X
Churpek, 2017 (S24)	NEWS	✓	✓	✓	✓	✓	✓	✓	X	X
Churpek, 2017 (S24)	MEWS	✓	✓	✓	✓	✓	X	X	X	X

Cildir, 2013 (S43)	MEWS	✓	✓	✓	✓	✓	X	X	X	X
Corfield, 2014 (S28)	NEWS	✓	✓	✓	✓	✓	✓	✓	X	X
De Groot, 2014 (S27)	NEWS	✓	✓	✓	✓	✓	✓	✓	X	X
De Groot, 2014 (S27)	MEWS	✓	✓	✓	✓	✓	X	X	X	X
Delahanty, 2019 (S20)	NEWS	✓	✓	✓	✓	✓	✓	✓	X	X
Delahanty, 2019 (S20)	MEWS	✓	✓	✓	✓	✓	X	X	X	X
Faisal, 2019 (S23)	NEWS	✓	✓	✓	✓	✓	✓	✓	X	X
Geier, 2013 (S47)	MEWS	✓	✓	✓	✓	✓	X	X	X	X
Ghanem-Zoubi, 2011 (S31)	MEWS	✓	✓	✓	✓	✓	X	X	X	X
Goulden, 2018 (S29)	NEWS	✓	✓	✓	✓	✓	✓	✓	X	X
Hung, 2017 (S49)	MEWS	✓	✓	✓	✓	✓	X	X	X	X
Khwannimit, 2019 (S30)	NEWS	✓	✓	✓	✓	✓	✓	✓	X	X
Khwannimit, 2019 (S30)	SOS	✓	✓	✓	✓	✓	X	X	✓	X
Khwannimit, 2019 (S30)	MEWS	✓	✓	✓	✓	✓	X	X	X	X
Martino, 2018 (S30)	MEWS	✓	✓	✓	✓	✓	X	X	X	X
Pong, 2019 (S36)	NEWS	✓	✓	✓	✓	✓	✓	✓	X	X
Pong, 2019 (S36)	MEWS	✓	✓	✓	✓	✓	X	X	X	X
Prabhakar, 2019 (S37)	MEWS	✓	✓	✓	✓	✓	X	X	X	X
Prabhakar, 2019 (S37)	NEWS	✓	✓	✓	✓	✓	✓	✓	X	X
Redfern, 2018 (S21)	NEWS	✓	✓	✓	✓	✓	✓	✓	X	X
Saeed, 2019 (S32)	NEWS	✓	✓	✓	✓	✓	✓	✓	X	X
