
Article:
Sabir, L. orcid.org/0000-0001-6488-3314, Ramlakhan, S. and Goodacre, S. orcid.org/0000-0003-0803-8444 (2022) Comparison of qSOFA and Hospital Early Warning Scores for prognosis in suspected sepsis in emergency department patients : a systematic review. Emergency Medicine Journal, 39 (4). pp. 284-294. ISSN 1472-0205

https://doi.org/10.1136/emermed-2020-210416

Comparison of qSOFA, and Hospital Early Warning Scores for prognosis in suspected sepsis in Emergency Department patients: a systematic review.

Sabir LR[1], Ramlakhan S, Goodacre S

Corresponding author[1]: Dr Lisa Ruby Sabir

Work address: Centre for Urgent and Emergency Care Research, School of Health and Related Research, University of Sheffield, Regent Court, 30 Regent Street, Sheffield, S1 4DA, UK

Email: l.sabir@sheffield.ac.uk

ORCID iD: 0000-0001-6488-3314

Dr Shammi Ramlakhan

Sheffield Children's Hospital NHS Foundation Trust, Western Bank, Sheffield, S10 2TH
Email: sramlakhan@nhs.net
ORCID iD: 0000-0003-1792-0842

Professor Steve Goodacre

Centre for Urgent and Emergency Care Research, School of Health and Related Research, University of Sheffield, Regent Court, 30 Regent Street, Sheffield, S1 4DA.
Email: s.goodacre@sheffield.ac.uk
ORCID iD: 0000-0003-0803-8444

Word count: 3005
Number of figures: 1
Number of tables: 7
PROSPERO Registration: CRD: 42019131414

Funding: No funding source.
Conflict of interest statement: None to declare

Author contributions: All authors made substantial contribution to the conception and design (LS, SR, SG), search strategy, study selection, data extraction (LS and SR), analysis and interpretation (LS, SR and SG). LS drafted the article and all other authors revised it critically.

What is already known on this subject?

- Recognition of sepsis is challenging; definitions have been redefined over the years, most recently the international consensus definition recommends the use of qSOFA in the emergency department to rapidly identify those who are likely to have poor outcomes.
- Several diagnostic and prognostic studies have compared qSOFA and SIRS, few have assessed EWS despite these being more routinely used clinically. If EWS could provide the same information, then they could be used earlier and allow standardisation and streamlining of effort.

What does this study add?

- This is the first systematic review that focuses on head-to-head comparisons of the most widely used scores – EWS and qSOFA, in the same cohort at recommended thresholds.
- Highlights the heterogeneity of evidence – sepsis definitions, determination of scoring thresholds and relevance of outcomes of interest.
- There is little to choose between these scores, however, at the current recommended thresholds NEWS has better sensitivity than qSOFA which has a better specificity.

Abstract

Background

Sepsis is a major cause of morbidity and mortality and many tools exist to facilitate early recognition. This review compares two tools: the quick Sequential Organ Failure Assessment (qSOFA) and Early Warning Scores (National/Modified Early Warning Scores (NEWS/MEWS)) for predicting intensive care (ICU) admission and mortality when applied in the Emergency Department.

Methods

A literature search was conducted using Medline, CINAHL, Embase, and Cochrane Library, hand searching of references and a grey literature search with no language or date restrictions. Two authors selected studies and quality assessment completed using QUADAS-2. Area under the Receiver Operating Characteristic Curve (AUROC), sensitivities, and specificities were compared.

Results

13 studies were included, totalling 403,865 patients. All reported mortality and six reported ICU admission.

The ranges for AUROC estimates varied from little better than chance to good prediction of mortality (NEWS: 0.59-0.88; qSOFA: 0.57-0.79; MEWS 0.56-0.75), however, individual papers generally reported higher AUROC values for NEWS than qSOFA. NEWS values demonstrated a tendency towards better sensitivity for ICU admission (NEWS≥5 46%-91%; qSOFA≥2 12%-53%) and mortality (NEWS≥5 51%-97%; qSOFA≥2 14%-71%) but lower specificity (ICU: NEWS≥5 25%-91%; qSOFA≥2 67%-99%; Mortality: NEWS≥5 22%-91%; qSOFA≥2 58%-99%).

Conclusion

The wide range of AUROC estimates and high heterogeneity limit our conclusions. Allowing for this, the NEWS AUROC was consistently higher than qSOFA within individual papers. Both scores allow threshold setting, determined by the preferred compromise

between sensitivity and specificity. At established thresholds NEWS tended to higher sensitivity whilst qSOFA tended to a higher specificity.

Introduction

Sepsis, defined as "*life threatening organ dysfunction due to a dysregulated host response to infection*"[1] is a leading cause of death worldwide. A global estimate of annual incidence is 31.5 million, and an estimated 5.3 million deaths annually[2]. In the UK, an estimated 52,000 patients die with sepsis annually. Consequently, many guidelines exist to enable early recognition and treatment to improve outcomes[3].

However, recognition is challenging, as reflected in the redefinition of sepsis over the years. Previously, the systemic inflammatory response syndrome (SIRS) criteria have been used to identify sepsis (the Sepsis-1 definition[4,5]), but replaced due to inadequate sensitivity and specificity[6]. There have been two further International Consensus definitions (Sepsis-2[7] and Sepsis-3[8]), with the latter recommending the use of the quick Sequential [Sepsis-related] Organ Failure Assessment (qSOFA) in the Emergency Department (ED) to rapidly identify those who are more likely to have poor outcomes secondary to sepsis; a score of two or more predicts a three to fourteen-fold increase in rate of in-hospital mortality[9]

Earlier management decisions such as ICU admission result in lower mortality[10,11]; a tool identifying those who may have poorer outcomes will facilitate these decisions.

In the acute setting, patients routinely get Early Warning Scores (EWS) calculated from physiological parameters. This is not condition-specific but is designed to indicate deterioration and trigger a response. The two most common EWS have been included in this review – the Modified Early Warning Score (MEWS) and the National Early Warning Score (NEWS). The online supplemental material has detailed information of the score components. In the UK, there has been a drive to make these scores consistent across all hospitals[12]. NEW score of 5 or more has been validated as a way of detecting suspected sepsis patients at risk of deterioration and recommended by NHS England[13].

Several studies have compared qSOFA and SIRS[14]. Few studies have assessed EWS, despite these being more routinely used clinically. If EWS are as accurate as other scoring tools, then they could be used earlier and allow standardisation and streamlining of

effort. Additionally, looking specifically at studies that compare EWS and qSOFA would allow direct comparison of the tests applied to the same population rather than looking at one scoring system in isolation.

This systematic review aims to compare qSOFA with EWS (NEWS/NEWS2/MEWS) in predicting ICU admission and mortality in ED patients.

Objective

To compare the accuracy of qSOFA with EWS (NEWS/NEWS2/MEWS) at predicting ICU admission and/or mortality in adult ED patients with suspected sepsis.

Methods

This study was registered on the PROSPERO database (CRD: 42019131414)[15].

Data sources and search strategy

This review was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analysis guidelines[16].

After conducting scoping searches, the studies included were identified by searching the following electronic databases: Medline (OVID), CINAHL (EBSCO), Embase (OVID), and Cochrane Library.

Reference lists for eligible papers were hand searched to identify additional studies. Google Scholar was used to forward search to identify additional studies that have subsequently cited eligible papers. In addition, Open Grey, and the Grey Literature Report were searched as well as ClinicalTrials.gov for ongoing trials. Authors of included papers needing additional data were contacted.

