An Roinn Sláinte
Department of Health

Sepsis Management for Adults (including maternity)

National Clinical Guideline No. 26

SUMMARY 2021

National Patient Safety Office
Oifig Náisiúnta um Shábháilteacht Othar

NATIONAL CLINICAL EFFECTIVENESS COMMITTEE

This National Clinical Guideline (NCG), has been developed by the Sepsis Guideline Development Group (GDG), within the HSE National Sepsis Programme (NSP). The National Clinical Effectiveness Committee (NCEC) was requested by the Minister for Health to commission the 2014 guideline arising from a significant patient safety/policy matter and this is the scheduled update.

Using this summary National Clinical Guideline

This summary should be read in conjunction with the full version NCEC NCG, the full version is available at:

https://www.gov.ie/en/collection/c9fa9a-national-clinical-guidelines/

The complete list of references and appendices can be found in the full version. Only relevant appendices are included in this summary.

Disclaimer

NCEC National Clinical Guidelines do not replace professional judgment on particular cases, whereby the clinician or health professional decides that individual guideline recommendations are not appropriate in the circumstances presented by an individual patient, or whereby an individual patient declines a recommendation as a course of action in their care or treatment plan. In these circumstances the decision not to follow a recommendation should be appropriately recorded in the patient's healthcare record.

Users of NCEC National Clinical Guidelines must ensure they have the current version by checking the relevant section in the National Patient Safety Office on the Department of Health website: https://www.gov.ie/en/collection/c9fa9a-national-clinical-guidelines/

Whilst every care has been taken to ensure that all the information contained in this publication is correct, the Department of Health cannot accept responsibility for any errors or omissions which may have occurred.

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Membership of the Guideline Development Group (GDG)

The GDG was chaired by Dr Vida Hamilton BE, MB, BAO, LRCP & SI, FCARCSI, EDIC, FJFICMI, National Clinical Lead for Sepsis (2014 – 2018). This NCG is supported by HSE Clinical Design and Innovation.

Membership nominations were sought from a variety of clinical and non-clinical backgrounds so as to be representative of all key stakeholders within the acute sector. GDG members included those involved in clinical practice, education, administration, research methodology and 2 persons representing patients and the public. The terms of reference for this group are outlined in Appendix 1.

Table 1. The National Clinical Guideline Development Group Membership

Name	Job title and affiliation
Dr Vida Hamilton (Chair)	National Clinical Advisor and Group Lead (Acute Hospitals) National Sepsis Clinical Lead (2013 – 2018)
Dr Martina Healy	National Sepsis Clinical Lead (2018 onwards)
Ciara Hughes **Christina Doyle**	Programme Manager National Sepsis (2019 onwards) Programme Manager National Sepsis (2013 – 2018)
Mary Bedding	Group Sepsis ADON RCSI Hospital Group
Dr Karn Cliffe	Group Sepsis ADON/M Dublin Midlands Hospital Group
Celine Conroy	Group Sepsis ADON Ireland East Hospital Group
Yvonne Young	Group Sepsis ADON University Limerick Hospital Group
Ronan O'Cathasaigh **Fidelma Gallagher**	Group Sepsis ADON Saolta Hospital Group (2016 – 2018) Group Sepsis ADON Saolta Hospital Group (2019 onwards)
Sinead Horgan **Catherine (Kay) O'Mahony**	Group Sepsis ADON South / South West Hospital Group (2015 – 2018 and 2020 onwards) Group Sepsis ADON South / South West Hospital Group (2019)
Dr Fidelma Fitzpatrick	Chair of Steering Group / Consultant Microbiologist
Dr Miriam Bell	Project Lead for National Early Warning System Guideline 2020 update
Dr Dorothy Breen	Consultant Anaesthetist, Cork University Hospital
Avilene Casey	Lead for the Deteriorating Patient Improvement Programme (Response and Recognition)
Dr Garry Courtney	Clinical Lead for the National Acute Medicine Programme
Jacqui Curley	Healthcare Pricing Office, HSE
Barbara Egan	Patient Representative
Dr Lynda Fenelon	Consultant Microbiologist
Jamie Logan	Nurse Lead for the National Clinical Programme for Surgery
Dr Anna Moore	Consultant in Emergency Medicine, Tullamore Hospital
Dr Gerry McCarthy	Clinical Lead for the Emergency Medicine Programme
Fiona McDaid	Nurse Lead for the Emergency Medicine Programme
Julieanne Mealy	Patient Representative

Dr Deborah McNamara	Clinical Lead for the National Clinical Programme for Surgery		
Michelle O'Neill	HRB-CICER /HIQA (Health Economics Expertise)		
Dr Michael Power	Clinical Lead for the Critical Care Programme		
Dr Karen Power	Irish Maternity Early Warning System representative		
Dr Yvonne Smith	Clinical Lead for the National Acute Medicine Programme		
Dr Omar Tujjar	Consultant Anaesthetist and Intensivist, Sligo University Hospital		
Gethin White	Clinical Librarian – Research, Information and Economic expert		
Experts co-opted on to GDG	Susan Ahern (HIQA) (Health Economics Expertise)		
	Subgroup of ICU Dietitians Group of INDI (Irish Nutrition and Dietetic Institute)		
	Jennifer Caffrey	Senior Dietitian	SVUH
	Aine Kelly	Senior Dietitian	TUH
	Carmel O'Hanlon	Clinical Specialist Dietitian	Beaumont
	Marcella Richardson	Senior Dietitian	UHL
	Geraldine Sexton	Senior Dietitian	MRHT
	Lisa Shanahan	Clinical Specialist Dietitian	MMUH
	Marie Sheahan	Senior Dietitian	CUH
	Clare Twomey	Senior Dietitian	CUH

Credits

The role of the NCEC is to prioritise, quality assure and recommend clinical guidelines to the Chief Medical Officer for endorsement by the Minister for Health. It is intended through Ministerial endorsement that full implementation of the guideline will occur through the relevant service plans.

The NCEC and the Department of Health acknowledge and recognise the Chair and members of the Guideline Development Group (GDG) for development of the guideline. The NCEC and Department of Health wish to express thanks and sincere gratitude to all persons contributing to this National Clinical Guideline; especially those that give of their time on a voluntary basis.

Acknowledgments

Sepsis is a common and time dependent medical emergency. It can affect any person of any age, from any social background and can strike irrespective of underlying good health or concurrent medical condition. This National Clinical guideline is intended to be relevant to all healthcare staff involved in the care of patients with sepsis and the suspicion of sepsis in the Republic of Ireland.

