Using this National Clinical Guideline
The aim of the National Clinical Guideline is to facilitate the early recognition and appropriate treatment of sepsis in Ireland in order to maximise survival opportunity and minimise the burden of chronic sequelae.

The summary document of the National Clinical Guideline is available at:
www.health.gov.ie/patient-safety/ncec
www.hse.ie/sepsis

Recommendations are presented with practical guidance. The recommendations are linked to the best available evidence and/or expert opinion using the grades for recommendations. The National Clinical Guideline recommendations have been cross-referenced where relevant with other National Clinical Guidelines.

National Clinical Guideline No. 6
ISSN 2009-6259
Published November 2014
Supplementary methodological information added (page 57) February 2015

Disclaimer
The Guideline Development Group’s expectation is that healthcare staff will use clinical judgement, medical, nursing and midwifery knowledge in applying the general principles and recommendations contained in this document. Recommendations may not be appropriate in all circumstances and the decision to adopt specific recommendations should be made by the practitioner taking into account the individual circumstances presented by each patient/resident and available resources. The National Clinical Guideline recommendations do not replace or remove clinical judgement or the professional care and duty necessary for each specific patient case. Therapeutic options should be discussed with a clinical microbiologist or infectious disease physician on a case-by-case basis as necessary.
The National Clinical Effectiveness Committee (NCEC) is a Ministerial committee established as part of the Patient Safety First Initiative. The NCEC role is to prioritise and quality assure National Clinical Guidelines and National Clinical Audit so as to recommend them to the Minister for Health to become part of a suite of National Clinical Guidelines and National Clinical Audit. National Clinical Guidelines which have been quality assured and recommended by NCEC for implementation provide robust evidence-based approaches to underpin or define models of care as appropriate. They provide guidance and standards for improving the quality, safety and cost-effectiveness of healthcare in Ireland. The implementation of clinical guidelines can improve health outcomes, reduce variation in practice and improve the quality of clinical decisions.

NCEC Terms of Reference
- Apply criteria for the prioritisation of clinical guidelines and audit for the Irish health system
- Apply criteria for quality assurance of clinical guidelines and audit for the Irish health system
- Disseminate a template on how a clinical guideline and audit should be structured, how audit will be linked to the clinical guideline and how and with what methodology it should be pursued
- Recommend clinical guidelines and national audit, which have been quality assured against these criteria, for Ministerial endorsement within the Irish health system
- Facilitate with other agencies the dissemination of endorsed clinical guidelines and audit outcomes to front-line staff and to the public in an appropriate format
- Report periodically on the implementation of endorsed clinical guidelines.

In response to the HIQA Patient Safety Investigation Report into Services at University Hospital Galway (2013), the NCEC was requested by the Minister for Health to commission and quality assure a number of National Clinical Guidelines. The National Clinical Guideline for sepsis management is one of these guidelines. The National Clinical Guideline – Sepsis Management has been quality assured by NCEC and endorsed by the Minister for Health for implementation in the Irish healthcare system.

Information on the NCEC and endorsed National Clinical Guidelines is available at

www.health.gov.ie/patient-safety/ncec
www.hse.ie/sepsis
Sepsis is common and is a time-dependent medical emergency. It can affect a person of any age, from any social background and can strike irrespective of underlying good health or concurrent medical conditions. International sepsis campaigns that have introduced and promoted an approach to sepsis care based on early recognition of sepsis with resuscitation and timely referral to critical care have reported reductions in mortality from severe sepsis/septic shock in the order of 20-30%.

This National Clinical Guideline is intended to be relevant to all healthcare staff involved in the care of patients who have sepsis. The Guideline Development Group consisted of a subgroup of the National Sepsis Steering Committee with expertise in guideline and early warning score implementation, sepsis management and emergency care. The Guideline Development Group has provided a number of recommendations to assist healthcare staff in the identification and management of patients with sepsis. A summary version of the National Clinical Guideline outlining the key recommendations, is available at: [www.health.gov.ie/patient-safety/ncec](http://www.health.gov.ie/patient-safety/ncec)

The recommendations align with the aims of the national sepsis work stream. Key recommendations are linked with other recommendations, practical guidance, roles, responsibilities and processes. The recommendations are linked to the best available evidence and/or expert opinion using the GRADE system for grading recommendations.

This guideline is available to all clinicians in the Republic of Ireland involved in the diagnosis and management of patients with sepsis.

We wish to acknowledge all the members of the National Sepsis Steering Committee and the Guideline Development Group members (Appendix 1) who gave freely of their time and expertise. A special word of thanks to the external expert, Prof. Kevin Rooney, National Clinical Lead on Sepsis, Healthcare Improvement Scotland and Professor of Care Improvement, University of the West of Scotland and the validators Dr. John Bates from the Joint Faculty of Intensive Care Medicine in Ireland and Dr. Christian Subbe, Consultant in Acute, Respiratory and Critical Care Medicine and Senior Clinical Lecturer at the School of Medical Sciences, Bangor University, UK.

Many thanks go to Ms. Clodagh Murray, Library Assistant, HSE South East Library Service, University Hospital Waterford for prompt research support and also to Ms. Grainne Cosgrove, Health Information Unit, Department of Health for providing extensive support regarding HIPE data analysis. We also wish to acknowledge the contribution of the National Cancer Control programme (NCCP) in support of this guideline.

Dr. Fidelma Fitzpatrick, Chair, National Sepsis Steering Committee, November 2014

Dr. Vida Hamilton, National Sepsis Lead, Chair, Guideline Development Group November 2014
# Table of Contents

## Section 1: Sepsis impact
1.1 Definitions 9  
1.2 Clinical impact of sepsis 10  
1.2.1 The burden of sepsis in Ireland 12  
1.3 Adapting the Surviving Sepsis Campaign guidelines 15  
1.4 Pathway of care for sepsis 15  
1.4.1 Diagnostic criteria for sepsis 17  
1.4.2 Detection and recognition 19  
1.4.3 Communication – ISBAR communication tool 22  
1.4.4 Resuscitation and referral 22  
1.4.5 Source control 23

## Section 2: National Clinical Guideline recommendations 25
2.1 National recommendations 25  
2.1.1 Screening, Sepsis 6, 3 hour and 6 hour bundles 26  
2.1.2 Initial resuscitation and infection issues 35  
2.2 Other national recommendations 39  
2.2.1 Haemodynamic support and adjunctive therapy 39  
2.2.2 Other supportive therapy of severe sepsis 42  
2.2.3 Special considerations in paediatrics 47

## Section 3: National Clinical Guideline processes 56
3.1 Aim and scope of the National Clinical Guideline 56  
3.2 Methodology 56  
3.2.1 Preparation module 56  
3.2.2 Adaptation process 57  
3.3 Financial impact of sepsis 59  
3.4 External review 59  
3.5 Procedure for update of this guideline 59  
3.6 Implementation of this guideline 60  
3.6.1 Emergency department/Acute Medical Assessment Units (AMAUs) 60  
3.6.2 Education program 60  
3.6.3 Process of implementation 60  
3.7 Audit criteria 62  
3.7.1 Measuring Improvements in hospitals 63  
3.7.2 Measuring Improvements in Ireland 63  
3.7.3 Measurement plan 63  
3.7.4 Balancing measures 64
List of tables

Table 1  Prevalence of sources of sepsis 10
Table 2  Hospital Inpatient Enquiry: Proportion of deaths with a diagnosis of sepsis or infections, 2013 13
Table 3  Hospital Inpatient Enquiry: Inpatients with a diagnosis of sepsis or infections, 2011 - 2013 13
Table 4  Infection, documented or suspected, and some of the following: 17
Table 5  Risk Factors for the development of sepsis in pregnancy 20
Table 6  Sources of maternal infection in severe sepsis 20
Table 7  Organisms isolated in severe maternal sepsis 20
Table 8  Modified SIRS criteria for maternity patients 21
Table 9  GRADE evidence quality classification 25
Table 10  Summary of national recommendations 26
Table 11  Lactate levels and associations with percentage mortality 28
Table 12  Balancing measures for monitoring implementation of Sepsis 6 64

List of Figures

Figure 1  Summary of diagnosis of sepsis 18
Figure 2  Summary of pathway of care for patients presenting with sepsis 18
Figure 3  Care pathway for the deteriorated critically ill pregnant woman 21
Figure 4  ISBAR communication tool 22
Figure 5  Adult sepsis management algorithm 32
Figure 6  Number of retrieved and reviewed guidelines 58
Figure 7  Surviving Sepsis Campaign Agree II domain scores 58
Sepsis impact

“Sepsis is a life threatening condition that arises when the body’s response to an infection injures its own tissues and organs. Sepsis leads to shock, multiple organ failure and death especially if not recognised early and treated promptly. Sepsis remains the primary cause of death from infection despite advances in modern medicine, including vaccines, antibiotics and acute care. Millions of people die of sepsis every year worldwide.”

Merinoff Symposium 2010: Sepsis

International estimates of incidence vary, but consensus points to approximately 300 cases per 100,000 population per annum. (1) As comparators, myocardial infarction affects 208 patients per 100,000 per year (2) and stroke 223. (3) Mortality from sepsis is currently as high as mortality from acute myocardial infarction was in the 1960s. (4)

According to the Centers for Disease Control and Prevention, sepsis affects more than 800,000 Americans annually and is the ninth leading cause of disease-related deaths. The Agency for Healthcare Research and Quality lists sepsis as the most expensive condition treated in U.S. hospitals, costing more than $20 billion in 2011. In the U.K. sepsis is estimated to claim 37,000 lives annually and cost the NHS approximately £2.5 billion. (5)

Sepsis mortality ranges between 15% and 37% in the U.S. (and much higher in other jurisdictions) depending on whether the healthcare providers are thoroughly trained in identifying and treating sepsis. Sepsis incidence is predicted to grow at a rate of 1.5% annually. (6) This is partly due to an aging population, increased numbers of invasive procedures and the increasing number of people living with co-morbidities and on long-term immunosuppressive therapies. Multiple studies have shown that programs aimed at early identification and treatment of patients with sepsis lead to reduced mortality, intensive care unit (ICU) admission, ICU length of stay and hospital length of stay. (7, 8)

1.1 Definitions

Infection is defined as a pathological process caused by invasion of normally sterile tissue or fluid or body cavity by pathogenic or potentially pathogenic micro-organisms. It is important to point out that, frequently, infection is strongly suspected without being microbiologically confirmed.

Sepsis is the clinical syndrome defined by the presence of both infection and the systemic inflammatory response syndrome (SIRS). (9) However, since infection cannot be always microbiologically confirmed, the diagnostic criteria are infection, suspected or confirmed and the presence of some of the SIRS criteria. (9)

Severe sepsis refers to sepsis complicated by organ dysfunction. (9) In the 8th Edition of the ICD-10-AM/ACHI/ACS this is extended to include organ failure. This difference does not affect the guideline diagnostic criteria which identify a minimum level of organ dysfunction beyond which severe sepsis is diagnosed.

Septic shock is defined as severe sepsis with circulatory shock with signs of organ dysfunction or hypoperfusion in the 8th Edition of the ICD-10-AM/ACHI/ACS. The diagnostic criteria in this guideline are applied after 30mls/kg isotonic fluid has been administered to reverse any

1. Australian Modification of ICD-10 incorporating the Australian Classification of Health Interventions and the Australian Coding Standards
hypovolaemia and are persistent systolic blood pressure <90 mmHg, MAP < 65 mmHg, decrease by 40 mmHg from baseline and/or lactate > 4 mmol/l. (18)

The sources of sepsis are very consistent in the industrialised world with respiratory sepsis being the most common with rates between 35% and 50%. Table 1 reports the findings of the IMPRESS trial a 24 hour point prevalence study of severe sepsis/septic shock in Emergency Departments and Intensive Care units in Europe, the US and Asia which were presented at the European Society of Intensive Care Medicine Annual Congress in September 2014.

### Table 1 Prevalence of sources of sepsis

<table>
<thead>
<tr>
<th>Source</th>
<th>Prevalence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Respiratory</td>
<td>35%</td>
</tr>
<tr>
<td>Urinary</td>
<td>21%</td>
</tr>
<tr>
<td>Intra-abdominal</td>
<td>16.5%</td>
</tr>
<tr>
<td>Catheter-related blood stream infection</td>
<td>2.3%</td>
</tr>
<tr>
<td>Device-related</td>
<td>1.3%</td>
</tr>
<tr>
<td>CNS</td>
<td>0.8%</td>
</tr>
<tr>
<td>Others e.g. cellulitis, intra-articular</td>
<td>11.3%</td>
</tr>
</tbody>
</table>

### 1.2 Clinical impact of sepsis

Sepsis claims more lives than lung cancer, and more than breast cancer, bowel cancer and HIV/AIDS combined. Mortality in adults with severe sepsis/septic shock a decade ago was 37 – 53% with a mortality of approximately 10% in paediatric sepsis. (10, 11)

Since then the Surviving Sepsis Campaign, The UK Sepsis Trust, the Australian Commission for Clinical Excellence, the Global Sepsis Alliance and other worldwide organisations have introduced and promoted an approach to sepsis based on early recognition and resuscitation and timely referral to critical care with reductions in mortality from severe sepsis/septic shock to 20–30%. (10, 12-14) Despite this there is a lack of awareness of sepsis and the fact that it is a time-dependent medical emergency.

It is not always easy to diagnose sepsis particularly in the early stages. The definition of sepsis is sensitive but not specific and sepsis represents a continuum through sepsis, severe sepsis and septic shock with increasing mortality as the disease progresses. It can be difficult to recognise, for example, up to 60% of patients with sepsis may present without a febrile response and the presenting complaint in the elderly may be a fall. (15)

As Niccolo Machiavelli stated in The Prince in 1513:

“...as the physicians say it happens in hectic fever, that in the beginning of the malady it is easy to cure but difficult to detect, but in the course of time, not having been either detected or treated in the beginning, it becomes easy to detect but difficult to cure”.

A full history and examination with appropriate blood tests and radiological examinations will aid in making the diagnosis.

A 2010 report by the Scottish Trauma Audit Group of sepsis management in Scotland reported that 1.7% of new patient hospitals attendances developed the criteria for sepsis within two days of initial attendance, 34% of patients with sepsis met the criteria for severe sepsis within two days of initial attendance and of these 48% (637) met the criteria before leaving the emergency department (ED). (16) Using estimated bed-day costs, the total annual cost of care for emergency
patients with sepsis within NHS Scotland was estimated to be in excess of £79 million. Notably, the vast majority of patients were managed initially by doctors in training, indicating the importance of non consultant hospital doctor (NCHD) involvement and training in managing patients with sepsis. The overall mortality for patients who met the criteria for sepsis within two days of initial attendance was 14%. For patients who met the criteria for severe sepsis within two days of initial attendance mortality was 24%.

Patients with sepsis have prolonged hospital stay and often require critical care input. In the UK sepsis consumes 30% of critical care expenditure and it is estimated to cost £20,000 to treat each patient. (5) Simple interventions such as the administration of antibiotics within one hour of diagnosis have been shown to save lives and reduce length of hospital stay, yet are delivered in less than one-fifth of cases. Systems (root cause) analysis in Australia has identified inadequate recognition as being the most common feature identified, being present in more than 90% of reported cases with poor outcome. (17)

A recent UK report from the Health Service Ombudsman outlined a number of key areas that needed to be improved when the management of ten patients who died of sepsis was reviewed. These included:

- Lack of timely history and examination (including adequate nurse triage) on presentation
- Lack of necessary investigations
- Failure to recognise the severity of the illness
- Inadequate first-line treatment with fluids and antibiotics
- Delays in administering first-line treatment
- Inadequate physiological monitoring of vital signs
- Delay in source control of infection
- Delay in senior medical input, and the lack of timely referral to critical care.

The Surviving Sepsis Campaign was created with the aim of reducing mortality in patients with sepsis, and an expert group was formed to look at the consistent findings in the centres with the best outcomes and reviewing the evidence for different treatment modalities. (18) A reduction in mortality from sepsis has been demonstrated in hospitals that have implemented the Surviving Sepsis guidelines in conjunction with an education program with a 5.4% adjusted decrease in mortality. (19) Staff turnover including doctors in training is a possible barrier to the sustainability of improvements in compliance with sepsis bundles. (20) The National Sepsis Steering Committee recommends, therefore, that a nationwide education campaign is undertaken to implement and sustain best practice in the recognition and management of sepsis in Ireland. The education programme needs to be sustained, reflect the evolving nature of medical practice, include new evidence as it emerges and be tailored to the needs of the target group.

The surviving sepsis guidelines were formulated and the third edition published in February 2013. (18) The National Sepsis Steering Committee (appendix 1) recommended this document be adapted as a guide to the management of severe sepsis/septic shock in Ireland along with a mechanism for early recognition and treatment of sepsis. It is recommended that each healthcare facility and each National Clinical Programme identify a pathway for the recognition, treatment of sepsis and appropriate referral of patients with severe sepsis/septic shock to critical care based on these guidelines.
1.2.1 The burden of sepsis in Ireland

Sepsis represents a significant burden on Irish patients and the Irish healthcare service. Currently in Ireland the only method to estimate the incidence of sepsis is through analysis of ICD-10-AM diagnosis codes for hospital discharges recorded in the Hospital Inpatient Enquiry Scheme (HIPE). There is no mechanism to record sepsis in the community. The current analysis of diagnosis codes from HIPE may be an under or over estimation of sepsis incidence as there are a number of ICD-10-AM diagnosis codes which include either sepsis or infection. This is not unusual and in the UK, it is also noted that there may be underestimation of sepsis morbidity due to errors in coding for sepsis2.

While hospital statistics do not capture underlying cause of death data in Ireland, for 2013, up to 60% of all hospital deaths had a sepsis or infection diagnosis with approximately 16% of all hospital deaths designated with a sepsis specific ICD-10-AM diagnosis code, table 1. The total number of cases with a diagnosis of sepsis was 8,831 in 2013 and these cases accounted for a total of 221,342 bed days.

In addition, in 2013, the mortality rate of patients with a diagnosis of sepsis who were admitted to an intensive care environment was 28.8%. The corresponding figure for 2011 is 32.4% and 31.3% for 2012. Note however that this data is based on the discharge code of patients who had a diagnosis of sepsis and who were admitted to any type of intensive care environment (including ICU, HDU, CCU etc) at some point during their hospitalisation. It is not possible to conclude that these patients were admitted to ICU as a result of sepsis, or that sepsis was the cause of death. See appendix 15 for specific HIPE codes used for this analysis. A multicentre study of intensive care population demographics performed by the Irish Critical Care Trials Group was performed over a ten-week period on the 14 ICUs in the group (both Republic and Northern Ireland) in 2006. This study documented a severe sepsis/septic shock prevalence of 35% and a mortality of 24.6%.3

Current HIPE data is likely to be an underestimate of the true burden of sepsis in Ireland. Patients with sepsis are frequently coded according to their likely site of infection (e.g. pneumonia, urinary tract infection) rather than the systemic diagnosis of ‘respiratory sepsis’ or ‘urosepsis’. The HIPE data for sepsis above represents the number of hospital discharges with any diagnosis (i.e. primary or additional diagnosis) of sepsis using ICD-10 AM codes A40 Streptococcal Sepsis and A41 Other Sepsis (which includes sepsis due to Group A Streptococcus, Haemophilus influenzae, anaerobes, gram-negative organisms, E. coli and unspecified sepsis). The 8th Edition of ICD-10-AM/ACHI/ACS, to be implemented in 2015, has explicit codes for sepsis, severe sepsis and septic shock. Documentation of sepsis, severe sepsis and septic shock in the case notes will facilitate the capture of this data by HIPE. It is anticipated these changes in coding practices will lead to an increase in the recorded burden of sepsis in Ireland.

The average length of stay (ALOS) in 2013 for a patient is approximately 5.59 days, a patient with a sepsis diagnosis has an ALOS of up to 26 days, which is approximately 5 times longer than the average non-sepsis patient stay [children: for 2013, 22.01 with sepsis code vs. 3.08 without sepsis code and in maternity: for 2013, 5.46 with sepsis code vs. 2.61 without sepsis code]. Patients with an associated infection also have an increased ALOS of up to 10 days, table 2.

Sepsis is a leading global health and financial burden and is expected to increase further with an aging population. Fixed direct costs associated with the spectrum of sepsis, such as increased ICU LOS, ICU staffing, medications and new technologies are significant. Equally concerning are

---

2 An audit performed by the Intensive Care National Audit and Research Centre (ICNARC) conservatively estimated that 102,000 cases of sepsis arises annually in the UK with 36,800 deaths as a result. (Reference: Sepsis management as an NHS clinical priority. Briefing - Professor Sir Mike Richards [Internet]. 2013. Available at: http://www.england.nhs.uk/wp-content/uploads/2013/12/spesis-brief.pdf)

the indirect costs associated with sepsis such as loss of earnings, productivity and mortality. In fact indirect costs may account for up to 70% of the total costs of sepsis. (21) European studies estimate that a typical episode of severe sepsis will cost a healthcare institution around €25,000. (22) One year healthcare use has also been shown to be elevated after severe sepsis. In addition, long-term mortality in previously healthy patients with severe sepsis/septic shock has been shown to be worse than that of those patients with non-septic critical illness and of the underlying general population. See appendix 14 for more details on the budget impact assessment for the National Clinical Guideline.

Table 2 Hospital Inpatient Enquiry:
Proportion of deaths with a diagnosis of sepsis or infections, 2013

<table>
<thead>
<tr>
<th>Total for All Hospitals</th>
<th>Percentage of hospital deaths with a sepsis diagnosis code</th>
<th>Percentage of hospital deaths with a sepsis or infection diagnosis code</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>16.3%</td>
<td>60.2%</td>
</tr>
</tbody>
</table>

Source: This table has been produced by the Information Unit, Department of Health, and is based on Hospital Inpatient Enquiry (HIPE) data.

Note: See appendix for list of sepsis and infections codes.

Table 3 Hospital Inpatient Enquiry:
Inpatients with a diagnosis of sepsis or infections, 2011–2013

<table>
<thead>
<tr>
<th>Patient Type</th>
<th>Category</th>
<th>2011</th>
<th>2012</th>
<th>2013</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adults</td>
<td>Inpatients with a Specific Seps Diagnosis Code</td>
<td>Cases</td>
<td>6,478</td>
<td>7,204</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Bed Days</td>
<td>185,942</td>
<td>192,844</td>
</tr>
<tr>
<td></td>
<td></td>
<td>ALOS</td>
<td>28.70</td>
<td>26.77</td>
</tr>
<tr>
<td></td>
<td>Inpatients with an Infection Diagnosis Code</td>
<td>Cases</td>
<td>78,400</td>
<td>84,972</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Bed Days</td>
<td>1,016,898</td>
<td>1,030,084</td>
</tr>
<tr>
<td></td>
<td></td>
<td>ALOS</td>
<td>12.97</td>
<td>12.12</td>
</tr>
<tr>
<td></td>
<td>All other cases</td>
<td>Cases</td>
<td>282,226</td>
<td>308,359</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Bed Days</td>
<td>1,601,970</td>
<td>1,646,020</td>
</tr>
<tr>
<td></td>
<td></td>
<td>ALOS</td>
<td>5.68</td>
<td>5.34</td>
</tr>
<tr>
<td></td>
<td>Total for All Inpatients</td>
<td>Cases</td>
<td>367,104</td>
<td>400,535</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Bed Days</td>
<td>2,804,810</td>
<td>2,868,948</td>
</tr>
<tr>
<td></td>
<td></td>
<td>ALOS</td>
<td>7.64</td>
<td>7.16</td>
</tr>
<tr>
<td>Children</td>
<td>Inpatients with a Specific Seps Diagnosis Code</td>
<td>Cases</td>
<td>753</td>
<td>786</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Bed Days</td>
<td>18,771</td>
<td>16,788</td>
</tr>
<tr>
<td></td>
<td></td>
<td>ALOS</td>
<td>24.93</td>
<td>21.36</td>
</tr>
<tr>
<td></td>
<td>Inpatients with an Infection Diagnosis Code</td>
<td>Cases</td>
<td>22,713</td>
<td>23,818</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Bed Days</td>
<td>89,840</td>
<td>84,665</td>
</tr>
<tr>
<td></td>
<td></td>
<td>ALOS</td>
<td>3.96</td>
<td>3.55</td>
</tr>
<tr>
<td></td>
<td>All other cases</td>
<td>Cases</td>
<td>71,107</td>
<td>74,073</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Bed Days</td>
<td>220,808</td>
<td>226,074</td>
</tr>
<tr>
<td></td>
<td></td>
<td>ALOS</td>
<td>3.11</td>
<td>3.05</td>
</tr>
<tr>
<td></td>
<td>Total for All Inpatients</td>
<td>Cases</td>
<td>94,573</td>
<td>98,677</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Bed Days</td>
<td>329,419</td>
<td>327,527</td>
</tr>
<tr>
<td></td>
<td></td>
<td>ALOS</td>
<td>3.48</td>
<td>3.32</td>
</tr>
<tr>
<td>Maternity</td>
<td>Inpatients with a Specific Sepsis Diagnosis Code</td>
<td>Cases</td>
<td>190</td>
<td>192</td>
</tr>
<tr>
<td>-----------</td>
<td>-----------------------------------------------</td>
<td>-------</td>
<td>-----</td>
<td>-----</td>
</tr>
<tr>
<td></td>
<td>Bed Days</td>
<td>1,185</td>
<td>1,148</td>
<td>1,473</td>
</tr>
<tr>
<td></td>
<td>ALOS</td>
<td>6.24</td>
<td>5.98</td>
<td>5.46</td>
</tr>
<tr>
<td>Inpatients with an Infection Diagnosis Code</td>
<td>Cases</td>
<td>5,170</td>
<td>5,261</td>
<td>5,294</td>
</tr>
<tr>
<td></td>
<td>Bed Days</td>
<td>17,408</td>
<td>18,310</td>
<td>19,119</td>
</tr>
<tr>
<td></td>
<td>ALOS</td>
<td>3.37</td>
<td>3.48</td>
<td>3.61</td>
</tr>
<tr>
<td>All other cases</td>
<td>Cases</td>
<td>122,088</td>
<td>121,951</td>
<td>113,301</td>
</tr>
<tr>
<td></td>
<td>Bed Days</td>
<td>314,721</td>
<td>309,760</td>
<td>295,751</td>
</tr>
<tr>
<td></td>
<td>ALOS</td>
<td>2.58</td>
<td>2.54</td>
<td>2.61</td>
</tr>
<tr>
<td>Total for All Inpatients</td>
<td>Cases</td>
<td>127,448</td>
<td>127,404</td>
<td>118,865</td>
</tr>
<tr>
<td></td>
<td>Bed Days</td>
<td>333,314</td>
<td>329,218</td>
<td>316,343</td>
</tr>
<tr>
<td></td>
<td>ALOS</td>
<td>2.62</td>
<td>2.58</td>
<td>2.66</td>
</tr>
<tr>
<td>Total</td>
<td>Inpatients with a Specific Sepsis Diagnosis Code</td>
<td>Cases</td>
<td>7,421</td>
<td>8,182</td>
</tr>
<tr>
<td></td>
<td>Bed Days</td>
<td>205,898</td>
<td>210,780</td>
<td>221,342</td>
</tr>
<tr>
<td></td>
<td>ALOS</td>
<td>27.75</td>
<td>25.76</td>
<td>25.06</td>
</tr>
<tr>
<td>Inpatients with an Infection Diagnosis Code</td>
<td>Cases</td>
<td>106,283</td>
<td>114,051</td>
<td>115,164</td>
</tr>
<tr>
<td></td>
<td>Bed Days</td>
<td>1,124,146</td>
<td>1,133,059</td>
<td>1,156,670</td>
</tr>
<tr>
<td></td>
<td>ALOS</td>
<td>10.58</td>
<td>9.93</td>
<td>10.04</td>
</tr>
<tr>
<td>All other cases</td>
<td>Cases</td>
<td>475,421</td>
<td>504,383</td>
<td>498,222</td>
</tr>
<tr>
<td></td>
<td>Bed Days</td>
<td>2,137,499</td>
<td>2,181,854</td>
<td>2,102,790</td>
</tr>
<tr>
<td></td>
<td>ALOS</td>
<td>4.50</td>
<td>4.33</td>
<td>4.22</td>
</tr>
<tr>
<td>Total for All Inpatients</td>
<td>Cases</td>
<td>589,125</td>
<td>626,616</td>
<td>622,217</td>
</tr>
<tr>
<td></td>
<td>Bed Days</td>
<td>3,467,543</td>
<td>3,525,693</td>
<td>3,480,802</td>
</tr>
<tr>
<td></td>
<td>ALOS</td>
<td>5.89</td>
<td>5.63</td>
<td>5.59</td>
</tr>
</tbody>
</table>

**Source:** This table has been produced by the Information Unit, Department of Health, and is based on Hospital Inpatient Enquiry (HIPE) data

**Note:**

Data refer to inpatients grouped according to three mutually exclusive categories:

(i) inpatients with any diagnosis of a specific sepsis code;

(ii) inpatients with any diagnosis of an infection code (excluding cases with a specific sepsis diagnosis code already included in (i).) Note that some of the infections codes may included sepsis but not necessarily. E.g. T81.1 is included in this category. This code refers to shock during or resulting from a procedure, but includes collapse, endotoxic shock, hypovolaemic shock amd septic shock during or following a procedure.