The search strategy was conducted using relevant subject headings for each database (such as Medical Subject Headings for MEDLINE) and free-text search terms (Table 1). There were no date restrictions, studies were included that were published up to

the search date (January 2019 and rerun in March 2019). There were no language restrictions or methodological search filters to limit study design.

Table 1 Keyword combinations used in literature searches

Sepsis	AND	**qSOFA**	AND	**EWS**	AND	**OUTCOME**
Sep*		Quick sepsis/sequential organ failure assessment		National early warning score*		Hospitlization/Hospitalisation
Bacteraemia		Organ dysfunction score*		Early warning score*		Mortality
				EWS/NEWS/NEWS2/MEWS		Prognos*
				Modified early warning*		Admission

Inclusion and exclusion criteria

Table 2 demonstrates the inclusion and exclusion criteria.

Table 2 Inclusion and exclusion criteria for study selection

	Include	**Exclude**
Patient population	Adult patients	Obstetric patients Paediatric patients
	Suspected sepsis	Organ dysfunction without evidence of infection
Index Test	qSOFA and NEWS/NEWS2/MEWS scores	Only one scoring method Neither scoring methods of interest used
Reference standard	Admission to level 2 or 3 care AND/OR Mortality documented	No report of outcomes or other outcomes reported such as length of hospital stay.
Setting	Emergency setting/department	Intensive Care Unit/Other non-Emergency setting
Study design	Observational/cohort/RCT/cross-sectional	Case studies

Participants

The population included were adult patients with suspected sepsis. Paediatric and obstetric patients were excluded as specific scoring methods are used for these groups.

Given the diagnostic difficulties and nomenclature changes, the inclusion of patients with “suspected sepsis” included the Sepsis 1 (SIRS response and infection), Sepsis 2 or Sepsis 3 definitions or the NICE criteria definitions[1,4,8]. It also included those coded as per International Classification of Disease (ICD) codes, clinician identified, or laboratory identified (such as cultures).

Index test

The index tests of interest were the qSOFA score and the NEWS/NEWS2/MEWS score. Studies that did not include both applied to the same cohort were excluded, as were those which only looked at one score in isolation. This allowed direct comparison of threshold effects in the same population.

Outcomes

The primary outcome was accuracy of scoring methods to predict ICU admission, with the secondary outcome being mortality. Sensitivity, specificity, positive and negative predictive values (PPV, NPV), positive and negative likelihood ratios (PLR, NLR), and the Area under the Receiver Operating Characteristic Curve (AUROC) were used to compare the tools.

Setting

Studies were included where the scoring methods had been applied in an emergency setting where undifferentiated patients are initially assessed by a clinician. This allows assessment of applicability for use in an acute/emergency setting. ICU studies were excluded as these populations were likely to have been considered for higher level care based on either these scores or certain physiological parameters already.

Study selection

All identified articles were collated in a referencing software (www.zotero.org/) and duplicates removed. Titles and/or abstracts of the studies retrieved by the search strategy were screened independently by both reviewers (LS and SR) using a pre-specified screening selection tool (*Table 2)*. The full text of those that met criteria or were ambiguous were assessed by two authors independently (LS and SR) and discrepancies identified and resolved.

Data extraction

Data were extracted by LS using a standardised and piloted data extraction form. Extracted information included: study characteristics: (author, year, country, funding, study design, and sample size); patient characteristics (age, sex); location; definitions of sepsis;

index tests; time of score measurement; ICU admission and mortality including sensitivity and specificity data.

Quality appraisal

Quality was assessed using the QUADAS-2 tool for Quality Assessment of Diagnostic Accuracy Studies[17]. It comprises four domains covering patient selection, index test, reference standard, and flow and timing. All were assessed in terms of the "risk of bias", and the first three domains were also assessed in terms of "concerns regarding applicability". The tool signalling questions were used independently by LS and SR and discrepancies discussed. Each item was scored "low", "high", or "unclear". No studies were excluded, but quality issues were considered. Studies scoring "low" on all four domains were considered low risk of bias and applicability. Any that scored "high" or "unclear" were considered "at risk of bias and concerns regarding applicability".

Statistical analysis

Statistical analysis was conducted using Microsoft Excel. Observing the results, a level of heterogeneity was present such as study population selection, definitions of sepsis, definitions of the outcomes of interest which precluded meaningful meta-analysis. Therefore as per the Centre for Reviews and Dissemination guidelines for systematic reviews[18], a descriptive narrative synthesis has been presented rather than a meta-analysis.

For studies where the PPV, NPV, PLR or NLR were not given, these have been calculated producing 2x2 tables using the reported measures of accuracy, prevalence and sample sizes given.

When comparing AUROC, the commonly used definition of >0.9 excellent, 0.8-0.9 good, 0.7-0.8 fair, 0.6-0.7 poor is used[19].

Results

Study identification

Figure 1 demonstrates the search strategy identified 1124 articles. Initial screening based on the inclusion and exclusion criteria and strategy described, and then examination of full text articles resulted in 13 studies included in the analysis[20–31]. One non-English language paper was identified and translated[27].

Study characteristics

All thirteen studies were published between 2017 and 2019. Three were conducted in the UK[20,23,26], three in the Netherlands[25,31,32], two in the US[21,22], two in Italy[28,29], one in Singapore[24], one in Spain[27] and one in China[30]. Eleven were single-centre studies[20–22,24,26–32], and two were multicentre [23,25]. Study design included ten observational studies[21–25,27–31], and three cohort studies[20,26,32]. Ten of the studies reported the prognostic accuracy of previously developed scoring systems[20–23,25,28–32], and three compared a novel scoring method with existing tools[24,26,27]. The supplemental material summarises the study characteristics.

Participant characteristics, methodology, and outcomes

Table 3 demonstrates the participant characteristics. The 13 studies totalled 403,865 patients. The proportion of women varied between 34.35-53%. Four studies included the ED but also included wards, medical assessment units or direct specialty referrals[20,21,23,26]. Where given, the ED results were separated for comparison. One study looked at ED-HDU where the HDU was based in and managed by Emergency clinicians[28]. Two studies looked at all patients presenting to the ED and applied the scoring criteria to all of these patients to look at the diagnostic ability to predict sepsis[22,31]. Patients were included in whom there was a suspicion of sepsis. This was either purely clinical[20], clinical but initially flagged with a scoring system such as NEWS ≥3[23] or other abnormal physiological parameters[27,30], by triage category[24,25], blood cultures and IV antibiotics[21,22,32], or based on final diagnosis or coding[22,26,28,29,31].

Seven studies compared NEWS and qSOFA[20,22–24,26,27,32], two compared both NEWS and MEWS with qSOFA[21,25] and four compared MEWS and qSOFA[28–31].

Scores were either calculated at time of arrival[20,22,24], retrospectively from records[21,25,28–32] or from a vital signs database[26], calculated from the point sepsis was suspected[23], or finally, both initial and worst measurements used[24].

Four studies did not investigate admission to ICU[22,27,30,32], one study reported scores on admission to ICU but not the proportion admitted[28]. Two studies combined either ICU admission with Medium Care Unit (MCU) admissions[25], or in-hospital mortality when giving the proportion[26]. Four studies reported the proportion of patients admitted to ICU, two of these had no further analysis on this outcome[23,31], and two had further analysis but as a composite outcome with in-hospital mortality[21] or in-hospital mortality and intubation[24]. Only two studies investigated ICU admission as a separate outcome and provided AUROC values[29] or both AUROC and sensitivity and specificity data[20]. The prevalence of admission to ICU varied from 3%[20] to 26%[21]. The study reporting the highest proportion only included suspected sepsis cases based on intravenous antibiotics and blood cultures and were therefore likely have a higher severity and hence higher admission rate to ICU.

