NATIONAL CLINICAL GUIDELINES

THE DIAGNOSIS & MANAGEMENT OF SEPSIS

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المبادئ الإرشادية السريرية لدولة قطر
NATIONAL CLINICAL GUIDELINES FOR QATAR

وزارة الصحـــة العامـــة
Ministry of Public Health
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Abbreviations

The abbreviations used in this guideline are as follows:

ABG	Arterial Blood Gas
ACD	Acid Citrate Dextrose
CBC	Complete Blood Count
CVC	Central Venous Catheter
CMP	Comprehensive Metabolic Panel
CPR	Cardiopulmonary Resuscitation
CSF	Cerebrospinal Fluid
CT	Computed Tomography
DNAR	Do Not Attempt Resuscitation
EDTA	Ethylene Diamine Tetra Acetic Acid
EMR	Electronic Medical Record
EOS	Early Onset Sepsis
EWS	Early Warning System
F_iO_2	Fraction of Inspired Oxygen
GA	Gestational age
GBS	Group B *Streptococcus*
GIR	Glucose Infusion Rate
HIV	Human Immunodeficiency Virus
HMC	Hamad Medical Corporation
ICU	Intensive Care Unit

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IO	Intraosseous route
IV	Intravenous route
LOS	Late Onset Sepsis
LP	Lumbar Puncture
MEWS	Modified Early Warning Scoring Tool
MOPH	Ministry of Public Health
MRI	Magnetic Resonance Imaging
MRSA	Methicillin Resistant *S. aureus*
MSSA	Methicillin Sensitive *S. aureus*
PEWS	Paediatric Early Warning System
PHCC	Primary Health Care Corporation
PICU	Paediatric Intensive Care Unit
POC	Point of Care testing
QEWS	Qatar Early Warning System
qSOFA	Quick Sequential (Sepsis-Related) Organ Failure Assessment Score
RBC	Red Blood Cells
RRT	Rapid Response Team
$ScVO_2$	Central Venous Oxygen Saturation
SpO_2	Percentage of Oxygen Saturation
TPN	Total Parenteral Nutrition
UTI	Urinary Tract Infection

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1 Information about this Guideline

1.1 Objective and Purpose of the Guideline

The purpose of this guideline is to define the appropriate diagnosis and management of sepsis in neonates, children and adults, including women in pregnancy and the puerperium. The objective of this guideline is to improve the early recognition and appropriate management of patients with suspected or proven sepsis, presenting to healthcare organisations in Qatar. It is intended that the guideline will be used primarily by healthcare providers in all healthcare settings.

1.2 Scope of the Guideline

The following aspects of care are included within this Guideline:

- Early recognition of sepsis, including:
  - Signs/symptoms indicative of sepsis by different age groups.
  - Criteria for emergency referral in different age groups.
- Sepsis screening.
- Immediate management using the Sepsis-6 Bundle.
- Further Management
- Considerations for patient preferences in relation to care.
- Key Performance Indicators.

1.3 Editorial Approach

This guideline document has been developed and issued by the Ministry of Public Health of Qatar (MOPH), through a process which aligns with international best practice in guideline development and localisation. The guideline will be reviewed on a regular basis and updated to incorporate comments and feedback from stakeholders across Qatar.

The editorial methodology, used to develop this guideline, has involved the following critical steps:

- Extensive literature search for well-reputed published evidence relating to the topic.
- Critical appraisal of the literature.
- Development of a draft summary guideline.
- Review of the summary guideline with a Guideline Development Group, comprised of practising healthcare professionals, subject matter experts and patient representatives, from across Qatar.
- Independent review of the guideline by the National Clinical Guidelines & Pathways Committee, appointed by the MOPH, from amongst stakeholder organisations across Qatar.

Whilst the MOPH has sponsored the development of the guideline, the MOPH has not influenced the specific recommendations made within it.

1.4 Sources of Evidence

The professional literature has been systematically queried using specially developed, customised, and tested search strings. Search strategies are developed to allow efficient yet comprehensive analysis of relevant publications for a given topic and to maximise retrieval of articles with certain desired characteristics pertinent to a guideline.

For each guideline, all retrieved publications have been individually reviewed by a member of the Editorial Team and assessed in terms of quality, utility, and relevance. Preference is given to publications that:

1. Are designed with rigorous scientific methodology.
2. Are published in higher-quality journals.
3. Address an aspect of specific importance to the guideline in question.

Further information about the literature search and appraisal process is included in the *Appendix*.

1.5 Evidence Grading and Recommendations

Recommendations made within this guideline are supported by evidence from the medical literature and where possible the most authoritative sources have been used in the development of this guideline. In order to provide insight into the evidence basis for each recommendation, the following evidence hierarchy has been used to grade the level of authoritativeness of the evidence used, where recommendations have been made within this guideline.

Where the recommendations of international guidelines have been adopted, the evidence grading is assigned to the underlying evidence used by the international guideline. Where more than one source has been cited, the evidence grading relates to the highest level of evidence cited:

- **Level 1 (L1):**
  - Meta-analyses.
  - Randomised controlled trials with meta-analysis.
  - Randomised controlled trials.
  - Systematic reviews.

- **Level 2 (L2):**
  - Observational studies, examples include:
    - Cohort studies with statistical adjustment for potential confounders.
    - Cohort studies without adjustment.
    - Case series with historical or literature controls.
    - Uncontrolled case series.
  - Statements in published articles or textbooks.

- **Level 3 (L3):**
  - Expert opinion.
  - Unpublished data, examples include:
    - Large database analyses.
    - Written protocols or outcomes reports from large practices.

In order to give additional insight into the reasoning underlying certain recommendations and the strength of recommendation, the following recommendation grading has been used, where recommendations are made:

- **Recommendation Grade A (RGA):** Evidence demonstrates at least moderate certainty of a net benefit from the recommendation.
- **Recommendation Grade B (RGB):** Evidence is insufficient, conflicting, or poor and demonstrates an incomplete assessment of net benefit vs harm; additional research is recommended.
- **Recommendation Grade C (RGC):** Evidence demonstrates potential harm that outweighs benefit; additional research is recommended.
- **Recommendation of the GDG (R-GDG):** Recommended best practice on the basis of the clinical experience of the Guideline Development Group members.

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1.6 Guideline Development Group Members

The following table lists members of the Guideline Development Group (GDG) nominated by their respective organisations and the National Clinical Guidelines & Pathways Committee. The GDG members have reviewed and provided their feedback and approval of the guideline document. Each member has completed a declaration of conflicts of interest, which has been reviewed and retained by the MOPH.

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1.7 National Clinical Guidelines & Pathways Committee Members

The following table lists members of the National Clinical Guidelines & Pathways Committee (NCGPC), appointed by the MOPH. The NCGPC members have reviewed and provided their feedback and approval of the guideline document. Each member has completed a declaration of conflicts of interest, which has been reviewed and retained by the MOPH.

National Clinical Guidelines & Pathways Committee (NCGPC) Members		
Name	**Title**	**Organisation**
Ms Huda Amer Al-Katheeri	Chair of the NCGPC, Director of Strategic Planning & Performance Department	Ministry of Public Health
Shk Dr Mohammed Hamad J. Al Thani	Co-Chair of the NCGPC, Director of Public Health	Ministry of Public Health
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Dr Chris Kenny	Executive Director Clinical and Service Development, Office of the Chief Medical Officer	Hamad Medical Corporation
Dr Egon Toft	VP and Dean of College of Medicine	College of Medicine, Qatar University

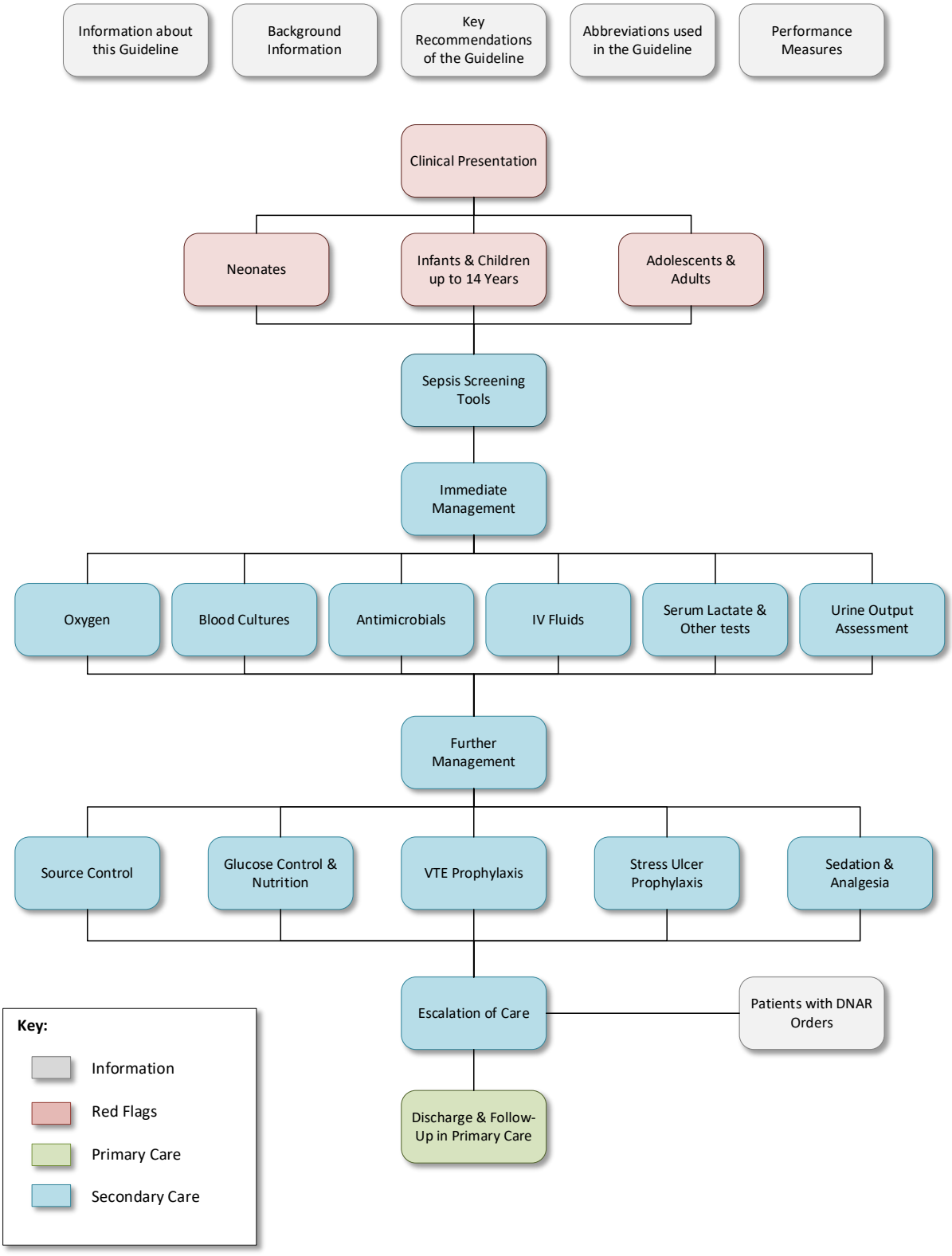
1.8 Responsibilities of Healthcare Professionals

This guideline has been issued by the MOPH to define how care should be provided in Qatar. It is based upon a comprehensive assessment of the evidence as well as its applicability to the national context of Qatar. Healthcare professionals are expected to take this guidance into account when exercising their clinical judgement in the care of patients presenting to them.