(iii) all other inpatients, excluding cases already included in (i) and (ii).

See appendix 15 for list of sepsis and infections codes.

ALOS refers to the average length of stay in days.
1.3 Adapting the Surviving Sepsis Campaign guidelines

Using the ADAPTE process, the Guideline Development Group recommends the Surviving Sepsis Campaign Guideline and the Sepsis 6 bundle as the guide to the management of sepsis in Ireland. The adaptation process is detailed in the methodology section 3.2.2. ADAPTE has been advocated internationally as the most appropriate systematic approach to facilitate the adaptation of guidelines to align with the context of each setting and one that fosters valid and high-quality adapted guidelines. This sepsis guideline is the first National Clinical Guideline to use this process.

This guideline represents an adaptation of the International Guideline for the Management of Severe Sepsis and Septic Shock: 2012 (http://www.survivingsepsis.org) and the Sepsis 6 bundle for the initial management of all patients diagnosed with sepsis (http://sepsistrust.org).

The purpose of the adaptation is to align these international guidelines with the structures and functions of the Irish healthcare system and to inform pathways of care for patients with sepsis and severe sepsis/septic shock within all Irish medical disciplines. Thus, these adaptations endeavor to be accessible to all disciplines and offer practical guidance on each recommendation and its implementation.

In order to achieve the primary aim of reducing mortality from sepsis in Ireland, clinicians need to have an understanding of sepsis, be able to diagnose it and have systems in place that facilitate the timely treatment and referral of patients for their appropriate care. Thus, this National Clinical Guideline includes explanatory notes on the burden of sepsis and its recognition and treatment. It is recognised that an education programme is vital to ensure successful implementation and that without audit it would be difficult to ensure that the guideline is being achieved. Audit facilitates the identification of gaps in knowledge, resources and capacity that can act as barriers to guideline implementation and once identified these barriers can be addressed. Both education and audit are essential to support the sustainability of the implementation programme.

We are very grateful to the Society of Critical Care Medicine, the UK SepsisTrust and the Commission for Clinical Excellence, New South Wales for their permission to adapt their work to the Irish healthcare setting. Further information available at: http://www.survivingsepsis.org; www.cecc.health.nsw.gov.au/ and http://sepsistrust.org. It is not the Guideline Development Group’s intent to change the meaning of content rather to make it accessible in the Irish context. Therefore this National Clinical Guideline applies only in the Republic of Ireland.

1.4 Pathway of care for sepsis

From SurvivingSepsis.org, Reproduced with permission copyright © 2014 Society of Critical Care Medicine

The management of the septic patient in the first hour is a time critical emergency and requires a team based approach involving all relevant healthcare staff members. This will have to be adapted for the local context depending on the composition of the team. A patient may present to an emergency department (ED) or other healthcare setting (e.g. a GP practice or specialty assessment area such as an oncology day ward) with sepsis or may develop sepsis during hospital admission. There are essentially 4 steps in the management of patients with sepsis; detection, communication, recognition (and diagnosis), and treatment (resuscitation and referral) (Figure 2). An example of the national early warning scoring card is given in appendix 2, the ISBAR communication tool in appendix 3, a sepsis screening tool in appendix 4, an emergency department sepsis pathway in appendix 5 and the ‘Start Smart, then Focus’ approach to antimicrobial stewardship in appendix 6 and a fluid resuscitation algorithm in appendix 8. These have been adapted for specific patient groups (e.g., paediatric, maternity) and hospital settings.
(e.g. ED, wards) and may need to be adapted for other healthcare settings (e.g. pre-hospital care).

Pathways of care for identification and management of patients with sepsis should include a mechanism to trigger sepsis screening to facilitate early recognition, a treatment pathway which includes the Sepsis 6 and a mechanism of risk stratification for the early identification of patients with severe sepsis and septic shock to facilitate referral to critical care. Pathway compliance will be audited and the content and compliance rates reviewed by the National Sepsis Steering Committee and the Health Service Executive (HSE).

This National Clinical Guideline is part of a suite of guidelines that relate to the acutely deteriorating patient. National Clinical Guidelines include:

- National Clinical Guideline No. 1 National Early Warning Score (NEWS)
- National Clinical Guideline No. 4 Irish Maternity Early Warning System (IMEWS)
- National Clinical Guideline No. 5 Communication (Clinical Handover) in Maternity Setting
- National Clinical Guideline - Paediatric Early Warning System (PEWS) – in process
- National Clinical Guideline - Clinical Handover in acute hospitals – in process


HSE guidance includes:

1.4.1 **Diagnostic criteria for sepsis**

Table 4 Infection, documented or suspected, and some of the following:

<table>
<thead>
<tr>
<th>General variables</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fever (&gt; 38.3°C); ≥ 38°C in pregnancy</td>
</tr>
<tr>
<td>Hypothermia (core temperature &lt; 36°C)</td>
</tr>
<tr>
<td>Heart rate &gt; 90/min⁻¹ or more than two SD above the normal value for age; ≥ 100/min⁻¹ in pregnancy</td>
</tr>
<tr>
<td>Tachypnoea</td>
</tr>
<tr>
<td>Altered mental status</td>
</tr>
<tr>
<td>Significant oedema or positive fluid balance (&gt; 20 mL/kg over 24 hr)</td>
</tr>
<tr>
<td>Hyperglycemia (plasma glucose &gt; 7.7 mmol/L) in the absence of diabetes</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Inflammatory variables</th>
</tr>
</thead>
<tbody>
<tr>
<td>Leucocytosis (WBC count &gt; 12,000 μL⁻¹); &gt; 16.9 μL⁻¹ in pregnancy</td>
</tr>
<tr>
<td>Leucopenia (WBC count &lt; 4000 μL⁻¹)</td>
</tr>
<tr>
<td>Normal WBC count with greater than 10% immature forms</td>
</tr>
<tr>
<td>Plasma C-reactive protein more than two SD above the normal value</td>
</tr>
<tr>
<td>Plasma procalcitonin more than two SD above the normal value</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Haemodynamic variables</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arterial hypotension (SBP &lt; 90 mm Hg, MAP &lt; 70 mmHg, or an SBP decrease &gt; 40 mmHg in adults or less than two SD below normal for age); MAP &lt; 65 mmHg in pregnancy</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Organ dysfunction variables</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arterial hypoxaemia (PaO₂/FIO₂ &lt; 300)</td>
</tr>
<tr>
<td>Acute oliguria (urine output &lt; 0.5 mL/kg/hr for at least 2 hrs despite adequate fluid resuscitation)</td>
</tr>
<tr>
<td>Creatinine increase &gt; 0.5 mg/dL or 44.2 μmol/L</td>
</tr>
<tr>
<td>Coagulation abnormalities (INR &gt; 1.5 or aPTT &gt; 60s)</td>
</tr>
<tr>
<td>Ileus (absent bowel sounds)</td>
</tr>
<tr>
<td>Thrombocytopenia (platelet count &lt; 100,000 μL⁻¹)</td>
</tr>
<tr>
<td>Hyperbilirubinaemia (plasma total bilirubin &gt; 4 mg/dL or 70 μmol/L)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Tissue perfusion variables</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hyperlactataemia (&gt; 1 mmol/L)</td>
</tr>
<tr>
<td>Decreased capillary refill or mottling</td>
</tr>
</tbody>
</table>

WCC = white cell count; SBP = systolic blood pressure; MAP = mean arterial pressure; INR = international normalized ratio; aPTT = activated partial thromboplastin time.


**Severe sepsis**

Severe sepsis is defined as sepsis-induced tissue hypoperfusion or organ dysfunction (any of the following thought to be due to the infection). [18]

- Lactate above upper limits laboratory normal
- Urine output < 0.5 mL/kg/hr for more than 2 hrs despite adequate fluid resuscitation
- Acute lung injury with PaO₂/FIO₂ < 250 in the absence of pneumonia as infection source
- Acute lung injury with PaO₂/FIO₂ < 300 in the presence of pneumonia as infection source
- Creatinine > 176.8 micromol/l
- Bilirubin > 34.2 micromol/l
- Platelet count < 100,000 μL⁻¹
- Coagulopathy (INR > 1.5)
- Sepsis induced hypotension.
**Septic shock**

Septic shock is defined as sepsis-induced tissue hypoperfusion persisting after resuscitation with 30mls/kg intravenous isotonic crystalloid fluid as evidenced by:

- Systolic blood pressure < 90 mmHg or MAP < 65 mmHg
- Decrease in systolic blood pressure by 40mmHg from baseline and/or
- Lactate > 4 mmol/l. (18)

### Figure 1 Summary of diagnosis of sepsis

- **SIRS**
  - Clinical response arising from a non specific insult.
  - Infections and non infectious causes.

- **Sepsis**
  - SIRS plus
  - Presumed or confirmed infection.

- **Severe Sepsis**
  - Sepsis plus
  - Sepsis-induced organ dysfunction or tissue hypoperfusion.

- **Septic Shock**
  - Sepsis-induced hypoperfusion or hypotension persisting despite 30mls/kg fluid resuscitation.

### Figure 2 Summary of pathway of care for patients presenting with sepsis

- **Detection**
  - Early Warning System
  - Triage

- **Communication**
  - ISBAR

- **Recognition**
  - Clinical evaluation
  - Sepsis screening tool

- **Resuscitate & Refer**
  - Sepsis 6 within one hour
  - Referral to senior clinicians and critical care as appropriate
1.4.2 Detection and recognition

The Emergency Department (ED)
It is recommended that patients presenting to the ED with a history suggestive of infection have sepsis screening (use the sepsis screening tool) at triage or the assessment area, according to local procedure and patients with two systemic inflammatory response (SIRS) criteria have a point of care lactate measurement performed. If the lactate is greater than 2 mmol/L or the patient has other signs of serious illness they are escalated directly for medical review.

**ED trigger**

- Presenting complaint suggestive of infection or unwell and in at risk group for neutropenia
- Two SIRS criteria
- Lactate > 2 mmol/L

**OR**

- Signs of serious illness

**Escalation to medical review**

The adult in-patient
The first step in the appropriate management of the adult in-patient with sepsis is timely recognition. Standardised scoring systems have the advantage of reducing inter-clinician variation and alerting them that action is required to prevent further patient deterioration. If a scoring system is being used, it is essential that there are clear links between when to screen for sepsis and a threshold score. The Guideline Development Group recommends that when an adult in-patient has a new National Early Warning Score (NEWS) of 4 (5 if already on supplementary O\textsubscript{2}) or higher, as part of the patient review, infection should be considered as a possible cause of the physiological deterioration. If, on history and examination, infection is suspected, sepsis screening should be performed.

**Adult in-patient trigger**

- New NEWS score of 4 (5 if on O\textsubscript{2}) or higher = medical review

**Sepsis screening:**

- Infection suspected as cause of physiological deterioration
- Two SIRS criteria = Sepsis
- Organ dysfunction and/or shock = Severe sepsis/septic shock

Sepsis may also be diagnosed on routine medical examination and by other means.

The maternity patient
Septic shock is relatively uncommon in maternity patients. However, in the period 2006-2008 sepsis was the leading cause of maternal mortality with a rate of 1.13/100,000 deliveries, underpinning this is a much larger burden of morbidity.\textsuperscript{4}

A number of risk factors have been identified that are associated with increased incidence of sepsis and should prompt consideration for sepsis screening if such a patient presents unwell.
Table 5 Risk factors for the development of sepsis in pregnancy

<table>
<thead>
<tr>
<th>Non-Pregnancy</th>
<th>Pregnancy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age &gt; 35</td>
<td>Cerclage</td>
</tr>
<tr>
<td>Minority ethnic group</td>
<td>PPROM</td>
</tr>
<tr>
<td>Vulnerable socio-economic background</td>
<td>Retained products</td>
</tr>
<tr>
<td>Obesity</td>
<td>History of group B Streptococcus infection</td>
</tr>
<tr>
<td>Diabetes</td>
<td>History of pelvic infection</td>
</tr>
<tr>
<td>Immunocompromised e.g. Systemic lupus erythromatosis</td>
<td>Group A Streptococcus infection in close contacts</td>
</tr>
<tr>
<td>Chronic renal failure</td>
<td>Amniocentesis</td>
</tr>
<tr>
<td>Chronic liver failure</td>
<td></td>
</tr>
<tr>
<td>Chronic heart failure</td>
<td></td>
</tr>
</tbody>
</table>

The pattern of site of infection is different from the non-pregnant population as are the organisms.

Table 6 Sources of maternal infection in severe sepsis

<table>
<thead>
<tr>
<th>Source</th>
<th>Antepartum (%)</th>
<th>Postpartum (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Genital tract</td>
<td>20.2</td>
<td>37.2</td>
</tr>
<tr>
<td>Urinary tract</td>
<td>33.6</td>
<td>11.7</td>
</tr>
<tr>
<td>Wound</td>
<td>0.0</td>
<td>14.3</td>
</tr>
<tr>
<td>Respiratory</td>
<td>9.0</td>
<td>3.5</td>
</tr>
<tr>
<td>Other</td>
<td>7.5</td>
<td>9.5</td>
</tr>
<tr>
<td>Unknown</td>
<td>29.9</td>
<td>23.8</td>
</tr>
</tbody>
</table>

Source: Severe Maternal Sepsis in the UK, 2011-2012: A National Case-Control Study

Table 7 Organisms isolated in severe maternal sepsis

<table>
<thead>
<tr>
<th>Organism</th>
<th>Antepartum</th>
<th>Postpartum</th>
</tr>
</thead>
<tbody>
<tr>
<td>E. Coli</td>
<td>24.6</td>
<td>19.1</td>
</tr>
<tr>
<td>Group A Streptococcus</td>
<td>1.5</td>
<td>13.0</td>
</tr>
<tr>
<td>Group B Streptococcus</td>
<td>9.7</td>
<td>7.4</td>
</tr>
<tr>
<td>Other Streptococcus</td>
<td>4.5</td>
<td>6.5</td>
</tr>
<tr>
<td>Staphylococcus</td>
<td>1.5</td>
<td>9.1</td>
</tr>
<tr>
<td>Mixed organisms</td>
<td>3.7</td>
<td>6.1</td>
</tr>
<tr>
<td>Other</td>
<td>9.0</td>
<td>5.6</td>
</tr>
<tr>
<td>Unknown</td>
<td>3.7</td>
<td>0.4</td>
</tr>
<tr>
<td>No laboratory confirmed infection</td>
<td>41.8</td>
<td>32.9</td>
</tr>
</tbody>
</table>

Source: Severe Maternal Sepsis in the UK, 2011-2012: A National Case-Control Study

The physiological changes of pregnancy can mimic the usual SIRS criteria leading to additional difficulties in diagnosis. Some SIRS criteria have been modified in order to allow for this (see tables 4 and 8) but these are pending validation and care needs to be taken to interpret SIRS criteria in the clinical context. The modified SIRS criteria are subject to study by the UK Obstetric Surveillance System and will be amended as further data becomes available.
When IMEWS or any other trigger prompts a review of the obstetric patient and history and examination is suggestive of infection, sepsis screening should be performed. Sepsis may also be diagnosed on routine medical examination or by other means; examination of the extended SIRS criteria or other investigations may be required in order to make the diagnosis. Once sepsis is diagnosed the Sepsis 6 should be completed within one hour. Patients need to be risk stratified into sepsis, severe sepsis and septic shock and those with severe sepsis/septic shock referred to critical care as per the local referral pathway and consistent with the Guidelines for the Critical Ill Women in Obstetrics (HSE, 2014).

Please see appendix 9 for a list of guidelines relevant to the obstetric patient and for the Irish Maternity Early Warning System (IMEWS) chart.

<table>
<thead>
<tr>
<th>Obstetric in-patient trigger</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sepsis screening:</td>
</tr>
<tr>
<td>IMEWS review</td>
</tr>
<tr>
<td>Infection suspected as cause of physiological deterioration + 2 SIRS criteria present* = Sepsis</td>
</tr>
<tr>
<td>Presence of organ dysfunction and/or shock = Severe sepsis/septic shock.</td>
</tr>
</tbody>
</table>

*Table 8 Modified SIRS criteria for maternity patients

- Temperature ≥ 38°C or < 36°C
- HR ≥ 100 beats/min
- RR ≥ 20 breaths/min
- WCC > 16.9 μL-1 or < 4 μL-1
- BSL > 7.7mmol/l (in the absence of diabetes mellitus)
- Altered mental status

The remaining SIRS criteria as per Surviving Sepsis Campaign guidelines are unmodified.

Further information in relation to the National Clinical Guideline No. 4 IMEWS can be found at:
www.health.gov.ie/patient-safety/ncec
http://www.hse.ie/eng/about/Who/clinical/natclinprog/obsandgynaeprogramme/IMEWS

Figure 3 Care pathway for the deteriorated critically ill pregnant woman
1.4.3 Communication – ISBAR Communication Tool

Poor communication has been identified as a contributing factor to adverse incidents where clinical deterioration is not identified or properly managed. The recommended communication tool when communicating in relation to the deteriorating patient, is the ISBAR communication tool (figure 4, appendix 3).

**Figure 4 ISBAR communication tool**

<table>
<thead>
<tr>
<th>ISBAR Communication Tool SAMPLE</th>
<th>Patient Deterioration</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>I</strong> Identify</td>
<td>Identify:</td>
</tr>
<tr>
<td>1 Identify</td>
<td>You</td>
</tr>
<tr>
<td></td>
<td>Recipient of handover information</td>
</tr>
<tr>
<td></td>
<td>Patient</td>
</tr>
<tr>
<td><strong>S</strong> Situation</td>
<td>Situation:</td>
</tr>
<tr>
<td>2 Situation</td>
<td>Why are you calling?</td>
</tr>
<tr>
<td></td>
<td>(Identify your concerns)</td>
</tr>
<tr>
<td><strong>B</strong> Background</td>
<td>Background:</td>
</tr>
<tr>
<td>3 Background</td>
<td>What is the relevant background?</td>
</tr>
<tr>
<td><strong>A</strong> Assessment</td>
<td>Assessment:</td>
</tr>
<tr>
<td>4 Assessment</td>
<td>What do you think is the problem?</td>
</tr>
<tr>
<td><strong>R</strong> Recommendation</td>
<td>Recommendation:</td>
</tr>
<tr>
<td>5 Recommendation</td>
<td>What do you want them to do?</td>
</tr>
</tbody>
</table>

Reproduced and adopted with permission from Dr S. Marshall, Monash University, Australia.

1.4.4 Resuscitation and referral

Once the diagnosis of sepsis has been made it is recommended that ‘Sepsis 6’ is performed within one hour.

Patients in whom severe sepsis or septic shock is suspected should be reviewed by a registrar, or more senior medical staff, immediately. **THIS IS A TIME-DEPENDANT MEDICAL EMERGENCY** similar to myocardial infarction, stroke or trauma with a time-critical period within which to maximise the patient’s survival.
If following the Sepsis 6 bundle and after 30mls/kg of fluid has been administered, severe sepsis or septic shock persists (as evidenced by persistent organ dysfunction and/or shock), it is recommended that a critical care review be requested. These patients should be assessed for admission and ongoing treatment in the HDU/ICU setting as required. Patients with raised lactate levels on presentation should have repeat lactate levels performed within three hours. Those with persistent shock should have invasive monitoring and ongoing fluid resuscitation guided by urinary output, repeat lactate and/or ScvO₂ measurement and pressor administration, as required, to obtain a MAP > 65mmHg within 6 hours. Critical care input may be requested at any point in the patient’s process of care if the patients’ condition so indicates to manage their airway, breathing and/or circulation.

Once the diagnosis of severe sepsis/septic shock has been made it is recommended that a critical care consultation be requested.

1.4.5 Source control

Once antibiotics have been administered and the patient fluid resuscitated and haemodynamically stabilised, source control, if required, needs to be addressed. It is recommended that the least physiologically deranging method of achieving adequate control be used.

Patients need to be carefully examined to ensure that drainable foci have been identified. Infected collections, devitalised tissue, lines and devices will act as a persistent source of sepsis until removed as antimicrobials have limited penetration. Source control is also a time-dependent phenomenon in patients with severe sepsis/septic shock with a recommendation of a 12 hour window post stabilisation. Consideration must be given to the logistics of organising this with limited access to interventional radiology and operating theatre time. The time recommendations should be taken into consideration when planning what type of procedure as well as when it is to take place.
National Clinical Guideline recommendations

This guideline adapts the Surviving Sepsis Campaign guidelines 2012 (18) and Sepsis Six (23) to the Irish context.

The recommendations are grouped into the following:

- Sepsis screening for patients presenting unwell with infection or at risk of neutropenia, or as an in-patient deteriorating and requiring an early warning score (EWS) triggered review.
- **Sepsis 6 to be completed within 1 hour in all patients diagnosed with sepsis.**
- The 3 Hour Bundle to be completed in patients diagnosed with severe sepsis/septic shock. This includes the Sepsis 6 completed in the 1st hour.
- The 6 Hour Bundle to be completed in patients with severe sepsis/septic shock.
- Further initial resuscitation and infection issues.
- Haemodynamic support and adjunctive therapy.
- Other supportive therapy of severe sepsis.
- **Special considerations in paediatrics.**

Practical guidance is additional evidence-based, practical information to assist the clinical team in carrying out the recommendations.

The rationale supporting each recommendation is derived from the Surviving Sepsis Campaign guidelines and is not presented in this document unless there has been a modification of a particular recommendation to incorporate the Irish context. This modification and the reason and evidence behind is stated.

**Grading the recommendations**

In this National Clinical Guideline the recommendations are graded according to the Surviving Sepsis Campaign guideline which uses the GRADE system to classify the quality of evidence as high (Grade A), moderate (Grade B), low (grade C) or very low (grade D), see table 9.

In addition, recommendations have been assigned as strong (grade 1) or weak (grade 2). The committee of the Surviving Sepsis Campaign highlight that the assignment of strong or weak is considered of greater clinical importance than a difference in letter level of quality of evidence. They assessed whether the desirable effects of adherence would outweigh the undesirable effects and the assigned strength grade reflected the group’s degree of confidence in that decision.

**Table 9 GRADE evidence quality classification**

<table>
<thead>
<tr>
<th>Grade</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grade A</td>
<td>Evidence from a meta-analysis of RCTs, or from at least one RCT.</td>
</tr>
<tr>
<td>Grade B</td>
<td>Evidence based on one controlled trial without randomisation, a quasi-experimental study, or extrapolated from RCTs.</td>
</tr>
<tr>
<td>Grade C</td>
<td>Evidence from comparative studies, correlation studies, case control studies or extrapolated from category A or B.</td>
</tr>
<tr>
<td>Grade D</td>
<td>Evidence from expert committees, reports or opinions, the clinical experience of respected authorities, and the conclusions of the Guideline Development Group</td>
</tr>
</tbody>
</table>

Some recommendations have been ungraded (UG) in the original Surviving Sepsis guideline. These statements were deemed not appropriate for the GRADE process by the Surviving Sepsis Guideline Committee.
### 2.1 National recommendations

#### 2.1.1 Screening, Sepsis 6, 3 hour and 6 hour bundles

**Responsibility**

**Assessment nurse in the Emergency Department (ED):** Screen if presenting complaint indicates infection and alert doctor as per ED sepsis pathway.

**Ward Nurse:** EWS score and alert doctor as per EWS pathway.

**Doctor:** Patient review and if infection suspected perform sepsis screen.

**Hospital Senior Management Team (e.g., CEO, Director of Nursing/Midwifery, Clinical Director and Director of Finance):** System resourced to fulfil above duties.

**Recommendation 1**

Routine sepsis screening of patients who have either:

- A presenting complaint consistent with infection,
- A deteriorating early warning score (EWS) NEWS or IMEWS,
  or
- Picked up on routine history and examination,
  or
- By other means;

is recommended to be performed to allow earlier diagnosis and implementation of therapy.

It is recommended that patients undergoing anti-cancer treatment who present unwell and are at risk of neutropenia be treated as sepsis until proven otherwise. **Grade 1C**
Practical Guidance
The Surviving Sepsis Campaign recommends screening for sepsis. Recommendation 1 is the template for screening in Ireland.

**Sepsis** is diagnosed by the presence of systemic inflammatory response (SIRS) criteria due to suspected or proven infection. See appendix 7 (with Surviving Sepsis Campaign full SIRS criteria).

**Severe sepsis/septic shock** is diagnosed by the persistence of organ dysfunction, inadequate tissue perfusion or hypotension after an initial fluid bolus. See appendix 8 (criteria for dysfunction/shock).

In order to diagnose infection, a history must be taken and clinical examination performed. The clinical manifestations are variable depending on the source of infection, the patient’s baseline health status and the time-course of the illness. Whilst the common sources of infection are respiratory tract, urinary tract, intra-abdominal, device-related, catheter-related, CNS, soft tissue and intra-articular; consideration must be given to situation specific infections such as perioperative, maternity, haematology-oncology, tropical medicine, seasonal infections and outbreaks.

During outbreaks, national recommendations, advice and information updates are circulated by the HSE and the Health Protection Surveillance Centre (HPSC). For further information see [http://www.hpsc.ie/](http://www.hpsc.ie/)

It is not always possible to diagnose infection at the first review. However, as the clinical situation evolves, a system of monitoring and review with the results of investigations is recommended to assist in making a timely diagnosis and to pick up further deterioration.

It is suggested that a patient presenting with a lactate > 4 mmol/L and/or hypotension, of unknown aetiology, should be treated as septic shock, using the Sepsis 6 whilst further investigations to clarify the diagnosis proceed. It has been consistently demonstrated that these patients have an improved outcome with early antimicrobials and fluid resuscitation when the underlying cause is infection. Antimicrobials should be stopped if the cause is subsequently found not to be infection.

**Other patients:** A SIRS response caused by infection defines sepsis; however, in some groups overt signs of sepsis can be a late feature i.e. in infants, the elderly and the immuno-compromised. Patients who are unwell in these groups may require review of the extended SIRS criteria (see appendix 7) and more senior review in order to make or out-rule the diagnosis. Patients in these groups presenting with organ dysfunction/shock should be treated as severe sepsis/septic shock if the diagnosis is unclear and delay of > 1 hour in confirming the diagnosis is anticipated. If infection is subsequently found not to be the cause antimicrobials should be stopped.

**High Risk Group – Cancer Patients:** Febrile neutropenia is a common complication of cytotoxic chemotherapy. Progression to neutropenic sepsis can result in hospital admissions, treatment delays, dose reductions and death. Patient presentation may be non-specific and the possibility of infection must be considered in any patient undergoing treatment for cancer, particularly cytotoxic chemotherapy, who is unwell and particularly in those who are neutropenic (note: SIRS criteria may not be present). It is recommended that suspected neutropenic sepsis, defined as a patent at risk of neutropenia who presents unwell, be treated with the Sepsis 6 within one hour of arrival in the hospital.

**Neutropenia** – An abnormal decrease in the number of neutrophils in the blood. Neutropenia is associated with a profound impairment in the inflammatory response, leading to a lack or minimisation of the usual signs and symptoms of infection. Neutropenia is a common problem in oncology patients either following chemotherapy, or less commonly secondary to radiation treatment or marrow infiltration by malignancy. Neutropenia is most likely to occur 10-14 days post-chemotherapy but should remain a consideration after this period. Neutropenic sepsis is diagnosed in patients having anti-cancer treatment who present unwell with a neutrophil count 0.5 x 10^9 or lower, or less than 1 x 10^9 with a downward trend.

