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SEPSIS
TRUST

Toolkit: General Practice recognition & management of Sepsis in adults and children and young people over 12 years- 2016

This clinical toolkit has been developed with General Practitioners 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 in General Practice and Urgent Care settings. These solutions are compatible with the 2016 NICE Clinical Guideline on Sepsis (NG51), with toolkits designed for other clinical environments, and with the UK 5 Year Antimicrobial Resistance Strategy 2013 to 2018.

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1 Intended users

Doctors and nurses working in General Practice and Urgent Care.

2 Aims of this clinical toolkit

It is intended that this toolkit will:

- assist health professionals in developing and maintaining their knowledge of current recognition and therapeutic strategies for sepsis and septic shock
- provide a framework to assist in the recognition and risk stratification of sepsis in General Practice and Urgent Care in line with current NICE guidelines
- give an overview of current practice in sepsis management
- help those charged with the design and conduct of clinical systems, education and audit to do so in line with national strategy.

3 Objectives and rationales

i) Rationale for a focus on sepsis

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 year². 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 stroke³. Hospitalizations for sepsis have more than doubled over the last 10 years^{4,5}.

Sepsis is a time-critical condition. In the most severe cases, septic shock, for every hour that appropriate antibiotic administration is delayed, there is an 8% increase in mortality⁶. Reliable delivery of excellent sepsis care depends critically on early recognition and timely disposition, together with excellent communication with health professionals in receiving disciplines.

Sepsis is currently poorly recognized and treated within the NHS. 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 sepsis⁷. A College of Emergency Medicine (CEM) audit of performance against self-imposed standards for the management of sepsis and septic shock found antibiotics to be administered in only 32% of patients within the first hour from time of arrival in the ED⁸. More recently, the National Confidential Enquiry into Patient Outcome and Death (NCEPOD) report 'Just say Sepsis' attempted for the first time to describe the quality of care delivered in General Practice and found room for improvement in almost 39% of cases⁹. Expert reviewers found that 80% of infections giving rise to sepsis originated in the community. While not every patient with community-

acquired infection went on to develop sepsis in the community, 54% of patients with a hospital discharge diagnosis of sepsis had sepsis on arrival to hospital. Developing a whole-system solution akin to that for chest pain and stroke is likely to raise the profile of the patient with sepsis and significantly reduce variation in and time to therapy.

ii) Describe sepsis and septic shock, providing definitions and a recognition framework

There are challenges and opportunities around reliable sepsis identification in a General Practice or Urgent Care setting. General Practitioners and other health professionals working in these environments are highly skilled in assessing need for hospital assessment in patients with infection: it is not practicable to expect differentiation between viral and bacterial illness in all cases and clinical judgement remains of paramount importance. Patients who are obviously critically ill are likely to be identified without the need for new efforts. However, there are some patients with sepsis who have less immediately obvious signs of critical illness. Some of this group might be identified earlier with greater awareness and targeted clinical assessment including a risk stratification framework designed to support clinical decision-making.

This toolkit balances the academic definitions for sepsis and septic shock issued by the 2016 International Consensus Definitions Task Force¹⁰ with a pragmatic, risk-stratifying framework recommended by NICE¹¹. The intent is to develop a common language across our healthcare system.

iii) Give insight into the application of qSOFA, NEWS and NICE guidelines in clinical practice

There are a number of potential tools available to aid in the recognition of sepsis, its risk stratification and communication. The International Consensus Definitions Task Force recommend an 'official' definition¹⁰ (a change in the Sepsis-Associated Organ Failure Assessment of SOFA score) applicable in few environments outside Critical Care, together with an evidence-based (in hospital settings) 'bedside' recognition aid termed 'quick-SOFA' or qSOFA.

The UK Sepsis Trust and NICE agree that, while qSOFA represents a useful tool to identify patients who might have sepsis, a more structured system of determining which patients should be screened for sepsis, together with a risk stratification system acknowledging the importance of clinical judgement, will be more useful. We recommend that clinical acumen based upon clinician assessment and interpretation of patient or carer concern, with or without the use of the National Early Warning Score (NEWS), be used to determine which patients with routine infection should undergo sepsis risk stratification.

iv) Identify aspects of high quality practice in performing a risk assessment for sepsis

In order to facilitate seamless care delivery for patients with sepsis across the healthcare system, we believe it important that language and communication be standardized. We

present within this toolkit a number of solutions, including a decision support tool intended for use in General Practice and compatible with those intended for use in Prehospital Care and in Emergency Department Care, a description of clinical systems support solutions available, signposts to appropriate educational resources and *suggested* standards which practices and organizations may choose to aspire to in designing excellence in sepsis recognition and management.

