Toolkit: Prehospital management of Sepsis in adults and young people over 12 years- 2016

This clinical toolkit has been developed in partnership with the College of Paramedics and in full communication with the National Institute for Health and Care Excellence (NICE). It is designed to provide operational solutions to the complexities challenging the reliable identification and management of sepsis. This toolkit is compatible with the 2016 NICE Clinical Guideline on Sepsis (NG51), and complements clinical toolkits designed for other clinical areas.

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Staff working in the prehospital environment should be familiar with the significant morbidity and mortality associated with sepsis. The prehospital practitioner may be the first point of contact for patients with sepsis. This contact represents an opportunity to screen, identify, risk stratify and deliver immediate life-saving treatment for these patients. Concurrent to these processes, appropriate transportation, destination selection and communication will enable seamless care and further reduce the morbidity and mortality associated with sepsis.

Evidence from Europe and the USA shows that prehospital recognition of sepsis with appropriate destination selection and handover leads to a shorter delay to administration of antibiotics and early fluid therapy. These steps are independently associated with improved outcome.

**Background**

The UK mortality rate for patients admitted with sepsis is 30%\(^1\) - approximately 5 times higher than for ST elevation myocardial infarction and stroke - and is responsible for approximately 44,000 deaths and 150,000 hospital admissions in the United Kingdom (UK) per year\(^2\). The majority of these patients will arrive via the ED. In the United States, the number of patients transported by Emergency Medical Services with sepsis now outnumbers those with heart attack or stroke\(^3\). In 2007 in the UK, sepsis was found to account for 12% of early inpatient deaths after ED admission: this is likely to have been an underestimate due to a further 26% of deaths coded as of respiratory cause\(^4\). Hospitalizations for sepsis have more than doubled over the last 10 years\(^5,6\).

Sepsis is a time-critical condition. In the most severe cases, for every hour that appropriate antibiotic administration is delayed, there is an 8% increase in mortality\(^7\). The Sepsis Six is an initial resuscitation bundle designed to offer basic intervention within the first hour. In one prospective observational study, it was associated with survival suggesting a number needed to treat (NNT) to prevent one death of 4.6\(^8\). This compares to an NNT of 42 for Aspirin in major heart attack and 45-90 for PCI in ST elevation myocardial infarction.

This toolkit, first produced in 2015 and introducing the concept of Red Flag Sepsis as a simplified set of criteria to facilitate rapid initiation of care, has been updated for 2016 to take into account two significant new developments- the revised Consensus International Definitions for Sepsis published in JAMA in February 2016\(^9\), and the NICE Clinical Guideline on Sepsis released in July of that same year\(^10\).
Sepsis is common in the prehospital environment. In the United States:

- The number of patients transported by Emergency Medical Services (EMS) with sepsis now outnumbers those with heart attack or stroke.\(^1\)
- More than 40% of all sepsis hospitalizations arrived at the emergency department after EMS transport.\(^1\)
- Prehospital care intervals, on average, exceed 45 minutes for those hospitalized with sepsis: a significant proportion of the one hour in which the Sepsis Six should be delivered.
- In Scotland in a recent study, over 85% of patients diagnosed with severe sepsis or septic shock in Emergency Departments were transported to hospital by ambulance.\(^5\)

The prehospital phase represents both opportunity and risk. By recognizing sepsis early, life-saving elements of the Sepsis Six can be delivered and ongoing care (e.g. in the Emergency Department resuscitation area) can be facilitated. Failure to recognize Sepsis in the prehospital environment will lead to excess deaths. Conversely, over-triage of suspected sepsis is likely to burden Emergency Departments and risks detracting from care provided to other patients.

**Professional responsibility & accountability**

NHS England established sepsis as an indicator in both Domains 1 and 5 of the National Outcomes Framework, and issued a stage 2 alert on sepsis in September 2014. This signposted to clinical toolkits such as this, to education programmes, examples of good practice, and other available resources.