**Febrile Neutropenia** – occurs when a patient has a fever and a significant reduction in their neutrophil counts. The fever may be caused by an infectious agent, and when it is, prompt treatment is required. A patient with febrile neutropenia needs assessment for the possible source, type of infection and treatment until the cause is found or it subsides. The risk of infection increases directly in proportion to the degree of neutropenia and its duration. (24-27)
**Responsibility**

*It is the responsibility of hospital senior management team (e.g. CEO, Director of Nursing/Midwifery, Clinical Director and Director of Finance and the HSE to ensure that point of care lactate measurement is available to clinicians caring for patients with sepsis.***

**Recommendation 2**

Point of care lactate measurement should be accessible in each Emergency Department, Medical Assessment Unit, Critical Care Unit, Maternity Unit and readily accessible elsewhere within the hospital. **Grade 1D**

**Practical Guidance**

In patients with elevated lactate levels, resuscitation can be targeted to normalise lactate as a measure of tissue hypoperfusion. **Grade 2C.**

Lactate levels can be used to help differentiate severe sepsis/septic shock from sepsis, diagnose cryptic shock which occurs in 13.5 to 25% of septic shock cases, prognosticate on presenting levels and on response to fluid resuscitation. (10) See table 11 for lactate levels associated with percentage mortality.

Septic shock can be present with normal lactate levels and raised lactate levels occur with non-septic conditions, thus lactate levels need to be interpreted within the clinical context.

As with all point of care tests, point of care lactate measurement should be incorporated into the appropriate hospital governance system. (28)

### Table 11 Lactate levels and associations with percentage mortality

<table>
<thead>
<tr>
<th>Presenting Lactate level</th>
<th>Mortality</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low (0.7 – 1.9)</td>
<td>4.5%</td>
</tr>
<tr>
<td>Intermediate (2 – 3.9)</td>
<td>10.6%</td>
</tr>
<tr>
<td>High (4+)</td>
<td>27.3%</td>
</tr>
</tbody>
</table>

(Data from CEC HIE, Australia N=3851)

**Responsibility**

*It is the responsibility of the attending doctor, nurse and midwife to administer the elements of the Sepsis 6 within the recommended timeframe. If an element cannot be performed due to resource issues i.e. no lactate measurement available, the line manager should be informed with a view to having the deficit addressed.*
Recommendation 3
For patients diagnosed with sepsis it is recommended that the Sepsis 6 be performed within one hour. Grade 1C

Sepsis 6 in the Emergency Department when:
Presenting complaint consistent with infection, two SIRS criteria, unwell or lactate > 2 mmol/L
Or
Unwell and in a high risk group for neutropenia

Sepsis 6 in the in-patient when:
Deteriorating NEWS/IMEWS with sepsis screening diagnosed sepsis
Or
In a high risk group for neutropenia
Or
By any other method

Sepsis 6 in Adults

<table>
<thead>
<tr>
<th>TAKE 3</th>
<th>GIVE 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. <strong>CULTURES:</strong> Take blood cultures before giving antimicrobials (if no significant delay i.e. &gt;45 minutes) and consider source control.</td>
<td>1. <strong>OXYGEN:</strong> Titrate O₂ supplementation to saturations of 94-98% or 88-92% in chronic lung disease.</td>
</tr>
<tr>
<td>2. <strong>BLOODS:</strong> Check lactate and full blood count.</td>
<td>2. <strong>FLUIDS:</strong> Start IV fluid resuscitation if evidence of hypovolaemia and/or shock. 500ml–1000ml bolus of isotonic crystalloid over 15–30 minutes and give up to 30ml/kg, reassessing after each bolus for signs of hypovolaemia, euvoalaemia, or fluid overload.</td>
</tr>
<tr>
<td>3. <strong>URINE OUTPUT:</strong> Assess urine output and consider urinary catheterisation for accurate measurement in patients with severe sepsis/septic shock.</td>
<td>3. <strong>ANTIMICROBIALS:</strong> Give IV antimicrobials according to local antimicrobial guidelines.</td>
</tr>
</tbody>
</table>

Practical Guidance
The Sepsis 6 represents the minimum intervention. Other blood tests, cultures or investigations may be required depending on the clinical findings both to assist in making a diagnosis and also to assess the severity of the patients’ illness. Blood tests should be sent marked ‘urgent’ and should be reviewed and acted on in a timely fashion. This also applies to any investigations ordered.

Sepsis 6 does not have to be performed within one hour of review; it is within one hour of the diagnosis of sepsis.

Patients with sepsis can have absolute hypovolaemia, relative hypovolaemia and/or distributive shock. These are diagnosed by measuring heart rate, blood pressure, lactate and urinary output as well as assessing clinical signs of hypoperfusion such as altered mental state, prolonged capillary refill or mottling. Patients with hypovolaemia without hypotension require fluid resuscitation to restore euvoalaemia and normal organ perfusion as evidenced by return of normal mentation, skin perfusion, urinary output and lactate levels.

Patients presenting with systolic blood pressure (SBP) <90mmHg, mean arterial blood pressure <65mmHg, SBP decrease of 40mmHg from baseline or serum lactate levels > 4mmols/l should receive 30mls/kg of intravenous (IV) isotonic crystalloid fluid in the first hour unless fluid overload develops. If the patient develops signs and symptoms of overload, IV fluid administration should be stopped and vasoactive agents be used to restore SBP to > 90mmHg or mean arterial blood pressure (MAP) to > 65mmHg. After fluid resuscitation with 30mls/kg isotonic crystalloid, hypotension may persist requiring further fluid resuscitation and vasopressors. This is septic shock. Myocardial dysfunction may also occur.
Fluid resuscitation is performed by giving fluid boluses (e.g. 500mls – 1000mls) over a given time period (e.g. 15 – 30 minutes) and the patient’s response assessed by clinical examination after the bolus has been given and a decision made as to whether the patient needs further fluid resuscitation or not. The amount of the bolus and the time period over which it is given, depends on the co-morbidities of the individual patient. Serial measurement of lactate and urinary output measurement can help guide fluid resuscitation.

Sepsis represents a clinical continuum ranging from patients presenting haemo-dynamically stable with no overt fluid deficit as indicated by normal organ function, urinary output and lactate level who require little or no fluid resuscitation and only maintenance fluids if fasting, through those that have restoration of haemo-dynamics and organ function after fluid resuscitation as demonstrated by normalisation of mental status, skin perfusion, urinary output and lactate and then require only maintenance fluids, if fasting, to those with persistent hypotension and organ dysfunction post initial fluid resuscitation who require critical care input and consideration of invasive monitoring, advanced haemo-dynamic support (e.g. vasopressors) and further guided fluid resuscitation. An example of a fluid resuscitation algorithm is given in appendix 8.

Patients remain under the care of the attending doctor and ward staff pending transfer to another hospital setting (e.g. critical care), with critical care acting in a consultative manner, if required.

**Recommendation 4**

It is recommended that each clinical programme/healthcare facility create or adopt treatment pathways for sepsis care that includes triggers for sepsis screening, facilitates the diagnosis of sepsis, severe sepsis/septic shock, and the treatment, resuscitation and appropriate referral to critical care. These completed pathways signed by the treating clinician should be included in the patient chart and their presence audited by HIPE as a key performance indicator.

**Practical Guidance**

Examples of pathways for ED presentations and NEWS triggered reviews are included in appendix 5. Pathways should clearly identify the stratification of patients into sepsis, severe sepsis or septic shock, include likely source of infection, if known, and the time first dose antimicrobials were administered. A referral mechanism to critical care for patients with severe sepsis/septic shock should be included.

**Rationale**

The aim of these recommendations is to facilitate the early recognition, prompt treatment and appropriate referral of patients with sepsis and severe sepsis/septic shock, as it has been demonstrated that in jurisdictions where these principles have been applied there has been a sustained decrease in mortality from sepsis (Surviving Sepsis Campaign, ProCESS trial, (29) Australian ICU database (12), ARISE trial5).

Adopting these recommendations is associated with a decrease in ICU and hospital length of stay and savings in healthcare costs. There is a growing awareness of chronic health issues amongst survivors of severe sepsis/septic shock, (30) it is anticipated that by intervening early in the course of the illness by screening for early recognition and prompt appropriate therapy, this burden of morbidity can be reduced both for patients and the healthcare system.

In 2010, sepsis was identified as the 11th leading cause of death in the U.S and in 2012 as the single most expensive condition treated in hospitals. (34) Audit of US national patient databases has shown sepsis to be a component in two of five in-hospital patient deaths, with most of these patients having sepsis on presentation (35), and the Irish national database (HIPE) documents an infection/sepsis prevalence of 60% amongst patients with in-hospital death. The high prevalence of this disease justifies intense quality improvement efforts.

Performance improvement and quality assurance can only occur if practice is audited, thus local and national audits should be performed. These can be benchmarked intra- and inter-hospital and internationally. Barriers to implementation of the guidelines need to be reported via line-managers and process/resource change occur to remove/reduce those barriers.

Education in the identification and management of patients with sepsis is a key to ensure guideline implementation. The creation of a sepsis team would facilitate education, implementation and audit, its components depending on the size of the institution serviced.

The signs and symptoms of sepsis are subjective and non-specific with many non-inflammatory disorders having similar presentation, it is important to be aware of the risks of overtreatment as well as under treatment. Thus timelines are from time of diagnosis (not presentation) and audit of sepsis screening will feedback the appropriateness of subsequent therapy and facilitate the tailoring of the education process. An audit of EWS responses would give the incidence of sepsis as the cause for EWS review, insight into over and under treatment and compliance with Sepsis 6.

The publication of this guideline needs to be supported by a robust educational campaign and on-going and embedded sepsis education in the undergraduate and postgraduate medical, midwifery and nursing programmes in order to optimise the recognition of the deteriorating patient, diagnose sepsis and deliver the correct therapy.

Process change and pathway implementation need to be supported by the appropriate resources in order to ensure effective delivery of prompt and appropriate sepsis treatment.
Sepsis Management

Figure 5 Adult sepsis management algorithm

**National Clinical Guideline: Adult Sepsis Management Algorithm**

**SUSPECTED INFECTION**

PLUS

2 SIRS CRITERIA

= SEPSIS

---

**Sepsis 6 in 1 hour**

**Give**

1. **Oxygen** (94-98% SpO2 or 88-92% COPO Patients)
2. **IV Antimicrobials** (according to local guidelines)
3. **Fluids** (500mls bolus: give up to 30ml/kg & reassess)

**Take**

1. **Blood Cultures**
2. **Lactate and FBC**
3. **Urine Output measurement**

**If MAP**

≥65mmHg and/or

Lactate ≤2mmol/L

Document Sepsis

**If MAP**

<65mmHg and/or

Lactate ≥4 mmol/L

**Fluid resuscitation of 30ml/kg IV in 1 HOUR**

---

**Lactate**

If Lactate ≥4mmol/L and/or MAP <65mmHg

**Document Sepsis**

If Lactate 2-4 mmol/L and/or MAP ≥65mmHg or organ dysfunction

**If MAP**

≥65mmHg and/or Lactate ≤2mmol/L

**Document Sepsis**

---

If Lactate ≥4mmol/L and/or MAP <65mmHg

**This is SEPTIC SHOCK**

**Please document it.**

**Continue Fluid Resuscitation.**

**Call**

**Critical Care Medicine**

---

If Lactate ≥4mmol/L and/or MAP <65mmHg

**This is SEVERE SEPSIS.**

**Please document it.**

---

*MAP: Mean Arterial Pressure

For more information go to on National Clinical Guideline No 6. Sepsis Management go to:

www.health.gov.ie/patient-safety/ncec
Responsibility

It is the responsibility of the attending doctor to inform their senior clinician as per local arrangement, when a patient is diagnosed with severe sepsis/septic shock and to administer the 3 and 6-hour bundles. It is their or their delegated authority’s responsibility to assess the patients’ response to the fluid bolus and to prescribe further bolus as appropriate.

**Recommendation 5 (3 Hour Bundle)**

**FOR PATIENTS WITH SEVERE SEPSIS/SEPTIC SHOCK**

**TO BE COMPLETED WITHIN 3 HOURS OF DIAGNOSIS**

1. Complete Sepsis 6 within first hour.
2. Administer a minimum of 30 mL/kg isotonic crystalloid for hypotension or lactate >4mmol/L
3. Assess patient for response to resuscitation by monitoring clinical and haemo-dynamic response, measure hourly urinary output and repeat lactate measurement.

**Practical Guidance**

The Sepsis 6, which is administered to all deteriorating patients presenting with sepsis, is completed in the first hour with O₂ and antimicrobials given and IV fluid resuscitation underway.

Measuring lactate and urinary output aids the identification of those with severe sepsis/septic shock and these patients should receive 30mls/kg IV isotonic crystalloid fluid guided by their clinical response to fluid resuscitation. Some patients will need more than this to be fluid replete i.e. warm, well perfused, normal mental status, with normal lactate and urinary output.

Patients who develop fluid overload, (signs and symptoms include jugular venous distention, crepitations on chest auscultation, and decreased pulse oximetry readings), should have all IV fluids (boluses and background rate) discontinued until no longer deemed fluid overloaded.

Patients who have persistent organ dysfunction and/or shock after 30mls/kg IV fluid has been administered should have a critical care consultation considered. While some will stabilise with further fluid, others will require advanced cardiovascular support and early referral will facilitate this process. Patients who present extremely unwell may require early critical care input to secure the airway and breathing as well as the circulation.

Clinical handover forms may facilitate the accurate recording of diagnosis, investigations and treatments received and help ensure effective communication between clinical teams and as such their use is suggested. For further information refer to National Clinical Guideline No. 5 Communication (Clinical Handover) in Maternity Services.
**Responsibility**

*It is the responsibility of the critical care team to support the attending doctor in achieving the goals of the 6-hour bundle, if required. The patient remains under the primary care of the initial attending team until transferred to a critical care area (ICU or HDU) or accepted by the critical care team.*

**Recommendation 6 (6 Hour Bundle)**

**FOR PATIENTS WITH SEVERE SEPSIS/SEPTIC SHOCK**

**TO BE COMPLETED WITHIN 6 HOURS OF DIAGNOSIS**

1. Apply vasopressors (for hypotension that does not respond to initial fluid resuscitation) to maintain a mean arterial pressure (MAP) ≥ 65 mm Hg.
2. A sample fluid resuscitation algorithm is suggested as a guide to ongoing fluid resuscitation (see Appendix 8).
3. Re-measure lactate as indicated.

**Practical Guidance**

The elements of the 6-hour bundle may have to be initiated very early in patients presenting with profound hypotension. The 3 and 6-hour bundles do not have to be performed consecutively but rather according to patient need. However, the elements should be completed within their time frames i.e. Sepsis 6 within the first hour, and the bundles within 3 and 6 hours respectively.

The management of severe sepsis/septic shock is evolving and the ProCESS trial and ARISE trials have shown that CVP (central venous pressure) and ScvO2 (central venous oxygen saturation) measurement are not necessary components in the resuscitation bundle. Central venous access is required for the administration of vasopressors. Further fluid resuscitation trials are in progress and the guideline will be updated as appropriate.
2.1.2 Initial resuscitation and infection issues

A. Initial resuscitation

Responsibility
Fluid resuscitation should be started by the attending clinical team and assisted by critical care as required. Once the patient has been accepted by the critical care team they will take over responsibility for the patient’s on-going resuscitation.

Recommendation 7
Intravenous fluid resuscitation

Quantitative resuscitation of patients with sepsis-induced tissue hypoperfusion should be used (i.e. a fluid bolus given over a pre-determined time period and repeated as required).

Sepsis-induced tissue hypoperfusion is defined in this National Clinical Guideline as hypotension or blood lactate concentration ≥ 4 mmol/L persisting after initial isotonic crystalloid fluid challenge of 30mls/kg. Goals during the first 6 hours of resuscitation include:

SBP > 90mmHg or MAP > 65mmHg or within 10% of known baseline and not clinically deemed hypoperfused

Or

SBP > 90mmHg or MAP > 65mmHg, fluid replete/overloaded* and on vasopressors

Grade 1B (29)

(see appendix 8 sample fluid resuscitation algorithm)

Or

a) Central venous pressure 8–12 mm Hg

b) Mean arterial pressure (MAP) ≥ 65 mm Hg

c) Urine output ≥ 0.5 mL/kg/hr

d) Central venous (superior vena cava) or mixed venous oxygen saturation 70% or 65%, respectively. Grade 1B (31)

Practical Guidance
Clinical hypoperfusion diagnosed by, but not limited to SBP < 90, MAP < 65, lactate > 4, mottled skin, oliguria, altered sensorium.

Fluid replete/overloaded is defined in this National Clinical Guideline as a clinical diagnosis. Signs and symptoms of overload include jugular venous distention, crepitations on chest auscultation, and decreased pulse oximetry readings. Discontinue all IV fluids (boluses, background rate) once this occurs, until no longer deemed fluid overloaded.

The ProCESS trial demonstrates no mortality or morbidity difference between EGDT, protocol-based standard therapy and usual care. It should be noted that usual care in the study institutions resulted in mortality rates of 18.9% and care should be taken in translating these findings into less resource intensive institutions. For this reason a simplified initial fluid resuscitation algorithm is offered as an alternative to early goal-directed therapy as a guide to initial fluid resuscitation (appendix 8).
B. Diagnosis

Responsibility
It is the responsibility of the clinician administering the first dose of antimicrobials to ensure that blood cultures have been taken first. However, taking cultures should not lead to a delay in administering antimicrobials beyond the one hour time frame. In different institutions, different personnel take the cultures and institutional practices should be followed.

Recommendation 8
Appropriate cultures should be taken before antimicrobial therapy is started, as long as there is no significant delay (> 45 mins) in the start of antimicrobial(s). Grade 1C

At least two sets of blood cultures (both aerobic and anaerobic bottles) should be obtained before antimicrobial therapy with at least one drawn percutaneously and one drawn through each vascular access device, unless the device was recently (<48 hrs) inserted. Grade 1C

Practical Guidance
The taking of blood cultures represents the minimum requirement in terms of microbiological sampling, samples from all potentially infected sites should be sent for analysis. Blood cultures must be taken using an aseptic technique (32) to avoid contamination and in order to be clinically useful.

Imaging studies should be performed promptly to confirm a potential source of infection. UG

C. Antimicrobial therapy

Responsibility
The attending nurse, midwife or doctor should administer the antimicrobials according to availability in order to ensure the one hour time frame is achieved.

Recommendation 9
Administration of effective IV antimicrobials should occur within the first hour of recognition of septic shock (Grade 1B) and severe sepsis without septic shock, Grade 1C.

Responsibility
The attending doctor and followed up by the responsible team.

Recommendation 10
• Initial empiric antimicrobial therapy of one or more antimicrobials that have activity against all likely pathogens (bacterial and/or fungal or viral) and that penetrate in adequate concentrations into tissues presumed to be the source of sepsis is recommended. Grade 1B
• Local antimicrobial prescribing should be followed to guide best choice of empiric antimicrobial therapy. This is to ensure that the antimicrobial chosen is appropriate for the local epidemiology.
• The antimicrobial regimen should be reassessed daily for potential deescalation as outlined in the ‘Start smart, then focus’ national antimicrobial prescribing care bundle. (appendix 6). Grade 1B
Practical Guidance
Empiric antimicrobial prescribing: Antimicrobial prescribing should be based on locally approved
guidelines, the patients’ history of colonisation/infection with antimicrobial resistant organisms and the
site of infection as determined clinically.
- Antiviral therapy is suggested to be initiated as early as possible in patients with severe sepsis or septic
  shock of suspected viral origin. Grade 2C
- Antimicrobial agents should NOT be used in patients with severe inflammatory states determined to
  be of non-infectious cause. UG

Antimicrobials should be reviewed after 24-48 hours by a senior clinician and rationalised based on
culture results and clinical response as outlined in the national antimicrobial prescribing care bundle.

Due to the increasing incidence of antimicrobial resistant organisms in Ireland (33) it may be helpful to
discuss empiric antimicrobial therapy choices with a clinical microbiologist/Infectious diseases physician.

Combination Therapy: The Surviving Sepsis Guideline Development Group suggest combination empirical
therapy for neutropenic patients with severe sepsis, Grade 2B, and for patients with difficult-to-treat,
multi-drug resistant bacterial pathogens such as Acinetobacter and Pseudomonas spp. Grade 2B.

Duration of antimicrobial therapy: Empiric combination therapy should NOT be administered for more
than 3–5 days. Deescalation to the most appropriate single therapy should be performed as soon as the
antimicrobial susceptibility profile is known. Grade 2B

Duration of therapy of typically 7–10 days is suggested. This is dependent on the source of infection and
the clinical response to therapy. Longer courses may be appropriate in patients who have a slow clinical
response, undrainerable foci of infection, bacteraemia with S. aureus; some fungal and viral infections or
immunologic deficiencies, including neutropenia. Grade 2C

D. Source control

Responsibility
It is the responsibility of the attending team to organise and review appropriate investigations
in order to attempt to identify the source of infection and to request review by the appropriate
clinical team for the consideration of drainage of drainable foci (e.g. from surgery or interventional
radiology).

Recommendation 11
It is recommended that a specific anatomical diagnosis of infection requiring consideration
for emergent source control be sought and diagnosed or excluded as rapidly as possible, and
intervention be undertaken for source control within the first 12 hours after the diagnosis is made,
if feasible. Grade 1C

Practical Guidance
When infected peripancreatic necrosis is identified as a potential source of infection, it is suggested that
definitive intervention is best delayed until adequate demarcation of viable and nonviable tissues has
occurred. Grade 2B

When source control in a severely septic patient is required, the effective intervention associated with the
least physiologic insult should be used (e.g. percutaneous rather than surgical drainage of an abscess). UG

If intravascular access devices are a possible source of severe sepsis or septic shock, they should be
removed promptly after other vascular access has been established. UG
E. Performance improvement

**Recommendation 12**
Hospital–based performance improvement efforts should be carried out on the diagnosis, treatment and referral of patients with severe sepsis. UG

**Responsibility:**

*It is the responsibility of the HSE and hospital managers to put in place processes to facilitate the implementation of this guideline and associated clinical pathways.*

*It is the responsibility of the HSE and senior hospital management to ensure that clinicians have access to appropriate education resources in order to be able to be compliant with the national guideline.*

*It is the responsibility of clinicians to avail of these resources to ensure their familiarity with the management of the deteriorating patient with sepsis.*

*It is the responsibility of the National Clinical Lead for the Sepsis Workstream and the National Sepsis Steering Committee to advise the HSE and the Department of Health on the necessary process change and requirements for sepsis pathway implementation and audit.*

*It is the responsibility of hospital management and HSE to resource the audit of compliance with sepsis screening, including the audit of key performance indicators such as time to first dose antimicrobials, incidence of bacteraemia, incidence of blood culture contamination, total antimicrobial dispensing, and rates of C. difficile infections.*

*It is the responsibility of the HSE and hospitals to audit the incidence of sepsis, severe sepsis, septic shock and mortality from same as documented in the patients medical chart. It is the responsibility of the diagnosing clinician to document sepsis, severe sepsis and septic shock and the origin of same, if known, in the medical chart. It is the responsibility of the clinician documenting cause of death to include sepsis, severe sepsis or septic shock as appropriate and the source of sepsis, if known, in the patient case notes and death certificate.*

**Practical Guidance**

To track improvements in the management of patients with sepsis, the level of compliance with elements of Sepsis 6, especially time to first dose antimicrobials, should be monitored on an ongoing basis as part of a ward/unit/directorate quality sepsis improvement programme.

Each ward/unit/directorate should agree a measurement plan for sepsis that is practical and aligns with other measurements for improvement. The measurement strategy needs to reflect the reality that patients can present with sepsis on admission or develop sepsis while in hospital. It should also include consideration of measurement of some balancing measures (see section 3.7 of this guideline). Sources of data can include the patient’s medical notes, medication chart, observation/early warning score chart, and fluid balance chart. Patients with a terminal illness should NOT be excluded unless a decision not to escalate care clearly excludes further active treatment with antimicrobials or IV fluids in the ward setting.
F. Infection prevention

Responsibility:
Hospital Senior Management Team (e.g. CEO, Director of Nursing/Midwifery, Clinical Director and Director of Finance. Action to be performed by ICU nurse or delegated person.

Practical Guidance
It is suggested that oral chlorhexidine gluconate be used as a form of oropharyngeal decontamination to reduce the risk of ventilator-associated pneumonia in ICU patients with severe sepsis. Grade 2B

Subject to update as per the ventilator associated pneumonia (VAP) prevention bundle.

For further details on infection and prevention control guidance see http://health.gov.ie/patient-safety/ncec/national-clinical-guidelines/: National Clinical Guideline No. 2 Prevention and Control of Methicillin Resistant Staphloccus Aureus (MRSA) National Clinical Guideline No. 3 Surveillance, Diagnosis and Management of Clostridium difficile in Ireland

2.2 Other national recommendations

2.2.1 Haemodynamic support and adjunctive therapy

G. Fluid therapy of severe sepsis

Responsibility
Prescribing doctor.

Recommendation 13
It is recommended that isotonic crystalloids are used as the initial fluid of choice in the resuscitation of severe sepsis and septic shock. Grade 1B

Recommendation 14
The Guideline Development Group recommends AGAINST the use of hydroxyethyl starches for fluid resuscitation of severe sepsis and septic shock. Grade 1B

Practical Guidance
Albumin in the fluid resuscitation of severe sepsis and septic shock is suggested when patients require substantial amounts of crystalloids and a colloid is being considered. Grade 2C

Recommendation 15
An initial fluid challenge of 500-1000mls over 15 minutes to 30 minutes is recommended in patients with sepsis-induced tissue hypoperfusion with suspicion of hypovolemia. This should be repeated to achieve a minimum of 30 mL/kg of isotonic crystalloids (a portion of this may be albumin equivalent). More rapid administration and greater amounts of fluid may be needed in some patients. Grade 1C
Practical Guidance
A fluid challenge technique is recommended i.e. fluid administration is continued as long as there is hemodynamic improvement either based on dynamic (e.g., change in pulse pressure, stroke volume variation) or static (e.g., arterial pressure, heart rate) variables. **UG**

### H. Vasopressors

**Responsibility**
*Attending clinical team, supported by the critical care team if outside the critical care ward. The critical care team whilst in ICU/HDU.*

<table>
<thead>
<tr>
<th><strong>Recommendation 16</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>It is recommended that vasopressor therapy if required should initially target a mean arterial pressure (MAP) of 65mm Hg. <strong>Grade 1C</strong></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>Recommendation 17</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>Low-dose dopamine should NOT be used for renal protection. <strong>Grade 1A</strong></td>
</tr>
</tbody>
</table>

**Practical Guidance**
All patients requiring vasopressors should have an arterial catheter placed as soon as practical if resources are available. **UG**

Noradrenaline is recommended as the first choice of vasopressor. **Grade 1C**

Adrenaline (added to and potentially substituted for noradrenaline) may be used when an additional agent is needed to maintain adequate blood pressure. **Grade 2B**

Vasopressin 0.03 units/minute can be added to noradrenaline with intent of either raising MAP or decreasing noradrenaline dosage. **UG** Low-dose vasopressin is not recommended as the single initial vasopressor for treatment of sepsis-induced hypotension and vasopressin doses higher than 0.03-0.04 units/minute should be reserved for salvage therapy (failure to achieve adequate MAP with other vasopressor agents). **UG**

Dopamine as an alternative vasopressor agent to noradrenaline is only to be used in highly selective patients (e.g., patients with low risk of tachyarrhythmias and absolute or relative bradycardia). **Grade 2C**

Phenylephrine is not recommended in the treatment of septic shock except in circumstances where (a) noradrenaline is associated with serious arrhythmias, (b) cardiac output is known to be high and blood pressure persistently low or (c) as salvage therapy when combined inotrope/vasopressor drugs and low dose vasopressin have failed to achieve MAP target. **Grade 1C**
I. Inotropic therapy

Responsibility
Attending clinical team, supported by the critical care team if outside critical care ward. The critical care team whilst in ICU.

Recommendation 18
The Guideline Development Group recommends AGAINST using a strategy to increase cardiac index to predetermined supranormal levels. Grade 1B

Practical Guidance
It is suggested that a trial of dobutamine infusion up to 20 micrograms/kg/min be administered or added to vasopressor (if in use) in the presence of (a) myocardial dysfunction as suggested by elevated cardiac filling pressures and low cardiac output, or (b) ongoing signs of hypoperfusion, despite achieving intravascular volume repletion and adequate MAP. Grade 1C

J. Corticosteroids

Responsibility
Attending clinical team, supported by the critical care team if outside critical care area. The critical care team whilst in ICU/HDU.