Samsudin, 2018 (S45)	MEWS	✓	✓	✓	✓	✓	X	X	X	X
Samsudin, 2018 (S45)	NEWS	✓	✓	✓	✓	✓	✓	✓	X	X
Schmedding, 2019 (S41)	MEWS	✓	✓	✓	✓	✓	X	X	X	X
Siddiqui, 2017 (S52)	EWS	✓	✓	✓	✓	✓	✓	X	X	X
Tirotta, 2017 (S35)	MEWS	✓	✓	✓	✓	✓	X	X	X	X
Vorwerk, 2009 (S39)	MEWS	✓	✓	✓	✓	✓	X	X	X	X
Yoo, 2015 (S51)	MEWS	✓	✓	✓	✓	✓	X	X	X	X
Awad, 2017 (S54)	NEWS	✓	✓	✓	✓	✓	✓	✓	X	X
Baker, 2015 (S57)	NEWS	✓	✓	✓	✓	✓	✓	✓	X	X
Calvert 2016 (S53)	MEWS	✓	✓	✓	✓	✓	X	X	X	X
Gök, 2019 (S58)	MEWS	✓	✓	✓	✓	✓	X	X	X	X
Chen, 2019 (S56)	NEWS	✓	✓	✓	✓	✓	✓	✓	X	X
Jo, 2013 (S60)	HOTEL	X	✓	X	✓	✓	✓	X	X	✓
Jo, 2013 (S60)	VIEWS	✓	✓	✓	✓	✓	✓	✓	X	X
Moseson, 2014 (S59)	MEWS	✓	✓	✓	✓	✓	X	X	X	X
Reini, 2012 (S55)	MEWS	✓	✓	✓	✓	✓	X	X	X	X
Bulut, 2014 (S68)	MEWS	✓	✓	✓	✓	✓	X	X	X	X
Cattermole, 2009 (S82)	MEWS	✓	✓	✓	✓	✓	X	X	X	X
Cattermole, 2014 (S85)	WORTHING	✓	✓	✓	✓	✓	✓	X	X	X

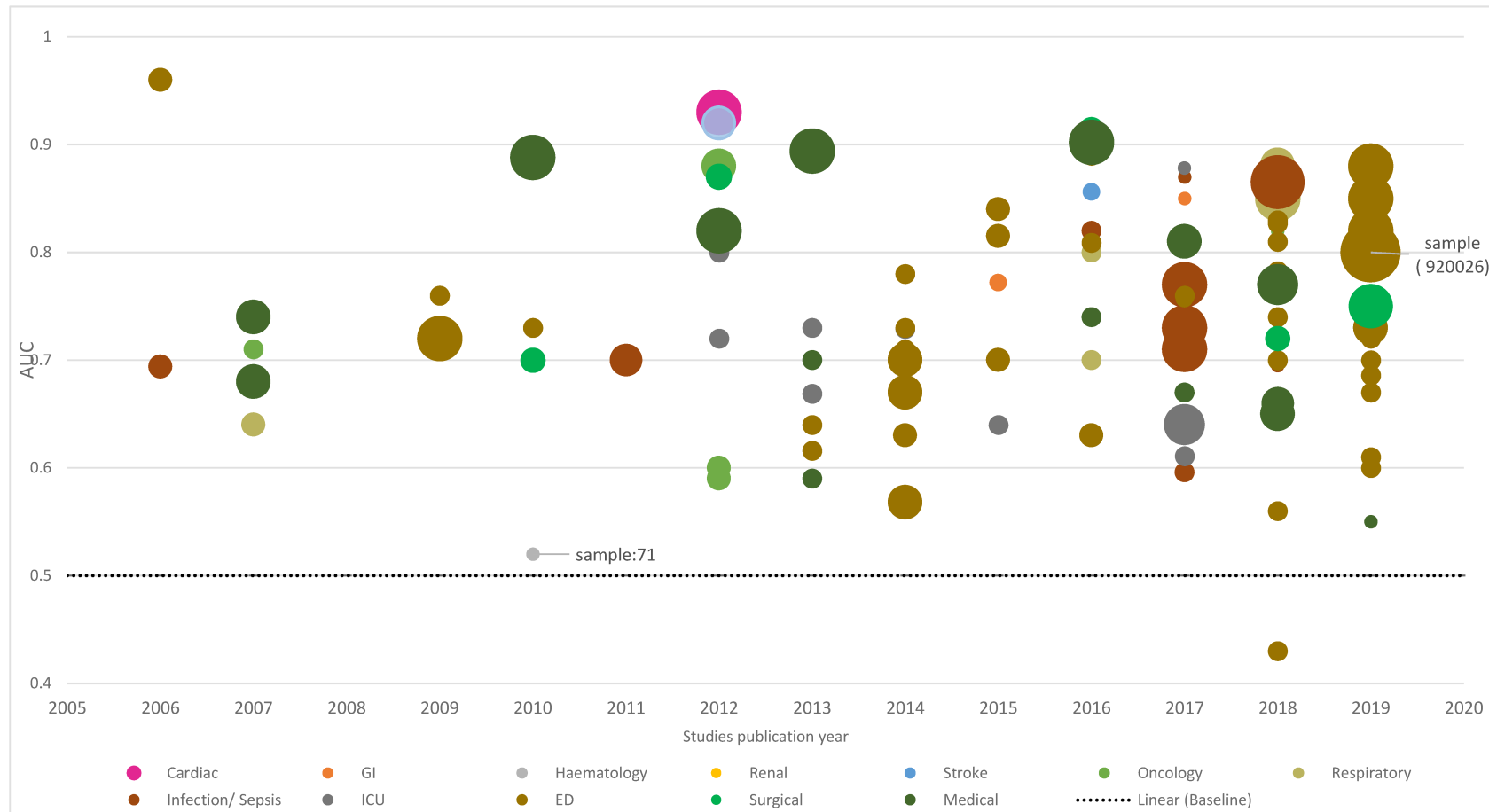
Cattermole, 2014 (S85)	NEWS	✓	✓	✓	✓	✓	✓	✓	X	X
Cattermole, 2014 (S85)	MEWS	✓	✓	✓	✓	✓	X	X	X	X
Heitz, 2010 (S83)	MEWS	✓	✓	✓	✓	✓	X	X	X	X
