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How can paramedics use an early warning score to prioritise adults with suspected sepsis?

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Introduction

Early recognition and treatment of sepsis is essential to reducing mortality. The Surviving Sepsis Campaign recommends treatment within one hour of presentation.[1] This can only be achieved if sepsis is prioritised in the emergency care system. However, systematic reviews [2,3] have identified few studies evaluating prehospital recognition of sepsis, and concluded that provider impression had poor sensitivity for sepsis [2] and recognition of sepsis by ambulance clinicians was poor.[3] Early warning scores use simple clinical measurements to calculate a score indicating the risk of adverse outcome.[4] Paramedics can use early warning scores to prioritise people with suspected sepsis for treatment, by pre-alerting the emergency department or starting treatment on the way to hospital, if the score exceeds a threshold.

The National Institute for Health and Care Excellence (NICE) recommends suspecting sepsis if a person presents with signs or symptoms that indicate possible infection, noting that people with sepsis may have non-specific presentations.[5] NICE guidance recommends that ambulance services pre-alert hospitals for high-risk patients with sepsis and recommends research to determine whether early warning scores can improve the detection of sepsis in pre-hospital settings. Guidelines from the Joint Royal Colleges Ambulance Liaison Committee (JRCALC) recommend considering sepsis in all patients with non-specific, non-localised presentations and using a structured screening tool and National Early Warning Score version 2 (NEWS2) to stratify risk, but does not specify which screening tool to use. The UK Sepsis Trust recommends that any adult who is unwell or has a NEWS2 score of five or above should be assessed for sepsis, using “red flag” criteria to prioritise those at higher risk.[6] The evidence-base for this recommendation is unclear and the implications of prioritising on this basis has not been extensively studied. International guidelines from the Surviving Sepsis Campaign recommend a bundle of treatments required within one hour of recognition of sepsis, but do not provide specific recommendations for paramedics.[1] A task force convened by the Society of Critical Care Medicine and the European Society of Intensive Care Medicine recommended use of the qSOFA score to rapidly identify patients at higher risk of adverse outcome in out-of-hospital and emergency department settings.[7]

Early warning scores may assist prehospital assessment of suspected sepsis in adults and children. However, differences in physiology, case mix, comorbidities, and causes of sepsis mean that the composition, accuracy, and impact of early warning scores differ markedly between adults and children. Here, we focus on early warning scores for adults.

What is the evidence of uncertainty?

The NICE Guideline Development Group [5] identified 12 studies evaluating four generic scores that could be used for suspected sepsis: the Simple Triage Scoring System (STSS), Rapid Emergency Medicine Score (REMS) or modified-REMS, the Modified Early Warning score (MEWS) and National Early Warning score (NEWS). All studies used hospital populations and were judged as being of very low quality. A systematic review of hospital studies suggested that early warning scores predicted mortality in sepsis with limited accuracy, based on poor quality data.[8] More recently, the qSOFA score has been derived and validated.[9] A systematic review of hospital studies suggested that qSOFA has better specificity for predicting adverse outcome at its recommended threshold but NEWS has better sensitivity.[10]

Hospital-based studies provide only limited evidence to guide prehospital use of early warning scores, given the differences between prehospital and in-hospital populations. Lane [2] and Smyth [3] undertook systematic reviews of prehospital identification of sepsis. They identified three studies that developed sepsis-specific prehospital scores (Prehospital Early Sepsis Detection (PRESEP), Prehospital Severe Sepsis (PRESS), and the Critical Illness Score (CIS)) and other studies evaluating MEWS, the Systemic Inflammatory Response Syndrome (SIRS) criteria, and the Robson tool. Lane [2] concluded that structured screening for sepsis demonstrated modest sensitivity and specificity, while Smyth [3] noted that the scores had not been validated in clinical practice. Both reviews recommended research to improve accuracy and validate the scores.