The **Surviving Sepsis Campaign** (SSC) is a global initiative which brings together professional organizations with the aim of reducing mortality from sepsis. The purpose of the SSC is to create an international collaborative effort to improve the treatment of sepsis and reduce the high mortality rate associated with the condition. The SSC published guidelines for Managing Sepsis and Septic Shock in 2012, and then in 2015, a consensus committee of 55 international experts representing 25 international organisations was

convened. The SSCG panel provided 93 statements on early management and resuscitation of patients with sepsis or septic shock.

The NSP is very grateful to the SSC for their kind permission to adopt the SSCG as the Irish National Clinical Guideline on Sepsis Management.

We also wish to acknowledge all the members of the National Sepsis Steering Committee (Appendix 2) and the Guideline Development Group (Table 1) who gave freely of their time and expertise. A special word of thanks to the external experts, Professor Kevin Rooney, National Clinical Lead on Sepsis, Healthcare Improvement Scotland and Professor of Care Improvement, University of the West of Scotland and the Dr. John Bates from the Joint Faculty of Intensive Care Medicine in Ireland.

A special word of thanks also to the National Sepsis Programme team for their hard work and dedication to seeing this project through to completion. To the group sepsis ADONS, Celine Conroy, Karn Cliffe, Mary Bedding, Yvonne Young, Fidelma Gallagher, Sinead Horgan, and the programme manager, Ciara Hughes. Thanks also to the former team members, Kay O'Mahony, Ronán O'Cathasaigh and Christina Doyle for their part in the initial phase of this project.

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We gratefully acknowledge the support and advice provided to the GDG from HRB-CICER and HIQA on the methodology and the budget impact analysis.

Finally, our appreciation goes to Dr Rob Cunney (HPSC) and AMRIC for their input to the antimicrobial stewardship section.

Dr Fidelma Fitzpatrick, Chair, National Sepsis Steering Committee.

Dr Vida Hamilton, National Clinical Advisor and Group Lead (Acute Hospitals), Chair, Guideline Development Group.

Dr Martina Healy, Clinical Lead for the National Sepsis Programme.

Signed by the Chair(s):

Fidelma Fitzpatrick Date: 30th January 2020

National Clinical Guidelines

Providing standardised clinical care to patients in healthcare is challenging. This is due to a number of factors, among them variations in environments of care and complex patient presentations. It is self-evident that safe, effective care and treatment are important in ensuring that patients get the best outcomes from their care.

The Department of Health is of the view that supporting evidence-based practice, through the clinical effectiveness framework, is a critical element of the health service to deliver safe and high-quality care. The National Clinical Effectiveness Committee (NCEC) is a Ministerial committee set up in 2010 as a key recommendation of the report of the Commission on Patient Safety and Quality Assurance (2008). The establishment of the Commission was prompted by an increasing awareness of patient safety issues in general and high-profile health service system failures at home and abroad.

The NCEC on behalf of the Department of Health has embarked on a quality assured National Clinical Guideline development process linked to service delivery priorities. Furthermore, implementing National Clinical Guidelines sets a standard nationally, to enable healthcare professionals to deliver safe and effective care and treatment while monitoring their individual, team and organisation's performance.

The aim of NCEC National Clinical Guidelines is to reduce unnecessary variations in practice and provide an evidence base for the most appropriate healthcare, in particular circumstances. As a consequence of Ministerial mandate, it is expected that NCEC National Clinical Guidelines are implemented across all relevant services in the Irish healthcare setting.

The NCEC is a partnership between key stakeholders in patient safety. NCEC's mission is to provide a framework for national endorsement of clinical guidelines and clinical audit to optimise patient and service user care. The NCEC has a remit to establish and implement processes for the prioritisation and quality assurance of clinical guidelines and 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. The aim of the suite of National Clinical Guidelines is to provide guidance and standards for improving the quality, safety and cost-effectiveness of healthcare in Ireland. The implementation of these National Clinical Guidelines will support the provision of evidence-based and consistent care across Irish healthcare services.

NCEC Terms of Reference

1. Provide strategic leadership for the national clinical effectiveness agenda.
2. Contribute to national patient safety and quality improvement agendas.
3. Publish standards for clinical practice guidance.
4. Publish guidance for National Clinical Guidelines and National Clinical Audit.
5. Prioritise and quality assure National Clinical Guidelines and National Clinical Audit.
6. Commission National Clinical Guidelines and National Clinical Audit.
7. Align National Clinical Guidelines and National Clinical Audit with implementation levers.
8. Report periodically on the implementation and impact of National Clinical Guidelines and the performance of National Clinical Audit.
9. Establish sub-committees for NCEC workstreams.
10. Publish an annual report.

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1 National Clinical Guideline recommendations

1.1 Summary of recommendations

The glossary of terms and abbreviations used throughout this document are explained in Appendix 3.

SSC Guideline: https://journals.lww.com/ccmjournal/Fulltext/2017/03000/Surviving_Sepsis_Campaign___International.15.aspx provides explanation on grading of recommendations and levels of evidence (Rhodes et al., 2017).

Table 2. The Surviving Sepsis Campaign (SSC) recommendations are adopted in total for this guideline.

Section	Recommendation	Quality of Evidence	Strength of Recommendation
Screening for sepsis and performance improvement	1. We recommend that hospitals and hospital systems have a performance improvement program for sepsis, including sepsis screening for acutely ill, high-risk patients. (SSCG Section B, Recommendation 1)	Low	Best Practice Statement (BPS).
Initial resuscitation	2. Sepsis and septic shock are medical emergencies, and we recommend that treatment and resuscitation begin immediately. (SSCG Section A, Recommendation 1)	Low	BPS
	3. We recommend that, in the resuscitation from sepsis-induced hypoperfusion, at least 30 mL/kg of IV crystalloid fluid be given within the first 3 hours. (SSCG Section A, Recommendation 2) **SSCG 2018 Update:** The 3-h and 6-h bundles have been combined into a single "hour-1 bundle" with the explicit intention of beginning resuscitation and management immediately for patients with sepsis and septic shock. More than 1 hour may be required for resuscitation to be completed, but initiation of resuscitation and treatment, such as obtaining blood for measuring lactate and blood cultures, administration of fluids and antibiotics, and in the case of life-threatening hypotension, initiation of vasopressor therapy, are all begun immediately.	Low	Strong