Dundar, 2016 (S74)	MEWS	✓	✓	✓	✓	✓	X	X	X	X
Dundar, 2016 (S74)	VIEWS	✓	✓	✓	✓	✓	✓	✓	X	X
Dundar, 2019 (S79)	NEWS	✓	✓	✓	✓	✓	✓	✓	X	X
Eckart, 2019 (S70)	NEWS	✓	✓	✓	✓	✓	✓	✓	X	X
Eick, 2015 (S67)	MEWS	✓	✓	✓	✓	✓	X	X	X	X
Liu, 2015 (S77)	NEWS	✓	✓	✓	✓	✓	✓	✓	X	X
Liu, 2015 (S77)	MEWS	✓	✓	✓	✓	✓	X	X	X	X
Ho, 2013 (S71)	MEWS	✓	✓	✓	✓	✓	X	X	X	X
Jang, 2019 (S63)	MEWS	✓	✓	✓	✓	✓	X	X	X	X
Kivipuro, 2018 (S69)	NEWS	✓	✓	✓	✓	✓	✓	✓	X	X
Kwon, 2018 (S61)	MEWS	✓	✓	✓	✓	✓	X	X	X	X
Liu, 2014 (S73)	MEWS	✓	✓	✓	✓	✓	X	X	X	X
Lee, 2019 (S65)	MEWS	✓	✓	✓	✓	✓	X	X	X	X
Lee, 2019 (S65)	NEWS	✓	✓	✓	✓	✓	✓	✓	X	X
Lee, 2019 (S65)	TREWS	✓	✓	✓	✓	✓	X	X	X	✓
Naidoo, 2014 (S76)	TREWS	✓	✓	✓	✓	✓	X	X	X	✓
Najafi, 2018 (S86)	NEWS	✓	✓	✓	✓	✓	✓	✓	X	X
Singer, 2017 (S66)	MEWS	✓	✓	✓	✓	✓	X	X	X	X
Skitch, 2018 (S72)	HEWS	✓	✓	✓	✓	✓	✓	✓	X	X
Skitch, 2018 (S72)	NEWS	✓	✓	✓	✓	✓	✓	✓	X	X
So, 2015 (S78)	MEWS	✓	✓	✓	✓	✓	X	X	X	X
Srivilaithon, 2019 (S84)	NEWS	✓	✓	✓	✓	✓	✓	✓	X	X
Lam, 2006 (S80)	MEWS	✓	✓	✓	✓	✓	X	X	X	X
Usman, 2019 (S62)	NEWS	✓	✓	✓	✓	✓	✓	✓	X	X