4 Sepsis definitions 2016

Scientific understanding of sepsis continues to evolve, and in February 2016 the International Consensus Definitions for Sepsis Task Force published recommendations for a revised set of definitions termed 'Sepsis-3'¹⁰. It is almost certain that the definitions of sepsis and septic shock will continue to develop as an iterative process over time. International guidelines recommend the application of standards of care including first-hour antibiotics to patients with sepsis and septic shock.

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. According to the latest international definitions set, organ dysfunction is identified by an increase in the Sepsis-related Organ Failure Assessment (SOFA) score of ≥ 2 points, though several of its parameters are only available in hospital.

Mindful of this, we discuss in section 5 two potential surrogates which may have utility in identifying patients with likely sepsis in General Practice and Urgent Care: the 'bedside' quick-SOFA or q-SOFA proposed and retrospectively validated by the International Definitions Task Force, and the National Early Warning Score (NEWS). The Systemic Inflammatory Response Syndrome (SIRS) criteria¹² no longer form part of the diagnostic criteria for sepsis.

Septic shock is defined as a subset of sepsis where particularly profound circulatory, cellular and metabolic abnormalities substantially increase mortality. The international definitions require that hypotension requiring the use of vasoactive infusions and a high arterial lactate content be used to describe septic shock: in General Practice and Urgent Care hypotension in the presence of presumed infection is an appropriate surrogate to describe presumed septic shock.

5 Determining in whom to consider sepsis/ record physiological parameters

We acknowledge fully that a 'typical' General Practitioner will see one, maybe two, cases of sepsis per year among many thousands of patients with self-limiting or minor infection. No recognition pathway is a substitute for clinical acumen. NICE NG51 recommends that health professionals think 'could this be sepsis?' if a person presents with signs or symptoms that indicate possible infection.

i) At risk groups

In patients who have one or more of the risk factors below, the clinician should give particular consideration as to whether face-to-face assessment (as opposed to telephone consultation) in the context of a potential infection is appropriate. Factors triggering direct assessment might include behavioural change, suggestion of significant loss of function, evidence of circulatory or respiratory dysfunction, or a general deterioration without clear cause.

- Patients who are pregnant or who have recently been pregnant* (included for completeness- the care of women who are or have recently been pregnant in General Practice and Urgent Care with possible sepsis will be dealt with in a separate Clinical Toolkit)
- Immunocompromised patients**
- Children under 1 (included for completeness- the care of children in General Practice and Urgent Care with possible sepsis will be dealt with in a separate Clinical Toolkit)
- The elderly, defined by NICE as age over 75 years or patients over 65 years with complex illness or frailty
- Recently trauma, invasive procedure or surgery (within the last six weeks)
- Patients with indwelling devices or known breach of skin integrity
- Intravenous drug abusers

*Though the number of deaths from sepsis in pregnancy are mercifully small, patients in pregnancy or who have recently been pregnant (including where the pregnancy did not result in delivery of a live baby) do appear to be at an approximately 50% higher risk than non-pregnant individuals of similar age^{13,14}.

**Immunocompromise is clearly a spectrum. The threshold to undertake face-to-face consultation will, for example, be much lower in a patient who is known to be neutropenic or has recently undergone chemotherapy than in a patient with well-controlled diabetes mellitus or who has recently commenced low-dose oral steroid therapy. Patients at risk of neutropenia are likely to have been counseled in appropriate action in the context of fever, and existing local pathways for these patients should be followed. Patients suspected to have neutropenic sepsis should be immediately referred for assessment in secondary or tertiary care. NICE NG51 suggests the following groups of patients with potential immunocompromise be considered as at increased risk of sepsis:

- people being treated for cancer with chemotherapy
- people with diabetes, who have had a splenectomy, or people with sickle cell disease)
- people taking long-term steroids
- people taking immunosuppressant drugs to treat non-malignant disorders such as rheumatoid arthritis

ii) Consideration based upon presentation

In patients without clear risk factors, consideration should be given in patients presenting with likely infection as to whether a full set of observations should be recorded to identify possible sepsis.