The definition of mortality varied: eight studies reported in-hospital mortality[20–22,25–27,29,31], with one also reporting sepsis-related in-hospital mortality[22], others described 30-day in-hospital mortaltiy[24], 30 day all-cause mortality[23,32], or 28-day mortality[28,30]. Mortality varied between 3.6%[31] to 31%[28]. The paper with the lowest mortality included all medical patients, not just those with suspected sepsis. Conversely, the paper reporting the highest mortality, selected ED-HDU patients, described by the authors as a "sub-intensive care unit" therefore already excluding lower risk cohort.

Quality appraisal

Three studies were considered to have a low risk of bias[20,25,26], and the remaining were considered at risk of bias or concerns regarding applicability (*Table 4)*. The most

common category of concern was the “flow and timing” domain which relates to the timings of the index test and reference standard, and length of follow up.

Eight authors were contacted[21–24,26–30] for further statistical data including confidence intervals of the extracted data. Five authors[21–24,26] replied with data within the allocated time-frame and these have been included.

ICU admission

Table 5 details the summary statistics for the four studies that reported ICU admission: one reported this outcome alone[20] and the remaining as a composite with mortality[21], ICU admission or mortality[26], or composite with mortality and intubation[24]. For ICU admission alone, using the recommended cut-offs (NEWS≥5, qSOFA≥2), Goulden et al., (2018) reported a higher sensitivity for NEWS than qSOFA which had a better specificity. They did not demonstrate statistical significance for AUROC data, but NEWS (0.64) was higher than qSOFA (0.59) (*Table 6)*.

For the combined outcomes, NEWS results were fair (0.70[24],0.72[21],0.75[25],0.79[26]) compared to qSOFA (respectively 0.63[24],0.62[21],0.72[25],0.68[26]).

In the studies reporting combined outcomes, the general trend is similar with NEWS demonstrating a higher sensitivity and lower specificity for recommended thresholds than qSOFA. NEWS≥5 demonstrated a higher sensitivity than MEWS≥5, which in turn appears to have a higher sensitivity and lower specificity compared to qSOFA≥2, however there were only two studies looking at MEWS for ICU admission.

Table 3: Participant characteristics

Author, year, reference	Total no of patients, n. (group sizes)	Age (years) mean ± SD, median (IQR)	Gender (% female)	Location of patients	When were scores calculated?	Participant selection criteria	Comparators	Outcome: Admission to ICU % (number of patients)	Outcome: Measured mortality	Outcome: Prevalence of mortality % (number of patients)
Goulden et al., 2018[20]	1818	68 ± 19	49	ED and MAU	Based on arrival measurement	Suspected sepsis	qSOFA, NEWS, SIRS	3% (53)	In-hospital mortality	15% (265)
Churpek et al., 2017[21]	30677 all patients: (18523 ED; 12154 wards)	58 ± 18 all patients; 58 ± 18.9 ED; 57 ± 16.7 Wards	53 all 55 ED; 48 wards	ED and wards	Retrospective calculation	Suspected infection based on whether they have had a blood culture and IV antibiotics	qSOFA, NEWS, MEWS, SIRS	26% (4868 ED) 20% (2390 wards) No further data on this outcome alone (composite outcome)	In-hospital mortality	5% (920 ED) 6% (729 wards)
Usman et al., 2018[22]	115734 (930 SS/SS)	46.5 ± 19.7 all patients: 63 ± 17 SS/SS	50.8	ED	Based on arrival measurements	Sepsis codes or blood cultures, urine, or antibiotics or flagged by ED doctor.	qSOFA, NEWS, SIRS	Not investigated	Sepsis-related in-hospital mortality and all-cause mortality	17.6% (164) sepsis related (0.6% (730) all-cause mortality – not just septic patients.)
Szakmany et al., 2018[23]	380 all patients: (64 ED; 316 wards)	74 (61-83) all patients	53	ED and wards	Used measurements at time sepsis was suspected.	Suspected or proven infection in patients with a NEWS ≥3.	qSOFA, NEWS, SIRS, SOFA	3.7% (14) Given combined for ED and wards. No further data on this outcome.	30-day all-cause mortality	17.2% (11 ED) 21.2% (67 wards).
Samsudin et al., 2018[24]	214	66.9 ± 16.1 Combined from data in paper	49.5	ED	Arrival scores used for all scores except qSOFA where both initial and worst used.	Clinical suspicion of sepsis meeting 2 of 4 SIRS criteria in high triage category.	qSOFA, NEWS, HRV, SIRS	5.14% (11) No further data on this outcome alone (composite outcome.)	30-day in-hospital mortality	18.7% (40)
de Groot et al., 2017[25]	2280	61.1 ± 17.0	42.3	ED	Retrospective calculation	Suspected infection with a Manchester triage category of yellow, orange, red, or IV antibiotics.	qSOFA, NEWS, MEWS, MEDS, PIRO.	9.6% (220) Note: Authors combined ICU/MCU	In-hospital mortality	6.3% (143)
Redfern et al., 2018[26]	241996 all patients: (81170 ED admissions of which 40782 with an infection code)	63 ± 20 all patients	53	ED and direct specialty referrals	Retrospective calculation	All admissions separated into no infection or infection depending on “suspicion of sepsis” ICD 10 codes.	qSOFA, NEWS, qNEWS	9.65% (3937/40782) Primary or secondary infection codes admitted to ICU or death from the ED	In-hospital mortality	8.09% (3298/40782) Primary or secondary infection codes from the ED

Redondo-González et al., 2018[27]	349	72.7 (range 86)	45.6	ED	Retrospective calculation	Suspected infection plus two of a list of altered physiological parameters (including SIRS)	qSOFA, EWS (NEWS), SOFA, LODS	Not investigated	In-hospital mortality	21.8% (76)
Innocenti et al., 2017[28]	742	75 ± 14	47	ED-HDU and data taken from ED admission	Retrospective calculation	Patients admitted to ED-HDU with a diagnosis of sepsis, severe sepsis, or septic shock	qSOFA, MEWS, SOFA, MEDS, PRIO, APACHE II, CCI	Secondary outcome but no % given. (Looked at average scores at admission to ICU)	28-day mortality	31% (230)
Martino et al., 2018[29]	310	78 (64-84)	43	ED	Retrospective calculation	Coded as sepsis (ICD 9 codes)	qSOFA, MEWS, SOFA, SIRS	14.2% (43)	In-hospital mortality	24.7% (75)
Liu and Hu 2018[30]	584	59.5 ± 17.2	34.35	ED	Retrospective calculation	Severe sepsis (Sepsis-3 criteria)	qSOFA, MEWS, SIRS, MEDS, SOFA, APACHE II	Not investigated	28-day mortality	20.38% (119)
van der Woude et al.,2018[31]	577 all patients: (198 with probable infection)	55.3 ± 18.6 all patients	49.7 all patients	ED	Retrospective calculation	Random selection of medical patients in ED. Infection based on discharge diagnosis and independent review of the notes.	qSOFA, MEWS, SOFA, SIRS	6.4% (37) all patients	In-hospital mortality	3.6% (21) all patients
Brink et al.,2019[32]	8204	57 (41-68)	44.2	ED	Retrospective calculation	Consecutive patients with suspected sepsis, defined as administration of IV antibiotics, taking of cultures/viral diagnostics.	qSOFA, NEWS, SIRS	Not investigated	10- and 30-day mortality	3.5% (286) 10-day mortality 6.0% (490) 30-day mortality

