UNCERTAINTIES

Should prehospital early warning scores be used to identify which patients need urgent treatment for sepsis?

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What you need to know

- Many prehospital early warning scores have been developed, based on a limited range of routinely recorded variables
- Existing evidence is insufficient to recommend one early warning score over another or to determine how the scores should be used in practice
- 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)

Early recognition and treatment of sepsis is essential to reduce mortality, but this can only be achieved if patients with suspected sepsis receive priority treatment in the emergency care system. One suggested approach for identifying these patients is through the use of early warning scores. These use simple clinical measurements to calculate a score indicating the risk of adverse outcome, 1 and several guidelines make recommendations around their use in early recognition of sepsis (see box 1).

Box 1: Guidelines recommending the use of early warning scores to aid in early recognition of sepsis risk in adults

- The National Institute for Health and Care Excellence (NICE) recommends that ambulance services pre-alert hospitals when any high risk criteria are present (diagnostic and prognostic criteria, as defined by NICE), and recommends research to determine whether early warning scores can improve the detection of sepsis in prehospital settings. 2
- The UK Sepsis Trust recommends that any adult who is unwell or has a National Early Warning Score version 2 (NEWS2) of ≥5 should be assessed for sepsis, using “red flag” criteria to prioritise those at highest risk. 3 However, the evidence for recommending NEWS2 or selecting specific red flags is unclear, and the implications of prioritising on this basis have not been extensively studied.
- Guidelines from the international Surviving Sepsis Campaign recommends that treatments are initiated within one hour of recognition of sepsis but do not provide specific recommendations for prehospital care practitioners. 4
- Guidelines from the UK’s Joint Royal Colleges Ambulance Liaison Committee (JRCALC) recommend using a structured screening tool and NEWS2 to stratify risk but do not specify which screening tool to use. 5
- 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 high risk of adverse outcome in out-of-hospital and emergency department settings. 6

Early warning scores can be used by prehospital care practitioners (such as paramedics in the UK) to prioritise people with suspected sepsis for treatment; for example, by pre-alerting the emergency department or starting treatment on the way to hospital if the score exceeds a certain threshold. These 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 by prehospital care practitioners assessing suspected sepsis or to suggest that one score is superior to another.

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. This paper focuses on early warning scores for adults.

What is the evidence of uncertainty?

There is more evidence about in-hospital scoring than about prehospital scoring (see box 2).

Box 2: Evidence about in-hospital early warning scoring for sepsis

- The NICE Guideline Development Group 2 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 (NEWS), and the National Early Warning Score (NEWS). All studies used hospital populations and were judged by the NICE Guideline Development Group as being of very low quality using GRADE scoring
- A meta-analysis and systematic review of in-hospital studies suggested that early warning scores predicted mortality in sepsis with limited accuracy, based on poor quality data. 7
- In 2021, a systematic review comparing qSOFA and hospital early warning scores for prognosis in suspected sepsis in emergency department patients suggested that qSOFA has better specificity for predicting adverse outcome at its recommended threshold but NEWS has better sensitivity. 8

However, hospital based studies provide only limited evidence to guide prehospital use of early warning scores, given the differences between prehospital and in-hospital populations.
Systematic reviews published in 2016 identified few studies (cohort and observational studies) evaluating prehospital recognition of sepsis—these concluded that prehospital provider impression had poor sensitivity for sepsis and recognition of sepsis by ambulance clinicians was poor. Three of the studies from these systematic reviews evaluated sepsis-specific prehospital scores (Prehospital Early Sepsis Detection (PRESEP), Prehospital Severe Sepsis (PRESS), and the Critical Illness Score (CIS)), and the other studies evaluated MEWS, the Systemic Inflammatory Response Syndrome (SIRS) criteria, and the Robson tool. Researchers found that structured prehospital screening for sepsis demonstrated modest sensitivity and specificity and noted that prehospital scores had not been validated in clinical practice. Both reviews recommended research to improve accuracy and to validate the scores.