Recommendation 19
Corticosteroids should NOT be administered for the treatment of sepsis in the absence of shock. Grade 1D

Recommendation 20
It is suggested to NOT use IV hydrocortisone to treat adult septic shock patients if adequate fluid resuscitation and vasopressor therapy are able to restore haemodynamic stability. In case this is not achievable, it is suggested to use IV hydrocortisone alone at a total dose of 200mg per day. Grade 2C

Practical Guidance
It is suggested to NOT use the ACTH stimulation test to identify adults with septic shock who should receive hydrocortisone. Grade 2B

In treated patients, it is suggested that hydrocortisone be tapered when vasopressors are no longer required. Grade 2D

When low-dose hydrocortisone is given, it is suggested that continuous infusion rather than repetitive bolus injection should be used. Grade 2D
2.2.2 Other supportive therapy of severe sepsis

Responsibility
Attending clinical team, supported by the critical care team if outside critical care area. The critical care team whilst in ICU.

K. Blood product administration

Recommendation 21
Once tissue hypoperfusion has resolved and in the absence of extenuating circumstances such as myocardial ischaemia, severe hypoxemia, acute haemorrhage or ischaemic heart disease, red blood cell transfusion is recommended only when the haemoglobin concentration decreases to < 7.0g/dL to target a haemoglobin concentration of 7.0-9.0g/dL in adults. Grade 1B

Recommendation 22
In patients with severe sepsis, it is suggested that platelets should be administered prophylactically when counts are <10,000/mm³ (10 x 10⁹/L) in the absence of apparent bleeding. Prophylactic platelet transfusion can also be used when counts are <20,000/mm³ (20 x 10⁹/L) if the patient has a significant risk of bleeding. Higher platelet counts (>50,000/mm³ [50 x 10⁹/L]) are advised for active bleeding, surgery or invasive procedures. Grade 2D

Practical Guidance
Erythropoietin is NOT recommended as a specific treatment of anaemia associated with severe sepsis. Grade 1B

It is suggested NOT to use fresh frozen plasma/octaplas to correct laboratory clotting abnormalities in the absence of bleeding or planned invasive procedures. Grade 2D

Antithrombin is NOT recommended for the treatment of severe sepsis and septic shock. Grade 1B

L. Immunoglobulins

Responsibility
Attending clinical team, supported by critical care if outside critical care area. The critical care team whilst in ICU.

Practical Guidance
It is suggested that IV immunoglobulins are NOT recommended for use in adult patients with severe sepsis or septic shock. Grade 2B

M. Selenium

Responsibility
Attending clinical team, supported by critical care if outside critical care area. The critical care team whilst in ICU.

Practical Guidance
It is suggested that IV selenium is NOT recommended for treatment of severe sepsis. Grade 2C
N. Mechanical ventilation of sepsis-induced acute respiratory distress syndrome (ARDS)

Responsibility
Attending clinical team, supported by critical care if outside critical care area. The critical care team whilst in ICU.

Recommendation 23
A target tidal volume of 6mL/kg predicted body weight in patients with sepsis-induced ARDS is recommended. Grade 1A

Recommendation 24
Plateau pressures should be measured in patients with ARDS and the initial upper limit goal for plateau pressures in a passively inflated lung should be <30cm H2O. Grade 1B

Recommendation 25
Positive end expiratory pressure (PEEP) should be applied to avoid alveolar collapse at end expiration (atelectotrauma). Grade 1B

Practical Guidance
Strategies based on higher rather than lower levels of PEEP are suggested to be used for patients with sepsis-induced moderate or severe ARDS. Grade 2C

Recruitment manoeuvres are suggested to be used in sepsis patients with severe refractory hypoxaemia. Grade 2C

Prone positioning is suggested to be used in sepsis-induced ARDS patients with Pao2/FIO2 ratio < 100 mm Hg in facilities that have experience with such practices. Grade 2B

Recommendation 26
Mechanically ventilated sepsis patients are recommended to be maintained with the head of the bed elevated to 30-45 degrees to limit aspiration risk and to prevent the development of ventilator-associated pneumonia. Grade 1B

Practical Guidance
The use of noninvasive mask ventilation (NIV) may be used in that minority of sepsis-induced ARDS patients in whom the benefits of NIV have been carefully considered and are thought to outweigh the risks. Grade 2B

Recommendation 27
For mechanically ventilated patients with severe sepsis, it is recommended that a weaning protocol should be in place and they should undergo spontaneous breathing trials on a regular basis to evaluate the ability to discontinue mechanical ventilation when they satisfy the following criteria:

a) arousable
b) haemodynamically stable (without vasopressor agents)
c) no new potentially serious conditions
d) low ventilatory and end-expiratory pressure requirements
e) low FIO2 requirements which can be met safely delivered with a face mask or nasal cannula.

If the spontaneous breathing trial is successful, consideration should be given for extubation. Grade 1A
**Practical Guidance**
Routine use of the pulmonary artery catheter for patients with sepsis-induced ARDS is NOT advised. **Grade 1A**

A conservative rather than liberal fluid strategy is advised for patients with established sepsis-induced ARDS who do not have evidence of tissue hypoperfusion. **Grade 1C**

In the absence of specific indications such as bronchospasm, the use of beta 2-agonists for treatment of sepsis-induced ARDS is NOT advised. **Grade 1B**

---

**O. Sedation, analgesia and neuromuscular blockade in sepsis**

**Responsibility**
Attending clinical team, supported by critical care if outside critical care ward. The critical care team whilst in ICU.

**Practical Guidance**
Continuous or intermittent sedation should be minimised in mechanically ventilated sepsis patients, targeting specific titration endpoints. **Grade 1B**

Neuromuscular blocking agents (NMBA) should be avoided if possible in the septic patient without ARDS due to the risk of prolonged neuromuscular blockade following discontinuation. If NMBAs must be maintained, either an intermittent bolus as required or continuous infusion with train-of-four monitoring of the depth of blockade should be used. **Grade 1C**

A short course of NMBA of not greater than 48 hours may be used for patients with early sepsis-induced ARDS and a Pao₂/FIO₂ < 150mm Hg. **Grade 2C**

---

**P. Glucose control**

**Responsibility**
Attending clinical team, supported by critical care if outside critical care ward. The critical care team whilst in ICU.

**Recommendation 28**
Blood glucose management in ICU patients with severe sepsis is recommended, commencing insulin dosing when 2 consecutive blood glucose levels are > 10mmol/L. Targeting an upper blood glucose ≤ 10mmol/L rather than an upper target blood glucose ≤ 110 mg/dL (6mmol/L). **Grade 1A**

**Practical Guidance**
Blood glucose levels should be monitored every 1-2 hours until glucose values and insulin infusion rates are stable and then every 4 hours thereafter. **Grade 1C**

Glucose levels obtained with point-of-care testing of capillary blood should be interpreted with caution, as such measurements may not accurately estimate arterial blood or plasma glucose values. **UG**
Q. Renal replacement therapy

**Responsibility**

*Depending on the institution, renal replacement therapies in critical care are the responsibility of the critical care team or the nephrology team or a combination of both.*

**Practical Guidance**

- It is suggested that continuous renal replacement therapies and intermittent haemodialysis are equivalent in patients with severe sepsis and acute renal failure. **Grade 2B**
- Continuous therapies to facilitate management of fluid balance are suggested for use in haemodynamically unstable septic patients. **Grade 2D**
- The use of sodium bicarbonate therapy in NOT recommended for the purpose of improving haemodynamics or reducing vasopressor requirements in patients with hypoperfusion-induced lactic acidemia with pH ≥7.15. **Grade 2B**

R. Deep vein thrombosis prophylaxis

**Responsibility**

*Attending clinical team, supported by critical care if outside critical care ward. The critical care team whilst in ICU.*

**Recommendation 29**

Patients with severe sepsis should receive daily pharmacoprophylaxis against venous thrombosis (VTE). **Grade 1B** This should be accomplished with daily subcutaneous low-molecular weight heparin (LMWH), **Grade 1B** versus twice daily unfractionated heparin (UFH), **Grade 2C** versus three times daily UFH.

If creatinine clearance is <30mL/min, suggest use of dalteparin, **Grade 1A**, or another form of LMWH that has a low degree of renal metabolism, **Grade 2C** or UFH, **Grade 1A**.

**Practical Guidance**

- It is suggested that patients with severe sepsis should be treated with a combination of pharmacologic therapy and intermittent pneumatic compression devices whenever possible. **Grade 2C**
- Septic patients who have a contraindication for heparin use (eg, severe thrombocytopenia, severe coagulopathy, active bleeding, recent intracerebral haemorrhage) should NOT receive pharmacoprophylaxis, **Grade 1B**, but it is suggested that they receive mechanical prophylactic treatment, such as graduated compression stockings or intermittent compression devices, **Grade 2C**, unless contraindicated. When the risk decreases pharmacoprophylaxis may be commenced. **Grade 2C**

S. Stress ulcer prophylaxis

**Responsibility**

*Attending clinical team, supported by critical care if outside critical care ward. The critical care team whilst in ICU.*

**Recommendation 30**

Stress ulcer prophylaxis using H2 blocker or proton pump inhibitors should be given to patients with severe sepsis/septic shock who have bleeding risk factors. **Grade 1B**
Recommendation 31
It is suggested that patients without risk factors do NOT receive stress ulcer prophylaxis. Grade 2B

Practical Guidance
When stress ulcer prophylaxis is used, it is suggested that proton pump inhibitors be used rather than H₂ receptor antagonists (H₂RA). Grade 2D

T. Nutrition

Responsibility
Attending clinical team, supported by critical care if outside critical care ward. The critical care team whilst in ICU, supported by dietetics and administered by critical care nursing.

Recommendation 32
It is suggested that oral or enteral feedings should be administered as tolerated, rather than either complete fasting or provision of only intravenous glucose within the first 48 hours after a diagnosis of severe sepsis/septic shock. Grade 2C

Practical Guidance
Mandatory full caloric feeding should be avoided in the first week but rather low dose feeding (eg, up to 500 calories per day) is suggested, advancing only as the patient tolerates it. Grade 2B

It is suggested that intravenous glucose and enteral nutrition is used rather than total parenteral nutrition (TPN) alone or parenteral nutrition in conjunction with enteral feeding in the first 7 days after a diagnosis of severe sepsis/septic shock. Grade 2B

It is suggested that nutrition with no specific immunomodulating supplementation be used rather than nutrition providing specific immunomodulating supplementation in patients with severe sepsis. Grade 2C

U. Setting goals of care

Responsibility
The combined input of the critical care team and the admitting clinical team.

Recommendation 33
Goals of care and prognosis should be discussed with patients and families. Grade 1B

Practical Guidance
Goals of care should be incorporated into treatment and end-of-life care planning, utilizing palliative care principles where appropriate. Grade 1B

It is suggested that goals of care should be addressed as early as feasible but no later than within 72 hours of ICU admission. Grade 2C
### 2.2.3 Special considerations in paediatrics

In childhood, sepsis is defined as evidence of the systemic inflammatory response syndrome (SIRS) in the context of suspected, or confirmed, bacterial, viral or fungal infection. (36)

The diagnosis of SIRS in children has been modified from the diagnostic features in adults and is dependent on the presence of certain paediatric specific criteria.

**SIRS** is a response to a stimulus, which results in two or more of the following:

- Temperature > 38.5°C or < 36°C
- Heart rate > 2 SDs above normal, or bradycardia in children < 1 year old (< 10th centile for age)
- Respiratory rate > 2 SDs above normal (or pCO₂ < 4.25Kpa)
- Leukocyte count > 12,000 cells/mm³, < 4,000 cells/mm³, or > 10% band forms
- Hyperglycaemia
- Altered mental status
- Hyperlactaemia
- Increased capillary refill time (CRT)

Other important definitions in paediatric sepsis include:

**Severe sepsis** is sepsis and organ hypoperfusion (raised lactate, oliguria, prolonged CRT, reduced mental status) or organ dysfunction* (disseminated intravascular coagulopathy (DIC), acute respiratory distress syndrome (ARDS), acute renal failure (ARF)).

~~~

### Organ dysfunction criteria

**Respiratory:**

- PaO₂/FiO₂ <300 in the absence of cyanotic heart disease or pre-existing lung disease
- PaCO₂ > 6.5 kPa or 20mmHg over baseline PaCO₂
- Proven need for FiO₂ > 0.5 to maintain saturations > 92%
- Need for nonelective invasive or noninvasive mechanical ventilation

**Neurological:**

- Glasgow coma score (GCS) < 11
- Acute change in mental status with a decrease in GCS > 3 points from abnormal baseline

**Haematologic:**

- Platelet count < 80,000/mm³ or a decline of >50% in platelet count from the highest value recorded over the previous 3 days (for chronic haematology/oncology patients)
- International normalised ratio > 2

**Renal:**

- Serum creatinine > 2 times upper limit of normal for age or 2-fold increase in baseline creatinine

**Hepatic:**

- Total bilirubin > 4 mg/dl (not applicable for newborn)
- ALT 2 times upper limit of normal for age

~~~
Septic shock is sepsis and cardiovascular organ dysfunction.

**Cardiovascular dysfunction**

Despite administration of isotonic fluid bolus > 40ml/kg in 1 hour:

- Decrease in BP (hypotension) < 5th percentile for age or systolic BP > 2 SD below normal for age
- Need for vasoactive drug to maintain BP in normal range (dopamine > 5 μg/kg/min or dobutamine, adrenaline or noadrenaline at any dose)

Or

- Two of the following:
  - Unexplained metabolic acidosis: base deficit < 0.5 MEq/L, increased arterial lactate > 2 times the upper limit of normal, oliguria ie urine output < 0.5mls/kg/hr
  - Prolonged capillary refill > 5 seconds
  - Core to peripheral temperature gap > 3ºC

**Infection:** A suspected or proven (by positive culture, tissue stain, or polymerase chain reaction test) infection caused by any pathogen OR a clinical syndrome associated with a high probability of infection. Evidence of infection includes positive findings on clinical exam, imaging, or laboratory tests (e.g. white blood cells in a normally sterile body fluid, perforated viscous, chest X-ray consistent with pneumonia, petechial or purpuric rash, or purpura fulminans).

A. **Recognition of Sepsis**

The timely recognition of sepsis is a challenge for all paediatric staff. Clinical history and physical examination may reveal features in keeping with infection or some of the diagnostic criteria of SIRS. Some groups of children have an increased risk for sepsis including:

- Children younger than 3 months
- Children with chronic disease
- Children with immune deficiency, immunocompromise, asplenia or an incomplete vaccination record
- Children who have recently had surgery.

Keeping a high index of suspicion for sepsis in all children with signs of infection, risk factors or features of SIRS is the key to early diagnosis. The use of a Paediatric Early Warning Score (PEWS) highlights some of these features and facilitates their recognition and communication. A National Clinical Guideline PEWS is in development. If sepsis is suspected then tests that may confirm the diagnosis should be performed. In addition early management should commence as outlined in the “Paediatric Sepsis 6”.

**Recommendation 1P**

Sepsis screening should be used on all paediatric patients either presenting unwell or deteriorating whilst an in-patient as evidenced by deteriorating early warning scores (PEWS) or picked up on routine history and examination or by other means. **Grade 1C.**

Sepsis is diagnosed by the presence of SIRS criteria due to suspected or proven infection.

**Recommendation 2P**

Once the diagnosis of sepsis has been made it is recommended that the ‘paediatric Sepsis 6’ be performed within 1 hour, **Grade 1C.** The paediatric Sepsis 6 has been adapted from the adult Sepsis 6 and reflects some differences in priorities of management in the septic child.
### Paediatric Sepsis 6

<table>
<thead>
<tr>
<th>GET 3</th>
<th>GIVE 3</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>1. IV or IO assess and take bloods</strong>&lt;br&gt;• Blood culture&lt;br&gt;• FBC&lt;br&gt;• Glucose &amp; treat if low&lt;br&gt;• Blood gas</td>
<td><strong>1. High flow Oxygen</strong></td>
</tr>
<tr>
<td><strong>2. Urine output measurement</strong></td>
<td><strong>2. IV fluids</strong>&lt;br&gt;• Aim to restore circulating volume&lt;br&gt;• Titrate 20mls/kg isotonic fluid over 5-10 mins&lt;br&gt;• Repeat if necessary&lt;br&gt;• Caution for fluid overload&lt;br&gt;• Monitor for crepitations or hepatomegaly</td>
</tr>
<tr>
<td><strong>3. Early senior input</strong></td>
<td><strong>3. Broad spectrum antimicrobials</strong>&lt;br&gt;Within 1 hour</td>
</tr>
</tbody>
</table>

#### Practical guidance
As with the adult Sepsis 6, this represents the minimum intervention. Other blood tests, cultures or investigations may be required depending on the clinical scenario. Blood tests must be sent marked urgent and must be reviewed and acted upon in a timely fashion. This also applies to any investigations ordered.

The key difference between the adult and paediatric Sepsis 6 is the emphasis on early input from senior clinicians/specialists. In addition to senior clinical support at the bedside early involvement of Paediatric Intensive Care Unit (PICU) support is encouraged. Where PICU support is not on site a national 24 hour hotline is available for urgent referrals providing advice and arranging transfer. The national number is 1890 213 213.

#### Recommendation 3P
It is recommended that each healthcare facility create or adopt a treatment pathway for paediatric sepsis care that includes triggers for sepsis screening, facilitates the diagnosis of sepsis, severe sepsis/septic shock, and the treatment, resuscitation and appropriate referral to critical care.

These completed pathways should be included in the patient chart and their presence audited as a key performance indicator.

Pathways should clearly identify the stratification of patients into sepsis, severe sepsis or septic shock, include likely source of infection, if known, and the time first dose antimicrobials were administered. The paediatric Sepsis 6 should be included in the pathway.
The following apply to paediatric patients with severe sepsis/septic shock and act as a guide to implementation of the International Guidelines for the Management of Patients with Severe Sepsis and Septic Shock: 2012 in Ireland.


Recommendation 4P

To be complete within 3 hours Grade 1C

1. Complete the paediatric Sepsis 6
2. Measure lactate level
3. Fluid resuscitate for hypotension or lactate > 4 mmol/l with 20mls/kg isotonic crystalloid boluses - remember hypotension is a late sign in paediatric sepsis
4. Consider early mechanical ventilation if fluid resuscitation is > 40-60mls/kg*
5. Consider early use of inotropes and vasopressors for fluid refractory hypotension
6. Correct hypoglycaemia
7. Correct hypocalcaemia

*Rationale.
Due to low functional residual capacity, young infants and neonates with severe sepsis may require early intubation; however, during intubation and mechanical ventilation, increased intrathoracic pressure can reduce venous return and lead to worsening shock if the patient is not volume loaded.

Practical guidance
In patients presenting with severe sepsis/septic shock the 3 hour bundle is to be completed. This consists of the Sepsis 6, fluid resuscitation, antimicrobials, correction of electrolytes and early use of mechanical ventilation and inotropes unless shock is reversed.
Follow ACCM-PALS Guidelines.

Recommendation 5P

To be complete between 3 and 6 hours

1. Continue fluid resuscitation: obtain CVP measurement to guide; aim for > 8mmHg
2. Measure ScvO₂
3. ScvO₂ < 70% (cold shock): Transfuse HbG > 10g/dl; optimise arterial saturation through oxygen therapy, ventilation; consider adding milrinone 0.25 – 0.75 mcg/kg/min iv/io (intravenous or intraosseus) titrating to desired effect
4. ScvO₂ > 70% (warm shock): Noradrenaline 0.1 – 0.2 mcg/kg/min iv/io infusion, titrate to desired effect; consider vasopressin 0.2 – 2 mU/kg/min infusion titrated to desired effect
5. Remeasure blood gas and lactate
6. Consider adrenal insufficiency: hydrocortisone 2mg/kg (max 100mg) iv/io bolus; obtain baseline cortisol; if unsure, consider ACTH stimulation test; duration depends on response and laboratory evaluation
Reproduced with permission of Dr. Joseph Carcillo, MD.
B. Initial resuscitation

**Recommendation 6P**
For respiratory distress and hypoxaemia it is suggested to start with face mask oxygen or if needed and available, high flow nasal cannula oxygen or nasopharyngeal CPAP (NP CPAP). For improved circulation, peripheral intravenous access or intraosseus access can be used for fluid resuscitation and inotrope infusion when a central line is not available. If mechanical ventilation is required then cardiovascular instability during intubation is less likely after appropriate cardiovascular resuscitation, recognising that neonates/infants may require early intubation and ventilation. **Grade 2C**

**Recommendation 7P**
Therapeutic end points of resuscitation should be targeted. **Grade 2C**
These include:
- Heart rate normalised for age,
- Capillary refill of ≤2 seconds,
- Normal blood pressure for age,
- Normal pulses with no differential between peripheral and central pulses,
- Warm extremities,
- Urine output >1mL.kg⁻¹.hr⁻¹,
- Normal mental status,
- CVP > 8mmHg
- ScvO₂ saturation ≥70%
- Cardiac index between 3.3 and 6.0L/min/m²

**Recommendation 8P**
For the management of septic shock, Paediatric Intensive Care Unit Ireland recommends ACCM – PALS guidelines which is recommended by the Society of Critical Care Medicine.

**Recommendation 9P**
It is recommended to evaluate for and reverse pneumothorax, pericardial tamponade or endocrine emergencies in patients with refractory shock. **Grade 1C**

C. Antimicrobials and source control

**Recommendation 10P**
Empiric antimicrobials should be administered within one hour of the identification of severe sepsis. Blood cultures should be obtained before administering antimicrobials when possible but this should not delay administration of antimicrobials. The empiric drug choice should be changed as epidemic and endemic ecologies dictate (eg, H1N1, MRSA, chloroquine resistant malaria, penicillin-resistant pneumococci, meningococcal sepsis, recent ICU stay, neutropenia). **Grade 1D**

**Practical guidance**
The empiric drug choice should be tailored to age specific diseases e.g. neonates and group B Streptococcus.

**Recommendation 11P**
The use of clindamycin and anti-toxin therapies is suggested as appropriate treatment for toxic shock syndromes with refractory shock. **Grade 2D**

**Recommendation 12P**
Early and aggressive infection source control is recommended. **Grade 1D**
D. Fluid and electrolyte resuscitation

**Recommendation 13P**
In the industrialised world with access to inotropes and mechanical ventilation, it is suggested that initial resuscitation of hypovolaemic shock begins with infusion of isotonic crystalloids or albumin with boluses of up to 20mL/kg crystalloids (or albumin equivalent) over 5-10 minutes, titrated to reversing hypotension, increasing urine output and attaining normal capillary refill, peripheral pulses and level of consciousness without inducing hepatomegaly or crackles/crepitations.

If hepatomegaly or crackles exist then inotropic support should be implemented, not fluid resuscitation. In non-hypotensive children with severe haemolytic anaemia (severe malaria or sickle cell crises) blood transfusion is considered superior to crystalloid or albumin bolusing. **Grade 2C**

Target serum calcium levels > 1.0mmol/l

E. Inotropes/vasopressors/vasodilators

**Recommendation 14P**
Peripheral inotropic support is suggested to be used until central venous access can be attained in children who are not responsive to fluid resuscitation. **Grade 2C**

**Recommendation 15P**
It is suggested that patients with low cardiac output and elevated systemic vascular resistance states with normal blood pressure should be given vasodilator therapies in addition to inotropes. **Grade 2C**

It is recommended that inotropes be started if there is no adequate haemodynamic response to fluid boluses totalling 40-60mls/kg.

F. Extracorporeal membrane oxygenation (ECMO)

**Recommendation 16P**
It is suggested that ECMO should be considered for refractory paediatric septic shock and respiratory failure. **Grade 2C**

G. Corticosteroids

**Recommendation 17P**
It is suggested that timely hydrocortisone therapy be given in children with fluid refractory, catecholamine resistant shock and suspected or proven absolute adrenal insufficiency. **Grade 1A**
H. Blood products and plasma therapies

**Recommendation 18P**
There are similar haemoglobin targets for children as in adults. However, during resuscitation of shock with low superior vena cava oxygen saturation shock (<70%), haemoglobin levels of 10g/dL are targeted. After stabilization and recovery from shock and hypoxaemia then a lower target >7.0g/dL can be considered reasonable. **Grade 1B**

**Recommendation 19P**
Similar platelet transfusion targets in children as in adults are suggested. **Grade 1B**

**Recommendation 20P**
It is suggested that plasma therapies should be used in children to correct sepsis-induced thrombotic purpura disorders, including progressive disseminated intravascular coagulation, secondary thrombotic microangiopathy and thrombotic thrombocytopenic purpura. **Grade 2C**

I. Mechanical ventilation

**Recommendation 21P**
It is suggested that lung protective strategies should be used during mechanical ventilation. **Grade 2C**

**Practical guidance**
Consider early mechanical ventilation in refractory shock as per ACCM-PALS guidelines.

J. Sedation/analgesia/Drug toxicities

**Recommendation 22P**
The use of sedation with a sedation goal should be used in critically ill mechanically ventilated children with sepsis. **Grade 1D**

**Recommendation 23P**
Drug toxicity should be monitored because drug metabolism is reduced during severe sepsis, putting children at greater risk of adverse drug-related events. **Grade 1C**

K. Glycaemic control

**Recommendation 24P**
It is suggested that hyperglycaemia should be controlled using a similar target as in adults of ≤10mmol. Glucose infusion should accompany insulin therapy in newborns and children because some hyperglycaemic children make no insulin whereas others are insulin resistant. **Grade 2C**
L. **Diuretics and renal replacement therapy**

**Recommendation 25P**
It is suggested that diuretics should be used to reverse fluid overload once shock has resolved and if unsuccessful then continuous venovenous haemofiltration (CVVH) or intermittent dialysis to prevent >10% total body weight fluid overload should be considered. **Grade 2C**

M. **Deep Vein Thrombosis (DVT) prophylaxis**

**Recommendation 26P**
There is no recommendation on the use of DVT prophylaxis in prepubertal children with severe sepsis.

N. **Stress ulcer (SU) prophylaxis**

**Recommendation 27P**
There is no recommendation on the use of SU prophylaxis in prepubertal children with severe sepsis.

O. **Nutrition**

**Recommendation 28P**
Enteral nutrition is advised to be given to children who can be fed enterally and parenteral feeding in those who cannot. **Grade 2C**
3 National Clinical Guideline processes

3.1 Aim and scope of the National Clinical Guideline

The aim of the National Clinical Guideline is to facilitate the early recognition and appropriate treatment of sepsis in Ireland in order to maximise survival opportunity and minimise the burden of chronic sequelae. It is intended to be relevant to all healthcare staff involved in the care of patients who have sepsis.

This guideline outlines:
1. Broad measures that should be put in place for sepsis screening and subsequent action once sepsis is detected.
2. Key local, regional and national measures, including balancing measures (see section 3.7) that should be monitored to track improvements in sepsis management.

The purpose is to inform and guide healthcare staff in the recognition, treatment and appropriate referral of patients with sepsis with the intention of:
- Improving sepsis recognition
- Ensuring that patients with sepsis have ‘Sepsis 6’ (23) performed within one hour of sepsis recognition, identify patients with severe sepsis/septic shock and escalate care as appropriate
- Reducing mortality and morbidity from sepsis in Ireland
- Reducing the economic burden of sepsis.

3.2 Methodology

3.2.1 Preparation module

The National Sepsis Steering Group was established by the National Director of Clinical Strategy and Programmes in July 2013. This multidisciplinary group included representation from patients, acute and nonacute healthcare settings and a number of National Clinical Programmes as outlined in appendix 1. Prof. Kevin Rooney, National Clinical Lead on Sepsis, Healthcare Improvement Scotland and Professor of Care Improvement, University of the West of Scotland, was invited to join the group as an external advisor. The initial work of the group concentrated on the management of sepsis in the adult in-patient population and in the Emergency Department. The National Sepsis Steering Group agreed to adapt the surviving sepsis guidelines for Ireland as National sepsis guidelines.

A small working group (the Guideline Development Group) of the National Sepsis Steering Group was established in January 2014. This group was charged with adapting the surviving sepsis guidelines for Ireland in accordance with the National Clinical Effectiveness Committees (NCEC) requirements. It was agreed that the National Sepsis Steering Group would review drafts as appropriate and sign off the final version of the National Clinical Guideline prior to NCEC submission. The National Sepsis Steering Group nominated Dr. Vida Hamilton to lead this process and invited representation from members of the National sepsis Steering group as outlined in appendix 1. The Guideline Development Group members’ names, areas of the document they were primarily responsible for drafting and any potential conflicts of interest are outlined in appendix 1.