The guidance does not override individual professional responsibility to take decisions which are appropriate to the circumstances of the patient concerned. Such decisions should be made in consultation with the patient, their guardians, or caregivers and should consider the individual risks and benefits of any intervention that is contemplated in the patient's care.

2 Sepsis Diagnosis & Management Pathway

Click on a box below to see the relevant page of the Pathway.



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3 Key Recommendations of the Guideline

The key recommendations of this guideline are:

Early Recognition & Referral (*Section 5*):

- Common symptoms and signs in patients of all ages, include[3,10–12]:
  - Fever or low body temperature.
  - Tachycardia.
  - Tachypnoea.
  - Oliguria.
  - Prolonged capillary refill.
  - Signs of potential infection (e.g. increased redness, swelling or discharge at a surgical site, breakdown of a wound).
  - Altered mental state (e.g. decreased level of consciousness or agitation).
- Patients may **not** have a fever[1] and may have non-specific and non-localised presentations[1–4].
- A screening tool should be used by healthcare organisations to identify patients with sepsis.
- Screening and assessment tools that can be used, include:
  - *Qatar Early Warning System* (QEWS) [4].
  - *Paediatric Early Warning Scoring* (PEWS) tool [5].
  - *Modified Early Warning Scoring* (MEWS) tool [6].
  - *Sepsis-related Organ Failure Assessment (SOFA)* [4].
  - *Quick Sepsis-related Organ Failure Assessment (qSOFA)* [4,7].
- All people with suspected sepsis, who are seen outside of an acute hospital setting, should be referred to an Emergency Department, using the National Ambulance Service [**R-GDG**].

Immediate Management (*Section 6*):

- The **Sepsis Six Bundle** should be initiated by a clinician within 60 minutes of sepsis recognition or suspicion. It includes three therapeutic and three diagnostic steps[8] **[L2, RGA]**:
  - Administration of oxygen.
  - Measuring serum lactate.
  - Obtaining blood cultures.
  - Administration of IV broad spectrum antimicrobials.
  - Administration of IV fluids.
  - Measuring urine output.

Administration of Oxygen (*Section 6.1*):

- Give oxygen using the relevant respiratory route or apnoeic spills in neonates, if the SpO_2 in room air is less than 94% and in cases of respiratory distress or apnoea in children[1,4] **[L1, RGA]**.
- The target is to achieve a saturation of 94-98% (90-95% in neonates), unless there is cyanotic congenital heart disease or chronic lung disease[1,4].

Obtaining Blood Cultures (*Section 6.2*):

- All sepsis laboratory testing must be performed and reported as soon as possible, and samples must be labelled as STAT[4] **[L1, RGA]**.
- Abnormal or out of normal range results, and preliminary or final culture results should be reported to the requesting physician or the available physician in charge[4] **[L1, RGA]**.
- The first set of cultures should ideally be withdrawn prior to the administration of antibiotic treatment, unless this causes delay to the start of treatment.

- In adult patients, the second set should ideally be collected from a different puncture site (if possible) and within 30-60 minutes of the first set, but should not delay the administration of antibiotics within the first hour [4,9,10] **[L1, RGA]**.
- Although it is important to collect cultures from all *potential* sites of infections amongst all groups of patients, culture of all *possible* sites is not recommended as this can result in inappropriate treatment and antibiotic use[9].
- Unless the source of sepsis is not clinically evident, pan-cultures are not recommended[9] **[L1, RGC]**.

Administration of Antimicrobials (*Section 6.3*):

- Antimicrobial therapy ideally should be started within 60 minutes of sepsis recognition to reduce the risk of serious complications and death [2,4] [**L1, RGA**].
- In immunosuppressed patients with hemodynamic instability, antimicrobial therapy should be started within **30 minutes** of sepsis recognition[4].
- Antimicrobial administration should not be delayed because of the time taken for laboratory tests and cultures [4] [**L1, RGC**].
- Empirical antimicrobial therapy should be used for sepsis with unknown aetiology and source of infection[4,9] [**L1, RGA**].
- When culture and sensitivity results become available, antibiotic treatment must be reconsidered[4,9,11][**L1, RGA**].
- All antimicrobial prescriptions must be reviewed within 48 hours of initiation by a member of an Infectious Disease Team or equivalent antimicrobial steward [**R-GDG**].
- See *Section 6.3* for recommendations of treatment by age group.

Administration of IV Fluids (*Section 6.4*):

- IV fluids should be administered to all patients with sepsis-induced hypoperfusion[1,4,9] [**L1, RGA**].
- Use a pump or flow controller to deliver an IV fluid bolus[1].
- A syringe can be used for children under the age of 12 if a pump is not available. The pump or flow controller should deliver the fluid at a clinically appropriate rate [1].
- Hydroxyethyl starch solutions should **not** be used [1,4,9] [**L1, RGC**].
- Caution should be taken with fluid resuscitation among pregnant women as their colloid osmotic pressure tends to be lower than in other adults, thus the increased risk of pulmonary oedema [12].
- If physiological parameters do not improve after fluid resuscitation, vasopressor therapy should be considered in consultation with a senior physician[4,9] [**L1, RGA**].
- Corticosteroids should only be used in patients with septic shock if adequate fluid resuscitation and vasopressor therapy do not restore hemodynamic stability[9].
- Use blood as a volume expander for the following patients [4,9] [**L1, RGA**]:
    - Cardiopulmonary compromise with central venous oxygen saturation ($ScVO_2$) <70%.
    - Haemoglobin < 70g/L.
- Do not use erythropoietin for anaemia associated with sepsis. [**R-GDG**]

Measuring Serum Lactate and Additional Laboratory Tests (*Section 6.5*):

- Serum lactate is used as a biomarker to monitor the response to treatment.
- The test should be repeated every 2-4 hours and until the patient is stabilised [1,4,9].
- Tissue hypoperfusion is marked by a serum lactate level ≥ 2mmol/L [1,4,9] unless in children with known metabolic aetiology.
- See *Section 6.5* for lists of additional tests to be performed in different groups of patients.

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Measuring Urine Output (*Section 6.6*):

- Monitor urine output and record findings once every 4 hours in the first 24-48 hours and at least once every hour patient with septic shock [1,4].
- If for two consecutive hours and with fluid resuscitation, the urine output becomes <0.5 ml/kg/hour for children; or <30 ml/hour for adults - inform the physician in charge immediately [1,4].
- Catheterisation is not recommended unless clinically indicated [1,4].

Further Management (*Section 7*):

- Any required source control interventions should be implemented as soon as possible in patients with sepsis or septic shock [**R-GDG**].
- In an intensive care unit (ICU) setting, give intravenous insulin if blood glucose >180mg/dl after two consecutive measurements[9] **[L1, RGA]**.
- The goal is to achieve a level between 140-180 mg/dl [**R-GDG**]**.**
- Glucose levels should be monitored every 1-2 hours until the insulin infusion rate and glucose level stabilise in patients with insulin infusion [9].
- Proton pump inhibitors or histamine-2 receptors antagonists are recommended as a prophylaxis for sepsis patients at risk of gastrointestinal bleeding [9] **[L1, RGA]**.
- Early enteral feeding or early trophic/hypocaloric enteral feeding are recommended in critically ill patients if applicable [9].
- Early parenteral feeding or parenteral in combination with enteral are not recommended in those who can be fed enterally or during the first 7 days where enteral feeding cannot be done [9] **[L1, RGA]**.
- In adults, low molecular weight heparin for venous thromboembolism prophylaxis is recommended, providing no contraindications exist[9] **[L1, RGA]**.
- If pharmacological prophylaxis is contraindicated, mechanical prophylaxis should be used [9].
- See *Section 7.6* for sedation and analgesia.
- See *Section 7.8* for care escalation criteria.
- See *Section 7.9* for management of patients with DNAR orders.

NB: Venous thromboprophylaxis using low molecular weight heparin is not recommended in children.

Discharge (*Section 7.10*):

- Patients can be discharged from inpatient care if [4]:
    - The patient is clinically well.
        - Stable infants at ≥35 weeks gestation or older, who have been treated for sepsis, can be discharged the same day the antibiotics are discontinued.
    - All investigations are improving or acceptable.
    - A follow up appointment with a primary care physicians, has been arranged and a discharge plan should be provided to the patient and/or carers[4,13].
    - Age-appropriate safety-netting instructions have been provided to the patient and/or their caregiver.

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4 Background Information

4.1 Definition and Classification

Sepsis is a clinical syndrome that complicates severe infection and is characterized by systemic inflammatory response syndrome, immune dysregulation, microcirculatory derangements, and end-organ dysfunction. In this syndrome, tissues remote from the original insult display signs of inflammation including vasodilation, increased vascular permeability and leukocyte accumulation.

It includes at least one of the following signs of hypoperfusion, cardiovascular organ dysfunction, respiratory distress or two or more other organ dysfunctions that is new and not explained by other known aetiology of organ dysfunction:

- **Cardiovascular dysfunction**
  - Hypotension, blood pressure (BP) < 5th percentile for age or systolic BP < 2 SD below normal range for age.
  - Need for vasoactive drug to maintain BP in the normal range (dopamine or dobutamine, or epinephrine at any dose).
  - Two of the following:
    - Unexplained metabolic acidosis: base deficit > 5.0 mmol/L.
    - Increased arterial lactate > 2 times upper limit of normal.
    - Oliguria: urine output < 0.5 ml/kg/hr for at least two consecutive hours.
    - Prolonged capillary refill > 3 seconds.
    - Core to peripheral temperature gap > 3°C.
- **Respiratory**
  - PaO2/FiO2 < 300 in the absence of cyanotic heart disease or pre-existent lung disease.
  - PaCO2 > 65 mmHg or 20 mmHg increase over baseline PaCO2.
  - Proven need for > 50% FiO2 to maintain saturation ≥ 92%.
  - Need for nonselective invasive or non-invasive mechanical ventilation.
- **Other organs dysfunctions**
  - Paediatric Coma Score GCS ≤11.
  - Acute change in mental status with a decrease in GCS ≥ 3 points from abnormal baseline.
  - Platelet count < 80,000/mm3 or a decline of 50% in platelet count from highest value recorded over the past 3 days (for chronic haematology/oncology patients).
  - International normalized ratio INR > 2.
  - Serum creatinine ≥ 2 times upper limit of normal for age or 2-fold increase in baseline.
  - Total bilirubin ≥4 mg/dL (≥ 68 mmol/L) (not applicable for new-born).
  - Alanine amino transferase (ALT) greater than 2 times the upper limit of normal for age.