	4. We recommend that, following initial fluid resuscitation, additional fluids be guided by frequent reassessment of hemodynamic status. (SSCG Section A, Recommendation 3)	Low	BPS
	5. We suggest guiding resuscitation to normalize lactate in patients with elevated lactate levels as a marker of tissue hypoperfusion. (SSCG Section A, Recommendation 7)	Low	Weak
	6. We recommend further hemodynamic assessment (such as assessing cardiac function) to determine the type of shock if the clinical examination does not lead to a clear diagnosis. (SSCG Section A, Recommendation 4)	Low	BPS
	7. We suggest that dynamic over static variables be used to predict fluid responsiveness, where available. (SSCG Section A, Recommendation 5)	Low	Weak
	8. We recommend an initial target mean arterial pressure (MAP) of 65 mmHg in patients with septic shock requiring vasopressors. (SSCG Section A, Recommendation 6)	Moderate	Strong
	9. We recommend that a fluid challenge technique be applied where fluid administration is continued as long as hemodynamic factors continue to improve. (SSCG Section F, Recommendation 1)	Low	BPS
	10. We recommend crystalloids as the fluid of choice for initial resuscitation and subsequent intravascular volume replacement in patients with sepsis and septic shock. (SSCG Section F, Recommendation 2)	Moderate	Strong
	11. We suggest using either balanced crystalloids or saline for fluid resuscitation of patients with sepsis or septic shock. (SSCG Section F, Recommendation 3)	Low	Weak

Notes:

i. See Appendix 7 for grading system used by NICE (7a) for Recommendations 1 and 2, and the GRADE approach (7b) used for Recommendation 3.

ii. Fidelity in 3.5 is the degree to which the malnutrition screening tool is delivered exactly as set out and intended by those who developed it.

	12. We suggest using albumin in addition to crystalloids for initial resuscitation and subsequent intravascular volume replacement in patients with sepsis and septic shock when patients require substantial amounts of crystalloids. (SSCG Section F, Recommendation 4)	Low	Weak
	13. We **recommend against** using hydroxyethyl starches (HESs) for intravascular volume replacement in patients with sepsis or septic shock. (SSCG Section F, Recommendation 5)	High	Strong
	14. We suggest using crystalloids over gelatins when resuscitating patients with sepsis or septic shock. (SSCG Section F, Recommendation 6)	Low	Weak
Antimicrobial therapy	15. We recommend that appropriate routine microbiologic cultures (including blood) be obtained before starting antimicrobial therapy in patients with suspected sepsis or septic shock if doing so results in no substantial delay in the start of antimicrobials. (SSCG Section C, Recommendation 1)	Low	BPS
Start Smart	16. We recommend that administration of IV antimicrobials be initiated as soon as possible after recognition and within one hour for both sepsis and septic shock. (SSCG Section D, Recommendation 1)	Moderate	Strong
	17.We recommend empiric broad-spectrum therapy with one or more antimicrobials for patients presenting with sepsis or septic shock to cover all likely pathogens (including bacterial and potentially fungal or viral coverage). (SSCG Section D, Recommendation 2)	Moderate	Strong
	18. We recommend that dosing strategies of antimicrobials be optimized based on accepted pharmacokinetic/ pharmacodynamic principles and specific drug properties in patients with sepsis or septic shock. (SSCG Section D, Recommendation 5)	Low	BPS

	19. We suggest empiric combination therapy (using at least two antibiotics of different antimicrobial classes) aimed at the most likely bacterial pathogen(s) for the initial management of septic shock. (SSCG Section D, Recommendation 6)	Low	Weak
	20. We suggest that combination therapy not be routinely used for ongoing treatment of most other serious infections, including bacteraemia and sepsis without shock. (SSCG Section D, Recommendation 7)	Low	Weak
	21. We r**ecommend against** combination therapy for the routine treatment of neutropenic sepsis/bacteraemia. (SSCG Section D, Recommendation 8)	Moderate	Strong
Then Focus	22. We recommend that empiric antimicrobial therapy be narrowed once pathogen identification and sensitivities are established and/or adequate clinical improvement is note. (SSCG Section D, Recommendation 3)	Low	BPS
	23. If combination therapy is initially used for septic shock, we recommend de-escalation with discontinuation of combination therapy within the first few days in response to clinical improvement and/or evidence of infection resolution. This applies to both targeted (for culture-positive infections) and empiric (for culture-negative infections) combination therapy. (SSCG Section D, Recommendation 9)	Low	BPS
	24. We recommend daily assessment for de-escalation of antimicrobial therapy in patients with sepsis and septic shock. (SSCG Section D, Recommendation 13)	Low	BPS
	25. We recommend against sustained systemic antimicrobial prophylaxis in patients with severe inflammatory states of non-infectious origin (e.g., severe pancreatitis, burn injury). (SSCG Section D, Recommendation 4)	Low	BPS

	26. We suggest that measurement of procalcitonin levels can be used to support shortening the duration of antimicrobial therapy in sepsis patients. (SSCG Section D, Recommendation 14)	Low	Weak
	27. We suggest that procalcitonin levels can be used to support the discontinuation of empiric antibiotics in patients who initially appeared to have sepsis, but subsequently have limited clinical evidence of infection. (SSCG Section D, Recommendation 15)	Low	Weak
	28. We suggest that an antimicrobial treatment duration of 7 to 10 days is adequate for most serious infections associated with sepsis and septic shock. (SSCG Section D, Recommendation 10)	Low	Weak
	29. We suggest that longer courses are appropriate in patients who have a slow clinical response, undrainable foci of infection, bacteraemia with S. aureus, some fungal and viral infections, or immunologic deficiencies, including neutropenia. (SSCG Section D, Recommendation 11)	Low	Weak
	30. We suggest that shorter courses are appropriate in some patients, particularly those with rapid clinical resolution following effective source control of intra-abdominal or urinary sepsis and those with anatomically uncomplicated pyelonephritis. (SSCG Section D, Recommendation 12)	Low	Weak
Source Control	31. We recommend that a specific anatomic diagnosis of infection requiring emergent source control be identified or excluded as rapidly as possible in patients with sepsis or septic shock, and that any required source control intervention be implemented as soon as medically and logistically practical after the diagnosis is made. (SSCG Section E, Recommendation 1)	Low	BPS