In 2015 and 2016, the Secretary of State for Health issued public commitments to action on sepsis. This has resulted in actions including a national CQUIN commissioning lever for EDs in 2015/16, and a further CQUIN applying across the whole hospital for 2016/17. There is active consideration for ‘whole system’ commissioning which will include prehospital quality standards.

In her report of September 2013 entitled ‘A Time to Act’, the Parliamentary and Health Service Ombudsman called upon the NHS and the Department of Health to act rapidly to reduce unnecessary deaths from sepsis\(^12\). As a direct result of this work, NICE has produced a clinical guideline and will produce an accompanying Quality Standard against sepsis, the latter carrying statute for implementation.

We have learned valuable lessons from the report arising from the recent survey on sepsis conducted by the National Confidential Enquiry into Patient Outcome and Death (NCEPOD), in particular that ambulance service practitioners are commonly the first health care professionals to have contact with patients with sepsis – a huge opportunity for diagnosis, risk stratification and treatment. Delays at every stage of healthcare were identified and felt to be contributory to adverse outcome, in addition to delays in patients’ initial contact with healthcare\(^13\).
Delivering Excellent Sepsis Care:

**Defining sepsis:**

Sepsis is characterized by a dysregulated host response to infection mediated by the immune system and resulting in organ dysfunction, potentially multi-organ failure, shock and death. International guidelines recommend the application of standards of care including first-hour antibiotics to patients with sepsis and septic shock.

In February 2016, the International Consensus Definitions for Sepsis Task Force published recommendations for ‘Sepsis-3’. Major changes from earlier definitions included that the Systemic Inflammatory Response Syndrome (SIRS) criteria were no longer form to part of the diagnostic criteria for sepsis, and that earlier efforts to define organ dysfunction criteria would be replaced with organ dysfunction tool known as SOFA (Sepsis-related Organ Failure Assessment score). Furthermore, the term ‘severe sepsis’ was abandoned, such that the international consensus group recommended the use only of the terms ‘infection’, ‘sepsis’, and septic shock.

Following publication of the Sepsis-3 definitions and the NICE clinical guideline, the Sepsis Trust has agreed with stakeholders a pragmatic interim approach to the recognition of sepsis for the UK. This approach is detailed below.

We propose to accept the International Consensus Definitions Task Force terminology to the extent that patients are described as having an infection, or sepsis. The term septic shock remains relevant, but according to strict definitions can only be confirmed following involvement of staff skilled in managing vasoactive infusions. Hypotension following fluid resuscitation would seem a reasonable surrogate to describe and communicate septic shock.

Following the relatively large-scale acceptance of the term ‘Red Flag Sepsis’ to communicate patients requiring urgent attention, we propose that this be continued to describe those patients identified as having one of the ‘high risk’ criteria from NICE NG51, which were derived from the original Red Flag criteria. NICE also introduces a second tier of risk - a set of ‘moderate to high risk’ criteria. We propose that presence of one of these criteria be communicated as ‘Amber Flag Sepsis’ for consistency.

**Determining who to screen for sepsis: rationale for not recommending qSOFA in isolation:**

It is unrealistic to expect organisations or individuals to formally calculate a SOFA score at presentation (and particularly outside hospital) prior to initiating time-critical life saving therapy.

To this end, the International Consensus Definitions Task Force used a combination of retrospective analysis of large data sets and prospective validation of smaller data sets to construct an ‘optional’ tool, using a simplified set of criteria, called ‘quick-SOFA’ or ‘qSOFA’ (Appendix 2). This tool would require that an aggregate of two parameters breach
threshold, the combination of which in the analyses conducted predicted death or a prolonged Intensive Care stay.

qSOFA would present operational difficulty to many organisations to implement, as it would demand the introduction of an additional aggregate scoring system for patients who are likely to have already been identified as at risk using a track and trigger system such as the National Early Warning Score (NEWS). qSOFA has yet to be robustly prospectively validated, and particularly has not been shown to be superior to NEWS in identifying patients with infection at risk of deterioration.