Neonatal sepsis is classified into[4]:

- Early onset sepsis (EOS) (occurring within the first 3 days of birth).
- Late onset sepsis (LOS) (occurring after day 3 of life).

Maternal sepsis occurs in women during pregnancy and puerperium[4].

Septic shock is a subset of sepsis in which underlying circulatory, cellular and metabolic abnormalities are associated with a greater risk of mortality than sepsis alone[9,14]. Patients with septic shock can be clinically identified by a vasopressor requirement to maintain a mean arterial pressure of 65mmhg or greater AND serum Lactate level greater than 2 mmol/L in the absence of hypovolemia

Bacteraemia is the presence of viable bacteria in the blood[4]. However, it is not necessary for the development of septic shock.

4.2 Epidemiology

Every year, sepsis is estimated to affect over 30 million of people worldwide, of which 3 million are new-born babies and 1.2 million are children[15]. In the US, 1.7 million people are diagnosed with sepsis every year and 270,000 of them die[16]. In the UK, sepsis is estimated to kill 44,000 patients [8]. Furthermore, about 10% of all ICU admissions in the US are because of sepsis and this contributes to over 24 billion dollars in annual hospital costs[8].

Sepsis can occur due to community-acquired infections (over 60%), healthcare-associated infections (26%), or hospital-acquired infections (11%)[17]. The majority occur as the result of pneumonia, abdominal, and genitourinary infections[13].

The most common pathogens of sepsis include gram-positive (58%) and gram-negative (33%) bacteria, fungi (7%), and anaerobes (2%)[18]. Gram-positive Group B *Streptococcus* (GBS) and gram-negative *Escherichia coli* (*E. coli*) together account for about 70% of cases of the EOS in neonates[4].

4.3 Sources of Infection

It is not always possible to identify the specific source of sepsis, however the following sources of infection are frequently associated with sepsis[2].

- Lower respiratory tract infections (e.g. pneumonia).
- Appendicitis.
- Peritonitis.
- Urinary tract infection (UTI).
- Cholecystitis and cholangitis.
- Skin and soft tissue infections (e.g. cellulitis).
- Post-operative infections.
- Central nervous system infections (e.g., meningitis, encephalitis).
- Osteomyelitis.
- Endocarditis.
- Device-related infection.

4.4 Risk Factors for Development of Sepsis

The following groups are recognised to be at increased risk of developing sepsis[1–3]:

- Patients aged <1 year or >65 years.
- Immunocompromised individuals:
    - Treated with chemotherapy and radiation therapy. (i.e. cancer patients)
    - With impaired immune function (e.g. diabetes, splenectomy, sickle cell disease and autoimmune disease).
    - With drug-mediated immune suppression (corticosteroids, other immunosuppressants).
- Individuals who have had surgery (or other invasive procedures) in the past 6 weeks.
- Pregnant women and women who have given birth or had a miscarriage or abortion in the past 6 weeks.
- Individuals with any breach of skin integrity (e.g. cuts, burns, catheterisation or intubation).
- Individuals with chronic infections (e.g. HIV, UTI, pneumonia, non-healing dermal wounds).
- Individuals with chronic illnesses such as chronic obstructive pulmonary disease, asthma, and chronic heart disease.
- Individuals who misuse drugs intravenously.

- Individuals with indwelling lines or catheters.
- Individuals with intravascular devices.

In neonates, the following particular risk factors should also be considered [1]:

- History of invasive group B streptococcal infection in a previous baby.
- Suspected or confirmed infection in another baby in the case of a multiple pregnancy.
- Maternal GBS colonisation, bacteriuria or infection in the current pregnancy.
- Preterm birth following spontaneous labour (before gestational age (GA) of 37 weeks).
- Suspected or confirmed rupture of membranes for more than 18 hours (prolonged rupture of membranes).
- Intrapartum fever higher than 38C.
- Confirmed or suspected chorioamnionitis.
- Parenteral antibiotic treatment given to the woman for confirmed or suspected invasive bacterial infection (e.g., septicaemia) at any time during labour, or in the 24-hour periods before and after the birth (this does not refer to intrapartum antibiotic prophylaxis).

In infants and children up to the age of 14 years the following risk factors have also been identified [**R-GDG**]:

- Chronic debilitating medical conditions e.g. cardiac, respiratory, neuromuscular conditions.
- Recent hospitalisation.

4.5 Prognosis

Sepsis is a systemic disorder that can affect all organs of the body. Patients with sepsis resulting in multiple organ system failure have a high mortality rate[9]. Early recognition and appropriate management in the first hours after development of sepsis has a critical impact on the outcome[9].

4.5.1 Sepsis Mortality

Sepsis is the most common cause of death among critically ill patients in non-coronary ICUs. Mortality from sepsis increases by about 8% for every hour of delayed treatment after the golden hour (the first 60 minutes)[16].

The following factors increase the risk of mortality [3,19,20].

- Age (<1 year or >75 years old).
- Nosocomial bacteraemia.
- Polymicrobial infection.
- Multi-drug resistant pathogens.
- Gram-positive pathogen[21].
- Chronic or severe underlying diseases.
- Development of septic shock.

Mortality is as high as 50%, especially in patients with multiorgan failure.

Note:

- The absence of full renal recovery is associated with poor long-term outcomes [3,22].
- Obesity is associated with an increased risk of complications[3].
- Maternal sepsis is the underlying cause for 11% of all maternal deaths [23].

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4.5.2 Sepsis Morbidity

Sepsis survivors have a reduced life expectancy, a higher risk of readmissions and a higher risk of death after rehospitalisation[13,26].

Longer term complications of sepsis, include[13,26,27]:

- Functional limitations (e.g., inability to manage money, bathe, or toilet independently).
- Anxiety, delirium, and depression.
- Post-traumatic stress disorder.
- Cognitive impairments.
- Cardiovascular events.
- Renal dysfunction.
- Heart failure.
- Acute lung injury.
- Chronic obstructive pulmonary disease.
- Other complications (e.g., numbness, pain, visual disturbance, hair loss, problems with dentition and nails).

5 Early Recognition of Sepsis

Symptoms and signs listed immediately below are usually present in all age groups[1–4]. They are often accompanied by additional features specific to the groups listed in each of the subsequent sections. Common symptoms and signs in patients of all ages, include[1–4]:

- Fever or low body temperature.
- Tachycardia.
- Tachypnoea.
- Oliguria.
- Prolonged capillary refill.
- Signs of potential infection (e.g. increased redness, swelling or discharge at a surgical site, breakdown of a wound).
- Altered mental state (e.g. decreased level of consciousness or agitation).

NB: Patients may **not** have a fever[1] and may have non-specific and non-localised presentations (e.g. feeling very unwell) [1–4].

5.1 Features of Sepsis in Neonates

The following symptoms and signs are associated with sepsis in neonates [1,2,4]:

- Temperature instability.
- Absence of interest in feeding (in babies <1 month).
- Bile-stained (green), bloody or black vomit.
- Bulging anterior fontanelle.
- Weak, "whining" or continuous crying.
- Hypoactivity or irritability.
- Bradypnoea or apnoea.
- Signs of hypoperfusion, including:
    - Capillary refill time of ≥3 seconds.
    - Cold extremities.
    - Pallor or mottling of skin.
- Leg tenderness.

5.2 Features of Sepsis in Infants and Children up to 14 Years of Age

The following symptoms and signs are associated with sepsis in infants and children up to 14 years of age[1,2]:

- Respiratory distress.
- Poor oral intake.
- Altered mental state, including:
    - Confusion.
    - Hypoactivity or irritability
    - Lethargy or unresponsiveness
- Neck stiffness.
- Signs of hypoperfusion, including:
    - Capillary refill time of ≥3 seconds.
    - Cold extremities.
    - Pallor or mottling of skin.

Age	0–1 month	1-12 months	1-2 years	3-5 years	6-9 years	>10 years
Tachycardia	≥224bpm	≥199bpm	≥159bpm	≥139bpm	≥137bpm	≥119bpm
Bradycardia	≤100bpm	≤100bpm	≤90bpm	≤80bpm	≤75bpm	≤60bpm

Table 5.2: Heart rate of patients with suspected/proven sepsis.

5.3 Features of Sepsis in Adolescents and Adults

The following signs and symptoms are associated with sepsis in children aged ≥14 years, and adults[1,2]:

- Respiratory rate ≥25 breaths/min.
- Need for oxygen (≥40% FiO_2) to maintain oxygen saturation >92% (or >88% in chronic obstructive pulmonary disease).
- Systolic blood pressure ≤90 mmHg (or systolic blood pressure more than 40 mmHg below normal).
- Heart rate ≥130 bpm.
- Severely reduced urine output:
    - Not passed urine in the past ≥18 hours.
    - For catheterised patients, passed less than 0.5 ml/kg/h.
- Objective evidence of altered mental state.
- Mottled or ashen appearance.
- Cyanosis of skin, lips or tongue.
- Non-blanching rash of skin.

5.4 Emergency Referral

All people with suspected sepsis, who are seen outside of an acute hospital setting, should be referred to an Emergency Department using the National Ambulance Service, if either of the following conditions apply [**R-GDG**]:

- The patient has any of the features of sepsis, as listed in *Sections 5.1 – 5.5* above.
- If a definitive diagnosis is not reached, but sepsis is still suspected.

5.5 Screening Tools

A screening tool should be used by healthcare organisations to identify patients with sepsis. Screening and assessment tools that can be used, include:

- *Qatar Early Warning System* (QEWS) [4].
- *Paediatric Early Warning Scoring* (PEWS) tool [5].
- *Modified Early Warning Scoring* (MEWS) tool [6].
- *Sepsis-Related Organ Failure Assessment (SOFA)* [4].
- *Quick Sepsis-Related Organ Failure Assessment (qSOFA)* [4,7].

5.5.1 Qatar Early Warning System

The *Qatar Early Warning System* (QEWS) is used as a system of alerting clinicians to adult patients likely to have sepsis[4]. The system is presently being updated and will be reissued in due course.

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5.5.2 Paediatric Early Warning Scoring Tool

The *Paediatric Early Warning Scoring* (PEWS) tool can be used as well as QEWS to assess the risk among paediatric inpatients[5].