Yuan, 2018 (S75)	NEWS	✓	✓	✓	✓	✓	✓	✓	X	X
Yuan, 2018 (S75)	MEWS	✓	✓	✓	✓	✓	X	X	X	X
Wei, 2019 (S64)	MEWS	✓	✓	✓	✓	✓	X	X	X	X
Xie, 2018 (S81)	MEWS	✓	✓	✓	✓	✓	X	X	X	X
Bartkowiak, 2019 (S87)	NEWS	✓	✓	✓	✓	✓	✓	✓	X	X
Bartkowiak, 2019 (S87)	MEWS	✓	✓	✓	✓	✓	X	X	✓	X
Cuthbertson, 2007 (S94)	EWS	✓	✓	✓	✓	X	✓	X	X	X
Cuthbertson, 2007 (S94)	MEWS	✓	✓	✓	✓	X	✓	X	X	X
Garcea, 2010 (S50)	EWS	✓	✓	✓	✓	✓	X	X	✓	X
Gardner-Thorpe 2006 (S92)	MEWS	✓	✓	✓	✓	✓	X	X	✓	X
Hollis, 2016 (S91)	EWS	✓	✓	✓	✓	✓	✓	X	X	X
Kovacs, 2016 (S88)	NEWS	✓	✓	✓	✓	✓	✓	✓	X	X
Plate, 2018 (S89)	VIEWS	✓	✓	✓	✓	✓	✓	✓	X	X

Sarani, 2012 (S90)	MEWS	✓	✓	✓	✓	✓	X	X	X	X
Abbott, 2016 (S101)	NEWS	✓	✓	✓	✓	✓	✓	✓	X	X
Duckitt, 2007 (S99)	WPC	✓	✓	✓	✓	✓	✓	X	X	X
Duckitt, 2007 (S99)	EWS	✓	✓	✓	✓	✓	X	X	X	X
Colombo, 2017 (S100)	MEWS	✓	✓	✓	✓	✓	X	X	X	X
Ghosh, 2018 (S98)	NEWS	✓	✓	✓	✓	✓	✓	✓	X	X
Ghosh, 2018 (S98)	MEWS	✓	✓	✓	✓	✓	X	X	X	X
Graziadio, 2019 (S103)	NEWS	✓	✓	✓	✓	✓	✓	✓	X	X
Prytherch, 2010 (S95)	VIEWES	✓	✓	✓	✓	✓	✓	✓	X	X
Ramsussen, 2018 (S97)	NEWS	✓	✓	✓	✓	✓	✓	✓	X	X
Smith, 2013 (S96)	NEWS	✓	✓	✓	✓	✓	✓	✓	X	X