Health professionals may consider recording observations in patients for whom they are considering an antibiotic prescription or stewardship discussion, patients with “flu-like” illness or gastroenteritis particularly when a loss of function or change in behavior are reported, in patients who look unwell with a fever or recent history of fever, (or who have a low recorded temperature), and in the unwell patient without clear cause. Where infection is suspected, assessment should include consideration of the source of infection and the clinician should ask ‘could this be sepsis’.

iii) The use of clinical systems support in recognition

During 2015 and 2016, the major providers of informatics in General Practice and Urgent Care services (TPP, EMIS, Advanced Computer Software, INPS and Microtest) have been working with the Department of Health and the UK Sepsis Trust collaboratively to design and implement devices to automate prompts in the identification of sepsis. The aims have been to make suggestion as to when physiological observations may be beneficial, to fill data gaps which may assist decision making, to alert as to the presence of Red Flags or Amber Flags in the context of sepsis, and to embed a language and definitions set common to other areas of NHS practice.

This is an iterative process, and as this Toolkit launches the major providers will update their systems to reflect the 2016 NICE Guideline. There is intent to avoid alert fatigue where possible, and providers have undertaken to respond to feedback in a timely fashion.

Clinical systems are no substitute for clinical gestalt- the systems are there as a redundancy. They should provide assistance in reminding clinicians of Red and Amber Flag criteria, in facilitating referral to hospital, and in supporting clinicians in decisions to continue care in the community based upon documented observations and clinical system support.

iv) Consideration in patients referred by NHS 111 and in patients presenting in response to recognized safety netting resources

NHS Pathways has made improvements in the sensitivity of its algorithms to sepsis in releases 10 and 11, and will continue further iterations in release 12, whilst attempting not to over-triage. It has improved the language used within questions to be more relevant to the lay person.

The clinical systems providers and NHS Pathways intend in time to signpost patients and carers to safety netting resources developed with the UK Sepsis Trust. These will also be distributed on request to providers in General Practice and Urgent Care and secondary care.

6 Sepsis Risk Stratification

Patients in whom sepsis is considered should have a full set of physiological observations taken to include temperature, heart rate, respiratory rate, blood pressure, and level of consciousness. Where resources permit, the measurement of oxygen saturations using a pulse oximeter should be performed in addition to basic physiological assessment.

Normal observations are likely to reassure and reinforce decisions to manage in the community, and abnormal observations may identify deterioration before the clinical picture becomes evident. Particularly in remote locations where transit times to hospital can be prolonged, or where community-based care with scheduled review is planned, recording physiology at initial assessment can aid in the identification of subsequent deterioration or improvement. We recommend that clinicians in General Practice and Urgent Care stratify patients with suspected sepsis for perceived risk in terms of physiological derangement according to this toolkit's recommendations based upon NICE NG51.

NICE NG51 introduces an improved set of Red Flag Sepsis criteria ('high risk criteria'), together with a second group of 'moderate to high risk criteria' which we will term Amber Flag Sepsis criteria to identify patients at lower risk but who still warrant close assessment. The reliance on laboratory tests seen in earlier pathways is thus removed. Thus strategies to identify sepsis in General Practice and Urgent Care are now similar to strategies in secondary care, presenting opportunity to align language and to explore the commissioning of cross-system pathways of care.

It is not always possible to define a source of infection in a patient presumed to have sepsis, particularly at initial assessment. It is important to reinforce that patients with signs and symptoms of infection together with physiological deterioration in the absence of a clear source should continue to be presumed to have sepsis. The clinician should also question whether this acute illness might be explained by a non-infective illness such as pancreatitis, acute coronary syndrome, poisoning or pulmonary.

Should a patient have a relevant advance directive precluding active intervention, or a competent and informed patient refuse treatment, clearly treatment would be inappropriate. For some patients, severe co-morbidity and pre-existing limitations to functional status may make referral to hospital inappropriate, although basic interventions may remain appropriate and require admission- such cases should be considered carefully and discussed with the patient, family and colleagues as appropriate.