Our literature search

Using the search strategy described in box 3, we identified 13 studies evaluating 20 scores (fig 1). The most extensively studied score, qSOFA (studied in nine of the 13 studies) had sensitivity ranging from 0.16 to 0.86 and specificity ranging from 0.16 to 0.97.

Box 3: Search strategy for studies evaluating early warning scores for suspected sepsis in prehospital populations

We searched for primary research studies evaluating the sensitivity and specificity or the effect of implementation of early warning scores for suspected sepsis in a prehospital population (see below for search terms). We only included studies with validation data—that is, where the score was tested on a different data set from the one used for derivation. Two of the studies we identified had been included in the 2016 systematic reviews mentioned above. The available evidence is from healthcare systems with highly developed prehospital care delivered by trained practitioners. There is no evidence to guide practice in less developed settings, such as those in low and middle income countries.

Search strategy

- Ambulances /
- Air ambulances /
- Paramedic
- “Emergency service” [Title/Abstract]
- Allied health personnel /
- Emergency medical technicians /
- “Out of hospital”
- “Emergency medical service”
- EMS
- Prehospital [Title/Abstract]
- “Emergency treatment” /
- “Transportation of patients” /
- EMT
- 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
- Sepsis /
- Septicemia*
- Septicaemia*
- Sepsis
- Septic
- Systemic inflammatory response syndrome /
- “Systemic inflammatory response syndrome” [Title/Abstract]
- SIRS
- “Serious infection” [Title/Abstract]
- 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23
- Risk assessment / classification
- Risk assessment / methods*
- Point-of-care systems /
- Severity of illness index /
- EWS[Title/Abstract]
- “Early warning scoring” [Title/Abstract]
- “Early warning” [Title/Abstract]
- “Warning system” [Title/Abstract]
- “Warning scoring” [Title/Abstract]
- “Early detection” [Title/Abstract]
- Prediction [Title/Abstract]
- “Screening tool” [Title/Abstract]
- 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
- 14 and 24 and 37

Databases and registries searched

We searched the following to identify completed and ongoing studies to address the uncertainty

- Embase—167 search results
- CINHAL—81 search results
- Pubmed—562 search results
- Clinicaltrials.gov—0 search results
- ISRCTN—0 search results
- Research registry—1 search result
Table 1 shows the variables included in the early warning scores for prehospital sepsis: these used different combinations of six physiological measures and age, with few additional variables. Differences in study populations and outcomes (shown in table 2), rather than variation in the composition of the scores, may explain the marked differences in the accuracy of different scores. We are therefore unable to demonstrate that any score is superior to the others.
Table 1 | Variables included in early warning scores

| Early warning score | No of variables | Age | Temperature | Heart rate | Respiratory rate | Oxygen saturation | Level of consciousness | Systolic blood pressure | Other |
|---------------------|-----------------|-----|-------------|------------|-----------------|-------------------|------------------------|------------------------|-------|
| 90-30-90*           | 3               |     |             |            |                 |                   |                        |                        |       |
| Borelli             | 7               |     |             |            |                 |                   |                        |                        | Suspected infection     |
| CIS                 | 6               |     |             |            |                 |                   |                        |                        |       |
| HEWS                | 7               |     |             |            |                 |                   |                        |                        |       |
| MBIS                | 4               |     |             |            |                 |                   |                        |                        |       |
| MEWS                | 5               |     |             |            |                 |                   |                        |                        |       |
| NEWS                | 7               |     |             |            |                 |                   |                        |                        |       |
| PHANTASi            | 3               |     |             |            |                 |                   |                        |                        |       |
| PITSTOP             | 3               |     |             |            |                 |                   |                        |                        | Suspected infection     |
| PreSat              | 5               |     |             |            |                 |                   |                        |                        | Suspected infection     |
| PRESEP              | 5               |     |             |            |                 |                   |                        |                        |       |
| PRESS               | 8               |     |             |            |                 |                   |                        |                        | Chief complaint at dispatch† Nursing home resident |
| PSP                 | 4               |     |             |            |                 |                   |                        |                        |       |
| qSOFA               | 3               |     |             |            |                 |                   |                        |                        |       |
| RST                 | 5               |     |             |            |                 |                   |                        | Blood glucose >6.6 mmol/L (unless diabetic) |
| SEPSIS              | 8               |     |             |            |                 |                   |                        | Skin pallor, mottling, or jaundice |
| Sepsis Alert        | 6               |     |             |            |                 |                   |                        | Suspected or documented infection Hypoperfusion |
| Suffoletto strategy | 3               |     |             |            |                 |                   |                        | Suspected infection     |