	32. We recommend prompt removal of intravascular access devices that are a possible source of sepsis or septic shock after other vascular access has been established. (SSCG Section E, Recommendation 2)	Low	BPS
Vasoactive medications	33. We recommend norepinephrine as the first-choice vasopressor. (SSCG Section G, Recommendation 1)	Moderate	Strong
	34. We suggest adding either vasopressin (up to 0.03 U/min) (weak recommendation, moderate quality of evidence) or epinephrine (weak recommendation, low quality of evidence) to norepinephrine with the intent of raising MAP to target, or adding vasopressin (up to 0.03 U/min) to decrease norepinephrine dosage. (SSCG Section G, Recommendation 2)	Moderate	Weak
	35. We suggest using dopamine as an alternative vasopressor agent to norepinephrine only in highly selected patients (e.g., patients with low risk of tachyarrhythmias and absolute or relative bradycardia). (SSCG Section G, Recommendation 3)	Low	Weak
	36. We **recommend against** using low-dose dopamine for renal protection. (SSCG Section G, Recommendation 4)	High	Strong
	37. We suggest using dobutamine in patients who show evidence of persistent hypoperfusion despite adequate fluid loading and the use of vasopressor agents. (SSCG Section G, Recommendation 5)	Low	Weak
	38. We suggest that all patients requiring vasopressors have an arterial catheter placed as soon as practical if resources are available. (SSCG Section G, Recommendation 6)	Very Low	Weak

Corticosteriods	39. We suggest against using IV hydrocortisone to treat septic shock patients if adequate fluid resuscitation and vasopressor therapy are able to restore hemodynamic stability. If this is not achievable, we suggest IV hydrocortisone at a dose of 200 mg per day. (SSCG Section H, Recommendation 1)	Low	Weak
Blood products	40. We recommend that RBC transfusion occur only when haemoglobin concentration decreases to < 7.0 g/dL in adults in the absence of extenuating circumstances, such as myocardial ischemia, severe hypoxemia, or acute haemorrhage. (SSCG Section I, Recommendation 1)	High	Strong
	41. We **recommend against** the use of erythropoietin for treatment of anaemia associated with sepsis. (SSCG Section I, Recommendation 2)	Moderate	Strong
	42. We **suggest against** the use of fresh frozen plasma to correct clotting abnormalities in the absence of bleeding or planned invasive procedures. (SSCG Section I, Recommendation 3)	Very Low	Weak
	43. We suggest prophylactic platelet transfusion when counts are < 10 × 109/L (10,000/mm3) in the absence of apparent bleeding and when counts are < 20 × 109/L (20,000/mm3) if the patient has a significant risk of bleeding. Higher platelet counts ≥ 50 × 109/L (50,000/mm3) are advised for active bleeding, surgery, or invasive procedures. (SSCG Section I, Recommendation 4)	Very Low	Weak
Immunoglobulins	44. We **suggest against** the use of IV immunoglobulins in patients with sepsis or septic shock. (SSCG Section J, Recommendation 1)	Low	Weak
Blood purification	45. We make **no recommendation** regarding the use of blood purification techniques. (SSCG Section K, Recommendation 1)	N/A	N/A

Anticoagulants	46. We **recommend against** the use of antithrombin for the treatment of sepsis and septic shock. (SSCG Section L, Recommendation 1)	Moderate	Strong
	47. We make no recommendation regarding the use of thrombomodulin or heparin for the treatment of sepsis or septic shock. (SSCG Section L, Recommendation 2)	N/A	N/A
Mechanical Ventilation	48. We recommend using a target tidal volume of 6 mL/kg predicted body weight (PBW) compared with 12 mL/kg in adult patients with sepsis induced acute respiratory distress syndrome (ARDS). (SSCG Section M, Recommendation 1)	High	Strong
	49. We recommend using an upper limit goal for plateau pressures of 22mmHg (30cm H2O) over higher plateau pressures in adult patients with sepsis induced severe ARDS. (SSCG Section M, Recommendation 2)	Moderate	Strong
	50. We suggest using higher PEEP over lower PEEP in adult patients with sepsis induced moderate to severe ARDS. (SSCG Section M, Recommendation 3)	Moderate	Weak
	51. We suggest using recruitment manoeuvres in adult patients with sepsis induced, severe ARDS. (SSCG Section M, Recommendation 4)	Moderate	Weak
	52. We recommend using prone over supine position in adult patients with sepsis induced ARDS and a PaO2/Fio2 ratio < 20 KPA (150 mmHg). (SSCG Section M, Recommendation 5)	Moderate	Strong
	53. We **recommend against** using high-frequency oscillatory ventilation (HFOV) in adult patients with sepsis-induced ARDS. (SSCG Section M, Recommendation 6)	Moderate	Strong
	54. We make **no recommendation** regarding the use of non-invasive ventilation (NIV) for patients with sepsis induced ARDS. (SSCG Section M, Recommendation 7)	N/A	N/A

	55. We suggest using neuromuscular blocking agents (NMBAs) for ≤ 48 hours in adult patients with sepsis- induced ARDS and a PaO2/Fio2 ratio < 20 KPA (150 mmHg). (SSCG Section M, Recommendation 8)	Moderate	Weak
	56. We recommend a conservative fluid strategy for patients with established sepsis induced ARDS who do not have evidence of tissue hypoperfusion. (SSCG Section M, Recommendation 9)	Moderate	Strong
	57. We **recommend against** the use of β-2 agonists for the treatment of patients with sepsis induced ARDS without bronchospasm. (SSCG Section M, Recommendation 10)	Moderate	Strong
	58. We **recommend against** the routine use of the PA catheter for patients with sepsis induced ARDS. (SSCG Section M, Recommendation 11)	High	Strong
	59. We suggest using lower tidal volumes over higher tidal volumes in adult patients with sepsis induced respiratory failure without ARDS. (SSCG Section M, Recommendation 12)	Low	Weak
	60. We recommend that mechanically ventilated sepsis patients be maintained with the head of the bed elevated between 30 and 45 degrees to limit aspiration risk and to prevent the development of VAP. (SSCG Section M, Recommendation 13)	Low	Strong
	61. We recommend using spontaneous breathing trials in mechanically ventilated patients with sepsis who are ready for weaning. (SSCG Section M, Recommendation 14)	High	Strong
	62. We recommend using a weaning protocol in mechanically ventilated patients with sepsis induced respiratory failure who can tolerate weaning. (SSCG Section M, Recommendation 15)	Moderate	Strong