5.5.3 Modified Early Warning Scoring Tool

The M*odified Early Warning Score* (MEWS) is used for all hospitalised patients to evaluate clinical deterioration of the patient and the risk of sepsis. A score ≥5 or any parameter score of 3, require higher level of care including ICU admission [6].

	Points:	3	2	1	0	1	2	3
Clinical Criteria	**Systolic blood pressure (mmHg)**	≤70	71 - 80	81 – 100	101 - 199		>199	
	Heart rate (bpm)		<40	41 – 50	51 - 100	101 - 110	111 - 129	>129
	Respiratory rate (breaths/min)		≤8		9 - 14	15 - 20	21 - 29	>29
	Temperature (°C)		<35	35.1 – 36	36.1 – 38.0	38.1 – 38.5	>38.5	
	Urine output (ml/kg/h)	0	<0.5					
	Neurological				Alert	Reacts to voice	Reacts to pain	Unresponsive

Table 5.5.3: Modified Early Warning Score tool [6].

5.5.4 Sepsis-Related Organ Failure Assessment Tool

According to the fourth SSC guidelines in 2016, the SOFA score and or the qSOFA score should be used to assess patients with possible sepsis. The *Sepsis-Related Organ Failure Assessment* (SOFA) is a grading system from 0-4 evaluating the severity of organ dysfunction using on a variety of clinical findings and laboratory data[4]. It involves tests for six organ systems and is primarily used in the ICU setting.
In screening for sepsis, increased risk would be an acute increase in the SOFA score of 2 or higher and a suggestion of infection. A higher SOFA score is associated with an increased probability of mortality.

	Points:	0	1	2	3	4
Clinical Criteria	**Respiration** $PaCO_2$/ F_iO_2 (mmHg)	≥400	<400	<300	<200 (with respiratory support)	<100 (with respiratory support)
	Coagulation Platelets ($x10^3/\mu l$)	≥150	<150	<100	<50	<20
	Liver function Bilirubin (mg/dL)	<1.2	1.2 – 1.9	2.0 – 5.9	6.0 – 11.9	>12
	Cardiovascular function	MAP ≥70mmg	MAP <70 mmHg	*Dopamine* <5 or *Dobutamine* (any dose)	*Dopamine* 5.1 – 15 or *Epinephrine* ≤0.1 or *Norepinephrine* ≤0.1	*Dopamine* >15 or *Epinephrine* >0.1 or *Norepinephrine* >0.1
	Central nervous system function Glasgow Coma Scale	15	13 - 14	10 - 12	6 - 9	<6
	Renal function Creatinine (mg/dL) and or	<1.2	1.2 – 1.9	2.0 – 3.4	3.5 – 4.9	>5.0
	Urinary output (ml/day)				<500	<200

Table 5.5.4: Sepsis-related Organ Failure Assessment tool [4].

5.5.5 Quick-Sepsis-related Organ Failure Assessment Tool

The *Quick Sepsis-Related Organ Failure Assessment* (qSOFA) is a modification of SOFA that does not require multiple tests and can be used in a pre-hospital or the emergency department setting, outside the ICU. However it cannot substitute the SOFA tool completely, but may identify patients with suspected infection or sepsis who are at greater risk of poor outcomes [4,7]. One point is given for each clinical criteria, and a score of ≥2 is considered positive and in favour of sepsis diagnosis [4,7].

The clinical criteria include [4,7]:

- Altered mental status (Glasgow Coma Scale < 15).
- High respiratory rate (≥22 breaths/min).
- Low systolic blood pressure (≤100 mmHg).

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6 Immediate Management

Sepsis is considered a medical emergency; therefore, treatment and resuscitation must begin immediately. Initial goals are to restore effective tissue perfusion by fluids and vasoactive medications and treat the underlying cause.

The **Sepsis Six Bundle** should be initiated by a clinician within 60 minutes of sepsis recognition or suspicion. It includes three therapeutic and three diagnostic steps[8] **[L2, RGA]**:

- Administration of oxygen
- Measuring serum lactate.
- Obtaining blood cultures.
- Administration of antimicrobials.
- Administration of IV fluids.
- Measuring urine output.

6.1 Administration of Oxygen

Administer oxygen as follows:

- Give oxygen using the relevant respiratory route or apnoeic spills in neonates, if the SpO_2 in room air is <94% and in cases of respiratory distress or apnoea in children[1,4] **[L1, RGA]**.
- If the SpO_2 in room air is ≥95% in children and neonates and ≥98% in adults, oxygen supplementation is only required if there are signs of respiratory distress or hypoperfusion[1,4].
- Measure baseline ABG to confirm oxygenation levels and identify acid-base status[1,4].
- The target is to achieve a saturation of 94-98% (90-95% in neonates), unless there is cyanotic congenital heart disease or chronic lung disease[1,4].

6.2 Blood Cultures

All sepsis laboratory testing must be performed and reported as soon as possible, and samples must be labelled as STAT[4] **[L1, RGA]**. Abnormal or out of normal range results, and preliminary or final culture results should be reported to the requesting physician or the available physician in charge[4] **[L1, RGA]**.

In general, diagnostic kits for basic sepsis testing should be available and contain[4] **[L1, RGA]**:

- 2 aerobic and 2 anaerobic blood culture bottles (only 1 culture bottle is required for paediatrics).
- 2 sterile specimen containers.
- 2 ACD tubes (yellow top).
- 1 EDTA tube (purple top).
- 1 sodium heparin tube (green top).
- 1 sodium citrate tube (blue top).
- 1 Arterial blood gas (ABG) kit.

Routine microbiological blood cultures must be requested for sepsis patients (each culture set includes one aerobic and one anaerobic culture bottles). [1,4,9].(See *Section 5.5*)

- For neonates and children below the age of 14 years:
    - Only one set of cultures is required and should be collected using full aseptic technique[4,9,10] **[L1, RGA]**.
- For patients over the age of 14 years:
    - Two sets of peripheral blood cultures should be collected using full aseptic technique,

Taking blood cultures:

- The first set of cultures should ideally be withdrawn prior to the administration of antibiotic treatment, unless this causes delay to the start of treatment.
- The second set should ideally be collected from a different puncture site (if possible) and within 30-60 minutes of the first set, but should not delay the administration of antibiotics within the first hour[4,9,10] **[L1, RGA]**.
- In patients in whom a central venous catheter (CVC) has been in situ for more than 48 hours:
    - A peripheral blood culture and central blood cultures from all CVC lumens should be obtained prior to administration of antibiotics - unless this causes delays in the initiation of the treatment [9] **[L1, RGA]**.

Although it is important to collect cultures from all *potential* sites of infections amongst all groups of patients, culture of all *possible* sites is not recommended as this can result in inappropriate treatment and antibiotic use. Thus, unless the source of sepsis is not clinically evident, pan-cultures are not recommended[9] **[L1, RGC]**.

6.3 Administration of Antimicrobials

Time to treatment initiation:

- Antimicrobial therapy ideally should be started within **60 minutes** of sepsis recognition to reduce the risk of serious complications or death [2,4] [**L1, RGA**].
- In immunosuppressed patients with hemodynamic instability, antimicrobial therapy should be started within **30 minutes** of sepsis recognition[4].

NB: Antimicrobial administration should not be delayed because of the time taken for laboratory tests and cultures [4] [**L1, RGC**].

Note:

- Empirical antimicrobial therapy should be used for sepsis with unknown aetiology and source of infection[4,9] [**L1, RGA**].
- When culture and sensitivity results become available, antibiotic treatment must be reconsidered[4,9,11][**L1, RGA**].
- Multidrug empirical antibiotic therapy is not required for all patients with sepsis but may be justified for patients with a high risk for multidrug-resistant organisms [11] [**L1, RGA**].
- Duration of antibiotic therapy depends upon the microorganism identified on culture and the clinical course of the patient [4,11] [**L1, RGA**].
- Estimation of the procalcitonin level is feasible and safe in critically ill patients with infections [11] and may be used to guide duration of antimicrobial therapy [4,9] [**L1**].

The choice of antibiotic should be made on the basis of the following criteria [4,9] [**L1, RGA**]:

- Age of the patient.
- Comorbidities or underlying diseases.
- Presence or absence of chronic organ failure.
- Pregnancy status.
- Immune status.
- Pharmacokinetics and Pharmacodynamics parameters; which can vary significantly in critically ill patients and patients with sepsis.
- Recent infection or colonisation with specific pathogens.
- Patient's allergy for drugs and their components.

- Pathogen prevalence and susceptibility in Qatar.
- Infection site.
- Relevant drug interactions. (current medications)
- Location at the time of infection (community, nosocomial).
- History of recent antimicrobial use within the past 3 months.
- Patients at risk of multidrug-resistant pathogens such as MRSA, multidrug-resistant Pseudomonas, vancomycin-resistant enterococci.

NB: All antimicrobial prescriptions must be reviewed within 48 hours of initiation by a member of an Infectious Disease Team or equivalent antimicrobial steward [**R-GDG**].

Stewardship in Sepsis [**R-GDG**]**:**

- Antimicrobial stewardship is crucial to keep in mind when treating patients with sepsis.
    - In using antimicrobials in empiric therapy, do not "throw in the kitchen sink."
    - Use monotherapy, when appropriate:
        - Patients without septic shock
        - Patients not at risk of MRSA infections
- Overuse of antimicrobials can result in collateral damage:
    - Antimicrobial resistance
    - Superinfections such as *Clostridioides difficile.*
- De-escalate antimicrobial therapy as soon as possible:
    - Continue treatment for identified pathogen and discontinue other therapy.
    - Change antibiotic therapy as warranted, but do not continue unnecessary antimicrobials.
- Use short courses of antimicrobial therapy.
    - Prolonged treatment may potentiate the development of resistance.
    - Use procalcitonin, if available, to guide clinical evaluation of infection resolution.
- Antibiotic discontinuation
    - Discontinue antibiotics if it is determined there is no infection. (use clinical judgement)
    - Do not use antibiotics as prophylaxis for patients who do not have sepsis but who may have another non-infectious systemic inflammatory process such as burns or severe pancreatitis.

6.3.1 Neonates

The table below provides recommendations for the most appropriate empirical antimicrobial treatments according to the type of infection or clinical scenario[4]:

Diagnosis	Empirical Treatment Recommendations
• EOS • LOS • Suspected pneumonia • Community-acquired meningitis • UTI	• Ampicillin AND cefotaxime.
• Deep soft-tissue infection • Suspected osteomyelitis	• Cefotaxime AND vancomycin

Table 6.3.1: Empirical antimicrobial recommendations by suspected infection in neonates.

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Refer to the infectious disease team for consultation if the patient has [4] [**L1, RGA**]:

- Deep seated tissue infections (e.g., osteomyelitis, septic arthritis, brain abscess).
- Complicated post-surgical infections.
- Invasive infection with methicillin resistant staph aureus (MRSA).
- Septicaemia with multidrug resistance bacteria.
- All invasive fungal infections.
- No clinical response to antibiotic therapy for 72 hours.
- Proven meningitis.
- Proven viral infection (for consideration as to the relevance of the sepsis).