Schematic 1: Confirming that Sepsis Risk Stratification is required

1. In the context of presumed infection, are any of the following true:
(common sources: chest, UTI, abdominal organs)

Patient looks very unwell	<input type="checkbox"/>
Family or carer is very concerned	<input type="checkbox"/>
There is ongoing deterioration	<input type="checkbox"/>
Physiology is abnormal for this patient	<input type="checkbox"/>

Tick

NICE NG51 built upon the UK Sepsis Trust's Red Flag Sepsis approach, launched in 2015, for determining which patients should immediately be transferred for life saving therapy. The first step in Sepsis Risk Stratification should be to confirm or exclude the presence of any ONE high risk, Red Flag Sepsis criterion as detailed in Schematic 2:

Schematic 2: Red Flag Sepsis criteria

3. Is ONE Red Flag present?

New deterioration in GCS/ AVPU	<input type="checkbox"/>
Respiratory rate ≥ 25 per minute	<input type="checkbox"/>
Needs oxygen to keep SpO ₂ 92% (88% in COPD)	<input type="checkbox"/>
Systolic B.P ≤ 90 mmHg (or ≥ 40 mmHg below normal)	<input type="checkbox"/>
Heart rate ≥ 130 per minute	<input type="checkbox"/>
Not passed urine in last 18 hours	<input type="checkbox"/>
Non-blanching rash or mottled/ ashen/ cyanotic	<input type="checkbox"/>
Recent chemotherapy (within last 6 weeks)	<input type="checkbox"/>

Tick

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 transferred to hospital if appropriate (section 9). Patients who have no Red Flag Sepsis Criteria should immediately be screened for Amber Flag Sepsis (Schematic 3).

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 transferred to hospital

Schematic 3: Amber Flag Sepsis criteria

3. Is any ONE Amber Flag present?

	Tick
Relatives worried about mental state/ behaviour	<input type="checkbox"/>
Acute deterioration in functional ability	<input type="checkbox"/>
Immunosuppressed (without recent chemotherapy)	<input type="checkbox"/>
Trauma, surgery or procedure in last 6 weeks	<input type="checkbox"/>
Respiratory rate 21-24 OR dyspnoeic	<input type="checkbox"/>
Systolic B.P 91-100 mmHg	<input type="checkbox"/>
Heart rate 91-130 OR new dysrhythmia	<input type="checkbox"/>
Not passed urine in last 12-18 hours	<input type="checkbox"/>
Tympanic temperature ≤ 36 °C	<input type="checkbox"/>
Clinical signs of wound, device or skin infection	<input type="checkbox"/>

If under 17 & immunity impaired treat as Red Flag Sepsis

For patients 18 years old and over, NICE recommend that the presence of any ONE amber flag criterion prompt a binary clinical decision. Clinical judgment should be used to determine whether the patient can be managed in the community setting or requires hospital assessment. For those in whom community-based care is deemed safe and appropriate, consideration should be given to providing a scheduled review appointment, and a clear record should be made of the decision, rationale and any safety netting provided.

Written and verbal safety netting is essential for patients with Amber Flag Sepsis deemed appropriate to remain in the community (see Section 8).

If a patient with one or more Amber Flags is aged 17 years or younger AND is immunocompromised, they should be treated as Red Flag Sepsis and immediate transfer for hospital assessment arranged.

A patient with presumed infection who displays at least ONE Amber Flag Sepsis criterion (in the absence of Red Flag Sepsis) should be evaluated and a binary decision made as to whether ongoing care in the community is appropriate. This is likely to be informed in part by physiological status and background morbidity of the individual patient, and whether a source of infection can be identified with any degree of certainty.

Clinical judgment should be exercised in the context of a patient with one or more Amber Flags who is judged to require hospital assessment in determining the acuity of referral.

Amber Flags are included for completeness, since they include several of the qSOFA parameters and therefore have a (retrospective) evidence base. They do add complexity, however, and it is not yet known whether to include Amber Flags adds value above and beyond a simple statement 'no red flags, but I or the patient/ their relatives still have significant concern'.

If a patient with presumed new infection has neither Red Flag nor Amber Flag criteria (or for whom there is little clinical concern following assessment), they should be assumed to be at low risk and decisions to refer for hospital assessment made according to routine protocols supported by clinical judgment- most patients in this group will appropriately receive ongoing care in the community.

General Practice Sepsis Screening and Action Tool



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To be applied to all non-pregnant adults and children 12 years and over with fever (or recent fever) symptoms
NB there is no systems substitute for clinical experience & acumen, but Red Flag Sepsis will help with early identification of adults and older children with systemic response to infection

1. Is physiology abnormal (e.g. NEWS ≥ 3)? Tick

And/or does patient look very sick?