Sedation and analgesia	63. We recommend that continuous or intermittent sedation be minimized in mechanically ventilated sepsis patients, targeting specific titration end points. (SSCG Section N, Recommendation 1)	Low	BPS
Glucose control	64. We recommend a protocolized approach to blood glucose management in ICU patients with sepsis, commencing insulin dosing when two consecutive blood glucose levels are >10mmol/L (180mg/dL). This approach should target an upper blood glucose level ≤10mmol/L (180mg/dL) rather than an upper target blood glucose level ≤6.1mmol/L (110mg/dL). (SSCG Section O, Recommendation 1)	High	Strong
	65. We recommend that blood glucose values be monitored every 1 to 2 hours until glucose values and insulin infusion rates are stable, then every 4 hours thereafter in patients receiving insulin infusions. (SSCG Section O, Recommendation 2)	Low	BPS
	66. We recommend that glucose levels obtained with point-of-care testing of capillary blood be interpreted with caution because such measurements may not accurately estimate arterial blood or plasma glucose values. (SSCG Section O, Recommendation 3)	Low	BPS
	67. We suggest the use of arterial blood rather than capillary blood for point-of-care testing using glucose meters if patients have arterial catheters. (SSCG Section O, Recommendation 4)	Low	Weak
Renal Replacement Therapy	68. We suggest that either continuous RRT (CRRT) or intermittent RRT be used in patients with sepsis and acute kidney injury. (SSCG Section P, Recommendation 1)	Moderate	Weak
	69. We suggest using CRRT to facilitate management of fluid balance in hemodynamically unstable septic patients. (SSCG Section P, Recommendation 2)	Very Low	Weak

	70. We **suggest against** the use of RRT in patients with sepsis and acute kidney injury for increase in creatinine or oliguria without other definitive indications for dialysis. (SSCG Section P, Recommendation 3)	Low	Weak
Bicarbonate therapy	71. We **suggest against** the use of sodium bicarbonate therapy to improve haemodynamics or to reduce vasopressor requirements in patients with hypoperfusion-induced lactic acidaemia with pH ≥ 7.15. (SSCG Section Q, Recommendation 1)	Moderate	Weak
Venous Thromboembolism prophylaxis	72. We recommend pharmacologic prophylaxis (unfractionated heparin [UFH] or low-molecular-weight heparin [LMWH]) against venous thromboembolism (VTE) in the absence of contraindications to the use of these agents. (SSCG Section R, Recommendation 1)	Moderate	Strong
	73. We recommend LMWH rather than UFH for VTE prophylaxis in the absence of contraindications to the use of LMWH. (SSCG Section R, Recommendation 2)	Moderate	Strong
	74. We suggest combination pharmacologic VTE prophylaxis and mechanical prophylaxis, whenever possible. (SSCG Section R, Recommendation 3)	Low	Weak
	75. We suggest mechanical VTE prophylaxis when pharmacologic VTE is contraindicated. (SSCG Section R, Recommendation 4)	Low	Weak
Stress Ulcer Prophylaxis	76. We recommend that stress ulcer prophylaxis be given to patients with sepsis or septic shock who have risk factors for gastrointestinal (GI) bleeding. (SSCG Section S, Recommendation 1)	Low	Strong
	77. We suggest using either proton pump inhibitors (PPIs) or histamine-2 receptor antagonists (H2RAs) when stress ulcer prophylaxis is indicated. (SSCG Section S, Recommendation 2)	Low	Weak

	78. We **recommend against** stress ulcer prophylaxis in patients without risk factors for GI bleeding. (SSCG Section S, Recommendation 3)	Low	BPS
Nutrition	79. We r**ecommend against** the administration of early parenteral nutrition alone or parenteral nutrition in combination with enteral feedings (but rather initiate early enteral nutrition) in critically ill patients with sepsis or septic shock who can be fed enterally. (SSCG Section T, Recommendation 1)	Moderate	Strong
	80. We **recommend against** the administration of parenteral nutrition alone or in combination with enteral feeds (but rather to initiate IV glucose and advance enteral feeds as tolerated) over the first 7 days in critically ill patients with sepsis or septic shock for whom early enteral feeding is not feasible. (SSCG Section T, Recommendation 2)	Moderate	Strong
	81. We suggest the early initiation of enteral feeding rather than a complete fast or only IV glucose in critically ill patients with sepsis or septic shock who can be fed enterally. (SSCG Section T, Recommendation 3)	Low	Weak
	82. We suggest either early trophic/ hypocaloric or early full enteral feeding in critically ill patients with sepsis or septic shock; if trophic/hypocaloric feeding is the initial strategy, then feeds should be advanced according to patient tolerance. (SSCG Section T, Recommendation 4)	Moderate	Weak
	83. We **recommend against** the use of omega-3 fatty acids as an immune supplement in critically ill patients with sepsis or septic shock. (SSCG Section T, Recommendation 5)	Low	Strong
	84. We **suggest against** routinely monitoring gastric residual volumes (GRVs) in critically ill patients with sepsis or septic shock (weak recommendation, low quality of evidence). However, we suggest measurement of gastric residuals in patients with feeding intolerance or who are considered to be at high risk of aspiration. (SSCG Section T, Recommendation 6)	Very Low	Weak

	85. We suggest the use of prokinetic agents in critically ill patients with sepsis or septic shock and feeding intolerance. (SSCG Section T, Recommendation 7)	Low	Weak
	86. We suggest placement of post-pyloric feeding tubes in critically ill patients with sepsis or septic shock with feeding intolerance or who are considered to be at high risk of aspiration. (SSCG Section T, Recommendation 8)	Low	Weak
	87. We **recommend against** the use of IV selenium to treat sepsis and septic shock. (SSCG Section T, Recommendation 9)	Moderate	Strong
	88. We **suggest against** the use of arginine to treat sepsis and septic shock. (SSCG Section T, Recommendation 10)	Low	Weak
	89. We **recommend against** the use of glutamine to treat sepsis and septic shock. (SSCG Section T, Recommendation 11)	Moderate	Strong
	90. We make no recommendation about the use of carnitine for sepsis and septic shock. (SSCG Section T, Recommendation 12)	N/A	N/A
Setting goals of care	91. We recommend that goals of care and prognosis be discussed with patients and families. (SSCG Section U, Recommendation 1)	Low	BPS
	92. We recommend that goals of care be incorporated into treatment and end-of-life care planning, utilizing palliative care principles where appropriate. (SSCG Section U, Recommendation 2)	Moderate	Strong
	93. We suggest that goals of care be addressed as early as feasible, but no later than within 72 hours of ICU admission. (SSCG Section U, Recommendation 3)	Low	Weak

Key questions and evidence statements are available in the full guideline.