Monitoring:

- Serum therapeutic drug monitoring is necessary during antibiotic therapy for certain drugs[4] [**L1, RGA**].
- The initial antibiotic requirement (type, dose, frequency) should be reviewed within 48 hours of initiation, or sooner, if clinically indicated [4,28] [**L1, RGA**].
- A daily assessment for antibiotic de-escalation should be further performed according to patient's clinical improvement and microbiology results [4] [**L1, RGA**].

Duration of antibiotic therapy depends upon the microorganism identified on culture and the clinical course of the patient and if in doubt should be discussed with Infectious Disease or equivalent antimicrobial steward[4] [**L1, RGA**]:

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6.3.2 Infants and Children up to 14 years of age

When culture and sensitivity results become available, reconsider empirical antibiotic treatment following recommendations given in the table below for paediatric patients with and without organ dysfunction[4] [**L1**].

<table>
<tr><th colspan="2">Diagnosis</th><th colspan="2">Prescribing Recommendations</th><th>Type I Mediated Penicillin Allergy</th></tr>
<tr><td rowspan="2">Sepsis of Unknown Origin</td><td>Community-acquired, previously healthy patients.</td><td>• Ceftriaxone.</td><td rowspan="8">• Add vancomycin, if:
○ Evidence of central line infection.
○ Hypotension or other cardiopulmonary impairment.
○ Radiographically documented pneumonia.
○ Clinically suspected, serious catheter-related infection.
○ Skin or soft-tissue infection at any site.
○ Known colonisation with penicillin/cephalosporin resistant pneumococci or MRSA.
○ Substantial mucositis.
○ Previous history of infection with penicillin-resistant streptococci.
○ Recent intensive chemotherapy associated with a high risk of infection with such organisms.
• Discontinue if no vancomycin-susceptible bacteria are recovered from the patient within 2-3 days of treatment.
• Monitor kidney function closely.</td><td>• Aztreonam AND vancomycin.</td></tr>
<tr><td>Patients with any of the following:
• Central line.
• Chronic hospitalisation.
• Immunocompromised.
• Taking immunosuppressants.
• Recent hospitalisation (>4 days in the last 2 months).</td><td>• Meropenem.</td><td>• Aztreonam AND vancomycin.</td></tr>
<tr><td rowspan="2">Febrile neutropenia</td><td>With organ dysfunction.</td><td>• Meropenem.</td><td>• Aztreonam AND amikacin.</td></tr>
<tr><td>Without organ dysfunction.</td><td>• Piperacillin AND tazobactam.</td><td>NA</td></tr>
<tr><td rowspan="2">Deep soft tissue infection</td><td>With organ dysfunction.</td><td>• Ceftriaxone.</td><td rowspan="2">• Aztreonam AND vancomycin.</td></tr>
<tr><td>Without organ dysfunction.</td><td>• Cefazolin.</td></tr>
<tr><td rowspan="2">Community-Acquired Pneumonia</td><td>With organ dysfunction.</td><td>• Ceftriaxone</td><td rowspan="2">• Aztreonam AND vancomycin.</td></tr>
<tr><td>Without organ dysfunction.</td><td colspan="2">• Co-amoxiclav AND a macrolide</td></tr>
<tr><td rowspan="2">Hospital-Acquired Pneumonia</td><td>With organ dysfunction.</td><td colspan="2">• Piperacillin AND tazobactam.
Or:
• Meropenem,</td><td rowspan="2">• Aztreonam AND vancomycin.</td></tr>
<tr><td>Without organ dysfunction.</td><td colspan="2">• Piperacillin AND tazobactam.</td></tr>
</table>

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Diagnosis		Prescribing Recommendations		Type I Mediated Penicillin Allergy
Intra-abdominal infection	With organ dysfunction.	• Piperacillin AND tazobactam.		• Aztreonam AND metronidazole.
	Without organ dysfunction.	• Ceftriaxone AND metronidazole.		
Uncomplicated UTI	Without organ dysfunction.	• Co-amoxiclav or ceftriaxone.		• Aztreonam
Complicated UTI	With organ dysfunction.	• Meropenem.		• Aztreonam.
	Without organ dysfunction.	• Cefepime AND gentamycin.		
Meningitis	With organ dysfunction.	• Meropenem.	• Add Acyclovir if meningoencephalitis is suspected	• Aztreonam AND vancomycin.
	Without organ dysfunction.	• Ceftriaxone.		
Necrotizing fasciitis	With or without organ dysfunction.	Consider in addition to above regimens: • Clindamycin.		
Risk of Fungemia	Patients with central line and ≥2 of the following: • TPN. • Malignancy. • Persistent fever for 5 days whilst on antibiotics.	Consider in addition to the above regimens: • Liposomal amphotericin B. Or: • Caspofungin.		
Suspected Influenza	With or without organ dysfunction.	Consider in addition to the above regimens: • Oseltamivir.		

Table 6.3.2: Recommended Empirical Antimicrobial Treatments for Sepsis in Children up to 14 years of age [4].

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6.3.3 Adolescents and Adults

An empiric broad-spectrum therapy with one or more antimicrobials should be started as soon as possible[2,4] [**L1, RGA**]. The following types of antibiotics may be used[9] [**L1, RGA**]:

- Broad-spectrum carbapenems:
  - Meropenem.
- Extended-range penicillin/β-lactamase inhibitor combinations:
  - Piperacillin/tazobactam.
  - Ticarcillin/clavulanate.
- Third- or higher-generation cephalosporins. (cefepime, ceftazidime)

In case of patients at risk for MRSA infection, the following agents are recommended [4,9,29] [**L1, RGA**]:

- Vancomycin.
- Teicoplanin.
- Other anti-MRSA agents (Linezolid, daptomycin)

In patients at risk of fungal infections, an appropriate antifungal agent should be added.

- Echinocandins (caspofungin, anidulafungin, micafungin) used first line for Candida infections
- Triazoles (voriconazole, posaconazole)
- Amphotericin B (deoxycholate or lipid formulations)

In patients presenting with septic shock, adding an aminoglycoside or fluoroquinolone may be considered:

- Fluoroquinolones (ciprofloxacin, levofloxacin)
- Aminoglycosides (amikacin, tobramycin)
- MRSA therapy may be added if the patient is at risk of MRSA infection

NB:

- *Rifampicin* should not be used alone for antimicrobial therapy [30] [**L1, RGC**].
- When culture and sensitivity results become available, reconsider narrowing antibiotic treatment following recommendations given in the table below [9,29–32] [**L1, RGA**].
- Combination therapy in septic shock should be modified, including discontinuing unwarranted antimicrobials based on clinical improvement or infection evidence. [**R-GDG**]
- Procalcitonin may be used to evaluate the resolution of infection and the possibility of shortening the antimicrobial therapy duration.
- If uncertainty of appropriate patient-specific antimicrobial therapy remains, consult infectious disease team[9] [**L1**].
- Appropriate therapy also includes appropriate dosing; therefore, renal function, renal replacement therapy, and or pharmacodynamics or pharmacokinetics issues must be considered when designing a dosing regimen for patients with sepsis. [**R-GDG**]
- To combat resistance, dosing strategies such as extended or continuous infusions may be used to optimise therapy.
- Serum therapeutic drug monitoring should be performed as necessary [4] [**L1, RGA**].

Diagnosis	Antimicrobials	Notes
Acute rhinosinusitis	• Penicillin.	• Consider doxycycline or clarithromycin in penicillin-allergic patients.
Meningitis	• Third generation cephalosporin (cefotaxime or ceftriaxone) or benzylpenicillin.	• Patients aged ≥60 year or immunocompromised patients should receive IV ampicillin or amoxicillin in addition to a cephalosporin. • If penicillin resistance is suspected, add vancomycin or rifampicin. • Consider chloramphenicol in penicillin- or cephalosporin-allergic patients.
Pneumonia	• Amoxicillin and Clavulanate plus Clarithromycin or Azithromycin	• Continue treatment for 5 days. The course can be extended if improvement is not reached in 3 days.
Uncomplicated Lower UTI	• Nitrofurantoin or trimethoprim.	• Consider pivmecillinam. (pro-drug of a beta-lactam antibiotic) • If microorganism is sensitive, consider amoxicillin. • In high resistance risk, consider fosfomycin.
Upper UTI	• Ciprofloxacin or amoxicillin/clavulanate.	• If microorganism is sensitive, consider trimethoprim. • Do not use nitrofurantoin.
Enterococcal infections	• Ampicillin, penicillin, or vancomycin with aminoglycoside.	
S. aureus infection	• β-lactam antibiotics (cloxacillin or cefazolin).	• In proven MSSA. • Daptomycin may be considered.
	• Vancomycin and β-lactam antibiotics should be used along with the MRSA management plan.	• In culture positive MRSA. The Infection Control Team must be informed immediately. • Consider daptomycin instead of vancomycin in cases of severe sepsis or shock, recent use of vancomycin (past 30 days), and/or previous renal impairment.
Legionella infections	Macrolide or fluoroquinolone.	
Candida sepsis	Echinocandins (anidulafungin, micafungin, or caspofungin).	If microorganism is sensitive, consider triazoles in hemodynamically stable, less ill patients. Use liposomal amphotericin B if echinocandins are not suitable.
Leg ulcers	Flucloxacillin.	Continue treatment for 7-14 days. Consider clarithromycin in penicillin-allergic patients. Consider doxycycline in penicillin-allergic patients on statin.
Pilonidal sinus	Flucloxacillin with metronidazole.	Continue treatment for 7 days. Use clarithromycin instead of flucloxacillin in penicillin-allergic patients. Use erythromycin instead of flucloxacillin in penicillin-allergic patients who are pregnant or breast-feeding.
Mastitis	Lactating women: flucloxacillin.	Continue treatment for 7-14 days. Consider amoxicillin/clavulanate if no improvement is reached in 2 days. Consider erythromycin or clarithromycin in penicillin-allergic patients.
	Non-lactating women: amoxicillin/clavulanate.	Consider erythromycin or clarithromycin supplemented with metronidazole in penicillin-allergic patients.
Dental abscess	Amoxicillin or phenoxymethylpenicillin	May be supplemented with metronidazole. Consider metronidazole or clarithromycin in penicillin-allergic patients.

Table 6.3.3: Antimicrobial recommendations for adolescent and adult patients with sepsis[9,29–32].

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6.3.4 Maternal Sepsis

Management of sepsis in pregnant and nonpregnant patients is similar [12] [**L2**]. Antimicrobial drugs used to treat sepsis during pregnancy and the puerperium are largely the same as those used in nonpregnant patients [12] [**L2**].