We searched for studies evaluating the accuracy or the effect of implementation of early warning scores for suspected sepsis in a prehospital population (see Box). We only included studies with validation data, i.e. where the score was tested on a different data set from the one used for derivation. We identified 13 studies evaluating 20 scores. Table 1 outlines the characteristics of the studies and the sensitivity and specificity of the scores studied, using different thresholds for positivity where appropriate. The study populations included people transported to hospital by Emergency Medical Services (EMS) but varied in the use of selection criteria from including all medical cases to including only those with presumed or diagnosed sepsis. Definitions of the reference standard were inconsistent, and included diagnosis (sepsis), prognosis (mortality) or health service use (ICU admission). Some results suggest promising accuracy, but there was substantial variation in both sensitivity and specificity. The most extensively studied score, qSOFA (nine studies) had sensitivity ranging from 0.16 to 0.86 and specificity ranging from 0.16 to 0.97. Figure 1 shows the variables included in the scores, which used different combinations of six

physiological measures and age, with few additional variables. Differences in study populations and outcomes, shown in table 1, rather than variation in the composition of the scores, shown in figure 1, may explain the marked differences in the accuracy of different scores. We are therefore unable to conclude that any score is superior to the others.

Two studies evaluated the impact of implementing prehospital early warning scores. Polito et al [23] reported a single-centre study showing that implementation of the PRESS score improved sepsis recognition by prehospital personnel from 12% (11/51 patients) before to 60% (47/78) after implementation. Borelli et al [24] reported a single-centre study showing that implementation of prehospital sepsis screening tool improved 3-hour sepsis bundle compliance for 20 screening tool positive patients compared to 43 historical controls.

Is ongoing research likely to provide relevant evidence?

We also searched for ongoing and planned studies of prehospital early warning scores for suspected sepsis. The National Institute for Health Research (NIHR) has funded the PHEWS study (Pre-Hospital Early Warning for Sepsis) to determine the accuracy, impact and cost-effectiveness of prehospital early warning scores for adults with suspected sepsis.[25] The study will: (1) Estimate the accuracy of prehospital early warning scores for predicting potential to benefit from time-critical treatment for sepsis in adults with possible sepsis who are attended by emergency ambulance; and (2) Estimate the impact of using prehospital early warning scores to guide key prehospital decisions, in terms of the operational consequences, and the cost-effectiveness of alternative strategies. Based on the findings, further research may then be required, in the form of a randomised trial, to provide definitive evidence that use of an early warning score improves outcomes and is cost-effective.

What should we do in the light of the uncertainty?

The available literature provides little evidence to address the following key issues:

- Paramedics need to know what threshold of an early warning score gives an appropriate balance of sensitivity and specificity for decision-making. Using a low threshold optimises sensitivity at the expense of specificity. This ensures prioritisation of people with severe sepsis, but may lead to “over-triage” if people with a low risk of severe sepsis are prioritised, resulting in increased pressure on emergency departments to prioritise multiple patients and inappropriate prehospital treatment. Conversely, using a higher threshold to improve

specificity may reduce sensitivity, leading to “under-triage” if people with severe sepsis are not prioritised and do not receive urgent treatment.

- Paramedics need to know when they should use the score. Applying a score indiscriminately to patients with nonspecific symptoms is likely to yield a low prevalence of severe sepsis and consequent over-triage, while restricting the score to cases with clear evidence of infection may miss cases.
- Paramedics may use their clinical judgement to interpret and act on early warning scores. Clinical judgement can identify potential false positive and false negative scores, and thus improve their accuracy in practice, but clinical judgement may be subject to well-recognised cognitive biases that lead to errors of judgement.
- The available evidence is from healthcare systems with highly developed prehospital care delivered by trained paramedics. There is no evidence to guide practice in less developed settings, such as those in low and middle-income countries.

Early warning scores have been validated to the extent that a higher score indicates a higher risk of adverse outcome, but the existing evidence is insufficient to justify recommending their routine use or suggest that one score is superior to another. If paramedics choose to use an early warning score to assess the risk of adverse outcome, they need to use clinical judgement to determine when they should use the score and how the score should influence decision-making. They should recognise that decision-making involves a trade-off between sensitivity (under-triage) and specificity (over-triage), and draw upon knowledge of the emergency care system and interactions with receiving hospitals to determine when the score should trigger use of a pre-alert.

Competing interests

We have read and understood the BMJ Group policy on declaration of interests and declare grant support from the National Institute of Health Research to their employing institutions. The authors are co-investigators on the PHEWS study.