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.

* 90-30-90 score consists of systolic blood pressure <90 mm Hg, respiratory rate >30/min, and oxygen saturation <90%.
† Relates to the “sick person” category generated by the ambulance service dispatch system when a caller responds to scripted questions.
Table 2 | Characteristics and results of the studies

| Lead author, year | Study design         | No of participants | Population                                          | Outcome or reference standard                                                      | Scores evaluated (threshold) | Sensitivity | Specificity |
|-------------------|----------------------|--------------------|-----------------------------------------------------|-------------------------------------------------------------------------------------|-------------------------------|-------------|-------------|
| Bayer 2015        | 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       | Retrospective cohort | 114                | Adult medical EMS transfers at risk of sepsis      | PRESS                                                                               | 0.86                         | 0.47        |
| Dorsett 2017      | Retrospective cohort | 152                | Adult EMS transfers to ED diagnosed with infection | qSOFA (2)                                                                           | 0.16                         | 0.97        |
| Jouffroy 2018     | 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        |
| Smyth 2018        | Retrospective cohort | 6682               | Adult medical cases                                 | High risk of severe illness or death from sepsis (NICE)                           | qSOFA (2) 0.95               | 0.57        |
|                   | and 2019             |                    |                                                     |                                                      | SEPSIS (2) 0.8                | 0.78        |
|                   |                      |                    |                                                     |                                                      | SEPSIS (5) 0.37              | 0.96        |
| Koyama 2019       | Retrospective cohort | 925                | Adult EMS transfers to ED with presumed infection   | In-hospital mortality                                                               | qSOFA 0.71                   | 0.51        |
| Shu 2019          | Retrospective cohort | 2292               | Adult EMS transfers to ED                           | Sepsis and in-hospital mortality                                                   | qSOFA* 0.43                  | 0.94        |
| Silcock 2019      | 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         | Retrospective cohort | 266                | Adult EMS transfers to ED with sepsis               | ICU admission and 28-day mortality                                                 | qSOFA (2) 0.86               | 0.67        |
| Vaittinada Ayar   | Prospective cohort   | 332                | Adult EMS transfers to ED with suspicion of infection| 28-day mortality                                                                   | qSOFA (2) 0.60               | 0.67        |
| Lane 2020         | 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                  | 0.7         |
|                   |                      |                    |                                                     |                                                      | 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        |
### Table 2 | Characteristics and results of the studies (Continued)

| Lead author, year | Study design | No of participants | Population | Outcome or reference standard | Scores evaluated (threshold) | Sensitivity | Specificity |
|-------------------|--------------|-------------------|------------|--------------------------------|-----------------------------|------------|------------|
| Polito 2018<sup>23</sup> | 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 | 90-30-90 score (systolic blood pressure <90 mm Hg, respiratory rate >30/min, oxygen saturation <90%). CI=Critical Illness Score, ED=emergency department, EMS=emergency medical service. | | |
| Borelli 2019<sup>24</sup> | Before v after study | 63 | Adult EMS transfers to ED with severe sepsis or septic shock | Primary outcome: 3-hour sepsis bundle compliance | | | |

Table 2 outlines the characteristics of the studies and the sensitivity and specificity of the scores studied, using different thresholds for positivity where appropriate. All but one were retrospective studies, with associated risks of missing or erroneous data. The study populations included people transported to hospital by emergency medical services 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 (admission to intensive care). Some results suggest promising accuracy for identifying high risk of severe illness or death (such as NEWS2<sup>23</sup>), but there was substantial variation in both sensitivity and specificity across the studies.