NB:

- Refer to the infectious disease team for consultation and the dose calculation [4] [**L1**].
- When culture and sensitivity results become available, reconsider antibiotic treatment following recommendations given in the table below[4,12,29,33–36] [**L1**].
- Serum therapeutic drug monitoring should be performed as necessary [4] [**L1, RGA**].
- Estimation of the procalcitonin level is feasible and safe in critically ill patients with infections[11] and may be used to guide duration of antimicrobial therapy[4,9] [**L1**].
- Consider oseltamivir or zanamivir, if influenza is suspected[34] [**L1, RGA**].

Diagnosis	Drugs	Notes
Sepsis of Unknown Origin	If not critically ill: • Ceftriaxone 2g IV STAT once daily AND metronidazole 500mg every 8 hours	If penicillin or cephalosporin allergic: • Clindamycin 600mg-1.2g every 6-8 hours AND gentamicin 3mg/kg once daily. ○ Gentamicin poses no problems in normal renal function. ○ Serum levels must be monitored. • If MRSA is suspected: ○ Add vancomycin 25mg/kg IV STAT (rate1g/hr).
	Septic Shock: • Piperacillin-Tazobactam 4.5g 8hrly AND gentamicin 3mg/kg once daily.	
Suspected Group A Streptococcal Infection	Clindamycin 600mg to 1.2g, 6-8 hourly	If MRSA is suspected: • Add vancomycin 25mg/kg IV STAT (rate1g/hr).

Table 6.3.4: Antimicrobial recommendations in maternal sepsis [4].

6.4 Administration of IV fluids

IV fluids should be administered to all patients with sepsis-induced hypoperfusion[1,4,9] **[L1, RGA]**. Use a pump or flow controller to deliver an IV fluid bolus. A syringe can be used for children under the age of 12 if a pump is not available. The pump or flow controller should deliver the fluid at a clinically appropriate rate [1]. Hydroxyethyl starch solutions should **not** be used [1,4,9] **[L1, RGC].**

6.4.1 Neonates

IV fluid resuscitation in neonates:

- Use IO if an IV access is not available[4].
- Use normal saline, with a bolus of 10–20 ml/kg within 10-15 minutes[1,4,9] **[L1, RGA].**
- The first hour volume replacement limits are[4]:
    - 60 ml/kg for full term newborn.
    - 30 ml/kg for neonate with birth weight 1000-1500 g.
    - 20 ml/kg for neonate with birth weight < 1000 g.

- Avoid insufficient or excessive fluid resuscitation and assess further need according to the clinical response[4].
- If further fluid resuscitation is required, use vasoactive drugs and maintain volume intake depending on the gestational and postnatal age of the baby[4].
- Correct for hypoglycaemia (if blood glucose <2.2 mmol/L) [4]:
    - Confirm the diagnosis of hypoglycaemia by re-assessing blood glucose levels.
    - Give dextrose 10% IV bolus 2 ml/kg over 5 minutes.
    - Initiate infusion of dextrose 10% at a glucose infusion rate of 6 mg/kg/minute.
    - Measure blood glucose after 20 minutes:
        - If >2.6 mmol/L, decrease the rate of glucose checking gradually to 4-6 hourly.
        - If <2.6 mmol/L, increase glucose infusion rate in steps of 2mg/kg/minute, every 30 minutes, without exceeding 12 mg/kg/minute and keep measuring the blood glucose level.
    - In new-borns >48 hours old, the target blood glucose level should be >3.3 mmol/L.

6.4.2 Infants and Children up to 14 years of age

IV fluid resuscitation in infants and children aged up to 14 years.

- Use IO if IV access cannot be secured [4].
- Use normal saline, with a bolus of 20 ml/kg within 5-20 minutes [1,4,9] **[L1, RGA].**
- Assess the response to fluid resuscitation and evaluate whether additional fluid bolus is needed [4].
- In the first hour, a fluid volume of 60 ml/kg or more may be needed [4].
- Carefully titrate IV fluid in the following patients [4]:
    - In need of high flow oxygen.
    - Severe heart failure.
    - End stage renal disease or on dialysis.
- Correct for hypoglycaemia (if blood glucose <3.3 mmol/L) by giving 5-10 ml/kg of d*extrose* 10% [4].
- Correct for hypocalcaemia (if blood calcium <1.1 mmol/L) by giving 100 mg/kg of calcium gluconate (maximum 2g) or 10-20 mg/kg calcium chloride in a PICU setting [4].
- If the patient requires large volumes of crystalloids, consider using albumin [4].

6.4.3 Adolescents and Adults

IV fluid resuscitation in adolescents and adults:

- Give a balanced isotonic crystalloids fluid such as Ringer's solution of at least 30 ml/kg within the first 3 hours [1,4,9] **[L1, RGA].**
- IV fluid resuscitation should be maintained until adequate tissue perfusion is achieved [4].
- Colloids such as hetastarch or other hydroxyethyl starches are not recommended.
- Albumin can be considered if larger amounts of fluids are needed [4].
- Needs for additional fluids should be guided by frequent assessment of hemodynamic status[4] [**R-GDG**]
    - Evaluation of variables such as heart rate, blood pressure, arterial oxygen saturation, respiratory rate, temperature, urinary output.
    - Target a MAP of 65 mm Hg, especially in those also receiving vasopressor therapy.
    - Target returning serum lactate concentrations to normal (less than 2 mmol/L) because lactate can be a good indirect measure of tissue perfusion and more objective than physical examination and or urinary output.
- Carefully titrate IV fluid in the following patients [4]:
    - In need of high flow oxygen.
    - Severe heart failure.
    - End stage renal disease or on dialysis.

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6.4.4 Maternal Sepsis

IV fluid resuscitation in maternal sepsis:

- Give a balanced isotonic crystalloid solution of at least 30 ml/kg within the first 3 hours [1,4,9] **[L1, RGA].**
- Give 500 ml IV fluid STAT if the patient has a mean arterial pressure < 65mmHg [4].
- IV fluid resuscitation should be maintained until adequate tissue perfusion is achieved [4].
- Review response to fluid resuscitation and determine the need for further fluid[4].
- Albumin can be considered if larger amounts of fluids are needed [4].
- Carefully titrate IV fluid in the following patients [4,34]:
    - Pre-eclampsia or eclampsia.
    - In need of high flow oxygen.
    - Severe heart failure.
    - End stage renal disease or on dialysis.
- Caution should be taken with fluid resuscitation among pregnant women as their colloid osmotic pressure tends to be lower than in other adults, thus the increased risk of pulmonary oedema [12].

6.4.5 Vasoactive Drugs

If physiological parameters do not improve after fluid resuscitation, vasopressor therapy should be considered in consultation with a senior physician[4,9] [**L1, RGA**]:

- Norepinephrine 0.05-0.1 µg/kg/minute (drug of choice).
- Vasopressin 0.03 units/minute.
- Dopamine maximum 10 µg/kg/minute
- Epinephrine 0.05-0.3 µg/kg/minute.
- Drugs can be given IV or IO until a central venous access is secured.

NB:

- Dopamine should only be used as an alternative in select patients (i.e. patients at low risk of tachyarrhythmias or bradycardia-induced hypotension). Low-dose *dopamine* for renal protection ("renal dose" 0.5–2 mcg/kg/minute) is not recommended [9] [**L1, RGC**].
- Any patient requiring vasopressor therapy should have an arterial catheter placed as soon as possible for monitoring. [**R-GDG**]
- Phenylephrine is a pure α-adrenergic agonist that should be reserved for those who have not achieved their goal MAP with other agents and combinations. [**R-GDG**]
- Dobutamine may be initiated in patients with evidence of persistent hypoperfusion or reduced cardiac input despite fluid resuscitation and vasopressor therapy. [**R-GDG**]

6.4.6 Corticosteroids

Corticosteroids should only be used in patients with septic shock, if adequate fluid resuscitation and vasopressor therapy do not restore hemodynamic stability[9] (i.e. DO NOT use hydrocortisone in the absence of septic shock).

- When indicated, intravenous hydrocortisone is recommended with a dose of 200 mg administered daily by continuous or intermittent infusion; however, may result in an increased risk of hyperglycaemia.
    - Use as short a course as possible.
    - Taper hydrocortisone over 3 days or more when vasopressors are no longer require

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6.4.7 Blood Products

Use blood as a volume expander for the following patients [4,9] **[L1, RGA]:**

- Cardiopulmonary compromise with central venous oxygen saturation ($ScVO_2$) <70%.
- Haemoglobin < 70g/L.

Packed RBCs transfusion:

- Given Packed RBCs to reach a minimum Hb of 90 -100g/L in patients with known coronary artery disease or myocardial ischaemia. (if there are no signs of cardiopulmonary compromise such as myocardial ischaemia or acute haemorrhage, a Hb of 70g/L is acceptable)[4,9] **[L1, RGA].**

NB: Do not use erythropoietin for anaemia associated with sepsis.

Platelet transfusion:

- In cases of sepsis with a platelet count less than $10x10^3/\mu l$ in the absence of bleeding, consider having a platelet transfusion as prophylaxis [4,9] **[L1, RGA].**
- Consider platelet transfusion in children with risk of bleeding and a platelet count less than $20x10^3/\mu l$ [4,9] **[L1, RGA].**
- Consider platelet transfusion for patients with a count of $50x10^3/\mu l$ in the following cases [4,9]: **[L1, RGA].**
    - Actively bleeding.
    - Having surgery or invasive procedures for example tracheostomy or intercostal chest tube insertion.
- The platelet count increases by $10x10^3/\mu l$ for every 1 unit per m^2 transfused [4].

Fresh frozen plasma transfusion:

- Transfusion of 10 ml/kg over 2 hours is only recommended when the patient has bleeding with confirmed clotting factor deficiency [4,9] **[L1, RGA].**

NB:

- Routine use of fresh frozen plasma to correct laboratory clotting abnormalities in the absence of bleeding is not recommended.
- Other agents:
    - Immunoglobulins should not be used for the specific treatment of sepsis or septic shock.
    - In limited trials, antithrombin in patients with sepsis has increased the risk of bleeding. Until future studies are done, antithrombin should not be used in patients with sepsis/septic shock.

6.5 Measuring Serum Lactate and Additional Laboratory Tests

In addition to blood cultures, the following laboratory tests should be performed for all age groups and as clinically indicated [1,4,37,38] **[L1, RGA]**:

- **Serum lactate level**:
    - Serum lactate is used as a biomarker to monitor the response to treatment.
    - The test should be repeated every 2-4 hours and until the patient is stabilised [1,4,9].
    - Tissue hypoperfusion is marked by a serum lactate level ≥ 2mmol/L [1,4,9].
- Complete Blood Count (CBC).
- Comprehensive metabolic panel (CMP) including:
    - Electrolytes.
    - Renal function tests.
    - Liver function tests.