Abbreviations: *MAU* Medical assessment unit, *qSOFA* Quick Sequential [Sepsis-related] Organ Failure Assessment, *SOFA* Sequential [Sepsis-related] Organ Failure Assessment, *SIRS* Systemic inflammatory response syndrome, *NEWS* National Early Warning Score *MEWS* Modified Early Warning Scores, *PIRO* predisposition, infection (or insult), response and organ dysfunction, *HRV* heart rate variability, *ICU* Intensive care unit, *NICE* National Institute of Clinical Excellence, *qNEWS* quick National Early Warning Score, *LODS* Logistic Organ Dysfunction Score, *MEDS* Mortality in the Emergency Department Score, *APACHE II* Acute Physiology and Chronic Health Evaluation Score, *CCI* Charlson Comorbidity Index, *ED* Emergency Department, *ED-HDU* Emergency Department High-Dependency Unit, *MCU* Medium care unit, *EMU* Emergency multidisciplinary unit, *SS/SS* severe sepsis/septic shock

Table 4: Quality assessment (QUADAS-2)

Study	RISK OF BIAS				APPLICABILITY CONCERNS		
	PATIENT SELECTION	INDEX TEST	REFERENCE STANDARD	FLOW AND TIMING	PATIENT SELECTION	INDEX TEST	REFERENCE STANDARD
Goulden et al., (2018)	Low	Low	Low	Low	Low	Low	Low
Churpek et al., (2017)	Low	Low	Low	Unclear	Low	Low	Low
Usman et al., (2018)	Low	Low	Low	Unclear	Low	Low	Unclear
Szakmany et al., (2018)	Low	Low	Low	Low	Low	Unclear	Low
Samsudin et al., (2018)	High	Unclear	Low	Low	Unclear	Low	Low
de Groot et al., (2017)	Low	Low	Low	Low	Low	Low	Low
Redfern et al., (2018)	Low	Low	Low	Low	Low	Low	Low
Redondo-González et al., (2018)	Unclear	Low	Low	Unclear	Low	Low	Low
Innocenti et al., (2017)	Low	Unclear	Low	Low	Low	Unclear	Low
Martino et al., (2018)	Unclear	Low	Unclear	Unclear	Low	Low	Low
Liu and Hu (2018)	Unclear	Low	Low	Low	Unclear	Low	Unclear
van der Woude et al., (2018)	Low	Unclear	Low	Unclear	Low	Low	Low
Brink et al., (2019)	Unclear	Low	Low	Unclear	Low	Low	Low

Table 5: Study results: Predicting ICU admission[20], composite of ICU admission and mortality[21], ICU admission or mortality[26], composite of ICU admission, intubation and in-hospital death[24]

Score	Author, year, reference	Outcome (including composite outcomes)	Sensitivity % (95% CI)	Specificity % (95% CI)	Positive predictive value % (95% CI)	Negative predictive value % (95% CI)	Positive likelihood ratio (95% CI)	Negative likelihood ratio (95% CI)
qSOFA ≥2	Goulden et al., 2018[20]	ICU admission	36.0 (23-50)	77.0 (75-79)	5.0 (3-7)	98 (97-98)	1.57 (1.09-2.28)	0.83 (0.68-1.02)
	Churpek& et al., 2017[21]	ICU admission and mortality	52.59 (51.2-54)	67.15 (66.4-67.9)	36.3* (35.2-37.5)	79.9* (79.1-80.6)	1.60 (1.55-1.66)	0.71 (0.68-0.73)
	Samsudin^* et al., 2018[24]	ICU admission, intubation and in-hospital death	39.6 (25.7-53.4)	95.2 (91.9-98.4)	71.0* (52.3-84.6)	84.1* (78.2-88.7)	8.25 (3.85-17.7)	0.63 (0.51-0.80)
	Redfern** et al., 2018[26]	ICU admission or mortality	11.92 (11.2-12.66)	99.39 (99.32-99.47)	67.6* (64-71)	91.3* (91-92)	19.83 (16.73-22.83)	0.89 (0.88-0.90)
qSOFA ≥1	Goulden et al., 2018[20]	ICU admission	75.0 (61.9-84.7)	39.0 (36.8-41.3)	3.6* (2.6-4.8)	98.1* (96.8-98.9)	1.23 (1.05-1.44)	0.64 (0.40-1.03)
	Churpek& et al., 2017[21]	ICU admission and mortality	94.52 (94-95.1)	11.01 (10.5-11.5)	27.5* (26.8-28.1)	84.9* (83.2-86.5)	1.06 (1.05-1.07)	0.5 (0.44-0.57)
	Samsudin^* et al., 2018[24]	ICU admission, intubation and in-hospital death	64.6 (51.1-78.1)	65.1 (57.8-72.3)	35.5* (26.3-45.8)	86.1* (78.9-91.1)	1.85 (1.38-2.48)	0.54 (0.37-0.81)
	Redfern** et al., 2018[26]	ICU admission or mortality	44.53 (43.21-45.75)	85.85 (85.55-86.15)	25.2* (24.20-26.20)	93.5* (93.3-93.8)	3.13 (3.02-3.29)	0.65 (0.63-0.67)
NEWS ≥5	Goulden et al., 2018[20]	ICU admission	77.0 (64-88)	41.0 (39-44)	4.0 (3-5)	99.0 (97-99)	1.32 (1.13-1.53)	0.55 (0.33-0.90)
	Churpek& et al., 2017[21]	ICU admission and mortality	90.64 (89.9-91.4)	24.70 (24-25.4)	30.03* (29.3-30.8)	88.1* (87-89.1)	1.20 (1.19-1.22)	0.38 (0.35-0.42)
	Samsudin^* et al., 2018[24]	ICU admission, intubation and in-hospital death	87.5 (78.1-96.6)	41.6 (34.1-49.1)	30.8* (23.7-38.9)	91.8* (83.4-96.2)	1.50 (1.27-1.77)	0.3 (0.14-0.64)
	Redfern** et al., 2018[26]	ICU admission or mortality	45.99 (44.92-47.13)	91.17 (90.94-91.41)	35.8* (34.4-37.1)	94.0* (93.8-94.3)	5.23 (4.97-5.46)	0.59 (0.58-0.61)
MEWS ≥5	Churpek& et al., 2017[21]	ICU admission and mortality	60.57 (59.2-61.9)	68.40 (67.6-69.2)	40.6* (39.5-41.7)	83.0* (82.2-83.6)	1.92 (1.85-1.98)	0.58 (0.56-0.60)
	Samsudin^* et al., 2018[24]	ICU admission, intubation and in-hospital death	52.1 (38.0-66.2)	64.5 (57.2-71.7)	30.4* (21.6-40.9)	81.9* (74.4-87.6)	1.47 (1.05-2.06)	0.74 (0.54-1.02)

Abbreviations: *qSOFA* Quick Sequential [Sepsis-related] Organ Failure Assessment, *NEWS* National Early Warning Score, *MEWS* Modified Early Warning Score, *CI* Confidence interval.

*calculated values
&data from supplementary data sent by authors (ED data only).
^*data from supplementary data sent by authors. qSOFA here was the worst recorded not the initial qSOFA.
**data from supplementary data sent by authors (ED data only, and only included those coded as a sepsis code).

Table 6: AUROC data for ICU admission and mortality for qSOFA, NEWS and MEWS.