↓ Y

2. Is the history suggestive of infection? Tick

Yes, but source not obvious

Pneumonia/ likely chest source

Urinary Tract Infection

Abdominal pain or distension

Cellulitis/ septic arthritis/ infected wound

Device-related infection

Meningitis

Other (specify:)

↓ Y

3. Is ONE Red Flag present? Tick

New deterioration in GCS/ AVPU

Respiratory rate ≥ 25 per minute

Needs oxygen to keep SpO₂ 92% (88% in COPD)

Systolic B.P ≤ 90 mmHg (or ≥ 40 mmHg below normal)

Heart rate ≥ 130 per minute

Not passed urine in last 18 hours

Non-blanching rash or mottled/ ashen/ cyanotic

Recent chemotherapy (within last 6 weeks)

↓ Y

Red Flag Sepsis!

Immediate actions:

Dial 999

Arrange blue light transfer

Administer oxygen to maintain saturations $> 94\%$

If estimated transfer time > 1 h administer antibiotic intravenously

Low risk of sepsis

Use clinical judgement and/or standard protocols

↑ N

Give safety netting advice: call 999 if develop any of the features in Box 3, or call 111/arrange to see GP if condition changes or deteriorates or features of Box 4 develop. Signpost to available resources as appropriate

↑ N

4. Is any ONE Amber Flag present? Tick

Relatives worried about mental state/ behaviour

Acute deterioration in functional ability

Immunosuppressed (without recent chemotherapy)

Trauma, surgery or procedure in last 6 weeks

Respiratory rate 21-24 OR dyspnoeic

Heart rate 91-130 OR new dysrhythmia

Systolic B.P 91-100 mmHg

Not passed urine in last 12-18 hours

Clinical signs of wound, device or skin infection

Tympanic temperature ≤ 35.9 °C

If under 17 & immunity impaired treat as Red Flag Sepsis

↓ Y

Sepsis likely

Use clinical judgment to determine whether patient can be managed in community setting. If treating in the community, consider:

- planned second assessment
- brief written handover to colleagues
- specific safety netting advice

Communication

Write a brief clear handover including observations and antibiotic allergies where present

Ensure Paramedics pre-alert as 'Red Flag Sepsis'

Sepsis Six and Red Flag Sepsis are copyright to and intellectual property of the UK Sepsis Trust, registered charity no. 1158843. sepsistrust.org

7 The use of physiological triggers to prompt consideration of sepsis-NEWS and qSOFA

In their 2016 publication, the International Consensus Definitions Task Force used a combination of retrospective analysis of large (primarily secondary care) 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' (Box 1).

Box 1: qSOFA criteria¹⁰

- Altered mentation
- Systolic blood pressure \leq 100 mmHg
- Respiratory rate \geq 22

If two or more parameters are present, the risk of deterioration is high

This tool requires that an aggregate of two parameters breach threshold, the combination of which in the analyses conducted predicted death or a prolonged Intensive Care stay. The external validity of qSOFA in General Practice and Urgent Care environments has not been demonstrated. All qSOFA criteria are captured in the Red Flag and Amber Flag sections of the recognition algorithm, and we recommend that qSOFA not be used as a stand-alone tool in General Practice and Urgent Care.

We (UKST and NICE) do not currently recommend the use of qSOFA as a stand-alone rule-in test for sepsis in the U.K. It is likely to be a useful and important redundancy to clinical acumen and the National Early Warning Score

Some practices have begun to explore the use of the National Early Warning Score (NEWS, Box 2) in higher risk groups to identify and communicate potential for deterioration. qSOFA has not been shown to be superior (or inferior) to NEWS in identifying patients with infection at risk of deterioration.

Box 2: National Early Warning Score (NEWS)¹⁶

PHYSIOLOGICAL PARAMETERS	3	2	1	0	1	2	3
Respiration Rate	≤8		9 - 11	12 - 20		21 - 24	≥25
Oxygen Saturations	≤91	92 - 93	94 - 95	≥96			
Any Supplemental Oxygen		Yes		No			
Temperature	≤35.0		35.1 - 36.0	36.1 - 38.0	38.1 - 39.0	≥39.1	
Systolic BP	≤90	91 - 100	101 - 110	111 - 219			≥220
Heart Rate	≤40		41 - 50	51 - 90	91 - 110	111 - 130	≥131
Level of Consciousness				A			V, P, or U

Since the minimum NEWS score compatible with 2 qSOFA parameters is 4, we believe it reasonable to propose that the existing NEWS escalation recommendations of an individual parameter score of 3 or an aggregate score of 4 or higher be used as a trigger to screen for sepsis.