Furthermore, Sepsis-3 describes as only having ‘infection’ or ‘sepsis’. There is, unlike in the Red Flag Sepsis pathways and the 2001 definitions set, no ‘interim’ group in which early scheduled review can be readily recommended. Outside hospitals, on which the validity of data the Task Force have used is not entirely clear, it may well be that qSOFA (predicting death or prolonged Critical Care stay) occurs at a point in the course of illness later than ideal for transfer to hospital.

For these reasons, we (UKST, CoP and NICE) do not currently recommend the use of qSOFA as the primary bedside test for sepsis in the U.K. It is likely to be a useful and important redundancy to the proposed screening strategy in organisations benefiting from electronic observations and clinical prompts.

Describing the solutions – how can we be good at treating sepsis?

1) Determining who to screen for sepsis (the denominator population)

A high degree of vigilance is required for early identification of the septic patient. All personnel undertaking patient care in the prehospital environment should be trained in sepsis recognition.

All patients presenting with physiological disturbances in the presence of signs and symptoms compatible with an infective illness should be formally screened for sepsis. At each opportunity, a binary decision should be reached for all patients screened: this patient could have sepsis, or this patient does not have sepsis. If alternative diagnoses are suspected (for example, pancreatitis, amniotic fluid embolism, acute severe asthma, congestive cardiac failure) these should be dealt with using standard protocols- if the diagnosis is subsequently discounted sepsis should be re-considered.

Suspicion of an infective cause is all that is required. The most common causes are respiratory, urinary tract, abdominal and skin and soft tissue, but staff must also be aware that there are many other causes. A comprehensive list is beyond the scope of this document but must be included in training.

Since the minimum NEWS score compatible with a qSOFA score of 2 (the recommended trigger threshold) is 4, UKST, CoP and NICE believe it reasonable to propose that the
existing NEWS escalation recommendations of an individual parameter score of 3 (as used in the Sepsis Trust’s Red Flag Sepsis pathways) or an aggregate score of 4 or higher be used as a trigger to screen for sepsis. For organisations not using NEWS, any abnormal physiology in the context of a patient who appears unwell without other clear cause should trigger a screen.

Unlike the Critical Care-focused definition in Sepsis-3, health professionals working at the interface between community and hospital care need to identify those patients who are not yet critically ill, but are likely to become so. The qSOFA and SOFA criteria will all be captured in either the ‘moderate to high risk’ or ‘high risk’ criteria within the NICE guideline (which forms the basis for this toolkit), and we believe that this presents a safer and more operationally deliverable strategy within the UK.

We recommend that patients be screened for sepsis if they present with unexplained illness, if they clearly look unwell and have a likely infective cause, or if they present with (or subsequently deteriorate to) an individual parameter score of 3 or aggregate score of 4 or higher on the National Early Warning Score (NEWS) (or locally derived equivalent).

Screening and risk stratification:

This toolkit complements other toolkits for primary and community care. This toolkit also ‘jigsaws’ with patients’ ongoing care – either within a hospital or community setting. Particular care must be taken to re-risk stratify those referred from community settings e.g. GP practices.

Sepsis screening should be done as a two-part process; confirming that sepsis risk stratification is required and, in the population thus identified, screening for the level of severity of sepsis, or Sepsis Risk Stratification. During Sepsis Risk Stratification, as soon as Red Flag Sepsis, Amber Flag Sepsis or septic shock are confirmed, treatment should be initiated and the patient rapidly transported to an appropriate centre.
1) Confirming that sepsis risk stratification is required:

![Diagram of sepsis risk stratification]

2) Is this RED FLAG sepsis?