Membership of the National Sepsis Steering Group and of the Guideline Development Group was voluntary and this work was not funded by any public or private agency. In June 2014, Dr Vida Hamilton was appointed National Clinical Lead for Sepsis, a half-time secondment to the HSE for the purpose of leading the implementation process of the national guidelines.
The Guideline Development Group submitted drafts of the National Clinical Guideline to the National Sepsis Steering Group for feedback in February, March and June 2014. The final version of the National Clinical Guideline was accepted by the National Sepsis Steering Group in September 2014 and submitted to the National Clinical Effectiveness Committee on the 12th September.

### 3.2.2 Adaptation Process

**Search and Screen:** The guidelines that were of interest to the Guideline Development Group were those pertaining to the management of sepsis in adult, paediatric and maternity patients over the last three years, using the following parameters:

<table>
<thead>
<tr>
<th>Population:</th>
<th>Adult, paediatric and maternal patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intervention:</td>
<td>Management of sepsis</td>
</tr>
<tr>
<td>Timeframe:</td>
<td>Only guidelines published over the most recent three years (NICE, SIGN)</td>
</tr>
<tr>
<td>Literature sources:</td>
<td>Medline and EMBASE Plus ADAPTE guideline websites see below</td>
</tr>
<tr>
<td>Concept and Key words:</td>
<td>Sepsis, infection, guidelines, management.</td>
</tr>
</tbody>
</table>

The inclusion and exclusion criteria that were used assist in the search and retrieval of guidelines were the following:

<table>
<thead>
<tr>
<th>Inclusion criteria</th>
<th>Exclusion criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>Evidence-based guidelines only (guidelines must include a report on systematic literature and explicit links between individual recommendations and their supporting evidence)</td>
<td>Guidelines written by a single author not on behalf of an organisation (for validity a guideline needs multidisciplinary input)</td>
</tr>
<tr>
<td>National and/or international guidelines only</td>
<td>Guidelines published without references (it is necessary to know that the guidelines and recommendations were based on best, current evidence)</td>
</tr>
<tr>
<td>Peer reviewed publications only</td>
<td></td>
</tr>
<tr>
<td>Written in the English language</td>
<td></td>
</tr>
</tbody>
</table>

The initial systematic search for sepsis related guidelines was performed in mid-December, 2013 (13/12/2013). As part of this systematic search for guidelines, Sepsis 6 emerged as a piece of guidance but not as a complete guideline. The Sepsis 6 guidance, although technically excluded from the systematic review because it was not an actual guideline, was referenced a number of times in the literature, particularly associated with the Sepsis Trust and the ‘Survive Sepsis’ initiative so, the decision was taken by the Guideline Development Group to include this piece of guidance in the evidence evaluation process.

The databases searched included Medline and EMBASE plus the ADAPTE guideline websites outlined in appendix 10. The numbers of retrieved and excluded guidelines are shown in figure 6. Surviving Sepsis Campaign was the guideline chosen for consideration for use in the Irish context with additional incorporation of Sepsis 6 into the key recommendations.

---

6 NICE and SIGN routine practice for guideline update  
7 [http://sepsistrust.org/](http://sepsistrust.org/)  
8 [http://survivesepsis.org/](http://survivesepsis.org/)
Assessment of retrieved guidelines: The quality of the guideline was assessed by three appraisers from the Guideline Development Group and one from the Department of Health using the AGREE II tool. The overall results of the appraisal are shown in figure 7. Domain comments by reviewers are outlined in appendix 11.

Figure 7 Surviving Sepsis Campaign Agree II domain scores
The findings from the literature search and the quality of the retrieved guidelines supported the Guideline Development Group decision to adapt the Surviving Sepsis guideline for the Irish setting with inclusion of the Sepsis 6 as a recommendation.

**Decision and selection of recommendations:** Acceptability and applicability of each of the guideline recommendations was appraised by the Guideline Development Group in terms of organisational and cultural context such as health services, expertise and resources available to facilitate the implementation of the Surviving Sepsis guideline and Sepsis 6 recommendations.

Each recommendation was reviewed initially by the working group members of the Guideline Development Group which included representation from ICU, maternity, paediatric and microbiology specialties. The initial consideration of the recommendations was then brought to the wider Guideline Development Group for consultation. Where modifications to the original recommendations were made to accommodate the Irish context or due to higher grade of emerging evidence, these modifications were outlined and justified accordingly using the multidisciplinary, local expertise of the Guideline Development Group.

### 3.3 Financial impact of sepsis

The Guideline Development Group examined the economic impact of sepsis and its management and a budget impact analysis was completed with the support of HIQA. Full details of the findings are in appendix 14.

### 3.4 External review

The Guideline Development Group sent this National Clinical Guideline for review to Dr. John Bates, Consultant in Anaesthesia and Intensive Care, Galway University Hospital and Dr. Christian Subbe, Consultant in Acute Respiratory and Critical Care Medicine, School of Medical Sciences, Bangor university, UK, with no payment or gratuity.

The Guideline Development Group is very grateful to both reviewers and appreciate the time commitment that was involved in their review.

The guideline was noted to be extremely comprehensive and to have brought together a lot of resources. It is acknowledged that there is an update on sepsis definition ‘the San Francisco Definition’, which corresponds to the current severe sepsis definition, in progress. This update is evolving in order to try and address the problem of antimicrobial over-prescription. This guideline emphasises making the diagnosis of infection or suspected infection as fundamental to sepsis screening, along with the approach of reassessing the patient with the results of investigations and microbiological cultures and the prompt to stop antimicrobials if sepsis is found not to be the cause of the physiological deterioration, as per the ‘Start Smart, then Focus’ national antimicrobial prescribing care bundle. Other additions and amendments were made as appropriate.

### 3.5 Procedure for update of this guideline

The Guideline Development Group agreed that that it will review its publication on a three-yearly basis and update as appropriate, in accordance with the Surviving Sepsis Campaign and international best evidence. Therefore, this guideline will be reviewed again in 2017.
3.6 Implementation of this guideline

3.6.1 Emergency Department/Acute Medical Assessment Units (AMAUs)

In aiming to reduce sepsis mortality and morbidity in the Emergency Department (ED) and the AMAU, three key primary drivers have been described:

- Early identification of septic patients
- Ensuring best practices in the ED and the AMAU
- Seamless transitions of care.

Each of these drivers has a series of secondary drivers – key action strategies that will lead to successful improvement. An example of a driver diagram for the management of sepsis in the ED is outlined in appendix 12. Measurement of lactate is an essential component of the management of patients with sepsis – it is essential that EDs and AMAUs have access to timely lactate results, therefore the Guideline Development Group recommend that all EDs and AMAUs should have point of care lactate measurement available within the department to avoid any delays with results reporting and/or specimen transport.

3.6.2 Education program

It is recommended that sepsis education be embedded in undergraduate medical education so that qualifying doctors have a comprehensive understanding of the systemic inflammatory response and the pathophysiological changes manifested by this response, in particular the mechanism of evolution of organ dysfunction and shock.

It is recommended that sepsis education be embedded in nursing and midwifery undergraduate education leading to an understanding of the systemic inflammatory response and its manifestations.

It is recommended that attending a formal sepsis education programme be a mandatory criteria for postgraduate qualification in all medical disciplines and in order to work in the Irish Healthcare System.

It is recommended that ongoing sepsis recognition and treatment training occur in all acute hospitals and that this training be informed by audit data from the local institution and national database (HIPE).

Roles and responsibilities

- **Medical schools**: Implement sepsis education in undergraduate curriculum
- **Postgraduate training bodies**: Identify or embed a formal sepsis education programme (e.g. simulation training for the acutely deteriorating patient) and ensure all trainees attend.
- **Department of Health, HSE and Senior Hospital Management**: Support, resource and facilitate ongoing sepsis training and the collection of audit data for performance feedback.
- **Clinical staff**: Participate in ongoing sepsis training, upgrading of processes based on audit feedback and new development in sepsis treatment.

3.6.3 Process of implementation

The aim of implementing guidelines is to reduce variability in clinical practice and improve patient outcome.

Barriers to implementation include:

- **Lack of awareness of guidelines and lack of familiarity with the subject matter**: The implementation of the guidelines is to be accompanied by a robust education programme and the long term educational strategy is outlined in section 3.6.2.
• **Lack of agreement with guidelines:** This guideline was internally and externally peer reviewed prior to publication.

• **Lack of self-efficacy:** The initial diagnosis of sepsis particularly in the early phase can be difficult. Triggers for sepsis screening on presentation to the ED/AMAU and for both adult and paediatric in-patients as well as ongoing sepsis training will facilitate sepsis recognition and streamline treatment.

• **Lack of outcome expectancy:** Feedback from local and national audit will support practice change as will international data which supports these process improvements.

• **Inertia of previous practice:** Sepsis treatment is ongoing with considerable variation in practice and a possible gap between perception and reality of clinical practice. A survey of therapy habits in sepsis in Germany (37) reported wide gaps, for example, in low tidal volume ventilation for patients with acute lung injury or acute respiratory distress syndrome the perception of compliance was 79.9% whilst actual compliance was 2.6%. It is planned to involve treating clinicians in the implementation process and to resource this process with a view to easing workload and thus facilitate practice change. Audit data will support reducing the gap between perception and practice.

• **External barriers:**
  - **Guideline related:** Every effort has been made to make this guideline clear and user friendly, however, adaptations may be required for clarification, improvement and to include new treatment recommendations. A system of regional and national forums for discussion and feedback will ensure that all participants in sepsis care have a voice to enact improvement.
  - **Patient related:** Sepsis awareness in the population needs to be increased in order to ensure timely presentation to the healthcare system.
  - **Environment related:** Guidelines can not be successfully implemented if the resources required to follow them are not available. (38)

**Roles and Responsibilities**

- **Nationally:** The Department of Health to develop appropriate policy measures to underpin the implementation of this guideline and the HSE to provide the resources to implement and support the guidelines.

- **The National Sepsis Team** (National Clinical Lead, National Sepsis Steering and Advisory Committees, National Clinical Nurse Lead, Project Manager): The National Sepsis team is responsible for advising on guideline and guideline implementation and educational support.

- **The Regional Team:** A regional sepsis support officer to work with the hospitals in their region/ Hospital Group supporting implementation, interacting with Senior Hospital Management and the HSE on behalf of clinicians to ensure they have adequate resources. They would collate audit data for local, regional and national feedback, hosting local and regional forums for presenting data, discussing successes, failures and process adaptations. They would attend national forums for data feedback and process adaptation discussions and recommendations and bring back and help implement change.

- **The Local Team:** Each acute hospital should have a sepsis team consisting of a Lead Clinician and Nurse at the least, varying depending on the size of the institution. The local team will support guideline implementation, sepsis training and audit data collection. Hospital senior management must support the local team in their role. Each healthcare staff member has a role to play in the recognition and management of sepsis by adhering to best practice as outlined in this guideline. This guideline should be reviewed by the healthcare facilities senior management teams in conjunction with the relevant specialists to plan implementation of the recommendations. This will enable the facility to ensure that the recognition and management of sepsis is a key patient safety issue for the facility.

**Organisational responsibility:** Within each healthcare facility the CEO/General Manager has corporate responsibility for implementation of the National Clinical Guideline.
All healthcare staff should: Comply with this National Clinical Guideline, related policies and procedures; adhere to their code of conduct and scope of practice guidelines as appropriate to their role and responsibilities and maintain competency in the recognition and management of sepsis.

3.7 Audit criteria

To ensure that this guideline positively impacts on patient care, it is important that it is audited. Audit is recommended to support continuous quality improvement in relation to the implementation of the National Clinical Guideline. The roll out of the National Intensive Care Audit database will contribute to the collection of accurate data on patients with severe sepsis/septic shock including hospital origin (i.e. ED or ward), mortality rates and sources of infection.

**Primary outcome:** Mortality outcome of 20-30% in patients with severe sepsis/septic shock

<table>
<thead>
<tr>
<th>Number of deaths in patients with severe sepsis and septic shock</th>
<th>Number of patients with severe sepsis and septic shock</th>
</tr>
</thead>
</table>

**Secondary outcome:**
- Reduced ICU length of stay
- Reduced hospital length of stay.

**Audit requirements:**
- Clear coding for sepsis, severe sepsis and septic shock
- Clear documentation of ICU length of stay, this must identify the day that the patient is deemed fit for discharge from ICU by the critical care team
- Hospital length of stay, this must identify the day the patient is deemed fit for discharge home or to long-term residential facility
- Documentation of sepsis, severe sepsis and septic shock as cause of or contributory to death.

**For educational and research purposes:**
- Organism if identified e.g. pneumococcus or no organism identified
- Site of infection e.g. respiratory if known or site not known.
- Time to first dose antibiotics, blood cultures before antibiotics and early fluid resuscitation have been identified as being associated with improved outcome.
- Time to critical care review and ICU admission reflect adequacy of critical care staffing and capacity and have resource planning implications.
- ICU admission rates, ICU length of stay and hospital length of stay are all secondary outcomes.

* It is suggested that organ dysfunctions be listed in the medical chart as:
  - Acute renal failure
  - Acute hepatic failure (not raised LFTs)
  - Acute respiratory failure
  - DIC
  - Encephalopathy
  - Critical illness myopathy
  - Septic shock.

**Responsibility**

It is the responsibility of the National Sepsis team to advise on mechanisms to facilitate the collection of relevant data.

It is the responsibility of the regional and local sepsis teams to implement and feedback and adapt these mechanisms.

It is the responsibility of the treating clinician to document accurately and following the recommendations as appropriate.
3.7.1 Measuring Improvements in Hospitals

Audit data collection, analysis and feedback are a fundamental requirement to the successful implementation of any performance improvement initiative.

Responsibility

It is the responsibility of the HSE and senior hospital management team to ensure it is resourced for data collection and analysis.

3.7.2 Measuring Improvements in Ireland

The HIPE system will measure all cases with sepsis, severe sepsis and septic shock documented in the notes. Thus, relatively simple measures can result in good capture of the incidence of sepsis in Ireland and facilitate the monitoring of improvements in outcomes in response to this campaign.

The key is to ensure that sepsis, if present, is routinely recorded in the chart, and routinely coded in the discharge summary. Once HIPE includes the appropriate ICD-10-AM diagnosis codes, it can report easily on frequency and characteristics of varying presentations of sepsis, and deliver an accurate picture of the status of sepsis within Irish hospitals. By “piggy-backing” onto an existing data collection structure, it avoids having to set up a parallel data collection process, with all of its consequent repercussions in terms of time, resources, training and IT support (see appendix 15). Data analysis and reporting could be further facilitated through the NQAIS system of Health Atlas.

3.7.3 Measurement Plan

Each ward/unit/directorate should agree a measurement plan for sepsis that is practical and integrates into other measurements for improvement. Patients can present with sepsis on initial presentation to the ED or AMAU or develop sepsis while in hospital, therefore, it is important that measuring progress with sepsis management includes each instance.

Sources of data: The patient’s medical notes, medication chart, NEWS chart, IMEWS chart and fluid balance chart.

ED/AMU: A suggested plan would be to sample five patients with sepsis diagnosis per week. If total patient numbers are less than 20 per month, all patients should be included in sample. Take the sepsis diagnosis time as time zero. Patients who are diagnosed with sepsis should have interventions done within one hour of time zero.

Wards: Collect data on one day each week.  
- Look at all patients on the ward that day.  
- Identify any with NEWS 4 (5 when on supplementary O2) or more at any time during the past week.  
- Take time zero as the time the patient developed a NEWS score of 4 (5 when on supplementary O2) + two or more SIRS criteria + suspicion of infection, i.e. time of diagnosis of sepsis not time of NEWS call. Patients who develop sepsis should have interventions done within one hour of time zero.

Exclusion Criteria: Patients with a terminal illness should NOT be excluded unless the decision not to escalate care clearly excludes further active treatment with antibiotics or IV fluids in the ward. There may be a requirement to exclude patients from specific elements of Sepsis 6 based on patient specific clinical criteria, this should be clearly documented.
3.7.4 Balancing Measures

Excessive or inappropriate antibiotic use is associated with increased antimicrobial resistance, *C. difficile* infection and adverse drug reactions.

There are at least three potential unintended consequences of implementing Sepsis 6 screening:

1. Patients who have deteriorated but have no evidence of sepsis/potential infective source are commenced inappropriately on antibiotic therapy.
2. Patients with suspected sepsis are commenced on inappropriate antibiotic therapy that is not in line with local guidelines.
3. Empiric antibiotic therapy that has been commenced in a patient with suspected sepsis is not reviewed at 24-48 hours as recommended by the Start Smart, then Focus Antibiotic Care bundle. At this stage an antimicrobial prescribing decision needs to be made and one of the five prescribing decision options chosen as follows:

- Stop antibiotic(s) - no evidence of bacterial infection, or infection resolved
- Switch from intravenous to oral antibiotic(s) - if patient meets criteria for oral switch as outlined in local antibiotic prescribing guidelines
- Change antibiotic(s) to a narrower spectrum agent, if possible
- Continue current antibiotic(s) and review again after further 24 hours
- Outpatient parenteral antibiotic therapy (OPAT) - consult with local OPAT team.

All hospitals should have antimicrobial stewardship programmes in place that monitor process or outcome measures to ensure that antibiotic are not being prescribed unnecessarily, due to inappropriate application of Sepsis 6. Examples of process and outcome measures that would be appropriate for use as balancing measures are outlined in table 12. Ensuring antibiotics are use appropriately for all infections, not just those associated with sepsis, will help to ensure effective antibiotic therapy is available when cases of sepsis do occur.

### Table 12 Balancing measures for monitoring implementation of Sepsis 6

<table>
<thead>
<tr>
<th>Measure</th>
<th>Details</th>
</tr>
</thead>
</table>
| **Appropriate Antibiotic Use** | • Audit of compliance with the Start Smart, Then Focus antibiotic care bundle  
• Audit of proportion of empiric antibiotic prescription that complies with local prescribing guidelines  
• Monitoring of hospital antibiotic consumption, with particular emphasis on broad spectrum antibiotics (e.g. third generation cephalosporins, antipseudomonal penicillins, carbapenems, fluoroquinolones) |
| **Consequences of Antibiotic Use** | • Antimicrobial resistance rates – for example  
  – Proportion of antimicrobial resistance among bloodstream isolates,  
  – Rates of colonisation with antimicrobial resistant pathogens such as MRSA or multiple drug-resistant Gram-negative bacteria  
• New cases of hospital-acquired *Clostridium difficile* infection  
• New cases of hospital-acquired Candida infections |
| **Medication Safety** | • Medication safety incidents associated with antibiotic therapy |
Appendices

Appendix 1: National sepsis steering committee

Terms of Reference:
The Sepsis Steering Group was formed in July 2013 with the aim of developing a framework to improve awareness and recognition of sepsis in the pre-hospital and hospital environments. Specifically, the Sepsis Steering Group aims to:

In the pre-hospital environment:
- Use available data and consensus definitions to establish a robust, reproducible system of identifying patients with or at risk of sepsis, severe sepsis and septic shock in the pre-hospital environment.
- Create guidelines in the administration of therapies specific to sepsis in the pre-hospital environment. Disseminate by sharing existing good practice regarding sepsis recognition tools and pathways.
- Create new and develop existing education materials and electronic materials and recognition tools
- Make recommendations to relevant bodies to implement these guidelines nationally.
- Develop metrics and data sets to allow the HSE and partner organisations to monitor performance

In secondary care:
Use available data and consensus definitions to establish a robust, reproducible system of identifying patients with or at risk of sepsis, severe sepsis and septic shock in the hospital environment.
- Disseminate by sharing existing good practice regarding sepsis recognition tools and pathways
- Develop metrics and data sets to allow the HSE and partner organisations to monitor performance
- Create new and develop existing education materials and electronic materials and recognition tools

Organisationally:
- Engage and work with relevant bodies, medical colleges and professional health related organisations to embed standards for sepsis recognition and care.

Ultimately, the Sepsis Steering Group will aim to inform, provide the tools for benchmarking and provide guidance on the national implementation of sepsis recognition and immediate therapy.
**Membership** Full details of membership including contributions, affiliations, representative bodies and conflicts of interest are outlined below.

<table>
<thead>
<tr>
<th>Member</th>
<th>Title</th>
<th>Role</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fidelma Fitzpatrick</td>
<td>Consultant Microbiologist, RCPI/HSE Clinical lead – HCAI and AMR prevention</td>
<td>Chair</td>
</tr>
<tr>
<td>Kevin Rooney</td>
<td>National Clinical Lead on Sepsis Healthcare Improvement Scotland</td>
<td>Member</td>
</tr>
<tr>
<td>Áine Carroll</td>
<td>National Director Clinical Strategy and Programme</td>
<td>Honorary member</td>
</tr>
<tr>
<td>Philip Crowley</td>
<td>National Director Quality and Patient Safety</td>
<td>Member</td>
</tr>
<tr>
<td>Vida Hamilton</td>
<td>NCP for Anaesthesia Representative</td>
<td>Member</td>
</tr>
<tr>
<td>Gary Courtney</td>
<td>Lead of the NCP for Acute Medicine</td>
<td>Member</td>
</tr>
<tr>
<td>Eilish Croke</td>
<td>National Lead for Early Warning Score Project</td>
<td>Member</td>
</tr>
<tr>
<td>Michael Turner</td>
<td>Lead of the NCP for Obstetrics and Gynaecology</td>
<td>Member</td>
</tr>
<tr>
<td>Michael Power</td>
<td>Lead of the NCP for Critical Care</td>
<td>Member</td>
</tr>
<tr>
<td>Frank Keane</td>
<td>Lead of the NCP for Surgery</td>
<td>Member</td>
</tr>
<tr>
<td>Cathal O’Donnell</td>
<td>National Ambulance Service</td>
<td>Member</td>
</tr>
<tr>
<td>Una Geary</td>
<td>Lead of the NCP for Emergency Medicine</td>
<td>Member</td>
</tr>
<tr>
<td>John Fitzsimons</td>
<td>Chair of PEWS steering committee</td>
<td>Member</td>
</tr>
<tr>
<td>Gethin White</td>
<td>Library Services DSH</td>
<td>Member</td>
</tr>
<tr>
<td>Geoff King</td>
<td>Lead of the NCP for Transport Medicine and National Clinical Lead for Pre-hospital Care</td>
<td>Member</td>
</tr>
<tr>
<td>Colette Cowan</td>
<td>Director of Nursing/Midwifery reference group representative</td>
<td>Member</td>
</tr>
<tr>
<td>Nora O’Mahony</td>
<td>Nursing/Midwifery Practice Development Coordinator</td>
<td>Member</td>
</tr>
<tr>
<td>Linda Dillon</td>
<td>Patient advocacy representative</td>
<td>Member</td>
</tr>
<tr>
<td>Joe Clarke</td>
<td>Representative for primary care</td>
<td>Member</td>
</tr>
<tr>
<td>Colm Henry</td>
<td>Clinical Director representative</td>
<td>Honorary member</td>
</tr>
<tr>
<td>Declan McKeown</td>
<td>Public Health Doctor Representative Health intelligence</td>
<td>Member</td>
</tr>
<tr>
<td>Niamh Appleby</td>
<td>Specialist Registrar, NCHD representative</td>
<td>Member</td>
</tr>
<tr>
<td>Tony McNamara</td>
<td>CEO/Hospital manager representative</td>
<td>Member</td>
</tr>
<tr>
<td>Diarmuid O’Shea</td>
<td>Representative of NCP for Older Persons</td>
<td>Member</td>
</tr>
<tr>
<td>Robert Cunney</td>
<td>Representative from RCPI Hospital Antimicrobial Stewardship Committee</td>
<td>Member</td>
</tr>
<tr>
<td>Fiona McDaid</td>
<td>Emergency Nursing Representative</td>
<td>Member</td>
</tr>
<tr>
<td>Rachel Gilmore</td>
<td>Emergency Programme Representative</td>
<td>Member</td>
</tr>
<tr>
<td>Aveen Murray</td>
<td>Representative of National Director, CSP</td>
<td>Member</td>
</tr>
<tr>
<td>Karen Power</td>
<td>HSE Research Project Manager Obs and Gynae</td>
<td>Member</td>
</tr>
<tr>
<td>Idowu Akingbagbohun</td>
<td>Administrative Support</td>
<td></td>
</tr>
</tbody>
</table>
Paediatric Guideline Development Group: Dr. Cathy McMahon, Consultant Paediatric Intensivist, Our Lady’s Children’s Hospital, Crumlin, Dr. Dermot Doherty, Consultant Paediatric Intensivist, Children’s University Hospital, Temple Street. The National Sepsis Steering Committee are very grateful for their expert input into the development of the paediatric guideline.

Conflict of Interest
Membership of the Guideline Development Group was voluntary and the work was not funded by any public or private agency.

Professor Kevin Rooney, Consultant in Anaesthesia and Intensive Care Medicine Royal Alexandra Hospital and Professor of Care Improvement at University of the West of Scotland wishes to declare that in the last 5 years, he has received research grants and income from consultancy work from Abbott Point of Care but that he has no other conflicts of interest.

No conflicts of interest were declared by any other members of the Guideline Development Group.

Terms of Reference: National Sepsis Workstream
The purpose of the National Sepsis Workstream is to guide the implementation process of the National Clinical Guideline No. 6 Sepsis Management with the aim that every person in the Republic of Ireland who develops sepsis has a pathway to access appropriate care as outlined in the guidelines.

It is lead by the National Clinical Lead for Sepsis, and is supported by the National Sepsis Steering Committee and the National Sepsis Advisory Group. The Steering Committee will meet quarterly and has representation from relevant stakeholders as outlined in its terms of reference, it will act to advise the group on implementation issues and improvements within their area of expertise. The chair will be nominated by the Director of Clinical and Strategy Programmes for a minimum two-year term to a three-year maximum term.

The Advisory group has the more specific role in advising and developing education and awareness programmes and will be made up of individuals with expertise and enthusiasm in these two areas. The Advisory group will have an ongoing role with more frequent meetings and will report to the Clinical Lead and the Steering Committee. It will discuss and formulate updates to the National Guidelines every three years and present these to the National Sepsis Steering Committee for review and ratification.

The National Clinical Lead and National Sepsis Steering Committee will report to the National Director of Clinical Strategy and Programmes and that office will provide administrative support until the appointment of the workstream programme manager.

Patient Advocacy Representative
First and foremost from a patient perspective the early diagnosis of sepsis could become the difference between life and death. Therefore the pathways that a patient travels within the health system as a whole, and the identification of possible sepsis becomes vitally important for the patient to have the best chance of a good recovery.

If sepsis is suspected and identified and treatment is initiated in the timeframe outlined in the new National Clinical Guideline, this can clearly lead to a better outcome for the patient. Before any of the identifying and treatment begins, it is clear that sepsis needs to be in everyone’s mind as a possibility in all patient groups, not only the patients that present clearly very ill. This mindset will be a change for many medical professionals.
It is therefore imperative that all healthcare providers, the Department of Health, the Health Service Executive, Senior Hospital Management and all healthcare workers implement the National Clinical Guideline – Sepsis Management.

A dear friend, husband, father and brother aged 55 who had just started on interferon with an injection port, presented on a Monday very unwell, it was Tuesday before sepsis was diagnosed, by Wednesday the port was still in place, Wednesday evening the port was finally removed, Thursday he was placed on life support with the explanation to his wife that it would allow him to rest and allow the drugs to work. Two of their daughters were in Australia and his wife was not made aware of just how serious his condition was, so she therefore did not call her daughters home until the following Monday when his condition had deteriorated and he passed away on Tuesday one week after presenting to the hospital and his daughters arrived home on Wednesday.

The devastation of his loss to his family two years on continues, trying to deal with his very sudden loss is more then enough, without all the questions as to how and why, and if more could have been done. There were some formal inquests where some family members wanted to take matters further and some did not, and then there were all business affairs that needed attending and so the impact goes on and on.

Another friend’s parent having had very successful heart surgery and was recovering well seven days later became suddenly unwell and passed away from sepsis.

For the loved ones of any patient that has passed away from sepsis to now know that with the National Clinical Guideline – Sepsis Management in place there will be a greater chance of early pick up and therefore recovery will, I am sure, bring great comfort.

It has been my privilege to represent the patients on the Sepsis Steering Committee and I must thank our chairperson Fidelma Fitzpatrick and all the many contributors for their valued input and sense of urgency in bringing together the National Clinical Guideline – Sepsis Management.