We would therefore recommend that practices using NEWS continue to do so in higher risk groups and use an elevated NEWS score as a trigger to consider sepsis, but do not yet directly recommend wide-scale adoption of NEWS outside hospitals.

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). The presence of any significantly altered physiology in the context of presumed infection should alert the clinician to the possibility of sepsis.

8 Recommendations for safety netting

If the patient is not to be referred for hospital assessment, there must be adequate written and verbal safety netting. One example of a safety-netting tool is in the UK Sepsis Trust's 'Symptom Checker Cards' produced in collaboration with a survivor group. Any safety netting advice given should be clearly documented in the patient's notes, together with observations and antimicrobial therapy offered. It is good practice to agree a planned next day review assessment in any patient with Amber Flag Sepsis managed in the community,

together with an invitation for open self-referral should the patient deteriorate or they or their relatives be concerned.

SEPSIS IN ADULTS IS A SERIOUS CONDITION
that can initially look like flu, gastroenteritis or a chest infection. Sepsis affects more than 250,000 people every year in the UK.
The UK Sepsis Trust registered charity number (England & Wales) 1158843

Seek medical help urgently if you develop any or one of the following:

Slurred speech or confusion
Extrême shivering or muscle pain
Passing no urine (in a day)
Severe breathlessness
It feels like you're going to die
Skin mottled or discoloured

JUST ASK
"COULD IT BE SEPSIS?"
IT'S A SIMPLE QUESTION, BUT IT COULD SAVE A LIFE.

(Available from info@sepsistrust.org. Developed following a modified Delphi process with input from in excess of 100 adult survivors)

9 Communication with Ambulance Service and secondary care

Once a patient arrives in hospital, the All Party Parliamentary Group (APPG) on sepsis has made a recommendation that organizations should give 'consideration to the development of Sepsis Teams'¹⁶. Comparisons with heart attack and stroke, where teams are available to be mobilized when prehospital services or General Practice and Urgent Care pre-alert a suspected case, would make this seem obvious. It is vital that patients with sepsis should be reviewed at the earliest opportunity by the most senior available health professional. This should include in General Practice and Urgent Care- if a doctor in training (for example) identifies Red Flag Sepsis, a senior doctor should review the findings immediately or as soon as practicable.

Many patients with sepsis will have multiple co-morbidities, and may be elderly or frail. For such patients, decisions should be taken at senior level (in consultation with the patient and their family as appropriate) regarding the appropriateness of escalation of care to hospital.

i) Communication in cases of Red Flag Sepsis

For patients identified with Red Flag Sepsis, immediate arrangement should be made for urgent transfer for hospital assessment. This should be by 'blue light' ambulance, with a Paramedic crew if immediately available. The call should include direct reference to the acuity of the condition, using the term 'Red Flag Sepsis'. If the call is made in the presence of the patient or their relatives, it may be preferable to state that the patient has suspected

sepsis and give observations (such as using the NEWS score). It is reasonable to check that a Red 2 dispatch code has been applied.

A brief, clear handover should accompany the patient to include observations, any relevant medical history and antibiotic history including allergies. Where possible, a telephone referral to the receiving clinical team should be made, using the term 'Red Flag Sepsis' (see above). As secondary care organizations continue to develop sepsis teams, collaborative care pathways are likely to develop between secondary care

As described above, patients under 18 years of age with no Red Flag but with one or more Amber Flag who are also immunocompromised should be treated identically to those with Red Flag Sepsis.

ii) Communication in cases of Amber Flag Sepsis

Where there are one or more Amber Flags in the absence of any Red Flag, clinical judgment will determine appropriate action.

Patients with as yet 'minor' sepsis can deteriorate rapidly. Patients with Amber Flags who have one or more risk factors described in 5.i) should receive particularly careful consideration as to whether hospital assessment is required, as should patients who live alone with poor access to communication and transport. Where clinical assessment is unable to identify a suspected source of infection, hospital assessment should also be carefully considered.