Wheeler, 2013 (S102)	Hotel	✓	X	✓	X	✓	✓	X	X	✓
Wheeler, 2013 (S102)	MEWS	✓	✓	✓	✓	✓	X	X	X	X

Total	133
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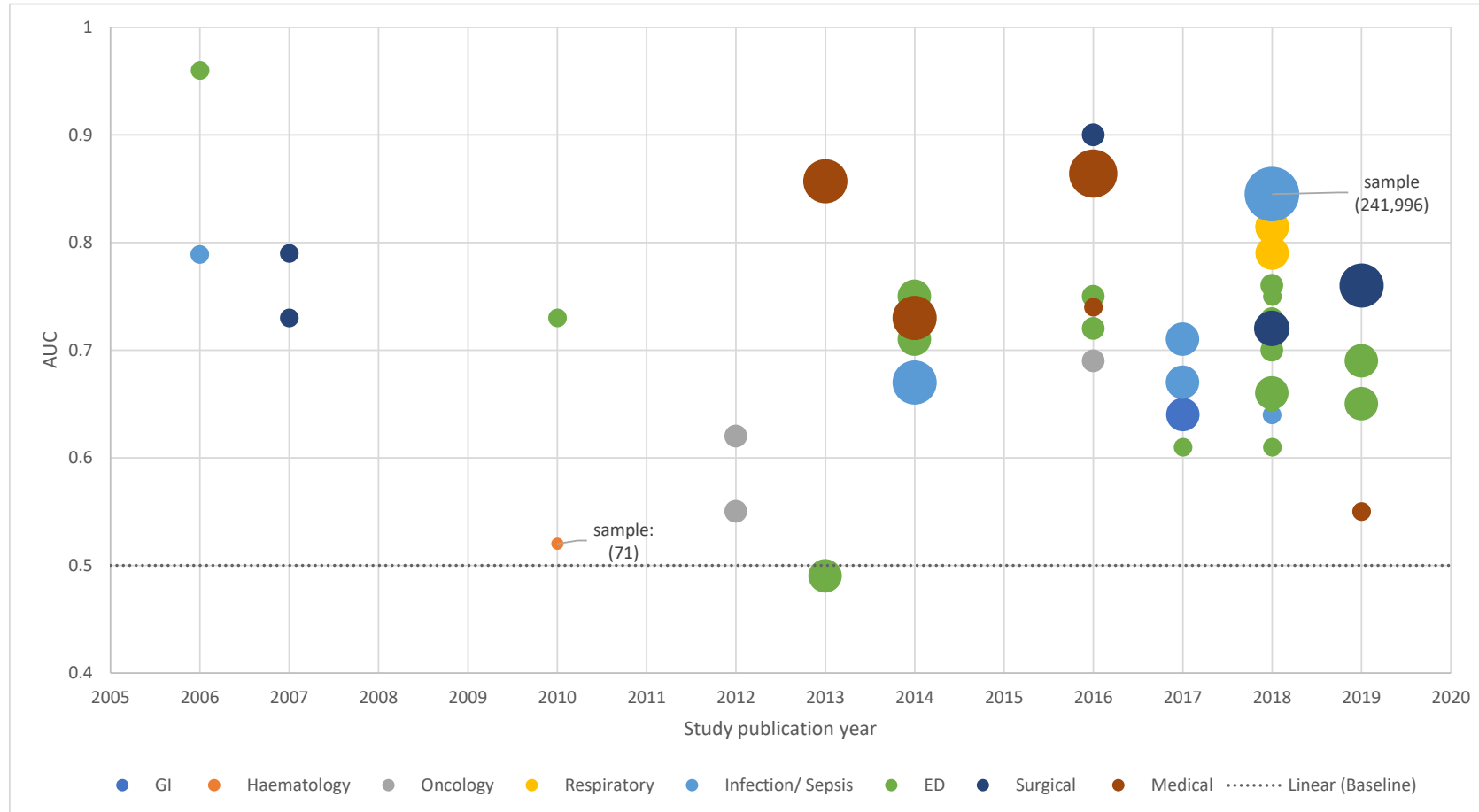
Abbreviations: HR: heart rate, SBP: systolic blood pressure, RR: respiratory rate, Temp: temperature, AVPU/LOC: alert, verbal response, physical response, unresponsive score or level of consciousness, O2 sat: Oxygen saturation, Supp O2: supplemental oxygen, Urine OP: urine output, Other: other parameters, i.e., blood biomarkers. VIEWES: Vitalpack early warning score, MEWS: modified early warning score, EWS: early warning score, NEWS: national early warning score, NEWS2: national early warning score 2, SOS: Search Out Severity score, Worthing: Worthing physiological scoring system, HOTEL: Hypotension, Oxygen saturation, Temperature, ECG abnormality, Loss of independence score, TREWS: Triage in Emergency department Early Warning Score, HEWS: Hamilton early warning score.