Outcome	Author, year, reference	qSOFA AUROC (95% CI)	NEWS AUROC (95% CI)	MEWS AUROC (95% CI)	Measured mortality
ICU admission	Goulden et al., 2018[20]	0.59 (0.52-0.67)	0.64 (0.57-0.71)	-	
	Churpek et al., 2017[21]	0.62* (0.60-0.63)	0.72* (0.70-0.73)	0.68* (0.66-0.70)	
	Samsudin et al., 2018[24]	0.63** (0.541-0.715)	0.70** (0.622-0.784)	0.61 (0.517-0.699)	
	de Groot et al., 2017[25]	0.72*** (0.68-0.75)	0.75*** (0.72-0.79)	0.71*** (0.68-0.75)	
	Redfern et al., 2018[26]	0.675^ (0.668-0.681)	0.791^ (0.785-0.796)	-	
	Martino et al., 2018[29]	0.61 (0.5-0.73)	-	0.66 (0.54-0.78)	
Mortality	Goulden et al., 2018[20]	0.62 (0.59-0.66)	0.65 (0.61-0.68)	-	In-hospital mortality
	Churpek et al., 2017[21]	0.71^* (0.68-0.72)	0.80^* (0.78-0.82)	0.75^* (0.73-0.76)	In-hospital mortality
	Usman et al., 2018[22]	0.79 (NG) [0.87]	0.88 (NG) [0.95]	-	In-hospital mortality [sepsis-related mortality]
	Szakmany et al., 2018[23]	0.57 (0.49-0.64)	0.59 (0.51-0.66)	-	30-day all-cause mortality
	Samsudin et al., 2018[24]	0.65 (0.557-0.741)	0.70 (0.615-0.788)	0.56 (0.462-0.659)	30-day in-hospital mortality
	de Groot et al., 2017[25]	0.68 (0.63-0.72)	0.67 (0.62-0.72)	0.63 (0.58-0.67)	In-hospital mortality
	Redfern et al., 2018[26]	0.675 (0.668-0.682)	0.79 (0.784-0.796)	-	In-hospital mortality
	Redondo-González et al., 2018[27]	0.67 (0.58-0.76)	0.73 (0.65-0.81)	-	In-hospital mortality
	Innocenti et al., 2017[28]	0.625 (0.579-0.671)	-	0.662 (0.618-0.705)	28-day mortality
	Martino et al., 2018[29]	0.75 (0.67-0.84)	-	0.74 (0.66-0.83)	In-hospital mortality
	Liu and Hu, 2018[30]	0.657 (0.617-0.695)	-	0.628 (0.587-0.667)	28-day mortality
	Brink et al., 2019[32]	0.697 (0.667-0.726)	0.779 (0.755-0.804)	-	30-day mortality

Abbreviations: *AUROC* Area under the Receiver Operating Characteristic Curve, *NG* Not given, *CI* Confidence interval, *qSOFA* Quick Sequential [Sepsis-related] Organ Failure Assessment, *NEWS* National Early Warning Score, *MEWS* Modified Early Warning Score.

*composite outcome of mortality and ICU admission. Taken ED only data from paper for this.
**composite outcome of in-hospital mortality, ICU admission and intubation within 30 days of ED admission.
***This paper included both ICU/MCU admission together.
^Taken ED data only, ICU admission OR in-hospital mortality.
^* Taken ED data only.

Mortality

Seven studies reported AUROC data for in-hospital mortality for NEWS and qSOFA. The range of estimates demonstrate overlap but the individual studies mostly appear to report a higher AUROC for NEWS (0.65[20],0.67[25],0.73[27],0.79[26],0.80[21],0.88[22]) than qSOFA (0.62[20],0.68[25],0.67[27],0.68[26],0.71[21],0.79[22]). AUROC for 30 day in-hospital mortality demonstrated a similar pattern (NEWS: 0.70[24], 0.78[32]; qSOFA: 0.65[24], 0.70[32]). One study reported data suggesting poor predictors of mortality for both NEWS (0.59) and qSOFA (0.57)[23]. The study that reported sepsis-related mortality demonstrated an AUROC for NEWS of 0.95 and 0.87 for qSOFA[22]. However, correlating this data with the specificity, it is high for both qSOFA≥2 (98.7%) and NEWS≥5 (90.2%) which is likely due to the inclusion of patients with other diagnoses as well as suspected infection as the authors wanted to show its use as a triage tool. A similar higher specificity is seen in two other papers that did not only look at suspected sepsis but also those with other diagnoses[26,31] *(Table 7).*

Ten studies reported data on qSOFA≥2, which generally demonstrates high specificity but low sensitivity[20–26,31,32]. Lowering the threshold to qSOFA≥1 improves the sensitivity but with the expected reduction of specificity[20–22,25–27,32]. The NEWS and MEWS scores were more variable but generally a NEWS≥5 had a higher sensitivity than qSOFA≥2 (50.5-97.3% and 13.6-71.1% respectively), but lower specificity, with some authors suggesting that NEWS≥7 is the optimal cut off[21].

Table 7: Predicting mortality (routine practice cut-offs (qSOFA≥2 and NEWS≥5))