2 Development of the National Clinical Guideline

2.1 Background

Sepsis is life-threatening organ dysfunction due to a dysregulated host response to infection (Singer et al., 2016). International estimates of incidence vary and despite declining age-standardised incidence and mortality, sepsis remains a major cause of health loss worldwide (Rudd et al., 2020). This study found that there were 48.9 million cases of sepsis in 2017 resulting in 11 million deaths worldwide, confirming that the actual rates are double than previously estimated, and that 20 per cent of global deaths are due to this under-reported but deadly medical condition. Information on the National Sepsis Programme and statistics on sepsis in Ireland are available at https://www.hse.ie/eng/about/who/cspd/ncps/sepsis/resources/

2.1.1 Definitions

It is recognised that in recent years, confusion has arisen with the changing definitions of sepsis and septic shock and the use of SIRS criteria. The understanding of sepsis has evolved over the years and as such so have the definitions (Table 3).

Table 3. History of Sepsis Definitions

Year	SRIS	Sepsis	Severe Sepsis	Septic Shock
Sepsis 1* (1992)	**Systemic inflammatory response syndrome** (SIRS) = the systemic inflammatory response to a variety of severe clinical insults in this instance infection: 1. Temperature >38°C or < 36°C 2. Heart rate >90 beats per minute 3. Respiratory rate >20 breaths per minute or PaCO2 < 32mmHg 4. White blood cell count >12,000 cells/µl <4,000/µl	**Sepsis** = the systemic response to infection, manifested by two or more of the SIRS criteria as a result of infection.	**Severe sepsis** = sepsis associated with organ dysfunction, hypoperfusion, or hypotension. Hypoperfusion and perfusion abnormalities may include, but are not limited to lactic acidosis, oliguria, or an acute alteration in mental status.	**Septic Shock** = sepsis-induced hypotension despite adequate fluid resuscitation along with the presence of perfusion abnormalities that may include, but are not limited to, lactic acidosis, oliguria, or an acute alteration in mental status.

Sepsis 2 (2001, 2008 & 2012)**	**Systemic inflammatory response syndrome** (SIRS) = the systemic inflammatory response to a variety of severe clinical insults in this instance infection: i. Temperature >38°C or < 36°C ii. Heart rate >90 beats per minute iii. Respiratory rate >20 breaths per minute or PaCO2 < 32mmHg iv. White blood cell count >12,000 cells/µl <4,000/µl (*Plus, general additional parameters under Sepsis)	**Sepsis** Infection documented or suspected and some of the following: General parameters* Fever (core temperature >38.3°C) Hypothermia (core temperature 90 bpm or >2 SD above the normal value for age Tachypnoea: >30 bpm Altered mental status Significant oedema or positive fluid balance (>20 mL kg-1 over 24 h) Hyperglycaemia (plasma glucose >110 mg dL-1 or 7.7 mM L-1) in the absence of diabetes **Also: Inflammatory parameters, Organ dysfunction parameters and Tissue perfusion parameters**	**Severe sepsis** = sepsis associated with organ dysfunction, hypoperfusion, or hypotension. Hypoperfusion and perfusion abnormalities may include, but are not limited to lactic acidosis, oliguria, or an acute alteration in mental status **(1992, 2001, 2008, 2012)**	**Septic shock** = a state of acute circulatory failure characterized by persistent arterial hypotension unexplained by other causes (2001, 2012). Sepsis induced tissue hypoperfusion is defined as either septic shock, an elevated lactate or oliguria **(2008, 2012).**
Sepsis 3* (2016)**	No longer utilised in sepsis definition	Sepsis is life-threatening organ dysfunction caused by a dysregulated host response to infection	No longer used as a definition	Septic shock is a subset of sepsis in which underlying circulatory and cellular/metabolic abnormalities are profound enough to substantially increase mortality

* **Sepsis 1** refers to the 1st consensus definition (Bone et al., 1992)

Sepsis 2 refers to the 2nd consensus definition (Levy et al., 2003) (Dellinger et al., 2008) (Martin, 2012)

***Sepsis 3** refers to the 3rd consensus definition (Rhodes et al., 2017)

The NCG has adopted the Sepsis 3 definition and the rationale are outlined below.

Sepsis 6 is the name given to a bundle of medical therapies designed to reduce mortality in patients with sepsis (Take 3 and Give 3). Sepsis 6 was developed by The UK Sepsis Trust (Daniels et al., 2011) as a practical tool to help healthcare professionals deliver the SSCG 1 hour bundle.

Sepsis 6 + 1 is the same as Sepsis 6 but + 1 refers to Fetal wellbeing. Resuscitating the mother will resuscitate the baby, however, it is important to assess fetal wellbeing and formulate a plan for delivery if required. Maternal sepsis with or without haemodynamic instability may present with fetal distress as the uteroplacental circulation is not auto-regulated (Chau, 2014). Thus any maternal circulatory insufficiency arising from sepsis may result in compromised fetal perfusion.

2.1.1.1 Systemic Inflammatory Response Syndrome (SIRS)

Much has been made of the removal of the systemic inflammatory response syndrome (SIRS) criteria from the definition of sepsis. However, this does not mean that SIRS have 'gone away'. It reflects the fact that self-limiting non-life-threatening infections may present with SIRS and that SIRS may be caused by infectious and non-infectious insults. The criteria for a systemic inflammatory response (SIRS) are fulfilled when 2 or more of the following are present (Bone et al., 1992).

Adult non-pregnant

- Heart rate > 90 beats/minute
- Respiratory rate > 20 breaths/minute
- Temperature > 38.3°C or < 36°C
- White cell count > 12 or < 4 x 109 cells/L or normal with > 10% immature forms
- Bedside glucose >7.7mmol/L in the absence of diabetes mellitus.

Maternity: Modified SIRS for women, pregnant and up to 42 days in the postnatal period. Physiological changes must be sustained not transient.

- Heart rate ≥ 100 beats/minute (Carlin, 2008, Hayes, 2012, Soma-Pillay et al., 2016)
- Respiratory rate ≥ 20 breathes/minute
- Temperature > 38°C or < 36°C (NWIHP, 2019, NCEC, 2019)
- White cell count > 16.9 or < 4 x 109 cells/L or > 10% immature bands
- Blood sugar level > 7.7 mmol/L (in the non-diabetic)
- Acutely altered mental status
- Fetal heart Rate > 160 bpm

The rationale behind the shift away from the SIRS-based definition of sepsis (Sepsis 2) is primarily three-fold.

- The over-sensitivity of the previous definition that included a cohort of patients who did not have a life-threatening illness and whose clinical course would not be impacted by escalated care (Churpek et al., 2015), (Comstedt et al., 2009).
- Its failure to recognise patients with a life-threatening acute organ dysfunction due to infection that would benefit from escalated care but who did not present with a SIRS response (Comstedt et al., 2009), (Kaukonen et al., 2015).
- The lack of specificity of the SIRS response that can be triggered by many non-infective insults (Thoeni, 2012).