Author contributions

SG conceived the articles and wrote the first draft. BT undertook the literature review and MS contributed additional data. All authors contributed to developing and redrafting the article. All authors approved the final draft.

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What you need to know

- Many prehospital early warning scores have been developed, based upon a limited range of routinely recorded variables
- Existing evidence is insufficient to recommend one early warning score over another or determine how the scores should be used in practice
- Paramedics need to balance the risk of missing sepsis (under-triage) against the potential to over-use pre-alerts to the emergency department or prehospital treatment (over-triage)

How patients were involved in the creation of this article

Two members of the Sheffield Emergency Care Forum (Enid Hirst and Linda Abouzeid) and an independent patient representative (Peter Hewkin) reviewed and commented on the paper.

What patients need to know

Paramedics can use early warning scores to decide when to alert the emergency department and start treatment for patients with sepsis. Many early warning scores have been developed but the available research does not tell us which is best or how paramedics should use them. Early warning scores need to be used in a way that achieves the best balance between the risk of missing cases of sepsis and the risks of over-diagnosis and over-treatment.

Education into practice

How do you decide which patients should be suspected of having sepsis?

If you use an early warning score, how do you decide what score should trigger initiation of treatment for sepsis and a pre-alert to the emergency department?

What are the consequences of under-triage and over-triage, and how would you know if either was occurring?

Box: Literature search for studies evaluating the accuracy or the effect of implementation of early warning scores for suspected sepsis in a prehospital population

Search strategy

1. Ambulances /
2. Air Ambulances /
3. paramedic*
4. “Emergency Service*” [Title/Abstract]
5. allied health personnel /
6. emergency medical technicians /
7. “out of hospital”
8. “Emergency Medical Service*"
9. EMS
10. Prehospital [Title/Abstract]
11. emergency treatment /
12. “transportation of patients" /
13. EMT
14. 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13
15. Sepsis /
16. Septicemia*
17. Septicaemia*
18. Sepsis
19. Septic
20. Systemic Inflammatory Response Syndrome /
21. “Systemic Inflammatory Response Syndrome” [Title/Abstract]
22. SIRS
23. “serious infection*” [Title/Abstract]
24. 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23
25. Risk Assessment / classification
26. Risk Assessment / methods*
27. Point-of-Care Systems /
28. Severity of Illness Index /
29. EWS[Title/Abstract]
30. “Early Warning Scoring”[Title/Abstract]

31. “early warning”[Title/Abstract]
32. “warning system*”[Title/Abstract]
33. "warning scoring*”[Title/Abstract]
34. “Early detection” [Title/Abstract]
35. Prediction [Title/Abstract]
36. “screening tool*”[Title/Abstract]
37. 24 or 25 or 26 or 27 or 28 or 29 or 30 or 31 or 32 or 33 or 34 or 35 or 36
38. 14 and 24 and 37

Databases and registries searched to identify completed and ongoing studies to address the uncertainty

Database or registry searched	**Number of search results**
EMbase	167
CINHAL	81
Pubmed	562
Clinicaltrials.gov	0
ISRCTN	0
Research registry	1

PRISMA flow chart.