Score	Author, year, reference	Sensitivity % (95% CI)	Specificity % (95% CI)	Positive predictive value % (95% CI)	Negative predictive value % (95% CI)	Positive likelihood ratio (95% CI)	Negative likelihood ratio (95% CI)
qSOFA ≥2	Goulden et al., 2018[20]	37.0 (31-43)	79.0 (77-81)	23.0 (19- 28)	88.0 (86-90)	1.78 (1.48-2.14)	0.80 (0.72-0.88)
	Churpek[&] et al., 2017[21]	71.13 (68.1-74)	63.51 (62.4-63.9)	9.2 (8.5-9.9)	97.7 (97.4-97.9)	1.93 (1.84-2.02)	0.46 (0.41-0.51))
	Usman et al**., 2018[22]	43.3 (35.3-51.7) Sepsis related	98.7 (98.6-98.8) Sepsis related	5.2 (4.1-6.5)	99.9 (99.9-99.9)	33.31 (27.93-40.96)	0.57 (0.50-0.66)
	Szakmany et al., 2018[23]	22.0 (14–33)	89.0 (85–92)	34.0 (22–49)	82.0 (77–85)	1.99 (1.17–3.39)	0.88 (0.78–0.99)
	Samsudin^* et al., 2018[24]	37.5 (22.5-52.5)	93.1 (89.3-96.9)	55.5[*] (37.3-72.4)	86.6[*] (81-90.8)	5.44 (2.76-10.69)	0.67 (0.53-0.86)
	de Groot et al., 2017[25]	32.0 (30-33)	87.0 (85-88)	11.0 (10-12)	95.0 (94-96)	2.46 (1.89-3.2)	0.78 (0.70-0.88)
	Redfern et al., 2018[26]	13.6 (12.8-14.5)	99.3 (99.3-99.4)	64.8[*] (61.2-68.3)	92.9[*] (92.6-93.1)	19.43 (17.98-24.35)	0.87 (0.86-0.88)
	Redondo-González et al., 2018[27]	65 (51-77)	58 (50-66)	36 (27-46)	82 (73-88)	1.55 (1.25-1.92)	0.60 (0.44-0.83)
	Van der Woude et al., 2018[31]	33.3 (14.6-57)	96.4 (94.5-97.8)	25.9[*] (13.1-44.6)	97.5[*] (95.8-98.5)	9.25 (4.40-19.43)	0.69 (0.51-0.94)
	Brink et al., 2019[32]	28.5 (24.7-32.7)	93.7 (93.1-94.2)	22.3* (19.2-25.7)	95.4* (94.9-95.8)	4.52* (3.84-5.33)	0.76* (0.72-0.81)
qSOFA ≥1	Goulden et al., 2018[20]	77.0 (0.72-0.82)	41 (0.39-0.44)	18.2[*] (16.1-20.6)	91.3[*] (88.9-93.1)	1.31 (1.21-1.41)	0.56 (0.45-0.71)
	Churpek[&] et al., 2017[21]	98.2 (97.1-98.9)	9.9 (9.5-10.4)	5.4[*] (5.1-5.7)	99.1[*] (98.5-99.4)	1.09 (1.08-1.10)	0.18 (0.11-0.29)
	Usman et al., 2018[22]	83.3 (76.6-88.4) Sepsis related	86.7 (86.5-87) Sepsis related	1.0 (0.8-1.2)	100 (100-100)	6.26 (5.84-6.77)	0.19 (0.13-0.28)
	Samsudin et al., 2018[24]	67.5 (53.0-82.0)	64.4 (57.3-71.5)	30.4[*] (21.8-40.6)	89.6[*] (83-93.8)	1.90 (1.41-2.54)	0.51 (0.32-0.80)
	de Groot et al., 2017[25]	83.0 (81-84)	47.0 (44-49)	10 (9-11)	98 (97-98)	1.57 (1.44-1.70)	0.36 (0.25-0.52)
	Redfern et al., 2018[26]	48.1 (46.8-49.5)	85.6 (85.3-86.0)	22.8[*] (21.8-23.8)	94.9[*] (94.7-95.2)	3.36 (3.21-3.50)	0.61 (0.59-0.63)
	Redondo-González et al., 2018[27]	98 (89-99)	14 (9-21)	29 (22-36)	95 (77-99)	1.14 (1.08-1.21)	0.14 (0.03-0.71)
	Brink et al., 2019[32]	69.9 (65.7-73.8)	59.5 (58.4-60.6)	9.9* (8.9-10.9)	96.9* (96.4-97.3)	1.73* (1.62-1.84)	0.51 (0.44-0.58)
NEWS ≥5	Goulden et al., 2018[20]	74.0 (68-79)	43.0 (41-46)	18.0 (16 to 21)	91.0 (88-93)	1.30 (1.19 to 1.41)	0.61 (0.55 to 0.61)
	Churpek[&] et al., 2017[21]	97.3 (96-98)	21.5 (20.9-22.1)	6.1[*] (5.7-6.5)	99.4[*] (99-99.6)	1.24 (1.22-1.26)	0.13 (0.08-0.18))
	Usman et al**., 2018[22]	87.9 (81.5-92.3) Sepsis related	90.2 (90-90.4) Sepsis related	1.4 (1.2-1.6)	100 (100-100)	8.97 (7.18-11.20)	0.13 (0.09-0.20)
	Samsudin^* et al., 2018[24]	85.0 (73.9-96.1)	39.7 (32.4-46.9)	24.5[*] (18.1-32.2)	92.0[*] (83.6-96.3)	1.41 (1.18-1.68)	0.38 (0.18-0.81)
	Redfern et al., 2018[26]	50.5 (49.3-51.7)	90.9 (90.7-91.2)	32.9[*] (31.6-34.2)	95.4[*] (95.2-95.6)	5.55 (5.31)	0.55 (0.53-0.56)
	Brink et al., 2019[32]	83.0 (79.4-86.1)	42.5 (41.4-43.6)	8.4* (7.7-9.2)	97.5 (96.9-98.0)	1.44* (1.38-1.51)	0.40* (0.33-0.49)

NEWS ≥6	Szakmany et al., 2018[23]	41.0 (30–53)	73.0 (67–77)	30.0 (26–35)	70.0 (65–74)	1.48 (1.02-2.16)	0.81 (0.67–0.98)
NEWS ≥7	Churpek[&] et al., 2017[21]	90.9 (88.8-92.6)	46.1 (45.3-46.8)	8.1[*] (7.6-8.6)	99.0[*] (98.7-99.2)	1.69 (1.64-1.73)	0.20 (0.16-0.24)
	Samsudin^* et al., 2018[24]	62.5 (47.5-77.5)	71.3 (64.5-78)	33.4[*] (23.7-44.6)	89.2[*] (83-93.4)	2.18 (1.56-3.05)	0.53 (0.35-0.79)
	Redfern et al., 2018[26]	30.4 (29.3-31.6)	97.7 (97.6-97.8)	53.7[*] (51.4-55.9)	94.1[*] (93.9-94.3)	13.22 (12.11-14.31)	0.71 (0.70-0.73)
	Redondo-González et al., 2018[27]	92 (80-96)	41 (33-49)	35 (27-43)	93 (84-97)	1.56 (1.38-1.76)	0.20 (0.09-0.42)
	Brink et al., 2019[32]	68.0 (63.7-72.0)	66.5 (65.4-67.5)	11.4* (10.3-12.6)	97.0 (96.5-97.5)	2.03* (1.90-2.17)	0.48* (0.42-0.55)
NEWS ≥8	de Groot et al., 2017[25]	63.0 (61-65)	63.0 (61-65)	10.0 (8-11)	96.0 (95-97)	1.70 (1.48-1.95)	0.59 (0.47-0.73)
MEWS ≥5	Churpek[&] et al., 2017[21]	75.4 (72.5-78)	62.4 (61.7-63.1)	9.5[*] (8.8-10.2)	98.0[*] (97.7-98.2)	2.01 (1.92-2.09)	0.39 (0.35-0.44)
	Samsudin^* et al., 2018[24]	45.0 (29.6-60.4)	62.1 (54.9-69.3)	21.4[*] (14-31.4)	83.1[*] (75.7-88.6)	1.19 (0.80-1.76)	0.89 (0.65-1.2)
	Van der Woude et al., 2018[31]	23.8 (8.2-47.2)	87 (83.9-89.7)	6.5[*] (2.8-14.3)	96.8[*] (94.9-98)	1.83 (0.83-4.06)	0.876 (0.69-1.12)
MEWS ≥7	de Groot et al., 2017[25]	42 (40-44)	77 (76-79)	11 (10-13)	95 (94-96)	1.83 (1.48-2.25)	0.75 (0.65-0.87)

Abbreviations: *qSOFA* Quick Sequential [Sepsis-related] Organ Failure Assessment, *NEWS* National Early Warning Score, *CI* Confidence interval, *NG* Not given, *ND* No data, *AUROC* Area under the Receiver Operating Characteristic Curve

[*]calculated values
[&]ED data only. Supplementary data sent by authors.
**PPV and NPV calculated from 2x2 tables sent by authors.
^*data from supplementary data sent by authors.

Discussion

To our knowledge, there are no previous systematic reviews looking at qSOFA and EWS at predicting ICU admission or mortality in the emergency setting for suspected sepsis. The recent publications included in this review are likely due to the recent implementation of EWS, in particular the modified versions (MEWS/NEWS). None of the studies included NEWS2 which is likely to change given its adoption nationally in the UK in March 2019[33].

The results demonstrate AUROC estimates were variable ranging from little better than chance to good prediction for mortality (NEWS: 0.59-0.88; qSOFA: 0.57-0.79; MEWS 0.56-0.75). However, individual papers mostly reported higher AUROC values for NEWS than qSOFA when compared directly at predicting mortality and ICU admission. This could be because NEWS includes more variables than qSOFA, and also has more points (20 versus 3).

At the commonly used thresholds NEWS trended to a better sensitivity than qSOFA for determining ICU admission and mortality, whereas qSOFA trended to a better specificity. Consequently, at the recommended thresholds for NEWS may be less likely to miss serious sepsis, which is necessary in an emergency setting, however, it may result in more over-triage than qSOFA. These results correlate with previous criticisms of qSOFA with high specificity for early risk assessment but a low sensitivity[34] and question whether qSOFA≥1 should be used instead[35]. These thresholds are set for a particular purpose: NEWS≥5 to identify those at risk of acute deterioration and trigger a response; qSOFA≥2 to recognise those at risk of poorer outcomes.