Linda Dillon
### Appendix 2: The National Early Warning score card

<table>
<thead>
<tr>
<th>The National Early Warning Score Card</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>SCORE</strong></td>
</tr>
<tr>
<td>Respiratory Rate (bpm)</td>
</tr>
<tr>
<td>SpO₂ (%)</td>
</tr>
<tr>
<td>Inspired O₂ (FiO₂)</td>
</tr>
<tr>
<td>Systolic BP (mmHg)</td>
</tr>
<tr>
<td>Heart Rate (BPM)</td>
</tr>
<tr>
<td>AVPU/CNS Response</td>
</tr>
<tr>
<td>Temp (°C)</td>
</tr>
</tbody>
</table>

Escalate care regardless of the score if you are concerned about a patient.
Appendix 3: ISBAR Communication tool – patient deterioration

<table>
<thead>
<tr>
<th>ISBAR Communication Tool SAMPLE</th>
<th>Patient Deterioration</th>
</tr>
</thead>
</table>
| **I** Identify | Identify:  
Recipent of handover information  
Patient |
| **S** Situation | Situation:  
Why are you calling?  
(Identify your concerns) |
| **B** Background | Background:  
What is the relevant background? |
| **A** Assessment | Assessment:  
What do you think is the problem? |
| **R** Recommendation | Recommendation:  
What do you want them to do? |

Reproduced and adopted with permission from Dr S. Marshall, Monash University, Australia.
Appendix 4: Adult in-patient sepsis screening form (sample)

Sepsis Screening Form

Complete this form and apply if the National Early Warning Score (NEWS) is ≥ 4 (5 on supplementary O2), or if infection is suspected

Doctor must review within 30 mins (use ISBAR). DOCTOR TO COMPLETE REMAINDER OF THIS DOCUMENT AS APPROPRIATE

Are any 2 or more modified Systemic Inflammatory Response Syndrome (SIRS) criteria present

☐ Respiratory rate > 20 (bpm)
☐ Heart rate > 90 (bpm)
☐ WCC < 4 or > 12 x 10^9/L
☐ Temperature <36 or >38.3 (°C)
☐ Acutely altered mental status
☐ Bedside glucose >7.7mmol/L (in the absence of diabetes mellitus)

+ INFECTION SUSPECTED

Note: Some groups of patients, such as older people, may not meet the modified SIRS criteria, even though infection is suspected. Where this occurs check for signs of organ dysfunction and raised biomarkers such as C-reactive protein (CRP)

☐ NO

☐ YES. THIS IS SEPSIS

Sepsis Six Regimen must be completed within 1 hour

Has a decision been made NOT to escalate care (excluding further treatment)?

☐ NO proceed

☐ YES do not proceed

SEPSIS SIX – aim to complete within 1 hour

1. Blood cultures before giving antibiotics
   Do not delay antibiotic administration >1 hour if blood cultures are difficult to obtain. Send samples from potentially infected sites eg. sputum, urine, wounds, WCC/CVC. Consider source control.
2. Lactate and FBC
3. Urine output measurement

Laboratory tests must be requested as EMERGENCY and aim to have results available and acted on within the hour

Look for signs of organ dysfunction:

☐ Systolic BP < 90 or Mean Arterial Pressure < 65 or Systolic BP more than 40 below patient’s normal
☐ New need for oxygen to achieve saturation > 90%
☐ Lactate > 2 mmol/L (following administration of fluid bolus)
☐ Urine output < 0.5 ml/kg for 2 hours – despite adequate fluid resuscitation
☐ Acutely altered mental status
☐ Glucose > 7.7 mmol/L (in the absence of diabetes)
☐ Creatinine > 177 micromol/L
☐ Bilirubin > 34 micromol/L
☐ PTR > 1.5 or aPTT > 60s
☐ Platelets < 100 x 10^9/L

Any organ dysfunction: THIS IS SEVERE SEPSIS

Registrar or Consultant to review immediately.

Reassess frequently in 1st hour.

Consider other investigations and management

Look for signs of septic shock

(following administration of fluid bolus)

☐ Lactate > 4 mmol/L
☐ Hypotensive (Systolic BP < 90 or MAP < 65)

If either present: THIS IS SEPTIC SHOCK

Critical care consult required

☐ Consultant referral

☐ Consider transfer to a higher level of care

Critical care consult requested

A critical care review may be requested at any point during this assessment, but is required for patients with Septic Shock. In a hospital with no critical care unit, a critical care consult must be made and transfer to a higher level of care considered, if appropriate, following the consult.

Doctor’s Name: ____________________________ MCRN: __________

Doctor’s Signature: ____________________________ Date: __________

Time: __________

Any organ dysfunction: THIS IS SEVERE SEPSIS

Registrar or Consultant to review immediately.

Reassess frequently in 1st hour.

Consider other investigations and management

File this document in patient notes - Document management plan.
Appendix 5 Emergency department sepsis pathway (sample)

Emergency Department Sepsis Pathway

ADULT PATIENTS

There is separate sepsis criteria for women in pregnancy

CLINICIAN TO COMPLETE THIS SECTION

Date: ____________________________ Time Started: ____________________________

Clinician's Name: ____________________________

Clinician's Signature: ____________________________

MCRN/NMBI PIN: ____________________________

Patient label here

INFECTION SUSPECTED +

any 2 or more modified Systemic Inflammatory Response Syndrome (SIRS) criteria present

☐ Respiratory rate > 20 (bpm) / Hypoxia
☐ Heart rate > 90 (bpm)
☐ WCC < 4 or > 12 x 10⁹/L
☐ Temperature <36 or >38.3 (°C)
☐ Acutely altered mental status
☐ Bedside glucose > 7.7 mmol/L
☐ Lactate > 2 mmol/L

Note: Some groups of patients, such as older people, may not meet the modified SIRS criteria, even though infection is suspected. Where this occurs check for signs of organ dysfunction and raised biomarkers such as C-reactive protein (CRP)

☐ YES. THIS IS SEPSIS

Sepsis Six Regimen must be completed within 1 hour

TAEK 3

1. Blood cultures before giving antimicrobial
   Do not delay antibiotic administration > 1 hour if blood cultures are difficult to obtain. Send samples from potentially infected sites eg. sputum, urine, wounds, IVC/CVC. Consider source control.
2. Lactate and FBC
3. Urine output measurement

Laboratory tests/Investigations must be requested as EMERGENCY and aim to have results available and acted on within the hour

Look for signs of organ dysfunction:

☐ Systolic BP < 90 or Mean Arterial Pressure < 65 or Systolic BP more than 40 below patient’s normal
☐ New need for oxygen to achieve saturation > 90%
☐ Lactate > 2 mmol/L (following administration of fluid bolus
☐ Urine output < 0.5ml/kg for 2 hours – despite adequate fluid resuscitation
☐ Acutely altered mental status
☐ Glucose > 7.7 mmol/L (in the absence of diabetes)
☐ Creatinine > 177 micromol/L
☐ Bilirubin > 34 micromol/L
☐ PTT > 1.5 or aPTT > 60s
☐ Platelets < 100 x 10⁹/L

Any organ dysfunction: THIS IS SEVERE SEPSIS

Registrar or Consultant to review immediately. Reassess frequently in 1st hour. Consider other investigations and management

( ALWAYS USE CLINICAL JUDGEMENT)

Look for signs of septic shock

( following administration of fluid bolus)

☐ Lactate > 4 mmol/L
☐ Hypotensive (Systolic BP < 90 or MAP < 65)

If either present: THIS IS SEPTIC SHOCK

Critical care consult required

☐ Consider transfer to a higher level of care

Critical care consult requested

A critical care review may be requested at any point during this assessment, but is required for patients with Septic Shock. In a hospital with no critical care unit, a critical care consult must be made and transfer to a higher level of care considered, if appropriate, following the consult.

Doctor's Name: ____________________________ MCRN: ____________________________

Doctor's Signature: ____________________________ Date: ____________________________

File this document in patient notes - Document management plan.

Time Completed: ____________________________
## Sepsis Antibiotic Prescription

<table>
<thead>
<tr>
<th>Date</th>
<th>Antibiotic</th>
<th>Dose</th>
<th>Route</th>
<th>Time</th>
<th>Signature</th>
<th>MCRN</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

## Sepsis Fluid Resuscitation Prescription

**Fluid:** Sodium Lactate or Normal Saline 0.9%*

<table>
<thead>
<tr>
<th>Date</th>
<th>Fluid</th>
<th>Volume</th>
<th>Rate</th>
<th>Assessment Hypotensive, Replete or Overloaded</th>
<th>Signature &amp; MCRN</th>
<th>Time</th>
<th>Sign &amp; PIN</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Comp.</td>
<td>500 mLs</td>
<td>15 Mins</td>
<td></td>
<td>Start Signature 1</td>
<td>Finish Signature 2</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Sodium Lactate or Normal Saline 0.9%*</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* √ Tick infusion of choice

Use Normal Saline 0.9% in patients with hyperkalaemia

Patients with **Severe Sepsis / Septic Shock** who develop respiratory compromise should not be managed with diuretics.

Consider using an infusion pump for fluid management for patients at risk of respiratory compromise.
Think Sepsis
For Adult Emergency Department Patients

Manchester Triage System
Suspected of confirmed infection?

YES

Does the patient have TWO of the following (SIRS criteria)?
- Heart rate >90 beats per minute
- Respiratory rate >20 breaths per minute
- Temperature >38°C or < 36°C
- Altered level of consciousness
- Glucose >7.7mmol/L (no diabetes)
- WCC <4 or >12 x 10^9/L

Caution in immunocompromised patients who may not mount typical SIRS response

YES

AT RISK OF SEPSIS

YES

Likely source of infection?
- Chest?
- Urinary?
- Abdomen?
- Skin/bone?
- Unknown?

Systolic blood pressure <90mmHg or Lactate >2mmol/L

Risk of uncomplicated sepsis
- Needs hourly review
- Continue sepsis pathway
- Do not return to Waiting Room
- Hourly vital signs until review by treating clinician
- Commence Sepsis 6 if sepsis diagnosis confirmed by treating clinician

NO

YES

High risk of severe sepsis/septic shock

Escalate immediately to Senior EM doctor
Sepsis 6 <1hr
Transfer to Resus of High obs area

Critical Care Consult if patient fails to respond or there is on-going concern

PLEASE NOTE:
- This algorithm applied to ALL adult patients.
- Apply caution regarding temperature data if anti-pyretic medication has been taken
- Consider Infection Prevention and Control requirements
Appendix 6: Start Smart, Then Focus antibiotic care bundle

Start Smart, Then Focus
An Antibiotic Care Bundle for Hospitals

Day 1: Start Smart...

1. Start antibiotics only if there is clinical evidence of bacterial infection
   - If there is evidence of bacterial infection, prescribe in accordance with your local antibiotic guidelines and appropriately for the individual patient (see notes below)

2. Obtain appropriate cultures before starting antibiotics

3. Document in both the drug chart and medical notes:
   - Treatment indication
   - Drug name, dose, frequency and route
   - Treatment duration (or review date)

4. Ensure antibiotics are given within four hours of prescription
   - Within 1 hour for severe sepsis or neutropenic sepsis

At 24-48 hours after starting antibiotics, make an Antimicrobial Prescribing Decision

- Review the clinical diagnosis
- Review laboratory/radiology results
- Choose one of the five options below
- Document this decision

Options

1. Stop antibiotic(s)
   - no evidence of bacterial infection, or infection resolved

2. Switch from intravenous to oral antibiotic(s)
   - if patient meets criteria for oral switch

3. Change antibiotic(s)
   - narrower spectrum, if possible; broader spectrum, if indicated

4. Continue current antibiotic(s)
   - review again after further 24 hours

5. Outpatient parenteral antibiotic therapy
   - consult with local OPAT team

When deciding on the most appropriate antibiotic(s) to prescribe, consider the following factors:
- History of drug allergy (document allergy type: minor (rash only) or major (anaaphylaxis, angioedema))
- Recent culture results (e.g., is patient colonised with a multiple-resistant bacterial?)
- Recent antibiotic treatment
- Potential drug interactions
- Potential adverse effects (e.g., C. difficile infection is more likely with broad spectrum antibiotics)
- Some antibiotics are considered unsafe in pregnancy or young children
- Dose adjustment may be required for renal or hepatic failure

Consider removal of any foreign body/indwelling device, drainage of pus, or other surgical intervention

For advice on appropriate investigation and management of infections, consult your local infection specialist(s) (microbiologist, infectious disease physician and/or antimicrobial pharmacist).
# Appendix 7: SIRS criteria

<table>
<thead>
<tr>
<th>General variables</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fever (&gt; 38.3°C)</td>
</tr>
<tr>
<td>Hypothermia (core temperature &lt; 36°C)</td>
</tr>
<tr>
<td>Heart rate &gt; 90/min⁻¹ or more than two SD above the normal value for age</td>
</tr>
<tr>
<td>Tachypnea</td>
</tr>
<tr>
<td>Altered mental status</td>
</tr>
<tr>
<td>Significant edema or positive fluid balance (&gt; 20 mL/kg over 24 hr)</td>
</tr>
<tr>
<td>Hyperglycemia (plasma glucose &gt; 140mg/dL or 7.7 mmol/L) in the absence of diabetes</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Inflammatory variables</th>
</tr>
</thead>
<tbody>
<tr>
<td>Leukocytosis (WBC count &gt; 12,000 μL⁻¹)</td>
</tr>
<tr>
<td>Leukopenia (WBC count &lt; 4000 μL⁻¹)</td>
</tr>
<tr>
<td>Normal WBC count with greater than 10% immature forms</td>
</tr>
<tr>
<td>Plasma C-reactive protein more than two SD above the normal value</td>
</tr>
<tr>
<td>Plasma procalcitonin more than two SD above the normal value</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Hemodynamic variables</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arterial hypotension (SBP &lt; 90mm Hg, MAP &lt; 70mm Hg, or an SBP decrease &gt; 40mm Hg in adults or less than two SD below normal for age)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Organ dysfunction variables</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arterial hypoxemia (Pao₂/FIO₂ &lt; 300)</td>
</tr>
<tr>
<td>Acute oliguria (urine output &lt; 0.5 mL/kg/hr for at least 2 hrs despite adequate fluid resuscitation)</td>
</tr>
<tr>
<td>Creatinine increase &gt; 0.5mg/dL or 44.2 μmol/L</td>
</tr>
<tr>
<td>Coagulation abnormalities (INR &gt; 1.5 or aPTT &gt; 60 s)</td>
</tr>
<tr>
<td>Ileus (absent bowel sounds)</td>
</tr>
<tr>
<td>Thrombocytopenia (platelet count &lt; 100,000 μL⁻¹)</td>
</tr>
<tr>
<td>Hyperbilirubinemia (plasma total bilirubin &gt; 4mg/dL or 70 μmol/L)</td>
</tr>
</tbody>
</table>
Tissue Perfusion Variables

Hyperlactatemia (> 1 mmol/L)

Decreased capillary refill or mottling

Severe Sepsis definition

Sepsis induced tissue hypoperfusion or organ dysfunction
(any of the following thought to be due to infection)

Sepsis induced hypotension

Lactate above upper limits laboratory normal

Urine output < 0.5 mL/kg/hr for more than 2 hrs despite adequate fluid resuscitation

Acute lung injury with PaO₂/FIO₂ < 250 in the absence of pneumonia as infection source

Acute lung injury with PaO₂/FIO₂ < 200 in the presence of pneumonia as infection source

Creatinine > 2.0 mg/dL (176.8 μmol/L)

Bilirubin > 2 mg/dL (34.2 μmol/L)

Platelet count < 100,000 μL

Coagulopathy (international normalized ratio > 1.5)
Appendix 8: Sample fluid resuscitation algorithm for adults with sepsis

**Fluid resuscitation algorithm for adults with sepsis**

**SBP <90mmHg or MAP <65mmHg, Lactate >2mmol/l**

**Give bolus 500mls isotonic crystalloid over 15 minutes and reassess.** *(Repeat lactate after 2 litres and if shock is persistent consider CRITICAL CARE)*

- Hypovolaemia
- Altered mentation
- Oliguria
- Cold/mottled skin
- Hypotension
- Raised lactate

15 Minute Observations

**SBP >90 mmHg MAP >65mmHg, and/or Lactate <2mmol/L**

> Stop all IVT
> Consider diuretic
> Consider NIV or intubation
> Continuous monitoring

**SBP <90 mmHg MAP <65 mmHg, and/or Lactate >2mmol/L**

> Stop all IVT
> Vasopressors
> Consider NIV or intubation
> Not for diuretic
> Continuous monitoring
> Call Critical Care

**SBP <90 mmHg MAP <65 mmHg, and/or Lactate >2mmol/L**

Despite adequate fluid resuscitation

> Vasopressors
> IV maintenance
> Continuous monitoring
> Call Critical Care

**SBP >90 mmHg MAP >65 mmHg, and/or Lactate <2mmol/L**

> Maintenance fluids
> 1/2 hourly observations
> Reassess for hypovolaemia

**Euvolaemia* or no longer fluid responsive**

**MAP:** Mean Arterial Pressure, **SBP:** Systolic Blood Pressure

* Euvolaemia can be difficult to assess in patients with distributive shock, the patients in the ProCESS and ARISE trials received, on average between 4 and 5 litres of isotonic crystalloid fluid in the first 6 hours, of this 30mls/kg and 34mls/kg of IVT was administered in the first hour respectively.

For more information go to on National Clinical Guideline No 6. Sepsis Management go to: www.health.gov.ie/patient-safety/ncec
Appendix 9: IMEWS chart (sample)

**Irish Maternity Early Warning System (IMEWS)
Escalation Guideline**

**ALL IMEWS TRIGGERS**
Consider context and complete full clinical assessment. Implement measures to reduce triggers if appropriate. Complete a full set of observations on IMEWS immediately. Inform the Midwife in charge.

1. **1 YELLOW**
   - Repeat full set of observations on IMEWS after 30 and before 60 minutes.

2. **2 YELLOWS OR 1 PINK**
   - Call the obstetrician to review.
   - Repeat a full set of observations after 30 minutes.

3. **>2 YELLOWS OR >2 PINKS**
   - Call the obstetrician and request immediate review.
   - Repeat a full set of observations within 15 minutes or monitor continuously.

**IMPORTANT:**
1. If concerned about a woman, escalate care regardless of triggers.
2. If action is not carried out as above, CMM/Midwife in charge must contact the senior obstetrician on duty.
3. Document all communication and management plans in notes.

**CONSIDER MATERNAL SEPSIS**
Are 2 or more of the following SIRS criteria present?
- Temperature ≥38°C or <36°C
- Respiratory rate ≥20 breaths per min
- Heart rate ≥100 beats per min
- White cell count >16.9 or <4.0 x 10⁹/L
- Bedside glucose >7.7 mmol/L (in the absence of diabetes)
- Acutely altered mental status

AND
If infection is suspected after medical review

**Intervention: within one hour**

**COMPLETE SEPSIS 6**
1. Appropriate cultures*
2. FBC +/- lactate
3. Start urine output chart
4. Maintain O₂ (94-98%)
5. Consider IV fluid bolus**
6. IV antibiotics

* e.g. blood, wound, vaginal swab, urine etc
**exercise caution in presence of pre-eclampsia
### Sepsis Management

**A National Clinical Guideline**

---

#### IMEWS Triggers Key

<table>
<thead>
<tr>
<th>IMEWS Trigger</th>
<th>Normal Values</th>
<th>Yellow Zone</th>
<th>Pink Zone</th>
</tr>
</thead>
<tbody>
<tr>
<td>Respiratory Rate (bpm)</td>
<td>11-19</td>
<td>20-24</td>
<td>≤10 or ≥25</td>
</tr>
<tr>
<td>SpO₂ (%)</td>
<td>96-100</td>
<td>-</td>
<td>≤95</td>
</tr>
<tr>
<td>Temperature (°C)</td>
<td>36.0-37.4</td>
<td>37.5-37.9 or 37.5-37.9</td>
<td>≤35 or ≥38</td>
</tr>
<tr>
<td>Maternal HR (BPM)</td>
<td>60-99</td>
<td>100-119</td>
<td>≤50 or ≥120</td>
</tr>
<tr>
<td>Systolic BP (mmHg)</td>
<td>90-139</td>
<td>140-159</td>
<td>≤90 or ≥160</td>
</tr>
<tr>
<td>Diastolic BP (mmHg)</td>
<td>60-89</td>
<td>90-99 or 90-99</td>
<td>≤40 or ≥100</td>
</tr>
<tr>
<td>AVPU</td>
<td>Alert</td>
<td>-</td>
<td>Voice, Pain or Unresponsive</td>
</tr>
</tbody>
</table>

### Contact appropriate doctor for early intervention if the woman triggers one or two **YELLOW** zones at any one time

#### Year: Date: Time:

| Resp. Rate | ≤25 | 20-24 | ≥25 |
| SpO₂ (%) | 96-100 | ≤95% | ≤95% |
| Temperature (°C) | 36.0-37.4 | 37.5-37.9 | ≤35 or ≥38 |
| Maternal HR (BPM) | 60-99 | 100-119 | ≤50 or ≥120 |
| Systolic BP (mmHg) | 90-139 | 140-159 | ≤90 or ≥160 |
| Diastolic BP (mmHg) | 60-89 | 90-99 or 90-99 | ≤40 or ≥100 |
| AVPU | Alert | - | Voice, Pain or Unresponsive |

#### Normal Values

| Respiratory rate (bpm) | 11-19 | 20-24 | ≤10 or ≥25 |
| SpO₂ (%) | 96-100 | - | ≤95 |
| Temperature (°C) | 36.0-37.4 | 37.5-37.9 | ≤35 or ≥38 |
| Maternal HR (BPM) | 60-99 | 100-119 | ≤50 or ≥120 |
| Systolic BP (mmHg) | 90-139 | 140-159 | ≤90 or ≥160 |
| Diastolic BP (mmHg) | 60-89 | 90-99 or 90-99 | ≤40 or ≥100 |
| AVPU | Alert | - | Voice, Pain or Unresponsive |

#### Woman's Name: Date of Birth: Healthcare Record No: Document Number (eg. 1, 2): Booking BP: / Gestational Age at Booking (weeks):
List of relevant national guidelines and reports for infection and pregnancy

1. National Clinical Guideline No. 4 Irish Maternity Early Warning System (IMEWS)
   www.health.gov.ie/patient-safety/ncec

2. Preterm Prelabour Rupture of membranes (PPROM)

3. Guidelines for the Critically Ill Woman in Obstetrics

4. Management of obstetric anal sphincter injury

5. HIV and pregnancy

6. Management of Second Trimester Miscarriage
Appendix 10: Guideline internet databases searched

<table>
<thead>
<tr>
<th>Guideline Internet sites</th>
<th>URL</th>
</tr>
</thead>
<tbody>
<tr>
<td>National Guidelines Clearinghouse (NGC)</td>
<td><a href="http://www.guideline.gov/">http://www.guideline.gov/</a></td>
</tr>
<tr>
<td>Guidelines International Network (G-I-N)</td>
<td><a href="http://www.g-i-n.net/">http://www.g-i-n.net/</a></td>
</tr>
<tr>
<td>Ontario Guidelines Advisory Committee (GAC) Recommended Clinical Practice Guidelines</td>
<td><a href="http://www.gacguidelines.ca/">http://www.gacguidelines.ca/</a></td>
</tr>
<tr>
<td>Institute for Clinical Systems Improvement (ICSI)</td>
<td><a href="https://www.icsi.org/">https://www.icsi.org/</a></td>
</tr>
<tr>
<td>National Institute for Clinical Evidence (NICE)</td>
<td><a href="https://www.nice.org.uk/guidance">https://www.nice.org.uk/guidance</a></td>
</tr>
<tr>
<td>Scottish Intercollegiate Guidelines Network (SIGN)</td>
<td><a href="http://www.sign.ac.uk/guidelines/index.html">http://www.sign.ac.uk/guidelines/index.html</a></td>
</tr>
<tr>
<td>Canadian Agency for Drugs and Technology in Health</td>
<td><a href="http://www.cadth.ca/">http://www.cadth.ca/</a></td>
</tr>
<tr>
<td>Canadian Medical Association Infobase</td>
<td><a href="https://www.cma.ca">https://www.cma.ca</a></td>
</tr>
<tr>
<td>The Cochrane library</td>
<td>www3.interscience.wiley.com/cgi-bin/mrwhome/106568753/HOME</td>
</tr>
<tr>
<td>Food and Drug Administration</td>
<td><a href="http://www.fda.gov/cder/guidance/index.htm">http://www.fda.gov/cder/guidance/index.htm</a></td>
</tr>
<tr>
<td>Centre for Reviews and Dissemination Health Technology Assessment Database</td>
<td><a href="http://www.crd.york.ac.uk/CRDWeb">http://www.crd.york.ac.uk/CRDWeb</a></td>
</tr>
<tr>
<td>Haute Autorité de Santé (HAS)</td>
<td><a href="http://www.has-sante.fr/portail/icms/tc_1249588/en/accueil">http://www.has-sante.fr/portail/icms/tc_1249588/en/accueil</a></td>
</tr>
<tr>
<td>CHU de Rouen – Catalogue &amp; Index des Sites Medicaux Francophones (CISMeF)</td>
<td><a href="http://doccismef.chu-rouen.fr/dc/#q=recommandations%20professionnelles">http://doccismef.chu-rouen.fr/dc/#q=recommandations%20professionnelles</a></td>
</tr>
<tr>
<td>Bibliothèque médicale AF Lemanissier</td>
<td><a href="http://www.bmiweb.org/consensus.html">http://www.bmiweb.org/consensus.html</a></td>
</tr>
<tr>
<td>Direction de la lutte contre le cancer – Ministere de la sante et des services sociaux du Quebec</td>
<td><a href="http://www.msss.gouv.qc.ca/sujets/probsante/cancer/index/php?id=76.105.0.0.1.0">http://www.msss.gouv.qc.ca/sujets/probsante/cancer/index/php?id=76.105.0.0.1.0</a></td>
</tr>
<tr>
<td>Registered Nurses Association of Ontario</td>
<td><a href="http://www.rnag.org">http://www.rnag.org</a></td>
</tr>
<tr>
<td>Agency for Quality in Medicine</td>
<td><a href="http://www.aezq.de/">http://www.aezq.de/</a></td>
</tr>
<tr>
<td>Finnish Medical Society of Clinical Oncology</td>
<td><a href="http://www.kaypahoito.fi">http://www.kaypahoito.fi</a></td>
</tr>
<tr>
<td>American Society of Clinical Oncology</td>
<td><a href="http://www.asco.org">http://www.asco.org</a></td>
</tr>
<tr>
<td>Cancer Care Ontario Practice Guideline Initiative</td>
<td><a href="http://cancercare.on.ca">http://cancercare.on.ca</a></td>
</tr>
<tr>
<td>National Cancer Institute</td>
<td><a href="http://www.cancer.gov">http://www.cancer.gov</a></td>
</tr>
<tr>
<td>National Comprehensive Cancer Network</td>
<td><a href="http://www.nccn.org">http://www.nccn.org</a></td>
</tr>
<tr>
<td>Agence Nationale de Sécurité du Médicament et des Produits de Santé</td>
<td><a href="http://ansm.sante.fr/L-ANSM2/Une-agence-de-expertise/L-ANSM-agence-d-evaluation-d-expertise-et-de-decision/(offset)/0">http://ansm.sante.fr/L-ANSM2/Une-agence-de-expertise/L-ANSM-agence-d-evaluation-d-expertise-et-de-decision/(offset)/0</a></td>
</tr>
</tbody>
</table>
Appendix 11: SCC Agree II reviewers comments