The urgency of hospital transfer is not as clear-cut as with Red Flag Sepsis, and clinical judgment will inform disposition. The call to the Ambulance Service should include direct reference to the acuity of the condition, using the terms 'Amber Flag Sepsis'. For patients not at immediate risk on clinical assessment, it may be necessary to reinforce that a Red 2 disposition is not required.

A brief, clear handover should accompany the patient to include observations, any relevant medical history and antibiotic history including allergies. Where possible, a telephone referral to the receiving clinical team should be made, using the terms 'Amber Flag Sepsis' or 'sepsis'. The presence of any risk factors and the rationale for the clinical decision to refer for hospital assessment should be discussed.

10 Early care options for patients with Sepsis (Red Flag Sepsis and Amber Flags where decision is made to refer for hospital assessment)

The key immediate interventions that increase survival are described in a bundle termed the Sepsis Six (Box 1). This bundle has been shown to be associated with significant mortality reductions when applied within the first hour¹⁷.

Box 1: The Sepsis Six (Source: <http://sepsistrust.org>)

1. Administer oxygen to maintain saturations >94%
2. Take blood cultures and consider infective source
3. Administer intravenous antibiotics
4. Consider intravenous fluid resuscitation
5. Check serial lactates
6. Commence hourly urine output measurement

While few General Practitioners will have the resources to provide the entirety of this bundle of care, it is included to illustrate the time-critical nature of Red Flag Sepsis and the need for collaborative care pathways.

Where resources permit, General Practitioners should initiate oxygen therapy to maintain target saturations of 94% or higher. Patients with sepsis are exempt from British Thoracic Society guidelines for the administration of oxygen to acutely ill adults as the pathophysiology of sepsis is such that organs become critically hypoxic. Hypoxia will kill before hypercapnia. Current theory suggests that hypercapnia occurring in response to oxygen therapy in patients with pulmonary disease is due not to the unproven theory of a loss of 'hypoxic drive' but to changes in ventilation-perfusion matching. Oxygen will not cause sudden apnoea in such patients.

Therefore where patients are known to have moderate to severe pulmonary disease (and where available), we still recommend that oxygen be administered but to maintain a lower target oxygen saturations above 88%.

II Advanced care options for patients with Sepsis (Red Flag Sepsis and Amber Flags where decision is made to refer for hospital assessment)

Particularly in remote areas, consideration should be given to the delivery of other elements of the Sepsis Six.

i) Antimicrobials

If transit times to hospital are routinely in excess of one hour, General Practitioners and organizations should consider whether it is appropriate and feasible to administer intravenous (or intramuscular) antimicrobials, since a delay of one hour in administering antimicrobials in septic shock is associated with an increase in mortality rates of 8%⁶. Organizations in areas where transit times can be prolonged (or where enhanced care is delivered as a routine such as Urgent Care) should risk assess the possibility of administering antimicrobials taking into account clinical need (risk, benefit and frequency of need), clinical skills, capacity, equipment and stock control needs.

If it is deemed appropriate to plan to deliver prehospital antimicrobials, the choice of agents will vary by region but ideally should be agreed with infection specialists locally. As regional sepsis networks spread, this will be facilitated. It is unreasonable to expect small practices to hold stocks of each first- and second-line intravenous antibiotic for each source of infection, but larger collaboratives and Urgent Care facilities may consider holding stocks for community-acquired pneumonia, urinary tract infection, skin and soft tissue infection and intra-abdominal infection which together account for 90% of cases of sepsis⁹.

ii) Blood cultures

If organizations elect to administer antimicrobials, the feasibility of sampling blood for culture should be evaluated.

While modern blood culture media are able to bind antimicrobials and thus increase the capture rate of organisms after antibiotic administration, this is not fully effective and capture rates remain higher if cultures are sampled first. The positive identification of organisms not only permits de-escalation of antimicrobial cover (or escalation if initial spectrum is inadequate) aiding antimicrobial stewardship, but has also been independently associated with improved outcomes. Intermediary plastic vessels are available for sampling should the use of standard glass blood culture bottles present a barrier.