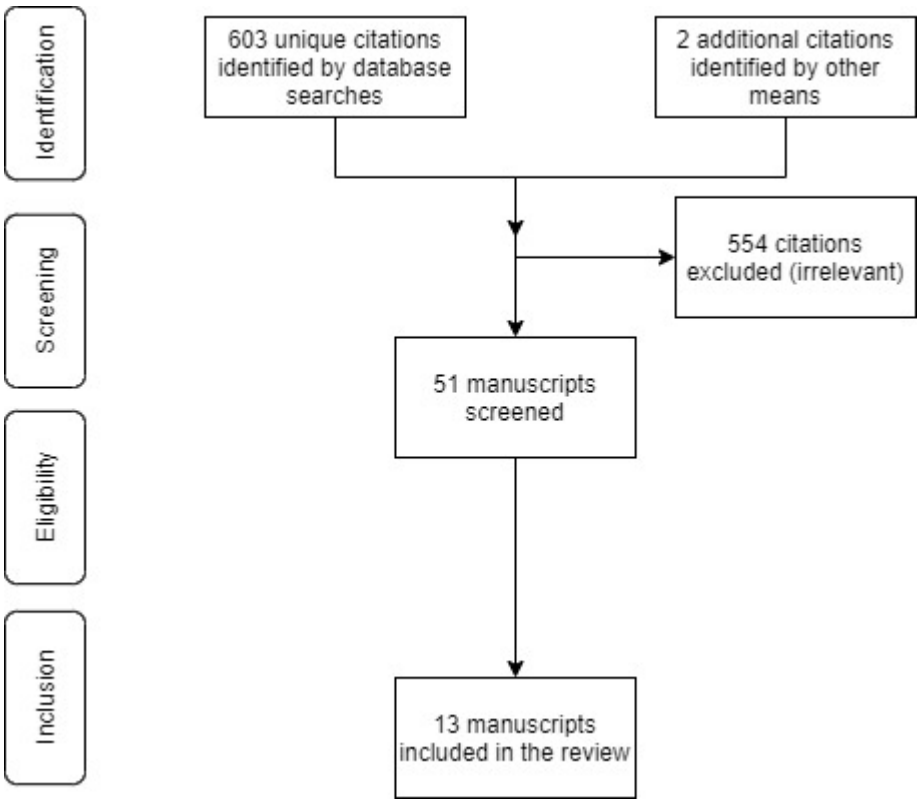
Identification
Screening
Eligibility
Inclusion
603 unique citations identified by database searches
2 additional citations identified by other means
554 citations excluded (irrelevant)
51 manuscripts screened
13 manuscripts included in the review

Table 1: Characteristics and results of the studies

Lead author, year	Study design	N	Population	Outcome or reference standard	Scores evaluated (threshold)	Sensitivity	Specificity
Bayer, 2015 [11]	Retrospective cohort	375	Adult EMS transfers to ED	Sepsis	RST	0.95	0.43
					MEWS (4)	0.74	0.75
					90-30-90	0.62	0.83
Polito, 2015 [12]	Retrospective cohort	114	Adult medical EMS transfers at risk of sepsis	Severe sepsis	PRESS	0.86	0.47
Dorsett, 2017 [13]	Retrospective cohort	152	Adult EMS transfers to the ED diagnosed with infection	Severe sepsis / septic shock	qSOFA (2)	0.16	0.97
Jouffroy, 2018 [14]	Retrospective cohort	37	Presumed septic shock	ICU admission	qSOFA (2)	0.62	0.16
					RST (2)	1.0	0.16
					MEWS (5)	0.85	0.33
					PRESEP (4)	0.92	0.29
Smyth, 2018 [15] & 2019 [16]	Retrospective cohort	6682	Adult medical cases	High risk of severe illness or death from sepsis (NICE)	SEPSIS (2)	0.95	0.57
					SEPSIS (3)	0.8	0.78
					SEPSIS (5)	0.37	0.96

					CIS	0.45	0.94
					PRESEP	0.61	0.87
					PRESS	0.18	0.97
					qSOFA	0.29	0.93
					90-30-90	0.63	0.97
					MEWS (4)	0.63	0.96
					NEWS (2)	0.99	0.87
					NEWS (3)	0.97	0.89
					NEWS (5)	0.85	0.93
Koyama, 2019 [17]	Retrospective cohort	925	Adult EMS transfers to ED with presumed infection	In-hospital mortality	qSOFA	0.71	0.51
Shu, 2019 [18]	Retrospective cohort	2292	Adult EMS transfers to ED	Sepsis and in-hospital mortality	qSOFA**	0.43	0.94
Silcock, 2019 [19]	Retrospective cohort	1713	Adult EMS transfers to ED	ICU admission or 30-day mortality	qSOFA (1)	0.61	0.71
					qSOFA (2)	0.18	0.97
					NEWS2 (5)	0.65	0.72
Usal, 2019 [20]	Retrospective cohort	266	Adult EMS transfers to ED with sepsis	ICU admission and 28-day mortality	MEWS (6)***	0.58	0.69
					qSOFA (2)***	0.86	0.47