The results have potential for a threshold effect; changing the NEWS threshold to a higher value would increase its specificity, at the expense of sensitivity whereas in ED triage a balance has to be struck so as not to miss those that are seriously unwell.

More research is necessary for accurate conclusions to change clinical practice. Given that the population is living longer with chronic conditions, specifically including studies

that report on possible differing physiological changes by age and reporting of co-morbidities as these factors are also likely to affect in-hospital mortality and admission to ICU.

Limitations

Due to the marked heterogeneity in patient selection, outcomes and settings, the data could not be pooled for metanalysis. Including studies reporting one scoring method would increase the number of articles included and hence likely produce more results that could be grouped for meta-analysis. However, as by definition, the groups studied would be different, this would lead to significant bias, and heterogeneity.

Regarding ICU admission, only two studies reported this alone, the remaining were composite outcomes without complete datasets for comparison. Furthermore, patients who die are often older than the overall study population, and also mostly not admitted to ICU[20,36], therefore this is likely to affect a prediction model for ICU admission for reasons such as ceilings of care or do not resuscitate decisions. Most of the studies did not look at factors such as comorbidities and age, but where this has been investigated the conclusions drawn are different[25]. de Groot et al., (2017) demonstrated that for older patients the diagnostic performance for each score with in-hospital mortality in the higher scoring categories (e.g. NEWS≥7) is not as extreme as that for younger patients relating to different physiological responses in the elderly to sepsis.

Finally, studies have calculated the scores at different times; for it to be effective in the emergency setting, the scores need to be taken as early as possible (initial triage) to help with decision making and predicting those that are likely to have a poorer outcome. The immediate decision often relates to the appropriateness of ICU level care.

Conclusions

Overall, there is a wide range of results and high degree of heterogeneity between the studies which limits the ability to draw conclusions.

There is little to choose between these scores, however, at the current recommended thresholds NEWS has better sensitivity than qSOFA which has a better specificity. Consequently, NEWS may be less likely to miss serious sepsis but may result in more over-triage than qSOFA.

References

1. NICE. Sepsis: recognition, diagnosis and early management | Guidance and guidelines | NICE [Internet]. 2016 [cited 2018 Sep 4]. Available from: https://www.nice.org.uk/guidance/ng51

2. Fleischmann C, Scherag A, Adhikari NKJ, Hartog CS, Tsaganos T, Schlattmann P, et al. Assessment of Global Incidence and Mortality of Hospital-treated Sepsis. Current Estimates and Limitations. Am J Respir Crit Care Med. 2015 Sep 28;193(3):259–72.

3. Dellinger RP, Levy MM, Rhodes A, Annane D, Gerlach H, Opal SM, et al. Surviving Sepsis Campaign: International Guidelines for Management of Severe Sepsis and Septic Shock 2012. Critical Care Medicine. 2013 Feb;41(2):580.

4. Bone RC, Balk RA, Cerra FB, Dellinger RP, Fein AM, Knaus WA, et al. Definitions for sepsis and organ failure and guidelines for the use of innovative therapies in sepsis. The ACCP/SCCM Consensus Conference Committee. American College of Chest Physicians/Society of Critical Care Medicine. Chest. 1992 Jun;101(6):1644–55.

5. Marik PE, Taeb AM. SIRS, qSOFA and new sepsis definition. J Thorac Dis. 2017 Apr;9(4):943–5.

6. Vincent J-L, Opal SM, Marshall JC, Tracey KJ. Sepsis definitions: time for change. The Lancet. 2013 Mar 2;381(9868):774–5.

7. Levy MM, Fink MP, Marshall JC, Abraham E, Angus D, Cook D, et al. 2001 SCCM/ESICM/ACCP/ATS/SIS International Sepsis Definitions Conference. Crit Care Med. 2003 Apr;31(4):1250–6.

8. Singer M, Deutschman CS, Seymour CW, Shankar-Hari M, Annane D, Bauer M, et al. The Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3). JAMA. 2016 Feb 23;315(8):801–10.

9. Seymour CW, Liu VX, Iwashyna TJ, Brunkhorst FM, Rea TD, Scherag A, et al. Assessment of Clinical Criteria for Sepsis: For the Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3). JAMA. 2016 Feb 23;315(8):762–74.

10. Anesi GL, Liu VX, Gabler NB, Delgado MK, Kohn R, Weissman GE, et al. Associations of ICU Capacity Strain with Disposition and Outcomes of Patients with Sepsis Presenting to the Emergency Department. Ann Am Thorac Soc. 2018 Aug 16;

11. Fernando SM, Rochwerg B, Reardon PM, Thavorn K, Seely AJE, Perry JJ, et al. Emergency Department disposition decisions and associated mortality and costs in ICU patients with suspected infection. Crit Care. 2018 Jul 6;22(1):172.

12. NHS England » National Early Warning Score (NEWS) [Internet]. [cited 2018 Nov 14]. Available from: https://www.england.nhs.uk/ourwork/clinical-policy/sepsis/nationalearlywarningscore/

13. NHS England approves use of National Early Warning Score (NEWS) 2 to improve detection of acutely ill patients [Internet]. RCP London. 2017 [cited 2018 Nov 14]. Available from: https://www.rcplondon.ac.uk/news/nhs-england-approves-use-national-early-warning-score-news-2-improve-detection-acutely-ill

14. Steyerberg EW, Vickers AJ, Cook NR, Gerds T, Gonen M, Obuchowski N, et al. Assessing the performance of prediction models: a framework for some traditional and novel measures. Epidemiology. 2010 Jan;21(1):128–38.

15. PROSPERO [Internet]. International prospective register of systematic reviews. [cited 2018 Dec 8]. Available from: https://www.crd.york.ac.uk/prospero/#searchadvanced

16. Moher D, Liberati A, Tetzlaff J, Altman DG, PRISMA Group. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. PLoS Med. 2009 Jul 21;6(7):e1000097.

17. Whiting PF, Rutjes AWS, Westwood ME, Mallett S, Deeks JJ, Reitsma JB, et al. QUADAS-2: a revised tool for the quality assessment of diagnostic accuracy studies. Ann Intern Med. 2011 Oct 18;155(8):529–36.

18. University of York. Our guidance - Centre for Reviews and Dissemination, The University of York [Internet]. [cited 2019 Apr 29]. Available from: https://www.york.ac.uk/crd/guidance/

19. Youngstrom EA. A Primer on Receiver Operating Characteristic Analysis and Diagnostic Efficiency Statistics for Pediatric Psychology: We Are Ready to ROC. J Pediatr Psychol. 2014 Mar;39(2):204–21.

20. Goulden R, Hoyle M-C, Monis J, Railton D, Riley V, Martin P, et al. qSOFA, SIRS and NEWS for predicting inhospital mortality and ICU admission in emergency admissions treated as sepsis. Emerg Med J. 2018 Jun;35(6):345–9.

21. Churpek MM, Snyder A, Xuan Han, Sokol S, Pettit N, Howell MD, et al. Quick Sepsis-related Organ Failure Assessment, Systemic Inflammatory Response Syndrome, and Early Warning Scores for Detecting Clinical Deterioration in Infected Patients outside the Intensive Care Unit. American Journal of Respiratory & Critical Care Medicine. 2017 4/1/2017;195(7):906–11.