Organizations in areas where transit times can be prolonged (or where enhanced care is delivered as a routine such as Urgent Care) and who intend to administer antimicrobials should also risk assess the possibility of sampling blood cultures taking into account clinical need (risk, benefit and frequency of need), clinical skills, capacity, equipment, transport of biomaterials and stock control needs.

iii) Point of care tests

For some patients, early risk stratification will only be complete after measuring lactate and creatinine levels, which would normally necessitate hospital referral. Whilst there exists no direct evidence of benefit in General Practice and Urgent Care, some organizations/practices may wish to assess the potential value of point-of-care-tests (POCTs) in facilitating and supporting admissions avoidance through the identification of sub-threshold values. Additional POCTs which may aid transfer (or antimicrobial prescribing) decisions include C-reactive protein and differential white cell count.

In Emergency Departments, the lactate level in sepsis is highly predictive of death¹⁸ and poor outcome. 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 shock¹⁹. Health professionals in General Practice and Urgent Care may find that the recording of a 'normal' lactate (less than 2 mmol/l) is reassuring in supporting their decision to continue caring for a patient in the community.

12 Educational resources

During 2016 and in communication with each body, each of the UK Sepsis Trust, Health Education England and BMJ Learning will produce peer-reviewed educational resources to support this toolkit. Future versions of this toolkit will signpost as these become available.

14 References

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Appendix I: summary of suggested clinical guidelines for the management of patients attending with sepsis in General Practice and Urgent Care

Amber Flag Sepsis:

- A documented decision whether to manage patient in the community or refer to hospital
- Discussion with a senior nurse or doctor (where initial assessment has been by trainee or junior health professional) within 30 minutes of diagnosis
- A full set of observations including heart rate, respiratory rate, blood pressure, temperature, conscious level and oxygen saturation (where available) recorded and documented
- If to be referred for hospital assessment, consideration given to the acuity of transfer and rationale documented
- If to be referred for hospital assessment, handover including relevant clinical history and antibiotic history including allergies to be provided
- If to be treated in the community, written and verbal safety netting advice offered and documented
- If to be treated in the community, arrangements to be made for scheduled review within 24 hours

Red Flag Sepsis

- Immediate discussion with a senior doctor (where initial assessment has been by trainee)
- Immediate request for 999 Ambulance with Paramedic crew if available
- Handover including relevant clinical history and antibiotic history including allergies to be provided
- Where resources available, administer oxygen therapy
- Where transfer times may be prolonged, consider need for intravenous antibiotics and fluid therapy if available
- Instruct Paramedics to pre-alert as Red Flag Sepsis

Appendix 2: Exemplar Standards for General Practice and Urgent Care management of Sepsis

The standards below are those which have been identified by the UK Sepsis Trust and the APPG for Sepsis as important in the management of sepsis with specific relevance to General Practice and Urgent Care . They are the 'Exemplar Standards' which organizations aiming to achieve excellence in sepsis care should aspire to deliver. Achieving these standards will place a General Practice and Urgent Care organization well on the road to the provision of excellent sepsis care.

1. Clear written guidance, policies and clinical pathways to be in place for the recognition and management of Red Flag Sepsis and Amber Flag Sepsis
2. Protocols in place to prevent assessment of patients with risk factors by telephone consultation alone in the context of a potential infection, fever (or recent history of fever) or who are unwell without clear cause
3. Telephone triage protocols available and used for all patients describing symptoms compatible with infection or who are unwell without clear cause
4. Clear written criteria as to which patients presenting for face-to-face consultation should be screened for sepsis
5. According to local criteria for screening, 100% of patients satisfying criteria to have heart rate, respiratory rate, blood pressure, conscious level, and oxygen saturations measured and recorded (unless precluded by equipment failure)
6. Risk assessment to be undertaken and maintained regarding the need for Point of Care Testing for lactate
7. 100% of patients identified with Red Flag Sepsis to be transported immediately for hospital assessment unless limitations of treatment agreed
8. Clear written and verbal handovers to accompany all patients referred for hospital assessment
9. Oxygen therapy to be available and considered for all patients with Red Flag Sepsis
10. Where transit times to hospital are routinely in excess of 60 minutes, risk assessment to be undertaken and maintained regarding the need for administration of antibiotics and intravenous fluids
11. Documented decision to treat in the community or transfer to hospital in 100% of patients with Amber Flag Sepsis
12. Where patients with Amber Flag Sepsis are to be managed in the community,

documented safety netting advice and review plans to be in place for all patients.