    - Glucose.
- Arterial blood gas (ABG), or capillary blood gas in neonates.
- C-reactive protein.
- Coagulation profile.
- Procalcitonin.
- Urinalysis, with microscopy and culture, if indicated.

6.5.1 Additional Laboratory Tests in Neonates

Additional tests that may be required for **neonates**, include[4]:

- Cerebrospinal fluid (CSF) culture:
    - Perform lumbar puncture (LP) before antibiotics administration if the delay does not influence the safety of the patient and is within the 60 minutes
    - In patients with EOS - within 3 days of life - LP is recommended where meningitis is highly suspected such as cases of seizures and abnormal consciousness.
    - In patients with LOS - LP is recommended only when clinical findings are highly suggestive of sepsis.
- CSF gram stain.
- CSF cell count with differential, protein and glucose.
- Urine culture:
    - Required for LOS and not for EOS.
    - Collect via a catheter or suprapubic aspiration.
- Other cultures as clinically indicated such as purulent eye drainage, skin lesions, pustules, peritoneal fluid, or tracheal aspirates in mechanically ventilated infants.

6.5.2 Additional Laboratory Tests in Infants and Children up to 14 Years of age

Additional tests that may be required for infants and children up to **14 years of age** [4]:

- CSF culture:
    - If clinical findings or laboratory results are highly suggestive of CNS infection.
    - If the patient's status is deteriorating while on antibiotics.
    - In febrile infants:
        - Appearing very ill.
        - Having seizures.
        - With clinically evident invasive infection.
- Other clinically relevant cultures (urine, sputum and wound).

6.5.3 Additional Laboratory Tests in Adolescents and Adults

Additional tests that may be required for older **adolescents and adults** as clinically indicated [4].

- Urine culture.
- Sputum culture.
- Wound swab culture.

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6.5.4 Additional Laboratory Tests in Maternal Sepsis

Additional tests that may be required for women in **pregnancy or within 6 weeks of birth**[4], include:

- Microscopy, culture, histopathology and sensitivity depending on the clinical presentation for the following specimens:
    - Throat swab.
    - Pre-moistened nose swab if MRSA status is unknown.
    - High or low vaginal swab.
    - Endocervical swab.
    - Wound swab.
    - Swab from baby.
    - Epidural site.
    - CSF.
    - Breast milk.
    - Placental tissue sample.
    - Whole placenta.
    - Midstream urine.
    - Stool.

Although it is important to collect cultures from all *potential* sites of infections amongst all groups of patients, culture of all *possible* sites is not recommended as this can result in inappropriate treatment and antibiotic use. Thus, unless the source of sepsis is not clinically evident, pan-cultures are not recommended[9] **[L1, RGC]**.

6.6 Assessment of Urine Output

The following recommendations are made:

- Perform point of care (POC) urinalysis or send for urine dipstick [1,4].
- Monitor urine output and record findings once every 4 hours in the first 24-48 hours and at least once every hour patient with septic shock [1,4].
- If for two consecutive hours and with fluid resuscitation, the urine output becomes <0.5 ml/kg/hour for children; or <30 ml/hour for adults - inform the physician in charge immediately [1,4].
- Catheterisation is not recommended unless clinically indicated [1,4].

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7 Further Management

7.1 Source Control

Despite adequate resuscitation efforts and appropriate antimicrobials, without control of the source of the infection, a patient may be unable to be stabilised. [**R-GDG**]

Any required source control interventions should be implemented as soon as possible in patients with sepsis or septic shock. Interventions include [**R-GDG**]:

- Drainage of abscesses.
- Necrotic tissue debridement.
- Surgical intervention for control of persistent microbial contamination.
- Gastrointestinal perforations.
- Debridement of deep space infections such as osteomyelitis and empyema.
- Removal of intravascular devices once other vascular access has been established.

7.2 Glucose Control

In an intensive care unit (ICU) setting, give intravenous insulin if blood glucose >180 mg/dl after two consecutive measurements[9] **[L1, RGA]**. The goal is to achieve a level between 140-180 mg/dl [**R-GDG**]

Glucose levels should be repeated every 1-2 hours until the insulin rate and glucose level stabilise in patients with insulin infusion [9]. If possible, glucose should be measured from arterial blood samples rather than capillary blood for POC testing, as the capillary blood sample does not necessarily reflect plasma glucose levels [9].

7.3 Stress Ulcer Prophylaxis

Stress ulcer prophylaxis such as proton pump inhibitors or histamine-2 receptors antagonists should be used in sepsis patients at increased risk of gastrointestinal bleeding (e.g. low platelets, prolonged mechanical ventilation) [9] **[L1, RGA]**.

NB:

- Do not use sucralfate.
- Avoid stress ulcer prophylaxis in patients without risk factors for gastrointestinal bleeding.

7.4 Nutrition Support

Early enteral feeding or early trophic/hypocaloric enteral feeding are recommended in critically ill patients if applicable [9]. Early parenteral feeding or parenteral in combination with enteral are not recommended in those who can be fed enterally or during the first 7 days where enteral feeding cannot be done [9] **[L1, RGA]**.

Supplementation with omega-3 fatty acids, the use of IV selenium, arginine and glutamine are not recommended [9] **[L1, RGC]**.

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7.5 Deep Venous Thrombosis Prophylaxis

The combination of pharmacologic prophylaxis and mechanical prophylaxis (compression) should be used, whenever possible, according to limited studies showing that this combination is more effective than either modality alone. [**R-GDG**]
Low molecular weight heparin for venous thromboembolism prophylaxis is recommended in adults, providing no contraindications exist[9] **[L1, RGA]**. However, if pharmacological prophylaxis is contraindicated, mechanical prophylaxis alone can be used [9].

NB: Venous thromboprophylaxis using low molecular weight heparin is not recommended in children.

7.6 Sedation and Analgesia

The following recommendations regarding sedation and analgesia are made [**R-GDG**]:

- Intermittent bolus or continuous infusion sedation should be minimised in mechanically ventilated patients with sepsis.
- Specific titration end points should be targeted.
- Limiting the use of sedation in mechanically ventilated patients reduces the time of ventilation and ICU length of stay.

7.7 Radiological Investigation

If clinically appropriate, the following radiology tests may be considered according to the history and clinical presentation [4,39]:

- Chest radiograph in case of respiratory distress.
- Abdominal radiograph in the presence of abdominal signs indicating necrotizing enterocolitis in neonates.
- Abdominal ultrasound.
- Pelvic ultrasound.
- CT/MRI scan.

7.8 Escalation of Care

Criteria for escalation of care in **neonates, infants and children up to 14 years of age** [4]:

- Sepsis care should be escalated whenever at least one of the following criteria is met:
    - The patient shows signs of worsening at the patient's current setting.
    - The attending team expects the patient to continue deteriorating despite best efforts, even if the patient is not yet in distress or septic shock.
    - Despite adequate fluid resuscitation:
        - Patient requires vasopressor support to maintain a mean arterial pressure ≥65mmHg, or
        - The lactate level is greater than 2mmol/L (>18mg/dL) in the absence of hypovolaemia

Note [4]:

- Neonates and infants with suspected/confirmed sepsis and hemodynamic instability should immediately be treated for septic shock without waiting for laboratory confirmation.
- Mechanical ventilation may have to be initiated if indicated.

- Neonates with septic shock may require transfer to a Level III Perinatal Centre after stabilisation if the baby requires cardiopulmonary support, parenteral nutrition or prolonged IV access.
- The multidisciplinary services available at larger centres may be necessary if the neonate's condition is acutely compromised.

Criteria for escalation of care in **adolescents and adults**:

- Sepsis care should be escalated as directed by facility protocols (e.g. ICU team or Rapid Response Team (RRT) where applicable), whenever at least one of the following criteria is met [4]:
    - The patient shows signs of worsening/persistent organ dysfunction not manageable at the patient's current setting.
    - The attending team expects the patient to continue deteriorating despite best efforts, even if the patient is not yet in distress or septic shock.
    - Despite adequate fluid resuscitation:
        - Patient requires vasopressor support to maintain a mean arterial pressure ≥65mmHg, or
        - The lactate level is greater than 2mmol/L (>18mg/dL) in the absence of hypovolaemia; or
        - The patient's clinical or biochemical parameters trigger QEWS response at both Clinical Review and RRT levels (see *Section 5.4*).

7.9 Patients with DNAR Orders

For all children who have been clinically agreed by the parent/s to be not for cardiopulmonary resuscitation (CPR) (i.e. those who have a *Do Not Attempt Resuscitation* (DNAR) order in place) [4]:

- The order of DNAR is not an order to forgo other treatment; it is strictly a decision concerning CPR if cardiopulmonary arrest occurs.
- It is recommended that the primary clinical teams caring for patients with DNAR order in place and diagnosed with sepsis (suspected or proven) to provide all of the recommended sepsis care and management unless this subject was discussed earlier with the infant parent/s and the agreement is not to treat.
- If there is agreement with the infant parent/s of not to provide part, or all, of the recommended sepsis management, then this must be clearly documented in the patient's medical records.

For all adult patients who have been clinically agreed not for cardio-pulmonary resuscitation (i.e. those who have a *Do Not Attempt Resuscitation* (DNAR) order in place), and those with a DNAR advance directive[4]:

- It is recommended that the primary clinical teams caring for patients with DNAR order in place and diagnosed with sepsis (suspected or proven) to conduct a multidisciplinary team (MDT) discussion(s) with the patient/patient's family on the most appropriate approach to their care on a case-by-case basis.
- If the consensus of the MDT discussion with the patient/patient's family is not to provide part, or all, of the recommended sepsis care and management as stated in this policy, then there must be clear documentation in the patient's medical records of:
    - The reason(s) for non-provision of recommended care.
    - The specific elements of care that will not be provided as recommended in this policy.
    - The tailored sepsis care and management agreed by the MDT for the patient.
    - Members of the team who made the consensus agreement.
    - Authorisation and countersignature of the most senior medical staff in charge of the patient's care (at least at consultant level).

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7.10 Discharge and Follow-Up in Primary Care

Patients can be discharged from inpatient care if[4]:

- The patient is clinically well.
    - Stable infants at ≥35 weeks gestation or older, who have been treated for sepsis, can be discharged the same day the antibiotics are discontinued.
- All investigations are improving or acceptable.
- A follow up appointment with a primary care physicians, has been arranged and a discharge plan should be provided to the patient and/or carers[4,13].
- Age-appropriate safety-netting instructions have been provided to the patient and/or their caregiver.