<table>
<thead>
<tr>
<th>Domain</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Scope and purpose</strong></td>
<td></td>
</tr>
</tbody>
</table>
| **Item 1**                  | • Objective is to provide an update of the previous surviving sepsis guidelines.  
                                 • For adult and paediatric patients with septic shock and severe septic shock.  
                                 • Management of patients with severe sepsis and septic shock.                                                                                           |
| **Item 2**                  | • Very clear and concise recommendations.  
                                 • Adult and paediatric patients with septic shock in the ITU and non-ITU setting.  
                                 • The specific aspects of management are separately described and rated.                                                                                     |
| **Item 3**                  | • Good use of segmentation of specific recommendations including severe sepsis, septic shock, adult and paediatric populations as well as the appropriateness for the ICU and non-ICU setting.  
                                 • All patients with severe sepsis/septic shock as defined as having 2 or more SIRS criteria with suspected/proven infection and organ dysfunction/shock. |
| **Stakeholder Involvement** |                                                                                                                                                                                                         |
| **Item 4**                  | • Selection was based on interest and expertise in specific aspects of sepsis as well as experience in the GRADE process application. There was also sponsorship by the Society of Critical Care Medicine and European Society of Intensive Care Medicine governing bodies.  
                                 • Group members from critical care, acute medicine, emergency medicine and other specialties represented.  
                                 • Clinical leads or designated representatives from the following clinical programmes medicine, surgery, ED, critical care, anaesthesia, microbiology, paediatrics, GP, ambulance services and patient representatives. |
| **Item 5**                  | • As far as I can tell the view of the target population were not consulted however this would be difficult to do. They do recommend that goals of care be discussed with patients and their families.  
                                 • This is not clearly stated.  
                                 • Patient representative present at all meetings, guidelines supported by the Irish Society of Intensive Care Medicine and Joint Faculty of Intensive Care Medicine. |
| **Item 6**                  | Yes, the recommendations are classified into 3 groups:  
                                 1. Those directly targeting severe sepsis  
                                 2. Those targeting general care of the critically ill patient and considered high priority in severe sepsis  
                                 3. Paediatric considerations.                                                                                                                                 |
| **Rigour of development**   |                                                                                                                                                                                                         |
| **Item 7**                  | A separate literature search was performed for each clearly defined question.                                                                                                                                 |
| **Item 8**                  | • All questions used in the previous guidelines publication were searched as were pertinent new questions generated by general topic related searches or recent trials.  
                                 • They were specifically asked to look for existing meta-analysis related to their question and search a minimum of one general database. |
| **Item 9**                  | Yes they followed the principles of the grading of recommendations Assessment, Development and Evaluation (GRADE) system to guide assessment of quality of evidence from high (A) to very low (D) and to determine the strength of recommendations. |
| **Item 10**                 | Yes, definition were created by Delphi consensus. GRADE representatives were available for advice throughout the process. Formal voting was used to resolve competing proposals etc.                                      |
| Item 11 | • A good review of the literature which had kept up to date with changes in practice.  
• This was taken into account when deciding on the strength of the recommendation. |
| Item 12 | • There is a rationale with evidence and references for every recommendation.  
• Each recommendation is supported by evidence based rationale. |
| Item 13 | • A consensus committee of 68 international experts representing 30 international organisations was used.  
• Peer reviewed by the SCC executive committee group head and the EBM lead, it is unclear if they were involved in the guideline production. No target population representatives included. |
| Item 14 | • The Surviving Sepsis Campaign and consensus committee members committed themselves to updating the guidelines regularly as new interventions are tested and results published. In fact, it is the second revision of the initial guidelines for 2003.  
• These are updated guidelines from first 2004 and then 2008, I do not see specific reference to when these guidelines are up for review again. |
| Clarity of presentation | | |
| Item 15 | There are clear recommendations with a rationale. |
| Item 16 | A strong recommendation is worded as „we recommend“ and a weak recommendation as „we suggest“. |
| Item 17 | They have within 3 and 6 hour bundles as well as recommendations for Initial resuscitation, haemodynamic monitoring, other supportive therapies and paediatric considerations. |
| Applicability | | |
| Item 18 | • They believed that the greatest outcome improvements could be made through education and process change for those caring for severe sepsis patients in the non-ICU setting and across the spectrum of acute care.  
• Performance monitoring of the SCC bundles is described in many sections, however, the authors do acknowledge that other areas/countries may not have the same resources to carry out all the recommendations.  
• The major barriers to implementation are identification of the target group and initiation of guidelines and these are addressed by the basic care pathway for all patients with sepsis, the ‘Sepsis 6’. |
| Item 19 | • They recommend protocolised quantitative targeted resuscitation.  
• SCC have easy web access with implementation tool kits available.  
• Recommendations are clear and having reviewed the surviving sepsis website, there is assistance to the implementation on the website. |
| Item 20 | • The document states that resource limitations in some institutions and countries may prevent physicians from accomplishing particular recommendations therefore the guidelines are intended to be best practice and are not created to represent a standard of care.  
• They acknowledge that some institutions may have difficulties implementing some recommendations and say that these are best practice guidelines rather than strict standard care models. Also it is based on the individual clinical decision given the available resources  
• Potential resource implications were taken into account as a factor towards a strong versus a weak recommendation but the specific details of each case not detailed with each recommendation.  
• There is a recognised capacity issue in critical care in Ireland which could lead to delays in appropriate treatment. |
**Item 21**

- The Surviving Sepsis Campaign committee hopes that over time particularly through education programs and formal audit and feedback performance improvement initiatives that the guidelines will influence bedside healthcare practitioner behaviour and reduce the burden of sepsis worldwide.
- These are outlined for the online resource kits and also in the special studies performed on some of the recommendations but not all.
- The surviving sepsis care bundles can easily be audited and there is a clear recommendation that performance improvement efforts should be used to improve outcome.
- The guideline does not address issues as how to monitor or audit.

**Editorial Independence**

**Item 22**

- There was no industry input into the guidelines development and all members displayed conflicts of interest.
- The conflicts of interest are very clearly stated.
- No industry funding for second edition of SSG.

**Item 23**

- A detailed description of the disclosure process and all author disclosures was published
- One reviewer - I don’t see record of this
- No competing interest.

**Overall Assessment**

This guideline has robust rigor of development that can be extrapolated for adoption. The resource implications of implementation will be considered separately for the Irish context.
Appendix 12: Sample driver diagram for improving care of patients with sepsis in the emergency department

Source: British Patient Safety Council
Appendix 13: Summary of ADAPTE process

Appendix 14: Budget impact analysis

Budget impact report

Key message
This review of the economic evaluation literature of the management of sepsis and the budget impact analysis support the clinical guideline recommendations.

The report was completed by Michelle O’Neill, Health Technology Assessment Directorate, Health Information and Quality Authority, Dr. Mary O’Riordán, Specialist in Public Health Medicine, Clinical Effectiveness Unit, Department of Health in collaboration with Dr Patricia Harrington and Dr. Máirín Ryan, Health Technology Assessment Directorate, Health Information and Quality Authority and Mr. Gethin White, Health Service Executive library services.

Economic literature review
A systematic review of economic studies was carried out to assess the available evidence for the management of sepsis. Studies were included if they examined the costs and consequences or just the costs of a sepsis management programme. Full details of the search are outlined below and the evidence table of results is presented in table 4. A total of 16 relevant studies were identified which included four overall costing studies, seven detection and intervention, four other specific discussion papers and one intervention study on education. All costs are reported as 2013 Irish Euros, unless otherwise stated.

Sepsis is the 10th leading cause of death worldwide and the leading cause of death in non-coronary intensive care units (ICUs)(39). The global burden of sepsis, which is exacerbated by aging populations in developed countries, is increasing worldwide (40). Sepsis, severe sepsis and septic shock are common reasons for admission to ICU.

In the US, 750,000 people develop sepsis each year with 1 in 4 dying from it (39). International consensus shows that there are approximately 300 cases per 100,000 population per annum (41). This compares with 208 cases of myocardial infarction per 100,000 population per annum and 223 cases of stroke.

An audit performed by the Intensive Care National Audit and Research Centre (ICNARC) conservatively estimated that 102,000 cases of sepsis arises annually in the UK with 36,800 deaths as a result (42). However, it was also noted that there may be underestimation of sepsis morbidity due to errors in coding for sepsis.

The financial burden is also escalating because of increasing fixed costs that dominate resource consumption in ICU and the development of expensive new drugs and technologies. Because of the high proportion of fixed costs (for example high staff ratios) in ICU, the total cost of ICU care mainly depends on length of stay in ICU. However, indirect costs (for example lost productivity) associated with severe sepsis are also considerable.

Overall cost implications
Critical care costs and utilisation have grown over the years. A study by Halpern et al. showed that in the US between 2000 and 2005, the overall cost of critical care medicine rose by 44% from $56.6 billion to $81.7 billion (equivalent to €76 billion to €109 billion) per annum (43).

International comparisons of the economic burden of sepsis vary; the variation can be attributed to differences in treatment and labour costs, standards of care and healthcare infrastructures in each country. Inpatient costs for sepsis are significant, but indirect costs and costs after the acute
episode may be even greater. In a study by Weycker et al, the mean cumulative cost of care for the five years post an initial admission for severe sepsis was two and half times the cost of the initial admission (44).

In studies looking at the burden of illness due to sepsis in Switzerland and Germany, indirect costs (for example productivity losses) due to sepsis were estimated to represent approximately 70% of the total costs while direct costs accounted for only 30% of total costs (21).

It has been estimated that approximately 70% of patients who have sepsis will require treatment in Critical Care Units (42).

While hospital statistics do not capture underlying cause of death data in Ireland, for 2013, up to 60% of all hospital mortality had a sepsis or infection diagnosis, with approximately 16% of all hospital deaths designated with a sepsis specific ICD-10-AM diagnosis code, see appendix 15. The total number of cases with a diagnosis of sepsis was 8,831 in 2013 and these cases accounted for a total of 221,342 bed days with an estimated cost of €125 million. Note that as specific inpatient costs for sepsis are not available in Ireland this estimate is based on international comparisons which may differ due to differences in treatment and labour costs.

In addition, in 2013, the mortality rate of patients with a diagnosis of sepsis who were admitted to an intensive care environment was 28.8%. The corresponding figure for 2011 was 32.4% and 31.3% for 2012. Note however that this data is based on the discharge code of patients who had a diagnosis of sepsis and who were admitted to any type of intensive care environment (including ICU, HDU, CCU etc) at some point during their hospitalisation. It is not possible to conclude that these patients were admitted to ICU as a result of sepsis, or that sepsis was the cause of death.

While the average length of stay (ALOS) in 2013 for a patient was approximately 5.6 days, a patient with a sepsis diagnosis has an ALOS of up to 26 days, which is 5 times longer than the average, non-sepsis patient stay. Patients with any associated infection have an ALOS of up to 10 days, table 1.
Table 1. Hospital Inpatient Enquiry: Inpatients with a Diagnosis of Sepsis or Infections, 2011–2013

<table>
<thead>
<tr>
<th>Patient Type</th>
<th>Category</th>
<th>2011</th>
<th>2012</th>
<th>2013</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adults</td>
<td>Inpatients with a Specific Sepsis Diagnosis Code</td>
<td>Cases 6,478</td>
<td>7,204</td>
<td>7,781</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Bed Days 185,942</td>
<td>192,844</td>
<td>202,701</td>
</tr>
<tr>
<td></td>
<td></td>
<td>ALOS 28.70</td>
<td>26.77</td>
<td>26.05</td>
</tr>
<tr>
<td></td>
<td>Inpatients with an Infection Diagnosis Code</td>
<td>Cases 78,400</td>
<td>84,972</td>
<td>88,218</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Bed Days 1,016,898</td>
<td>1,030,084</td>
<td>1,053,750</td>
</tr>
<tr>
<td></td>
<td></td>
<td>ALOS 12.97</td>
<td>12.12</td>
<td>11.94</td>
</tr>
<tr>
<td></td>
<td>All other cases</td>
<td>Cases 282,226</td>
<td>308,359</td>
<td>313,276</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Bed Days 1,601,970</td>
<td>1,646,020</td>
<td>1,586,636</td>
</tr>
<tr>
<td></td>
<td></td>
<td>ALOS 5.68</td>
<td>5.34</td>
<td>5.06</td>
</tr>
<tr>
<td></td>
<td>Total for All Inpatients</td>
<td>Cases 367,104</td>
<td>400,535</td>
<td>409,275</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Bed Days 2,804,810</td>
<td>2,868,948</td>
<td>2,843,087</td>
</tr>
<tr>
<td></td>
<td></td>
<td>ALOS 7.64</td>
<td>7.16</td>
<td>6.95</td>
</tr>
</tbody>
</table>

| Total        | Inpatients with a Specific Sepsis Diagnosis Code | Cases 7,421 | 8,182 | 8,831 |
|              |          | Bed Days 205,898 | 210,780 | 221,342 |
|              |          | ALOS 27.75 | 25.76 | 25.06 |
|              | Inpatients with an Infection Diagnosis Code | Cases 106,283 | 114,051 | 115,164 |
|              |          | Bed Days 1,124,146 | 1,133,059 | 1,156,670 |
|              |          | ALOS 10.58 | 9.93 | 10.04 |
|              | All other cases | Cases 475,421 | 504,383 | 498,222 |
|              |          | Bed Days 2,137,499 | 2,181,854 | 2,102,790 |
|              |          | ALOS 4.50 | 4.33 | 4.22 |
|              | Total for All Inpatients | Cases 589,125 | 626,616 | 622,217 |
|              |          | Bed Days 3,467,543 | 3,525,693 | 3,480,802 |
|              |          | ALOS 5.89 | 5.63 | 5.59 |

Source: This table has been produced by the Information Unit, Department of Health, and is based on Hospital Inpatient Enquiry (HIPE) data.

Note:
Data refer to inpatients grouped according to three mutually exclusive categories:
(i) inpatients with any diagnosis of a specific sepsis code;
(ii) inpatients with any diagnosis of an infection code (excluding cases with a specific sepsis diagnosis code already included in (i).) Note that some of the infections codes may include sepsis. For example, T81.1 refers to shock during or resulting from a procedure, but includes collapse, endotoxic shock, hypovolaemic shock and septic shock during or following a procedure.
(iii) all other inpatients, excluding cases already included in (i) and (ii).
See appendix 15 for list of sepsis and infections codes.
ALOS refers to the average length of stay in days.
Total includes all adult, maternity and paediatric patients.
Detection and Intervention costs and savings

Implementation of integrated sepsis protocols or early goal directed therapy (EGDT), such as the Surviving Sepsis Campaign, has the potential to reduce mortality due to sepsis. The reduction in practice variation by using a protocol has been shown to reduce mortality and lead to a reduction in ICU costs of 35% (45). In contrast, the failure to administer appropriate antibiotics in severe sepsis has been associated with a 2 day increase in length of stay (46).

Compliance with the Sepsis 6 protocol has shown a reduction in the relative risk of death from sepsis by 46.6% which equates to one additional life being saved for every five episodes of care (42). An unpublished NIHR-funded research study examining the outcomes of those patients receiving Sepsis 6 showed that these patients stayed an average of 2 days less in critical care and 3.4 hospital days less in total (42).

A Heart of England Foundation trust (HoEFT) carried out a business case analysis in 2012 based on the above NIHR-funded sepsis improvement project performed at Good Hope Hospital, Solihull (47). The group estimated that if no change in sepsis management was to be put in place the cost of sepsis care to HoEFT was €250m over 5 years and 17,000 patients would die from sepsis over that time. If the sepsis improvement project was implemented across the jurisdiction, the project was estimated to save HoEFT €8m over 5 years and 1,165 additional deaths would be prevented over that time period. If the trust was to invest in systems that automate sepsis recognition and response, the team projected that the project would save HoEFT €13m over five years and prevent an additional 3,620 deaths over the same period.

In the US, healthcare group Kaiser Permanente developed a comprehensive sepsis care programme in their 21 medical centres which serve 3.25 million members. The programme included robust sepsis screening methods, early goal-directed therapy (EGDT) and serial serum lactate screening similar to the Surviving Sepsis Campaign recommendations. Between 2009 and 2011 during the roll-out of their programme, they achieved:
- A threefold increase in sepsis detection rate
- A 60% reduction in mortality for patients with sepsis
- A 25% reduction in risk-adjusted average length of stay for patients with sepsis.

If these success rates were achieved for the remainder of the US, it has been estimated that there would be 72,000 fewer sepsis-related deaths, 5 million fewer hospital days and a reduction in hospital costs of $11 billion dollars (8, 48).

Another intervention to reduce sepsis mortality was implemented in a nine hospital collaborative in California (49). This collaborative manages 400,000 ED visits and 70,000 inpatient admissions with an average sepsis mortality of 27.7%. They used patient sepsis screening criteria, fast-track diagnosis and treatment protocols based on the Surviving Sepsis Campaign protocols. Their outcomes from the 22 month long intervention study was an overall reduction in sepsis-related mortality by 44% during the study period, 54.5% post year 1 and sustained at 49.8% at year 2. A return on investment (ROI) analysis showed that the programme generated a 56% ROI. This estimate was based on a $2.5 million investment, the percentage decrease in mortality and the estimated cost saving per case avoided. The cost-savings were determined using the US industry standard cost for sepsis of $22,100 (Institute of Medicines Medication Safety Study)(39) and the cost was escalated by 1% for each year of the study.

A sepsis alert programme, similar to SCC, was introduced in another US collaborative Christiana Care Health System (50). This collaborative admits approximately 58,000 patients and receives 175,000 ED visits per annum. The retrospective analysis over a two year period showed a decrease in sepsis-related mortality from 61.7 to 16.7 percent. ICU LOS was reduced from 11.9 to 4.1 days. In addition, the percentage of patients discharged home following an ICU admission increased by 199% which suggests that fewer patients experienced prolonged health decline from an extended ICU stay.
Suarez et al. examined the cost of implementing Surviving Sepsis in 59 Spanish ICUs. They reported an increased cost per patient of €2,165 mostly due to an increase in length of stay and an incremental cost-effectiveness ratio (ICER) of €5,531 per life year gained and an ICER of €8,017 per quality adjusted life year gained (QALY). So despite the increase in cost per patient, the SCC appears to be a cost-effective option for severe sepsis (51). In another Spanish before-and-after intervention study, delivery of SCC was associated with 6 fewer days in hospital and 2.5 fewer days in critical care (52).

In another study by Talmor et al, although the implementation of an integrated sepsis protocol resulted in a mean increase in cost of €9,732 per patient, life expectancy and QALYs were higher in those patients where an integrated sepsis protocol was used; 0.78 and 0.54 respectively. In addition, using such a protocol was associated with an incremental cost of €12,458 per-life year gained and a cost of €18,021 per QALY gained. The integrated sepsis protocol used was considered cost-effective and compared favourably to other acute care interventions (53). A prospective cohort study using historical controls by Assuncao et al, examined a managed protocol for severe sepsis in Brazil (n=414). The mortality rate was 57% in the control group and 38% in the protocol group. The cost of hospitalisation in the ITU was reduced significantly from €121,945 in the control group to €75,410 in the protocol group, with an average of 3.2 life-years gained after hospital discharge in the protocol group (54).

Early goal-directed therapy (EDGT) has also been shown to be cost-effective. Huang et al have shown that three different EDGT programmes (Emergency department based, mobile intensive care unit team, and intensive care unit based) do have set up costs but these are off-set by decreased LOS such that the net hospital costs reduced by between €8,919 and €9,519 per patient depending on the programme. However, the implementation of EDGT increased the lifetime costs because of greater survival and hence higher post-hospital costs resulting in an ICER of between €2,915/QALY and €7,442/QALY from the societal perspective(55). Jones et al showed that EGDT was associated with a cost of €5,501 per QALY gained (56).

**Other specific treatment costs**

Fixed costs account for the majority of ICU consumption costs and due to the longer length of stay they incur higher total costs. However the daily costs are also higher in septic patients. Two studies examining costs of ICU demonstrate that medications which includes antibiotics, account for between 15.6% and 21.7% of costs (57, 58). At all levels of care, septic patients have been shown to incur consistently higher daily costs than non-septic patients.

**Education**

Clinical and cost-effectiveness outcomes pre and post implementation of a multi-faceted sepsis education programme were reviewed in 10 hospitals in Brazil; comprising 1,650 hospital beds, 2,120 patients, between May 2010 and January 2012. The intervention included screening strategies, multidisciplinary education and case management sessions with continuous performance assessment(59). The main outcome was the level of compliance with the resuscitation bundle. Secondary outcomes included hospital mortality, hospital and ICU LOS, QALY gain and cost-effectiveness. Post implementation, compliance with the resuscitation bundle improved significantly from 13% at baseline to 62%. Hospital mortality decreased significantly from 55% to 26%. There was a reduction in total cost per patient from €25,600 to €15,300 with a mean difference of -10,340 (95% CI -16,282 to -4,672). The mean QALY increased from 2.63 (95% CI 2.15-3.14) to 4.06 (95% CI 3.58 – 4.57). Full compliance saved €4,711 per QALY (59).

**Summary of literature**

Sepsis is a leading global health and financial burden, the incidence of which is expected to increase further with an aging population. Fixed direct costs associated with the spectrum of sepsis, such as increased ICU LOS, ICU staffing, medications and new technologies are significant. Equally concerning are the indirect costs associated with sepsis such as loss of earnings, productivity and mortality. In fact, indirect costs may account for up to 70% of the total costs.
of sepsis. Healthcare use has also been shown to be elevated for one year after an episode of severe sepsis. In addition, long-term mortality in previously healthy patients with a history of severe sepsis/septic shock has been shown to be worse than both for patients with a history of non-septic critical illness and the underlying general population.

With these increasing costs, prevention and early detection appear to offer opportunities to mitigate the effects of sepsis syndrome. Integrated sepsis protocols and early goal-directed therapies like SCC have been shown to be highly cost-cost effective and significantly reduce sepsis-related mortality. However, there is some conflicting evidence on whether adherence to a sepsis protocol reduces the length of stay. Studies in the UK using the Sepsis 6 protocol have shown that it results in an estimated cost saving of €4,500 per patient. (42) In the US, sepsis mitigation achieved by the Kaiser Permanente group (serving a population of 3.25 million) showed particular success such that if they were achieved for the remainder of the US, it has been estimated that there would be 72,000 fewer deaths, 5 million fewer hospital bed days and a reduction in hospital costs of $11 billion dollars. Education programmes to support the compliance with sepsis resuscitation bundles showed that a multifaceted education programme led to high compliance with the resuscitation bundle and was a cost-effective intervention with an associated reduction in sepsis-related mortality.

**Budget impact of the National Clinical Guideline**

**Scope of the budget-impact analysis**

Rather than cost each recommendation statement, the budget impact analysis focuses on the additional cost implications that may arise from implementation of this National Clinical Guideline, as determined by discussions with the Sepsis Management Guideline Development Group.

The specific areas for consideration include:

a. ‘Point of care’ (POC) lactate testing.

b. Sepsis management education programmes

c. Other measures to assist the implementation of this National Clinical Guideline

d. Hospital level audit

**a. Point of care lactate testing**

International guidance advocates POC lactate measurement as part of a suite of triggers to identify sepsis. Early identification of sepsis has been shown to be an overall cost-effective measure. There is a lack of economic literature to specifically determine the cost-effectiveness of handheld POC lactate measurement devices in isolation; however, when used as part of a bundle of interventions such as in the Surviving Sepsis Campaign Guidelines, it has been shown to be cost-effective.(51)

Traditionally lactate is measured on a blood gas machine. Blood gas machines, although accurate and necessary medical equipment, are expensive, require regular calibration and are not as robust as the smaller handheld POC machines on the market. An increased use of traditional lactate testing due to implementation of the sepsis guidelines may therefore have significant resource implications.

One Irish level three hospital currently has 10 handheld POC machines in use. These machines have been positioned in areas that frequently see the acutely ill patient. Table 2 outlines the areas where these machines are in use.
Table 2 Level three hospital current location of use and number of handheld POC machines

<table>
<thead>
<tr>
<th>Clinical Area</th>
<th>Number of hand held POC machines</th>
</tr>
</thead>
<tbody>
<tr>
<td>Emergency department</td>
<td>2</td>
</tr>
<tr>
<td>Intensive Care Unit</td>
<td>1</td>
</tr>
<tr>
<td>Acute Medical Assessment Unit</td>
<td>1</td>
</tr>
<tr>
<td>Paediatric Unit</td>
<td>1</td>
</tr>
<tr>
<td>Maternity Unit</td>
<td>1</td>
</tr>
<tr>
<td>Respiratory Ward</td>
<td>1</td>
</tr>
<tr>
<td>Coronary Care Unit</td>
<td>1</td>
</tr>
<tr>
<td>Medical Laboratory</td>
<td>1</td>
</tr>
<tr>
<td>Cardiac Nurse team</td>
<td>1</td>
</tr>
</tbody>
</table>

On discussion with a selection of users of handheld POC machine they report that it is easy to use, robust and timely. Some suggestions to improve the system of use of handheld POC machines included the following:

- To ensure that the system has the ability to interface with the current laboratory system so that the output from the POC machine is recorded into the laboratory records in addition to the simple print out from the POC machine.
- To ensure that there is an agreed central point of coordination for the machines so that there is a clear line of accountability for training, maintenance and resource monitoring so that the machines are allocated based on need.
- To incorporate external quality assessment for POC testing as is performed for other laboratory tests.
- To audit the clinical and economic impact of POC testing.

Table 3 outlines a summary of the cost considerations in terms of POC lactate. The costs attributed are approximations but it is estimated implementation will cost €1.9million (€1.4million will be incurred in the initial setup phase with ongoing annual costs of €0.5million) and lead to savings of up to €12million per annum. The Guideline Development Group suggests that a more detailed business case be developed around POC lactate testing to inform how best to implement this recommendation.

The requirements of POC lactate testing could be based on an analysis of the effectiveness of the current system in place in the level three hospital outlined above.
### Table 3. Summary of costing considerations for point of care lactate introduction, education, and local sepsis coordinator

<table>
<thead>
<tr>
<th>Category</th>
<th>Item</th>
<th>Comment</th>
<th>Cost</th>
<th>Savings</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Initial Phase</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Education</td>
<td>Who will need training?</td>
<td>All users of the POC machine</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Will this be additional or part of an existing training system? (e.g., NEWS)?</td>
<td>Initial training for use of the machine is provided by the manufacturer as part of the retail price of the unit. The training could subsequently be incorporated into the existing training as part of the sepsis module, with negligible additional cost.</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Simulation training module for the acutely deteriorating patient.</td>
<td>A full business case would need to be developed</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Technology</td>
<td>How many lactate testing kits will need to be purchased? One per ward/one per hospital/ICU wards/acute wards?</td>
<td>Handheld POC reader @ €5000 each, Integrated interface with LAB IT @€10,000***</td>
<td>€1,025000</td>
<td>€390,000</td>
</tr>
<tr>
<td></td>
<td>Are there any special storage requirements?</td>
<td>For the POC machine no special requirement above routine medical equipment maintenance. For the cartridge and validation reagents, cold storage is required.</td>
<td></td>
<td>Negligible</td>
</tr>
<tr>
<td><strong>On-going intervention costs</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Technology</td>
<td>Any maintenance contracts?</td>
<td>POC Machine is a reader device only and does not require a maintenance contract. External quality control @€600 per annum for 39 hospitals.</td>
<td>€23,400</td>
<td></td>
</tr>
<tr>
<td></td>
<td>What is the lifetime of the kit?</td>
<td>The POC machine is a reader device only so has a prolonged life. The cartridge is the part that performs the test.</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td></td>
<td>Calibration?</td>
<td>Cartridges require one off batch validation @ €200 for a box of controls that lasts at least 2 years. Costs are determined by the number of validations and cartridges used.</td>
<td>€7,800</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Sterilisation?</td>
<td>Routine infection control measures</td>
<td>Negligible</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Waste disposal?</td>
<td>Routine sharps disposal of cartridges, needle and syringe</td>
<td>Negligible</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Additional items, needles, vials?</td>
<td>For lactate, a venous sample from a regular blood sample/syringe can be used. When reviewing a deteriorating patient, routine bloods are typically drawn. Lactate test can be done using this blood sample. Single use cartridge @€10 each**</td>
<td>€80,367</td>
<td></td>
</tr>
</tbody>
</table>
Staff | Who will administer the test? | Clinical staff | Negligible
---|---|---|---
How long will it take? | 15-20 minutes. Once blood is in the machine the test takes 10 minutes | Negligible
Will there be additional tasks required? Sterilisation, waste, calibration | Nil other than described above | Negligible
On-going training | Note: The acutely deteriorating patient simulation training will be a separate cost that requires a full business case to be developed. The cost of on-going handheld POC lactate training in itself is considered negligible as it is included in the price of purchase of the hardware. | Negligible
Local sepsis coordinator | 6 WTE @ CNM2 Level | €410,000

Total Costs | €1,936,567

Savings

Material | Any material savings? Different needles/vials etc. | Non-heparinised syringes can be used | Negligible

Staff | Reduction in lab tests? | Lactate is traditionally tested on blood gas machines and is not a routine laboratory test | may lead to a reduction, as without POC there would be an increase in the resources required to implement the guidelines

Outcomes | Improved outcomes ICU bed days saved, reduction in mortality, post sepsis syndrome (full sepsis six or individualised elements?) | International literature shows that prevention and early detection of sepsis reduces sepsis related mortality, overall length of stay, decreased ICU costs. (Sepsis 6 showed that these patients stayed an average of 2 days less in critical care and 3.4 days less in total which was estimated to be a cost saving of approximately €4,500 per patient). (42) | €12 million (€4,500 per patient saved for full Sepsis 6)

Total Savings | €12m

Estimated Sepsis Costs per annum (€)* | €125m

---

*Number of POC machines required was calculated as one POC machine each per acute setting including AMU (MAU), SAU, ITU, CCU, ED, maternity units and one machine per a proportion of general medical and surgical wards (1 machine per 5 wards). This proportion is based on the numbers of POC machines currently in use in the general wards of the aforementioned level-3-hospital.