Figure S1. Predictive performance of early warning scores for mortality in studies from 2005 to 2020 for different disease subgroups and clinical settings



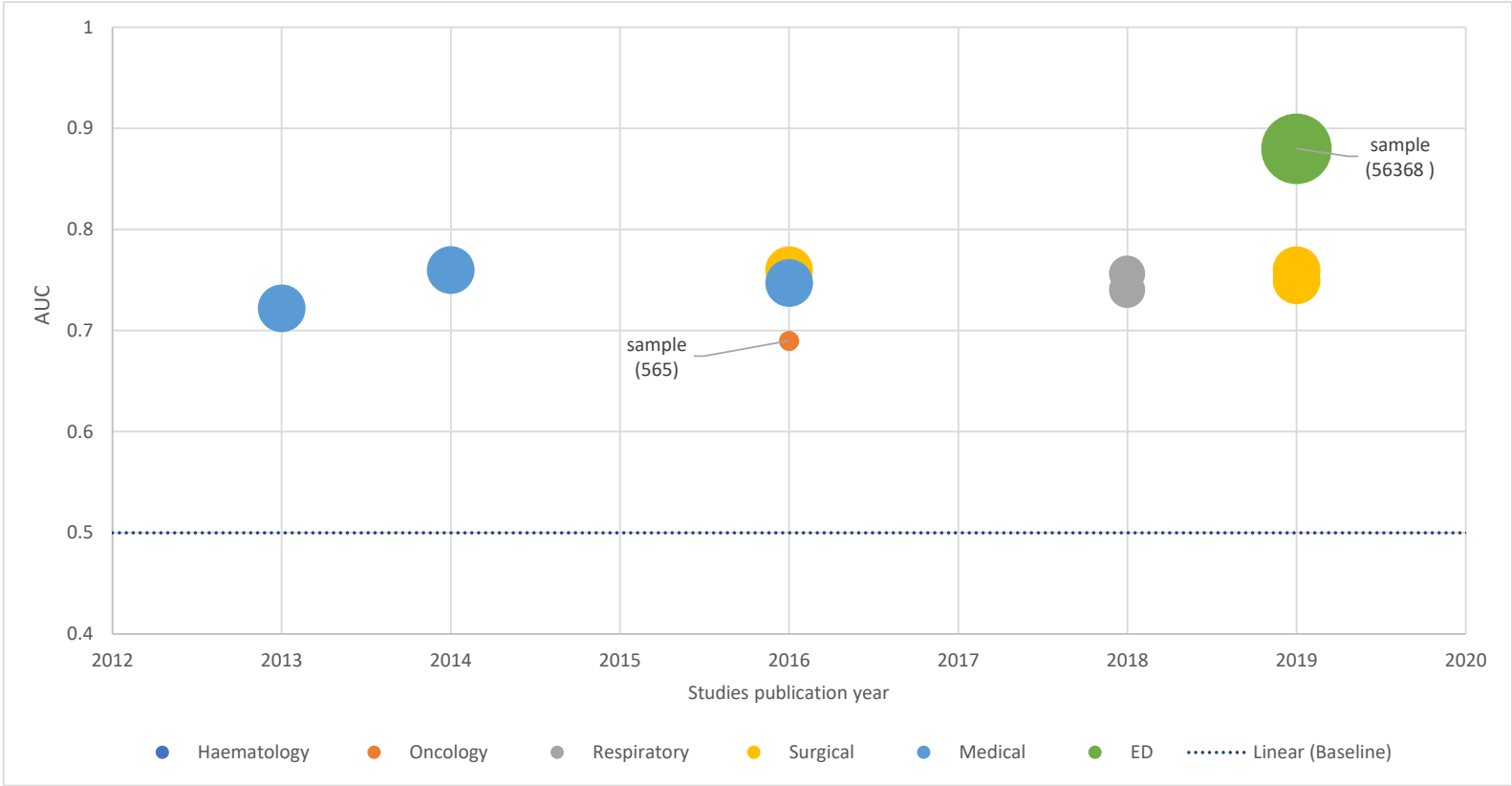
Abbreviations: AUC: Area Under the Curve; ED: Emergency Department; GI: Gastrointestinal diseases; ICU: Intensive Care Unit. *Note:* Bubbles sizes represents the sample size in each study.

Figure S2. Predictive performance of early warning scores for intensive care admission in studies from 2005 to 2020 for different disease subgroups and clinical settings



Abbreviations: AUC: Area Under the Curve; ED: Emergency Department; GI: Gastrointestinal diseases. *Note: Bubbles sizes represents the sample size in each study.*

Figure S3. Predictive performance of early warning scores for cardiac arrest in studies from 2012 to 2020 for different disease subgroups and clinical settings



Abbreviations: AUC: Area Under the Curve; ED: Emergency Department; GI: Gastrointestinal diseases. *Note: Bubbles sizes represents the sample size in each study.*