Whilst the presence of a systemic inflammatory response (SIRS) is helpful in diagnosing infection, it is no longer a requirement for the diagnosis of sepsis, (Singer et al., 2016).

2.1.1.2 Sepsis definitions for this NCG

Sepsis is life-threatening organ dysfunction caused by a dysregulated host response to infection (Singer et al., 2016).

Maternal sepsis is a life-threatening condition defined as organ dysfunction resulting from infection during pregnancy, childbirth, post-abortion or postpartum period (WHO, 2017).

The clinical application of this latest definition requires that there be evidence to support infection as the cause of the patient being unwell based on history, examination and clinical or biochemical evidence of acute organ dysfunction consequent to that infection. The guideline recognises that there is no single test that confirms the presence of infection or sepsis but rather the diagnosis is based on the presence of a suite of symptoms and signs supported by tests and investigations. It also recognises that whilst the identification of a pathological organism is very valuable in guiding treatment, that blood cultures are only positive in 40-55% of cases (Martin et al., 2003), (Brun-Buisson et al., 1995), and in some cases even lower (Coburn et al., 2012) (Jones and Lowes, 1996), and that a negative culture does not preclude the diagnosis of infection or sepsis.

2.1.1.3 Septic Shock definition

All adults

Septic shock is a subset of sepsis with circulatory and cellular/metabolic dysfunction associated with a higher risk of mortality (Singer et al., 2016). The sepsis definition taskforce has defined this as the requirement for vasopressors/ inotropes to achieve a mean arterial pressure of ≥ 65mmHg AND a lactate > 2mmols/l despite adequate fluid resuscitation (Singer et al., 2016). The rationale behind this definition is to identify the cohort of patients with a mortality risk of > 40% for the purposes of international comparison. Patients with a vasopressor requirement and normal lactate post resuscitation have a mortality risk of > 30% (Singer et al., 2016).

Patients who require vasopressors or inotropes to maintain adequate perfusion pressure post fluid resuscitation require critical care whether their lactate is raised or not. For this reason, this NCG uses the persistent requirement for vasopressors/inotropes post adequate fluid resuscitation as its definition of septic shock. This is a pragmatic decision for the purposes of facilitating clinical care, recognizing that lactate measurement is not always available and that the sepsis definition taskforce allowed for this:

'In settings in which lactate measurement is not available, the use of a working diagnosis of septic shock using hypotension and other criteria consistent with tissue hypoperfusion (e.g. delayed capillary refill) may be necessary' (Singer et al., 2016).

2.1.1.4. Criteria to support diagnosis of sepsis.

To assist healthcare professionals in diagnosing sepsis and septic shock, criteria outlined in Table 4 have been developed.

Table 4. Summary of diagnostic criteria used by the NCG

Infection	A clinical syndrome based on symptoms and signs caused by pathological organisms, which may or may not be identified.
Sepsis	One or more acute organ dysfunction consequent to infection. Of note this was formerly defined as "Severe sepsis". When used now, severe sepsis is a descriptive term rather than a definition much like severe pneumonia.
Septic shock	A vasopressor or inotrope requirement to maintain mean arterial pressure (MAP) ≥ 65mmHg despite adequate fluid resuscitation which has been triggered by infection.

What is the impact of sepsis in Ireland?

In 2018, sepsis or septic shock was documented in 14,639 non-pregnant adults and these patients had a mortality rate of 20.3% (HSE, 2019b). There were 12,005 patients, with a sepsis diagnosis, who were assigned to a medical diagnostic related group (DRG), and these patients had an average length of stay (AvLOS) of 17.1 days, which is 49.6% longer than those who had a diagnosis of infection. Medical patients with a hospital stay complicated by sepsis had a mortality rate of 19.4%. 2,634 patients were assigned to a surgical DRG and they had an AvLOS of 46.4 days, 127% longer than those with an infection diagnosis. Surgical patients whose hospital stay was complicated by sepsis had a mortality rate of 24.8%. 31.7% of all hospital inpatients were documented as having an infection or sepsis as part of their discharge diagnoses and they occupied 49.4% of the acute hospital beds.

Sepsis affected 3.33% of inpatients but contributed to 27% of all hospital deaths, a documentation rate of 303 cases per 100,000 population per annum. In 2017, chart review audits were performed by the Sepsis Group Assistant Directors of Nursing (ADONS) on 523 charts nationally. Charts were sampled from all acute hospitals and included patients with infection and acute kidney injury cared for by medical physicians, surgeons and emergency medicine physicians. This audit demonstrated that only 52% of cases that fulfilled the criteria for sepsis were actually documented as sepsis, applying this rate to national figures would lead to sepsis affecting up to 6.7% of hospital inpatients or approximately 583 per 100,000 population per annum. This is consistent with other jurisdictions that have published data based on administrative databases (Angus et al., 2001).

Three highly publicised maternal deaths have occurred in Ireland since 2007 identifying failings around assessment, monitoring and recognition of sepsis and septic shock. Mortality from maternal sepsis from direct causes is currently 0.5% (HSE, 2019b) and 0.44 per 100,000 maternities (Knight M, 2019). The Irish data is based on the number of women who developed sepsis in Ireland during 2018 (HSE, 2019b).

Table 5. Definitions of maternal deaths: (WHO 2010)

MATERNAL DEATH	Deaths of women while pregnant or within 42 days of the end of the pregnancy* from any cause related to or aggravated by the pregnancy or its management, but not from accidental or incidental causes.
Direct	Deaths resulting from obstetric complications of the pregnant state (pregnancy, labour and puerperium), from interventions, omissions, incorrect treatment or from a chain of events resulting from any of the above.
Indirect	Deaths resulting from previous existing disease, or disease that developed during pregnancy, and which was not the result of direct obstetric causes, but which was aggravated by the physiological effects of pregnancy
Late	Deaths occurring more than 42 days but less than 1 year after the end of pregnancy.
Coincidental‡	Incidental/accidental deaths not due to pregnancy or aggravated by pregnancy

* Includes giving birth, ectopic pregnancy, miscarriage or termination of pregnancy.

‡ Termed ''Fortuitous'' in the International Classification of Diseases (ICD)

Why is the pre-critical care setting important?

The Centres for Disease Control (CDC) in the U.S. have identified that 70-80% of sepsis cases arise in the community (CDC, 2016, NCEC, 2013). These patients present to the acute hospital sector via the emergency department (ED), the Acute Medical Unit (AMU), the Acute Surgical Assessment Unit (ASAU) and to a lesser extent the outpatient department (OPD). The remaining 20-30% of patients deteriorate with sepsis as an inpatient.