![Diagram of RED FLAG sepsis criteria]

Any patient with presumed sepsis who has one or more Red Flag Sepsis criteria should be assumed to have sepsis or septic shock, and immediately commenced on the PH Sepsis Pathway.
A patient who looks unwell with presumed infection who displays at least ONE Red Flag Sepsis criterion has Red Flag Sepsis and should immediately be placed on the PH Sepsis pathway.

The Red Flag Sepsis criteria detailed above are modified by NICE from an original set developed by the UK Sepsis Trust in September 2015. Red Flag Sepsis is intended to help identify patients with ‘formal’ sepsis according to a change in SOFA score in the PH environment – whilst awaiting the results of confirmatory tests / diagnostics which can only be delivered in the hospital environment.

4) In the absence of Red Flag criteria, patients should be screened for the presence of Amber Flag criteria:

4. Is any ONE Amber Flag present?

- Relatives concerned about mental status
- Acute deterioration in functional ability
- Immunosuppressed
- Trauma/ surgery/ procedure in last 6 weeks
- Respiratory rate 21-24 OR breathing hard
- Systolic B.P 91-100 mmHg
- Heart rate 91-130 OR new arrhythmia
- Not passed urine in last 12-18 hours
- Temperature < 36°C
- Clinical signs of wound, device or skin in

If immunosuppressed & under 18 treat as Red Flag Sepsis

If Amber Flag sepsis is present, the patient should be transferred to an appropriate destination. Handover should include the presence of ‘Amber Flag’ sepsis.

In the absence of Amber Flag criteria, each ambulance trust / PH organization should formalize a protocol for these lower risk patients. This protocol should include the consideration of other diagnoses, potential referral to other services and clear signposting with written patient information.
The PH Sepsis Pathway:

This is for all patients who trigger one or more of the Red Flag Sepsis Criteria. This pathway consists of two main parts: resuscitation and communication.

It should be noted that on-scene times should be minimised, and as much of the PH Sepsis Pathway as feasible should be delivered as concurrent activity alongside transportation to an appropriate centre.

PH practitioners will vary in their ability to deliver some aspects of this pathway.

**Resuscitation:**

- Fluid boluses:
  - 250ml boluses of 0.9% Sodium Chloride: administer a maximum of 250mls if the patient is normotensive, a maximum of 2000ml if the patient is persistently hypotensive or their lactate (if available) is > 2mmol/l. Deliver fluid challenges in divided boluses of 250-500 ml with reassessment of the patient's conditions between each - stop giving fluids if the patient develops signs of pulmonary oedema. Particular care must be taken with fluid challenges in the presence of significant coronary heart disease: in which 250ml boluses should be administered with careful reassessment between boluses.

- Oxygen:
  - Deliver to maintain oxygen saturations of >94% (88% in COPD).

Some patients with initial hypoperfusion may respond rapidly to smaller volumes. There is strong evidence that expedient delivery of ‘basic’ aspects of care limits the maximum acuity of intervention required - early resuscitation can prevent the requirement for invasive monitoring and vasoactive support later in hospital.

Monitor blood pressure, heart rate, urine output and if possible lactate during the resuscitation phase – return to base line levels indicates patient improvement.

**Oxygen**

Deliver oxygen to maintain oxygen saturations of >94% (88% in Chronic Obstructive Airways Disease).
Intravenous antibiotics (if available)

Some services may carry IV antibiotics for the treatment of sepsis. These may be condition-specific or generic: local protocols should be developed for their use.

Record lactate (if available)

Point of care lactate measurement devices may be useful in the PH environment, in the diagnosis and risk stratification of patients with sepsis.

The lactate level in sepsis is highly predictive of death\textsuperscript{16} (see Box 1) and poor outcomes and, when initially elevated, the degree of reduction following resuscitation (‘lactate clearance’) predicts survival\textsuperscript{17}. A significant proportion of patients with sepsis who have normal blood pressure have elevated serum lactate and outcomes for these patients with ‘cryptic shock’ are as poor as for those with overt septic shock\textsuperscript{18}.