Following discharge from inpatient care, primary healthcare professionals should focus on [1,4,13,40] [**L1**]:

- Reviewing and adjusting long-term medication.
- Screening for common treatable impairments after sepsis:
    - Functional disability.
    - Swallowing impairment.
    - Mental health impairments (anxiety, depression, post-traumatic stress disorder).
    - Hearing, vision, and developmental status after neonatal meningitis.
- Evaluating for conditions that might occur during hospitalisation, including:
    - Infection.
    - Organ failure.
    - Aspiration pneumonitis.
    - Exacerbation of chronic obstructive pulmonary disease.
- Identifying new physical, mental, and cognitive problems.
- Referring for appropriate treatment.
- Palliation of symptoms (if needed).
- Referrals to physical therapy (if needed).
- Educating patients and caregivers about:
    - Sepsis.
    - Long-term functional deficits.
    - Possible complications.
    - Dietary changes (if any).
    - Restrictions regarding driving, physical activity, etc.
    - Available support resources.

8 Key Considerations for Patient Preferences

Patient preferences refer to patient perspectives, beliefs, expectations, and goals for health and life, and to the steps employed by individuals in assessing the potential benefits, harms, costs, and limitations of the management options in relation to one another. Patients may have preferences when it comes to defining their problems, identifying the range of management options and selecting or ranking the outcomes used to compare these options.

It is important for healthcare professionals to develop an understanding of the patient as an individual and the unique way in which each person experiences a condition and its impact on their life.

The following recommendations are therefore made for physicians and other healthcare professionals regarding general principles of patient care in Qatar:

- **Respect Patients:** Treat patients with respect, kindness, dignity, courtesy and honesty. Ensure that the environment is conducive to discussion and that the patient's privacy is respected, particularly when discussing sensitive, personal issues. Ask the patient how they wish to be addressed and ensure that their choice is respected and used.

- **Maintain Confidentiality:** Respect the patient's right to confidentiality and avoid disclosing or sharing patients' information without their informed consent. In this context, students and anyone not directly involved in the delivery of care should first be introduced to the patient before starting consultations or meetings, and let the patient decide if they want them to stay.

- **Clarify Third-Party Involvement:** Clarify with the patient at the first point of contact whether and how they like their partner, family members or carers to be involved in key decisions about their care or management and review this regularly. If the patient agrees, share information with their partner, family members or carers.

- **Obtain Informed Consent:** Obtain and document informed consent from patients, in accordance with MOPH policy and guidance.

- **Encourage Shared Decision Making:** Ensure that patients are involved in decision making about their own care, or their dependent's care, and that factors that could impact the patient's participation in their own consultation and care including physical or learning disabilities, sight, speech or hearing impairments and problems with understanding, reading or speaking English are addressed.

- **Disclose Medical Errors:** Disclose errors when they occur and show empathy to patients.

- **Ensure Effective Communication:** Explore ways to improve communication including using pictures, symbols or involving an interpreter or family members. Avoid using medical jargon. Use words the patient will understand and confirm understanding by asking questions.

- **Ensure Continuity of Care:** Provide clear and timely sharing of patient information between healthcare professionals especially at the point of any transitions in care.

9 Performance Measures

Below is a list of potential performance measures that are proposed for the evaluation of provider concordance with guidelines recommendations [4]:

Number	Numerator	Denominator
S01	Number of patients who completed the sepsis six bundles (had lactate results; blood cultures collected; antibiotic, humidified oxygen, IVF administered; and urine output monitored within 60 minutes from time zero).	Total number of patients with sepsis and/or septic shock.
S02	Number of patients identified with sepsis and/or septic shock who had IV antibiotics administered within 60 minutes from time zero.	Total number of patients identified with sepsis and/or septic shock.
S03	Number of serum lactate test results released within 60 minutes from time zero.	Total number of patients identified with sepsis and/or septic shock.
S04	Number of patients who had blood culture collected within 60 min from time zero.	Total number of patients identified with sepsis and/or septic shock.
S05	Number of patients who had a fluid bolus administered within 60 minutes from time zero.	Total number of patients identified with sepsis and/or septic shock.
S06	Number of patients who had humidified oxygen administered within 60 minutes from time zero.	Total number of patients identified with sepsis and/or septic shock.
S07	Number of patients who had urine output monitoring started within 60 minutes from time zero.	Total number of patients identified with sepsis and/or septic shock.
S08	Number of patients who died due to sepsis and/or septic shock during a specified period of time.	Number of new patients identified with sepsis and/or septic shock during the same period.
S09	Number of patients who died in hospital due to sepsis and/or septic shock during a specific time.	Total number of deaths for all causes.
S10	Number of patients who were transferred to HLC due to sepsis and/or septic shock.	Total number of patients identified with sepsis and/or septic shock.
S11	Number of sepsis cases for whom Clinical Review (CR) and Rapid Response Team (RRT) was called.	Total number of sepsis patients.
S12	Length of stay for all sepsis cases.	Total number of sepsis cases.
S13	Length of stay in intensive care unit for all sepsis and/or septic shock cases.	Total number of sepsis and or septic shock cases.
S14	Number of patients with sepsis and/or septic shock with initial lactate of ≥ 2 mmol/L who had lactate re-measured within 4 hours	Total number of patients with sepsis and/or septic shock with initial lactate of ≥ 2mmol/L
S15	Number of medication safety incidents associated with antibiotic therapy.	Total number of sepsis patients receiving antibiotic therapy.
S16	Number of antimicrobial resistances among bloodstream isolates.	Total number of cultures.
S17	Number of empiric antibiotic prescription that complies with local prescribing guidelines.	Total number of antibiotic prescriptions
S18	Number of patients presenting with sepsis and/or septic shock who had blood cultures collected prior to antibiotic.	Total number of patients presenting with sepsis and/or septic shock who were given antibiotics

Table 9.1: Sepsis Performance Measures [4].

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Appendix: Detailed Description of the Literature Search

A systematic search for existing literature on sepsis was performed in the period May 1st - May 28th, 2019.

The search for clinical practice guidelines on sepsis diagnosis and/or management was performed in the *PubMed* database and websites of relevant organisations and societies including the *Sepsis Alliance*, *The Centers for Disease Control and Prevention* and *The UK Sepsis Trust*. The present guideline is primarily based on UK NICE, Surviving Sepsis Campaign and *HMC/Sidra* guidelines and is supplemented with other relevant studies.

Peer-reviewed scientific publications were found in PubMed and via *Google Scholar* Internet search engine. Non-peer reviewed studies were identified in *bioRxiv*. Books were checked on *Amazon* and via *Google* and *Google Scholar* search engines. Drug prescribing information sheets were found via Google search engine.

The included publications were identified using the term "*sepsis*" and specified with the following terms in combinations:

Septic shock, aetiology, prognosis, outcome, complication, presentation, symptom, diagnosis, treatment, antibiotics/antimicrobial therapy, obstetric, pregnancy, neonate, follow-up care, screening, culture, investigation, biomarker, test, urine output, lactate, oxygen, fluid, crystalloid, corticosteroids, transfusion, hypoglycaemia, glucose, nutrition, vasoactive drug, medication, thromboembolism, ulcer.

Figure A.1 on the next page demonstrates graphically the results of the search and application of exclusion criteria.

View Pathway

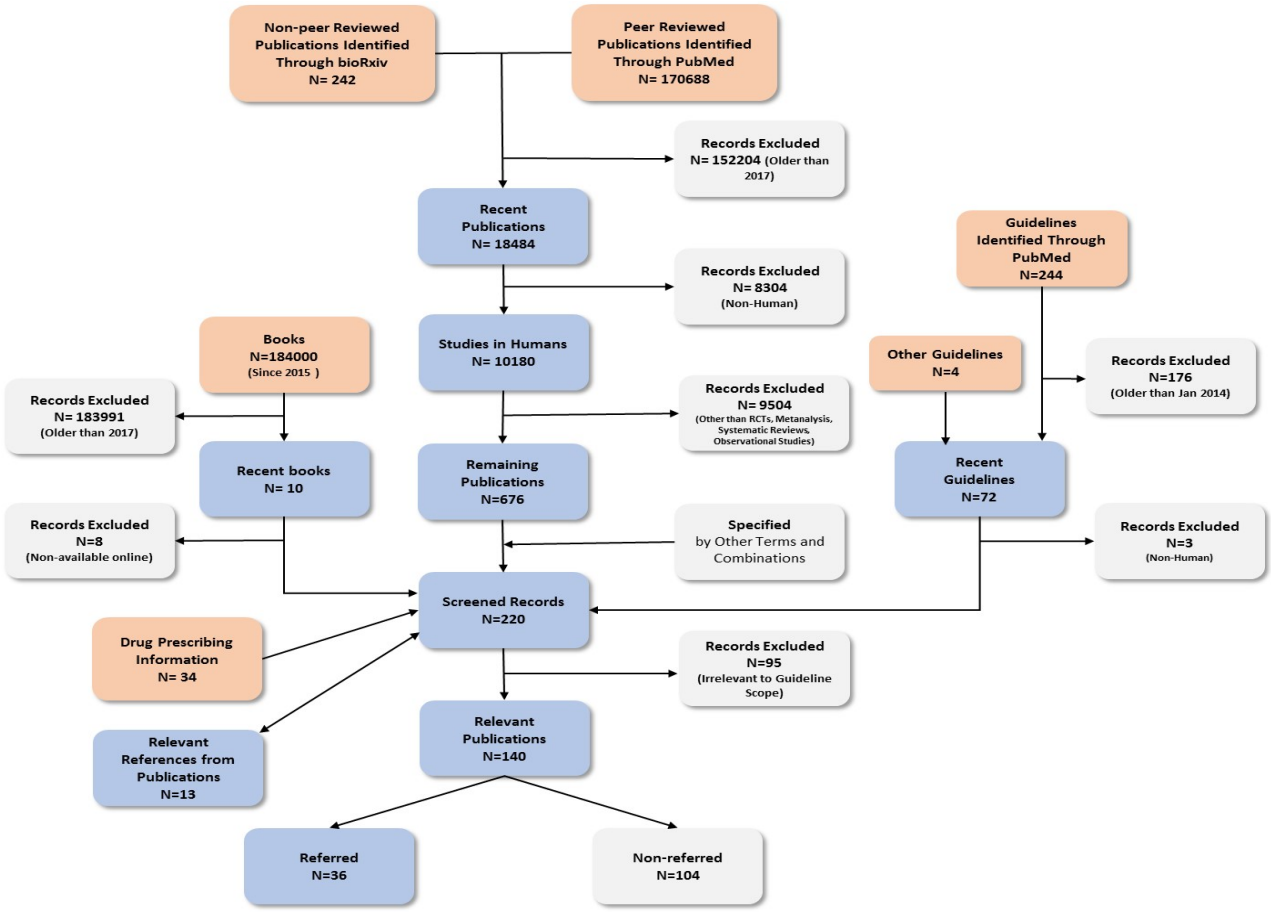

Fig A.1: Literature search results and application of exclusion criteria.

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MOPH National Clinical Guidelines Team:

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