Vaittinada Ayar, 2019 [21]	Prospective cohort	322	Adult EMS transfers to ED with suspicion of infection	28-day mortality	qSOFA (2)	0.60	0.67
Lane, 2020 [22]	Retrospective cohort	12740	Adult EMS transfers to ED with infection diagnosed in the ED	Sepsis	Sepsis Alert	0.07	0.99
					qSOFA*	0.40	0.94
					PITSTOP	0.02	1.0
					PRESS (2)	0.11	0.98
					SEPSIS (5)	0.26	0.94
					90-30-90 (1)	0.57	0.79
					Borrelli strategy (3)	0.49	0.86
					MEWS (4)	0.53	0.77
					PRESEP (4)	0.49	0.76
					MBIS	0.44	0.77
					PSP (2)	0.42	0.77
					PreSAT (2)	0.49	0.71
					PHANTASi	0.2	0.88
					RST (2)	0.75	0.54
					HEWS (2)	0.85	0.41
					Suffoletto strategy	0.7	0.38

Polito, 2018 [23]	Before v after study	285	Adult EMS transfers to ED with HR>90, SBP<110 or RR>20	Primary outcome: Proportion with prehospital recognition of sepsis			
Borelli, 2019 [24]	Before v after study	63	Adult EMS transfers to ED with severe sepsis or septic shock	Primary outcome: 3-hour sepsis bundle compliance			

90-30-90 score consisting of systolic blood pressure below 90mmHg, respiratory rate above 30/minute and oxygen saturation below 90%; CIS Critical Illness Score; ED emergency department; EMS emergency medical service; HEWS Hamilton Early Warning Score; MBIS Mecklenburg Bacterial Infection Scale; MEWS Modified Early Warning score; NEWS National Early Warning Score; PHANTASi Prehospital Antibiotics Against Sepsis; PITSTOP Paramedic Initiated Treatment of Sepsis Targeting Out-of-Hospital Patients clinical trial; PreSAT Prehospital Sepsis Assessment Tool; PRESEP Prehospital Early Sepsis Detection; PRESS Prehospital Severe Sepsis; PSP Prehospital Sepsis Project; qSOFA quick Sepsis Related Organ Failure Assessment; RST Robson Screening Tool; SEPSIS screening to enhance prehospital identification of sepsis.

*Results are for sepsis, mortality also reported in a separate paper (Lane 2020, PHEC)

**Results are for sepsis, mortality also reported

***Results are for ICU admission, mortality also reported

Figure 1: Variables included in early warning scores

Early Warning Score	Number of variables	Age	Temperature	Heart rate	Respiratory rate	Oxygen saturation	Conscious level	Systolic BP	Other
90-30-90	3				●	●		●	
Borelli	7	●	●	●	●	●	●	●	Suspected infection
CIS	6	●		●	●	●	●	●	
HEWS	6		●	●	●	●	●	●	
MBIS	4		●	●			●	●	
MEWS	5		●	●	●		●	●	
NEWS	7		●	●	●	●	●	●	Inspired oxygen
PHANTASi	3		●	●	●				
PITSTOP	2		●					●	
PreSAT	4		●	●	●			●	
PRESEP	1		●						
PRESS	5	●	●			●		●	Dispatch chief complaint of sick person; nursing home resident
PSP	4		●	●	●			●	
qSOFA	3				●		●	●	
RST	5		●	●	●		●		Glucose
SEPSIS	8	●	●	●	●	●	●	●	Skin appearance
Sepsis Alert	6	●	●	●	●				Suspected or documented infection, hypoperfusion
Suffoletto strategy	2		●					●	

90-30-90 score consisting of systolic blood pressure below 90mmHg, respiratory rate above 30/minute and oxygen saturation below 90%; CIS Critical Illness Score; HEWS Hamilton Early Warning Score; MBIS Mecklenburg Bacterial Infection Scale; MEWS Modified Early Warning score; NEWS National Early Warning Score; PHANTASi Prehospital Antibiotics Against Sepsis; PITSTOP Paramedic Initiated Treatment of Sepsis Targeting Out-of-Hospital Patients clinical trial; PreSAT Prehospital Sepsis Assessment Tool; PRESEP Prehospital Early Sepsis Detection; PRESS Prehospital Severe Sepsis; PSP Prehospital Sepsis Project; qSOFA quick Sepsis Related Organ Failure Assessment; RST Robson Screening Tool; SEPSIS screening to enhance prehospital identification of sepsis.