*Estimated using average hospital discharges with a sepsis diagnosis from HIPE, where 30% of these cases required critical care at a cost of €25,500 per case, and the remaining cases had a reduced estimated cost of €9,500 per case.

**Single cartridge use is based on the number of average of 8,036 sepsis discharges recorded per annum. This is an underestimation as more sepsis cases may have occurred than were recognised or recorded, and patients will be tested who do not prove to be septic.

***IT interface initial costs are based on the number of acute hospitals assuming that each acute hospital has one laboratory network and would require just one interface regardless of the size/extent of the hospital.

^Laboratory Quality Assurance costs are based on acute hospital number.
b. Sepsis management education programme
The international economic literature suggests that education programmes on sepsis recognition and management are cost-effective. A multifaceted sepsis management education programme has been shown to have a cost saving of €4,711 per QALY. (29)

Another key element to the management of sepsis is the education of clinicians around the appropriate response once sepsis has been recognised. The development of a simulation training programme (similar to Acute Cardiac Life Support training) for the management of the acutely deteriorating patient is considered, by the GDG, a key step to the appropriate management of patients with sepsis. Given the various models that could be used to implement this type of education programme and the significant cost that a robust simulation training would incur, a full business case would need to be developed. This business case would need to consider coordination with other programmes that exist in the system, for example the NEWS programme and ensure that the most cost-effective programme is developed for the Irish context.

All clinical responders to the acutely deteriorating patient would require this simulation education programme.

c. Other measures to assist the implementation
Local Sepsis Coordinator
Part of the success of the Kaiser Permanente Sepsis control initiative has been attributed to the ‘consistent approach to performance improvement’ which propelled local rapid improvement cycles and ‘joint problem solving across facilities’. To ensure this ‘top-down bottom-up approach to performance improvement’ the local coordination of sepsis management is a priority. The Guideline Development Group recommend the introduction of the role of a hospital sepsis coordinator for education, audit and evolution of the sepsis team. This would enable standardisation of sepsis care across Irish healthcare facilities. As a matter of priority, the Guideline Development Group recommend that a business case be prepared to consider the most cost-effective way to implement the role of the local hospital sepsis coordinator.

As part of the projected costings outlined in table 3, six additional WTEs were allocated to support sepsis implementation. The 6 WTEs was on the basis of 6 hospital groups and their role will be to support sepsis implementation in their hospital group, negotiate with the hospitals and HSE on behalf of clinicians, collate and present audit data, and host events regionally and nationally. These six sepsis lead coordinators will be based in the lead hospital in the group and also support the work of the sepsis staff in that hospital.

However it is also anticipated by the Guideline Development Group that there is also an additional need for audit/sepsis WTEs in each hospital as the audit collection is an integral part of the success of sepsis management implementation.

d. Audit costs
Audit in the hospital for sepsis KPIs represents new activity. The Guideline Development Group anticipate that additional resources may be required. The audit function will develop in line with the incremental nature of the implementation of the National Clinical Guideline. While it is acknowledged that this will require additional resources, the local organisations will be required to examine their requirements, maximise available resources and develop business cases as appropriate in a timely manner.
Methods for literature review
The search strategy is based on the developed PICOS (population, interventions, comparisons and outcomes) and a schema of concepts as outlined in Figure 1.

Figure 1 Concepts for systematic review of economic impact report of sepsis management
**PICOS Search Terms**

**Intervention 1: Sepsis detection**

| **Population:** | All patients who may be at risk of or may have sepsis in acute hospitals, obstetrics and paediatric units |
| **Intervention:** | Sepsis detection options |
| **Comparison:** | Between sepsis detection techniques and no sepsis detection techniques; between different options applied |
| **Outcomes:** | Resources and costs |

**Concepts and key words**

1. Early recognition of Sepsis
   a. Deteriorating
   b. SIRS criteria (Systemic Inflammatory Response criteria)
   c. Suspected infection, blood stream infection
   d. Septic shock, Septicaemia

2. Sepsis screening

3. Electronic Early Warning Score (EWS) generation

4. Point of care lactate
   a. POC LAC
   b. POC lactate
   c. Emergency department triage, ED triage
   d. Acute medical unit (AMU)
   e. Critical Care Units; Intensive Care Unit (ICU), High Dependency Unit (HDU), Paediatric Intensive Care Unit (PICU), Coronary Care Unit (CCU), Maternity Unit, Acute wards.

5. Sepsis Six, Sepsis 6

6. Surviving Sepsis
   a. Three hour bundle; 3-hour bundle
   b. Six-hour bundle; 6-hour bundle

7. Acute hospitals
   a. Acute Care
   b. Secondary Care
   c. Tertiary Care
   d. Inpatients
Intervention 2: Sepsis education

| Population: All staff who may be caring for patients at risk of sepsis in acute hospitals, obstetrics and paediatric units |
| Intervention: Sepsis education techniques |
| Comparison: Sepsis education interventions applied to target population compared with no sepsis education intervention applied |
| Outcomes: Resources and costs |

Concepts and key words

1. Sepsis education programmes:
   a. Suspected infection; sepsis; septic shock; septicaemia, blood stream infection, SIRS criteria
   b. techniques; programmes
   c. Surviving Sepsis Campaign
   d. ESICM (European Society of Intensive Care Medicine) PACT (Patient Centred Acute Care Training) modular learning programmes.

2. Specialist sepsis education coordinator:
   a. audit
   b. implementation.

3. Electronic learning tools for Sepsis

4. Smart phone applications for Sepsis

5. Undergraduate and post graduate sepsis training programmes

6. Acute hospitals
   a. Acute Care
   b. Secondary Care
   c. Tertiary Care
   d. Inpatients
Intervention 3: Sepsis treatment

**Population:** All patients who may be at risk of sepsis in acute hospitals, obstetrics and paediatric units
**Intervention:** Care options for Sepsis
**Comparison:** Between care options and no care options;
**Outcomes:** Resources and costs

Concepts and key words

1. Sepsis; infection, blood stream infection, septicaemia

2. Early recognition of Sepsis
   a. Deteriorating
   b. SIRS criteria (Systemic Inflammatory Response criteria)
   c. Suspected infection
   d. Septic shock

3. Early intervention
   a. Sepsis Six: Cultures; lactate; oxygen; fluids; crystalloids; Urine output; antibiotics; antimicrobials, antibacterial
   b. Three hour bundle
   c. Six hour bundle: Vasopressin, Central Venous Oxygen (SCVO$_2$), Corticosteroids, Haemoglobin transfusion, PEEP (Positive End Expiratory Pressure)

4. Critical Care; Intensive Care Unit (ICU), High Dependency Unit(HDU), Paediatric Intensive
   a. Care Unit (PICU), Coronary Care Unit (CCU),
   b. Ventilator
   c. Dopamine

Information sources

1. (With economic filter (Glanville et al 2009))
   - EmbaseClassic+Embase 1947 to June 2014
   - Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations and Ovid MEDLINE(R) 1946 to present, run through OVID on June 2014

2. Without economic filter (built into database type))
   - Database of abstracts of Reviews of Effects
   - NHS Economic Evaluation Database
   - Health Technology Assessment Database
   - Cochrane Central Register of Controlled Trials
   - Cochrane Database of Systematic Reviews
### Table 4 Sepsis management economic literature evidence table

<table>
<thead>
<tr>
<th>Study</th>
<th>Intervention</th>
<th>Analysis Details</th>
<th>Clinical &amp; QALY Outcomes</th>
<th>Costs</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adrie et al 2005</td>
<td>None. Costing study</td>
<td>Country: France&lt;br&gt;Discount rate: none&lt;br&gt;Perspective: hospital&lt;br&gt;Time Horizon: admission&lt;br&gt;Model Type: costing study</td>
<td>None. Costing study</td>
<td>Mean cost per day of €1,229 in patients with severe sepsis. ICU mean (SD) cost was €14,066 (€12,902) in patients with severe sepsis at ICU admission not followed by ICU-acquired severe sepsis.</td>
<td>Patients with severe sepsis at admission, hospital-acquired €16,879 (€14,280) vs. community-acquired infection €12,223 (€11,738). ICU cost more than twice as high in patients with €22,117 (€20,759) vs. without severe sepsis €9,312 (€8,342). ICU-acquired sepsis, increased to €35,504 (€24,833) in patients with vs. €31,720 (€22,990) without severe sepsis at ICU admission.</td>
</tr>
<tr>
<td>Bates et al 1993</td>
<td>None. Costing study</td>
<td>Country: US&lt;br&gt;Discount rate: none&lt;br&gt;Perspective: hospital&lt;br&gt;Time Horizon: admission&lt;br&gt;Model Type: costing study</td>
<td>The main outcome measures were LOS in total &amp; post-onset LOS</td>
<td>Total mean charges per patient 1) €256,236 nosocomial sepsis 2) €180,076 sepsis syndrome 3) €30,088 all other patients 4) €161,783 survivors sepsis syndrome 5) €27,920 all other patients survivors 6) €212,108 nonsurvivors sepsis syndrome 7) €115,103 all other patients nonsurvivors</td>
<td>Mean difference between sepsis syndrome &amp; all other admissions was €74,793, LOS 11.0 days. No statistically significant difference in resource utilisation between nosocomial &amp; community-acquired sepsis. Survivors of sepsis syndrome had a longer total LOS &amp; post-onset LOS, but lower charges than nonsurvivors.</td>
</tr>
<tr>
<td>Lagu et al. 2012</td>
<td>None, Costing study, direct costs of severe sepsis patients with organ dysfunction in US</td>
<td>Country: US&lt;br&gt;Discount rate: none&lt;br&gt;Perspective: 3rd Party Payer&lt;br&gt;Time Horizon: inpatient stay&lt;br&gt;Model Type: costing study</td>
<td>None. Costing study</td>
<td>Cost per patient €18,868 2007, total costs €23.7 billion in 2007</td>
<td>Increase in total costs from 2003 to 2007 (€15.0 billion €23.7 billion) &amp; decrease in costs per case (€19,727 vs. €18,868)</td>
</tr>
<tr>
<td>Moerer et al. 2002</td>
<td>None. Costing study, direct costs of severe sepsis patients in German intensive care units</td>
<td>Country: Germany&lt;br&gt;Discount rate: none&lt;br&gt;Perspective: 3rd Party Payer&lt;br&gt;Time Horizon: inpatient ICU stay&lt;br&gt;Model Type: costing study</td>
<td>None. Costing study</td>
<td>Mean direct ICU €31,524 ± 25,210/patient &amp; €1,783/day</td>
<td>Mean total direct total cost of care and mean daily care cost was higher for Non survivors than for survivors (€34,431 vs. €29,747) &amp; (€2,231 vs. €1,572).</td>
</tr>
<tr>
<td>Study</td>
<td>Intervention</td>
<td>Analysis Details</td>
<td>Clinical &amp; QALY Outcomes</td>
<td>Costs</td>
<td>Results</td>
</tr>
<tr>
<td>---------------</td>
<td>------------------------------------------------------------------------------</td>
<td>----------------------------------------------------------------------------------</td>
<td>---------------------------------------------------------------------------</td>
<td>----------------------------------------------------------------------</td>
<td>------------------------------------------------------------------------</td>
</tr>
</tbody>
</table>
| Suarez et al 2011 | Implementation of an SSC protocol comprising 2 bundles: the resuscitation bundle (within 6hrs of severe sepsis, measuring serum lactate, blood cultures, antibiotics within 3hrs for ED admissions & 1hr for non-ED admissions, fluids & EGDT), the post resuscitation bundle (within 24hrs low dose steroids, drotrecogin alfa, glucose control, respiratory plateau pressure) and a 2-month educational programme (training physicians & nursing staff for the ED, medical & surgical wards & ICU in early recognition of severe sepsis & in treatments included in the SSC protocol). The comparator was routine care. | Country: Spain  
Discount rate: 3%  
Perspective: 3rd Party Payer  
Time Horizon: lifetime  
Model Type: no model, costs collected alongside study | Life yrs gained 0.54 (95%CI 0.02-1.05), QALY 0.37 (95%CI 0.02-0.73) | increase in costs €2,165 (95%CI 142-4188) per patient, all in-hospital costs were included, educational costs excluded | €5,531 per life yr gained, €8,017 per QALY, cost per life saved €59,915 |
| Talmor et al 2008 | Integrated sepsis protocol incorporating: a) early goal-directed therapy, b) empirical antibiotics, c) steroids in adrenal suppression, d) assessment for activated protein C therapy e) tight glycaemia control f) low tidal volume ventilation for patients with acute lung injury. The comparator was routine care. | Country: US  
Discount rate: 3%  
Perspective: 3rd Party Payer  
Time Horizon: lifetime  
Model Type: no model, costs collected alongside study | life expectancy increase 0.78 (95%CI 0.73-0.84), QALY gain 0.54 (95%CI 0.50-0.58) | increase in costs €9,732 (95%CI €9,145–€10,318) per patient, all in-hospital costs were included | €12,458 per life yr gained, €18,021 per QALY |
<table>
<thead>
<tr>
<th>Study</th>
<th>Intervention</th>
<th>Analysis Details</th>
<th>Clinical &amp; QALY Outcomes</th>
<th>Costs</th>
<th>Results</th>
</tr>
</thead>
</table>
| Assuncao et al 2014 | Protocol based on SSC. Included lectures, e-learning modules for multidisciplinary team & distribution of explanatory brochures. Regular clinical staff & all physicians in ED & ICU included. SSC 6hr management (serum lactate measurement, blood cultures, antibiotics, EGDT, measurement of central venous or mixed O2 saturation & maintenance of central venous & mean arterial pressure) & 24hr management (glucose control, low doses of corticoids, protective strategy of mechanical ventilation & drotrecogin α). | **Country:** Brazil  
**Discount rate:** none  
**Perspective:** hospital  
**Time Horizon:** lifetime  
**Model Type:** none used as cost saving | Average gain 3.2 life-yrs after being discharged from hospital (8.8 ± 13.3 yrs control group & 12.0 ± 14.0 yrs protocol group). | Cost of hospitalisation in the intensive care unit was reduced significantly from €121,945 ± €178,563 in the control group to €75,410 ± €112,448 in the protocol group. | Given the incremental cost was lower than or equal to zero, the effectiveness of the protocol was justified by the significant increase in the life-yrs saved & the observed reduction in mortality. |
| Shorr et al 2007 | A protocol developed from literature & the SSC including: identification, fluid resuscitation, timely & appropriate antibiotic administration, vaspressors & inotropic support, indications for packed red cell transfusion, drotrecogin alfa (activated) & corticosteroids. | **Country:** US  
**Discount rate:** none  
**Perspective:** hospital  
**Time Horizon:** admission  
**Model Type:** cost consequence | 28-day mortality rate preprotocol was 48.8% compared with 30.0% following protocol. Median reduction in overall hospital LOS by 5 days. | Median per-patient cost €23,829 (€3,913 –108,166) before protocol & €17,454 (€3,734–111,033) following protocol. Savings of nearly €6,503/subject a total €621,064 between groups. | The protocol reduced overall costs & LOS. |
| Hutchison et al 2011 | Implementing an antimicrobial guide specific for severe sepsis | **Country:** US  
**Discount rate:** none  
**Perspective:** 3rd Party Payer  
**Time Horizon:** inpatient stay  
**Model Type:** cost and consequence | Time to 1st antibiotic (1.77 ± 1.13 hrs) vs. control group (14.90 ± 45.07 hrs). Similar mortality in both groups. Overall LOS mean, 9.8 [SD, 8.8] intervention vs. 14.7 [SD, 11.5] days control, difference 5 days. | The total cost was reduced by 30% in the intervention group, and the mean variable cost was reduced by €2,583 in the intervention group. | A reduced LOS (5 days), a significantly earlier time to 1st dose antibiotic (12hrs) lower total (30%) mean hospital costs (€2,583). |
<table>
<thead>
<tr>
<th>Study</th>
<th>Intervention</th>
<th>Analysis Details</th>
<th>Clinical &amp; QALY Outcomes</th>
<th>Costs</th>
<th>Results</th>
</tr>
</thead>
</table>
| Huang et al. 2009 | 3 implementation strategies 1)ED-based ED staff provide both screening & EGDT; 2) mobile team ED staff screen for candidates & alert ICU staff, who come to the ED to provide EGDT; 3)ICU-based ED staff screen & identify candidates but transfer them to the ICU where ICU staff provide EGDT. | **Country:** US  
**Discount rate:** 3%  
**Perspective:** 3rd Party & Societal  
**Time Horizon:** hospital stay & life time  
**Model Type:** CUA | Incremental QALYs gained/treated patient differed by strategy (ED, 0.59 0.27; team, 0.59 0.27; ICU, 0.47 0.26). | Hospital costs fell (€8,919– €9,519). Mean/patient lifetime costs €79,723 (95% CI, €66,447–€94,209) usual care & €83,088 (95% CI, €71,190–€95,603) EGDT, difference €3,365 (95% CI, €11,588 to €18,990). Incremental costs 1) €4,390 2) €4,335 3) €1,370 | ICERs 1)€7,442/QALY 2)€7,348/QALY 3)€2,915/QALY from the societal perspective |
| Jones et al. 2011 | Implementing EGDT as standard care. Resuscitation protocol, targeted 3 end points: central venous pressure, mean arterial pressure & central venous oxygen saturation. Patients cared for as a part of routine care in the ED without additional staff & did not mandate the entire resuscitation occur in the ED. | **Country:** US  
**Discount rate:** 3%  
**Perspective:** 3rd Party Payer  
**Time Horizon:** life time  
**Model Type:** CUA | Discounted sepsis-adjusted LE, mean (SD) 5.7 (9.20) before phase 7.2 (9.32) after phase, 1.5 difference  
Discounted QALYs, mean (SD) 5.1 (5.98) before phase, 6.4 (5.95) after phase 1.3, difference | Inhospital costs, mean (SD)€13,515.73 (14,159.87) before phase, €20,678 (19,776) after phase, €7163 difference | ICER €4,757/LYG, €5,501/QALY gained |
| Noritomi et al 2014 | The programme used a multifaceted approach: screening strategies, multidisciplinary educational sessions, case management & continuous performance assessment. | **Country:** Brazil  
**Discount rate:** 3%  
**Perspective:** 3rd Party Payer  
**Time Horizon:** lifetime  
**Model Type:** CUA | Average QALY increased from 2.63 (95% CI 2.15–3.14) to 4.06 (95% CI 3.58–4.57) | total cost/patient baseline to the last 3 months (-10,340; 95% CI-16,282 to-4,672), only in hospital costs included | For each QALY, the full compliance saves €4,711. |
| Burchardi et al 2004 | Review includes costing studies along with interventions covering a wide range of interventions. | **Country:** variety of countries  
**Discount rate:** none  
**Perspective:** varies  
**Time Horizon:** varies  
**Model Type:** descriptive review | A variety reported | Original cost year not presented costs incorrectly adjusted using exchange rates so cannot compare | Original cost year not presented costs incorrectly adjusted using exchange rates so cannot compare |
<table>
<thead>
<tr>
<th>Study</th>
<th>Intervention</th>
<th>Analysis Details</th>
<th>Clinical &amp; QALY Outcomes</th>
<th>Costs</th>
<th>Results</th>
</tr>
</thead>
</table>
| Chalupka et al 2012   | review includes costing studies along with some interventions covering a wide range of interventions | **Country:** variety of countries  
**Discount rate:** none  
**Perspective:** varies  
**Time Horizon:** varies  
**Model Type:** descriptive review                                                                                                                      | None reported focus is on the costs of interventions                                                                                                   | Cost year not presented with reported costs so cannot compare          | Cost year not presented with reported costs so cannot compare          |
| Merritt et al 2011    | discussion piece                                                              | **Country:** US  
**Discount rate:** none  
**Perspective:** not specified  
**Time Horizon:** not specified  
**Model Type:** discussion piece                                                                                                                       | Hospital-acquired sepsis has shown a 56% higher mortality, as high as a 75% increase in hospital length of stay | Average daily ICU cost to care for the patient with sepsis to be $934 to $1064, with total costs of $11,474 to $25,000 per episode.  
Cost year not specified.                                                                 | Every hour of delay in treatment increases mortality by 7.5%.  
Average daily ICU cost ($934-1,064) total costs ($11,474-$25,000) per episode.  
Cost year not specified.                                                                 |                                                                 |
| Sepsis Trust, UK 2013 | none briefing paper                                                            | **Country:** UK  
**Discount rate:** none  
**Perspective:** NHS  
**Time Horizon:** varies  
**Model Type:** not a modelled study                                                                                                                  | Compliance with the Resuscitation Bundle improved from 10.9% to 21.5%.  
Sampling of blood cultures before antibiotics, delivery of broad spectrum antibiotics & general Critical Care interventions such as 'gentle' ventilation & maintenance of normal blood sugars were shown to improve survival. | It has been estimated in European studies that a typical episode of severe sepsis costs a healthcare organisation approx €25,000.  
Patients receiving the Sepsis 6 protocol equates to a cost saving of circa €4,500/ patient.  
Cost year not specified.                                                                 | Achieving 80% delivery of the basic standards of care is likely to save at least 10,000 lives & €205 million yearly for the National Health Service. |
Appendix 15: HIPE codes used for Sepsis case analysis

List of Sepsis Codes
A40 Streptococcal sepsis
A41 Other sepsis
A02.1 Salmonella sepsis
A22.7 Anthrax sepsis
A26.7 Erysipelothrix sepsis
A32.7 Listerial sepsis
A42.7 Actinomycotic sepsis
B37.7 Candidal sepsis
O85 Puerperal sepsis
P36 Bacterial sepsis of newborn
T81.42 Sepsis following a procedure

List of Infection Codes
All codes in the OECD List of infections*, with the exception of the following codes (including all subdivisions):
K57.1 Diverticular disease of small intestine without perforation or abscess
K57.3 Diverticular disease of large intestine without perforation or abscess
K57.5 Diverticular disease of both small and large intestine without perforation or abscess
K57.9 Diverticular disease of intestine, part unspecified, without perforation or abscess

Also include the following codes (including all subdivisions):
J12 Viral pneumonia, not elsewhere classified
J16 Pneumonia due to other infectious organisms, not elsewhere classified
J17 Pneumonia in diseases classified elsewhere
J18 Pneumonia, organism unspecified
J69 Pneumonitis due to solids and liquids
P23 Congenital pneumonia
P24 Neonatal aspiration syndromes
A06 Amoebiasis
A07 Other protozoal intestinal diseases
A08 Viral and other specified intestinal infections
A09 Other gastroenteritis and colitis of infectious and unspecified origin
A83 Mosquito-borne viral encephalitis
A84 Tick-borne viral encephalitis
A85 Other viral encephalitis, not elsewhere classified
A86 Unspecified viral encephalitis
A87 Viral meningitis
G01 Meningitis in bacterial diseases classified elsewhere
G02 Meningitis in other infectious and parasitic diseases classified elsewhere
G03 Meningitis due to other and unspecified causes
G04 Encephalitis, myelitis and encephalomyelitis
G05 Encephalitis, myelitis and encephalomyelitis in diseases classified elsewhere
P37.52 Invasive neonatal candidiasis
T81.1 Shock during or resulting from a procedure, not elsewhere classified
O88.3 Obstetric pyaemic and septic embolism
O75.3 Other infection during labour
O86 Other puerperal infections
Notes
Inpatients are assigned to the sepsis category if any diagnosis (principal or any additional diagnosis) is within the list of codes specified, including all subdivisions of the codes.

Inpatients are assigned to the infections category if they have not already been assigned to the sepsis category, and if any diagnosis is within the range of codes specified. Note that the OECD list of infections includes some of the sepsis codes specified above, however these cases will already have been assigned to the sepsis category and so this won’t affect the results.

Inpatients are assigned to the all others category if they are not in either the sepsis or the infections category.

Day cases are excluded from the analysis.
### Appendix 16: Glossary of terms

<table>
<thead>
<tr>
<th>Acronym</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>AMR</td>
<td>Antimicrobial resistance</td>
</tr>
<tr>
<td>CCU</td>
<td>Coronary care unit</td>
</tr>
<tr>
<td>CNS</td>
<td>Central Nervous System</td>
</tr>
<tr>
<td>CSPD</td>
<td>Clinical Strategy and Programmes Directorate, HSE</td>
</tr>
<tr>
<td>CVP</td>
<td>Central Venous Pressure</td>
</tr>
<tr>
<td>DoH</td>
<td>Department of Health</td>
</tr>
<tr>
<td>ED</td>
<td>Emergency department</td>
</tr>
<tr>
<td>ESRi</td>
<td>The Economic and Social Research Institute</td>
</tr>
<tr>
<td>GDH</td>
<td>Glutamate dehydrogenase</td>
</tr>
<tr>
<td>GP</td>
<td>General practitioner</td>
</tr>
<tr>
<td>HCAI</td>
<td>Healthcare-associated infection</td>
</tr>
<tr>
<td>HCW</td>
<td>Healthcare worker/healthcare staff</td>
</tr>
<tr>
<td>HDU</td>
<td>High dependency unit</td>
</tr>
<tr>
<td>HIPE</td>
<td>Hospital Inpatient Enquiry Scheme</td>
</tr>
<tr>
<td>HPA</td>
<td>Health Protection Agency</td>
</tr>
<tr>
<td>HPSC</td>
<td>Health Protection Surveillance Centre</td>
</tr>
<tr>
<td>HIQA</td>
<td>Health Information and Quality Authority</td>
</tr>
<tr>
<td>HSE</td>
<td>Health Services Executive</td>
</tr>
<tr>
<td>IDSA</td>
<td>Infectious Disease Society of America (IDSA)</td>
</tr>
<tr>
<td>ICU</td>
<td>Intensive care unit</td>
</tr>
<tr>
<td>IMEWS</td>
<td>Irish Maternity Early Warning System</td>
</tr>
<tr>
<td>IV</td>
<td>Intravenous</td>
</tr>
<tr>
<td>IPC(T)</td>
<td>Infection prevention and control (team)</td>
</tr>
<tr>
<td>LOS</td>
<td>Length of stay</td>
</tr>
<tr>
<td>MAP</td>
<td>Mean arterial pressure</td>
</tr>
<tr>
<td>M EW S</td>
<td>Maternity Early Warning Score</td>
</tr>
<tr>
<td>NEWS</td>
<td>National Early Warning Score</td>
</tr>
<tr>
<td>NCP</td>
<td>National Clinical Programme</td>
</tr>
<tr>
<td>PEWS</td>
<td>Paediatric Early Warning Score</td>
</tr>
<tr>
<td>PPIs</td>
<td>Proton pump inhibitors</td>
</tr>
<tr>
<td>RCT</td>
<td>Randomised controlled trial</td>
</tr>
<tr>
<td>SAC</td>
<td>Scientific advisory committee</td>
</tr>
<tr>
<td>SCC</td>
<td>Surviving Sepsis Campaign</td>
</tr>
<tr>
<td>ScvO₂</td>
<td>Central Venous Oxygen Saturation</td>
</tr>
<tr>
<td>SPHM</td>
<td>Specialist in Public Health Medicine</td>
</tr>
<tr>
<td>US</td>
<td>United States</td>
</tr>
<tr>
<td>UFH</td>
<td>Unfractionated heparin</td>
</tr>
<tr>
<td>UK</td>
<td>United Kingdom</td>
</tr>
<tr>
<td>WHO</td>
<td>World Health Organisation</td>
</tr>
</tbody>
</table>
References


6. Regulatory impact statement New York State. Sections 405.2 and 405.4 of Title 10 (Health) of the Official Compilation of Codes, Rules and Regulations of the state of New York.


28. RCPI. Guidelines for the Safe and Effective Management and Use of Point of Care Testing. www.rcpi.ie/content/docs/000001/370_5_media.pdf


42. Sepsis management as an NHS clinical priority. Briefing - Professor Sir Mike Richards [Internet]. 2013.


50. Maheshwari V. Sepsis alert program leads to more timely diagnosis and treatment, reducing morbidity, mortality and length of stay. National Guideline Clearinghouse; 2013.