22. Usman O.A., Usman A.A., Ward M.A. Comparison of SIRS, qSOFA, and NEWS for the early identification of sepsis in the Emergency Department. Am J Emerg Med [Internet]. 2018;((Usman) Center for Health Policy, Primary Care and Outcomes Research, Stanford University, 117 Encina Commons, Stanford, CA 94305-6006, United States). Available from: http://www.journals.elsevier.com/american-journal-of-emergency-medicine/

23. Szakmany T., Pugh R., Kopczynska M., Lundin R.M., Sharif B., Morgan P., et al. Defining sepsis on the wards: results of a multi-centre point-prevalence study comparing two sepsis definitions. Anaesthesia. 2018;73(2):195–204.

24. Samsudin MI, Liu N, Prabhakar SM, Chong S-L, Kit Lye W, Koh ZX, et al. A novel heart rate variability based risk prediction model for septic patients presenting to the emergency department. Medicine. 2018 Jun;97(22):e10866–e10866.

25. de Groot B, Stolwijk F, Warmerdam M, Lucke JA, Singh GK, Abbas M, et al. The most commonly used disease severity scores are inappropriate for risk stratification of older emergency department sepsis patients: an observational multi-centre study. Scand J Trauma Resusc Emerg Med. 2017 Sep 11;25(1):91.

26. Redfern O, Smith G, Prytherch D, Meredith P, Inada-Kim M, Schmidt P. A Comparison of the Quick Sequential (Sepsis-Related) Organ Failure Assessment Score and the National Early Warning Score in Non-ICU Patients With/Without Infection. Critical Care Medicine. 2018 Dec 1;46(12):1923–33.

27. Redondo-Gonzalez A., Varela-Patino M., Alvarez-Manzanares J., Oliva-Ramos J.R., Lopez-Izquierdo R., Ramos-Sanchez C., et al. Assessment of the severity scores in

patients included in a sepsis code in an emergency departament. Rev Esp Quimioter. 2018;31(4):316–22.

28. Innocenti F, Tozzi C, Donnini C, De Villa E, Conti A, Zanobetti M, et al. SOFA score in septic patients: incremental prognostic value over age, comorbidities, and parameters of sepsis severity. Intern emerg medicine. 2018;13(3):405–12.

29. Martino IF, Figgiaconi V, Seminari E, Muzzi A, Corbella M, Perlini S. The role of qSOFA compared to other prognostic scores in septic patients upon admission to the emergency department. EUR J INTERN MED. 2018;53(9003220):e11–3.

30. Liu S.-J., Hu H. Comparison of six scoring systems for predicting the mortality of severe sepsis patients in the emergency department. Am J Emerg Med. 2018;36(5):902–4.

31. van der Woude S.W., van Doormaal F.F., Hutten B.A., Nellen F.J., Holleman F. Classifying sepsis patients in the emergency department using SIRS, qSOFA or MEWS. Neth J Med. 2018;76(4):158–66.

32. Brink A, Alsma J, Verdonschot RJCG, Rood PPM, Zietse R, Lingsma HF, et al. Predicting mortality in patients with suspected sepsis at the Emergency Department; A retrospective cohort study comparing qSOFA, SIRS and National Early Warning Score. PLOS ONE. 2019 Jan 25;14(1):e0211133.

33. NHS Improvement. Resources to support the safe adoption of the revised NEWS (NEWS2) [Internet]. [cited 2018 Nov 16]. Available from: https://improvement.nhs.uk/news-alerts/safe-adoption-of-NEWS2/

34. Song J-U, Sin CK, Park HK, Shim SR, Lee J. Performance of the quick Sequential (sepsis-related) Organ Failure Assessment score as a prognostic tool in infected patients outside the intensive care unit: a systematic review and meta-analysis. Crit Care. 2018;22(1):28.

35. Jiang J, Yang J, Mei J, Jin Y, Lu Y. Head-to-head comparison of qSOFA and SIRS criteria in predicting the mortality of infected patients in the emergency department: a meta-analysis. Scandinavian Journal of Trauma, Resuscitation and Emergency Medicine. 2018 Jul 11;26(1):56.

36. Kopczynska M, Sharif B, Cleaver S, Spencer N, Kurani A, Lee C, et al. Red-flag sepsis and SOFA identifies different patient population at risk of sepsis-related deaths on the general ward. Medicine (Baltimore). 2018;97(49):e13238.

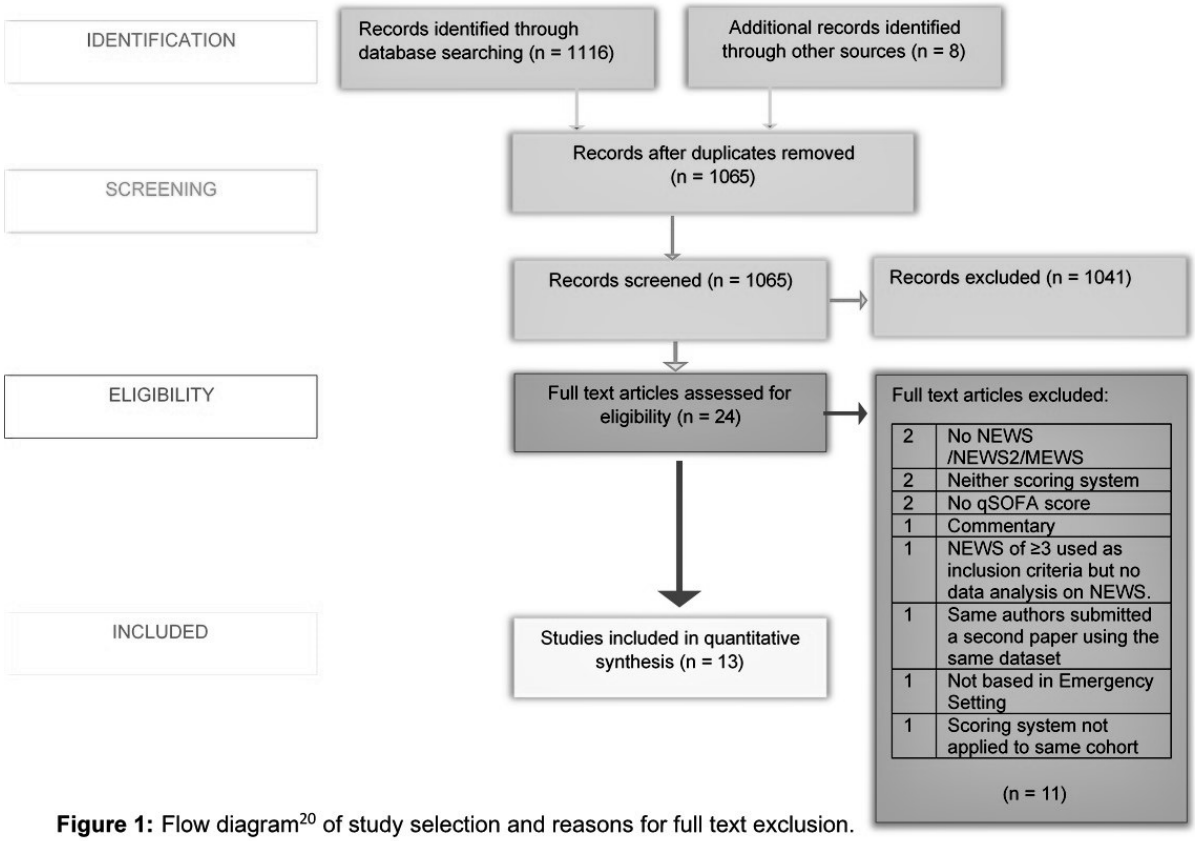

Figure 1: Flow diagram[20] of study selection and reasons for full text exclusion.