In the analysis of criteria predictive of death in Sepsis-3, at each level of qSOFA score, lactate provided additional predictive value for mortality\textsuperscript{19}.

Some PH services have access to POCT lactate measuring devices and have in recent years become increasingly familiar with the routine use of serum lactate in assessing risk in patients presenting with presumed sepsis. Therefore, whilst NICE NG51 recommends that lactate be sampled following confirmation of the presence of High Risk (or two or more moderate risk) criteria, operationally we recommend that lactate be included in the Red Flag Sepsis criteria sought at the first stage of Sepsis Risk Stratification. Here the NICE NG51 pathway and the pathway described here again converge, since NICE recommends that if a lactate of greater than 2 mmol/l is identified in the presence of any high risk or moderate risk criteria, a pathway of care equivalent to the Sepsis Six be commenced.

When cryptic shock has been identified from a venous or capillary lactate sample, this should be corroborated with an arterial sample once in hospital to exclude error arising from regional perfusion abnormalities. A capillary or venous lactate from a correctly calibrated device which is normal is reassuring as a stand-alone.

Box 1: The relationship of lactate level in sepsis to mortality

<table>
<thead>
<tr>
<th>Lactate</th>
<th>Mortality</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;2</td>
<td>15%</td>
</tr>
<tr>
<td>2-4</td>
<td>25%</td>
</tr>
<tr>
<td>&gt;4</td>
<td>38%</td>
</tr>
</tbody>
</table>

Exemplar Standards for the prehospital management of sepsis

Prehospital services have a key role to play in early sepsis management. The prehospital environment is where rapid identification of the septic patient must occur and where early intervention, communication and transfer can impact on mortality and morbidity. In designing clinical pathways, construction of both high level and low level process maps is a helpful starting point.

The standards below are those which have been identified by the UK Sepsis Trust and the All Party Parliamentary Group for Sepsis as important in the management of sepsis with specific relevance to prehospital care providers. They are the ‘Exemplar Standards’ which organizations should aspire to deliver. Achieving these standards will place prehospital care providers well on the road to the provision of excellent sepsis care.

1. Clear guidance, policies and clinical pathways to be in place for the recognition, management and communication of sepsis and Red Flag Sepsis.
2. All patients with a NEWS score above trigger threshold (or a single NEWS criterion scoring 3), or with physiological abnormality in the presence of clinical suspicion of infection to be screened for sepsis with Sepsis Risk Stratification undertaken, and the outcome of this screening process recorded on the Patient Care Record or electronic Patient Care Record (PCR/ePCR).
3. The PH Sepsis Bundle (or a modified prehospital equivalent) to be used as a delivery method for early sepsis care and to be delivered within 1 hour post diagnosis in ≥95% of cases in collaboration with receiving EDs.
4. Definitive, documented decision made and communicated about the presence/absence of sepsis and the level of severity at time of handover to ED or other clinical group.
5. Mandatory annual sepsis training for all clinical members of staff.
6. A minimum of 80% of permanent staff to have received appropriate sepsis training at any one time point, audited at least biannually.
7. A nominated clinical Sepsis lead within the prehospital providers organization.
8. Interdisciplinary meetings to be undertaken between the ED and prehospital service staff together with managers and commissioners as appropriate, with remit to refine care pathways for sepsis and ensure compatibility between clinical areas. This work should be undertaken within the remit of, or fed back to, the organization’s Sepsis Group.
9. Voluntary reporting of performance data into the public domain.
References:


4. Nafsi T, Russell R, Reid CM, et al. Audit of deaths less than a week after admission through an emergency department: how accurate was the ED diagnosis and were any deaths preventable? Emergency Medicine Journal 2007; 24: 691–695


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19. Seymour CW et al. JAMA. doi:10.1001/jama.2016.0288 Supplementary online content, eFigure 12