Only two of the studies considered how prehospital early warning scores potentially influence hospital management. One single centre study found that implementation of the PRESS score improved sepsis recognition by prehospital personnel from 12% (11/51 patients) before implementation to 60% (47/78) over 12 months after.<sup>23</sup> Another single centre study demonstrated weak evidence that implementation of a prehospital sepsis screening tool improved clinician compliance with Surviving Sepsis Campaign 3-hour sepsis bundle recommendations for 20 patients who were screening tool-positive compared with 43 historical controls.<sup>24</sup>

A formal systematic review of the evidence would involve additional steps to identify studies that may have been missed by our search, such as review of the grey literature, contact with experts in the field, or hand searching of relevant journals. This may identify additional studies, but they are unlikely to be high quality or add to the evidence identified here. We are reasonably confident that we have not missed any potentially important studies, and therefore would consider primary research to be a higher priority for future research than a formal systematic review.

### PRACTICE

**Is ongoing research likely to provide relevant evidence?**

We 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.<sup>25</sup> The study will (a) 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 (b) 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 light of the uncertainty?**

Based on the current evidence, the authors do not recommend that prehospital care practitioners use an early warning score to determine patient management in suspected sepsis. Further research is to be undertaken before an early warning score can be recommended as the basis for decision making. However, despite the limited evidence, some prehospital care teams may wish to use an early warning score as part of a general assessment of illness severity. In these instances, provide training so prehospital care teams can:

- Use early warning scores in a way that is consistent with other parts of the emergency care system, thus promoting good communication and shared understanding of illness severity.
- Understand that the sensitivity and specificity of the score for predicting severe illness depends on the threshold above which the score is considered to be positive. Using a low threshold optimises sensitivity at the expense of specificity: it increases recognition 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 many 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.
- Are confident to use clinical judgment to:
  - Recognise when it is appropriate to calculate an early warning score. Applying a score indiscriminately to patients with non-specific 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.
Interpret and act on early warning scores. Clinical judgment can identify potential false positive and false negative scores, and thus improve their accuracy in practice. However, as with all clinical judgment, this may be subject to cognitive biases that lead to errors.

- Draw on knowledge of the emergency care system and interactions with receiving hospitals to determine when to pre-alert the receiving hospital and when to initiate treatment in a prehospital setting
- Calculate an early warning score quickly and accurately. A simple score such as qSOFa is relatively easy to calculate. More complex scores may need to be supported by information systems, which may be assisted by adoption as a generic illness severity score across the health service (for example, NEWS2 in the UK NHS).

### What patients need to know

- Prehospital care practitioners can use early warning scores to decide when to alert the local 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 prehospital care practitioners should use them
- Early warning scores need to be used in a way that achieves the best balance between the risk of missing sepsis cases and the risks of over-diagnosis and over-treatment

### Education into practice

- When would you consider using an early warning sepsis score?
- What scores trigger initiation of treatment for sepsis and a pre-alert to the emergency department in your region?
- What are the consequences of under-triage and over-triage of sepsis?

### How patients were involved in the creation of this article

Public representatives from the Sheffield Emergency Care Forum (Enid Hirst and Linda Abouzeid) and an independent public representative (Peter Hawkin) reviewed and commented on the paper. Their comments, and those of the BMJ external peer reviewer, led to our recommendations for a consistent approach to early warning scoring across the emergency care system and using clinical judgment to determine when and how an early warning score is used.

This is one of a series of occasional articles that highlight areas of practice where management lacks convincing supporting evidence. You can read more about how to prepare and submit an Education article on our Instructions for Authors pages: https://www.bmj.com/about-bmj/resources-authors/article-types

Contributors: 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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