In order for patients to have the best opportunity to survive they need to present for medical review and have sepsis recognised and managed in an appropriate and timely manner. There is an important role for primary and community care in terms of risk recognition and for public awareness of the signs and symptoms of deterioration that may signal the development of sepsis, in order to ensure the right patient is in the right place at the right time to receive the right treatment; however, this is outside the remit of this guideline.

It is recognised that the presentation of sepsis is variable in symptoms, signs and time course. Thus, sepsis may not be present or not be diagnosed on first presentation and may not become apparent until the clinical condition evolves further. Deterioration whilst on treatment (including supportive) needs to be reviewed and diagnosis and treatment amended accordingly. The Irish National Early Warning System (2020) (INEWS) combined with clinical judgment should be deployed to recognise and respond to deterioration in the in-patient.

The Irish Maternity Early Warning System (IMEWS), (NCEC, 2019) combined with clinical judgement, should be deployed to detect deterioration in the pregnant woman.
Patient information leaflets and booklets are available at https://www.hse.ie/eng/about/who/cspd/ncps/sepsis/resources/

2.2 Clinical and financial impact of condition/disease/topic

A literature search was undertaken by the HSE Library Service to identify any economic literature published since the previous Sepsis NCG was published in 2014. The methodology is provided in Appendix 4.

The programme uses the Hospital Inpatient Enquiry (HIPE) database to extract data on the burden of sepsis in the acute hospital sectors and to identify the common characteristics of patients with sepsis.
The methodology uses specific HIPE codes which are based on ICD-10-AM. Appendix 5 describes the coding process and a list of the codes used for the extraction can be found in the annual Sepsis report 2018.

There are a number of limitations to using this dataset:

- Causality cannot be inferred from administrative data.
- Sepsis may be a direct or indirect contributor to morbidity and mortality.
- In patients admitted to critical care, the sepsis event may be unrelated to the cause of critical care admission and indeed may not have occurred during the critical care stay.

The reasons contributing to the above include:

- Sepsis is not routinely coded as the main diagnosis.
- There is no order of precedence in the subsequent diagnostic and procedural codes dx 2-30.

For example, a patient admitted for treatment of lymphoma might develop neutropenic sepsis and end up in an intensive care unit (ICU). Their main diagnosis, dx1, is likely to be coded as lymphoma and sepsis could appear anywhere in dx2-30, as will the ICU stay.

Another patient might be admitted electively for a surgical procedure with routine post-operative ICU admission, subsequently, on the ward, they develop sepsis but do not require or no critical care bed is available, and they have a prolonged hospital stay. Their dx1 will be the reason for the surgical procedure with sepsis anywhere between dx2-30, as will the ICU stay.

In the first example sepsis is clearly the cause of deterioration and ICU admission, in the second the sepsis episode is unrelated to the ICU admission but has clearly contributed to morbidity. In both cases the sepsis episode has had a profound effect on the patient and the healthcare costs.

Despite its limitations the use of administrative data has been validated for quality improvement programmes (Aylin et al., 2007).

In 2018, there were 14,639 patients who had sepsis included in their discharge coding. 4,002 of these patients required admission to a critical care bed at some point during their hospitalisation (HSE, 2019b).

The economic impact of sepsis can be looked at by assessing:

- Direct costs
- Economic and social burden
- 'Loss of wages technique'

Direct:
The average cost per in-patient stay per night in 2017 (latest data available) was €878, (HPO, 2018). This cost is not specific to sepsis patients. It is the average cost of an inpatient stay per night when all diagnoses are included. Sepsis is acknowledged as one of the more expensive inpatient diagnosis (Pfuntner A., 2013), so this analysis is at risk of underestimating the costs of sepsis care in the Irish acute hospital sector.

Table 6 describes the healthcare usage of patients with sepsis, both medical and surgical, and the difference, in terms of numbers of patients, number of bed days, average length of stay (AvLOS) and cost between this cohort and the patient with any uncomplicated infection.

The estimated direct costs of patients with sepsis causing or complicating their hospital admission is €288 million per annum (i.e. €19,667 x 14,639) with an AvLOS of 22.4 days. The difference between the average hospital stay complicated by infection rather than sepsis is 9.79 days or €8,603 per patient.

Table 6. Healthcare usage in sepsis vs. infection 2018 (HSE, 2019)

Diagnosis	No. of Inpatients	No. of Bed Days Used (BDU)	Average Length of Stay (Days) (No. of BDU ÷ No. of inpatients)	Cost per patient per day €	Total Cost per patient per stay (AvLOS X Cost per day)
Surgical Sepsis	2,634	122255	46.4	878	€40,739
Medical Sepsis	12,005	205638	17.1	878	€15,013
Total Sepsis	14,639	327,893	22.4	878	€19,667
Surgical Infection	12,802	261,636	20.4	878	€17,911
Medical Infection	102,301	1,050,662	10.3	878	€9,043
Total Uncomplicated Infection	115,103	1,312,298	11.4	878	€10,009
Difference between Sepsis and Infection	100,464	984,405	9.79	878	€8,603

The average length of stay for a patient in a surgical diagnostic-related group (DRG) with a sepsis diagnosis is 46.4days with a cost of €40,739. Surgical DRG patients with an infection diagnosis have an AvLOS of 20.4 days, a difference in cost of €22,828 per patient between sepsis and infection complicating their hospitalisation. This is a total cost differential of approximately €60 million between surgical patients with sepsis and surgical patients with any uncomplicated infection (Table 7).

Table 7. Calculation of the annual cost differential for surgical patients sepsis and all other infections 2018** (HSE, 2019)

No. of in-patients	Cost per day €	Average Length of Stay (AvLOS) Days	Total Cost (No x Cost x AvLOS)
2634 - Sepsis	878	46.4	€107 Million
2634 – Other infection	878	20.4	€47M
		Differential	€60 Million

The average length of stay for a patient in a medical diagnostic-related group (DRG) with a sepsis diagnosis is 17.1 days with a cost of €15,013. Medical DRG patients with an infection diagnosis have an AvLOS of 10.3 days, a difference in cost of €5,970 per patient between sepsis and infection complicating their hospitalisation. This is a total cost differential of approximately €72 million between medical patients with sepsis and medical patients with any uncomplicated infection (Table 8).

Table 8. Annual cost differential for medical patients sepsis and all other infections, 2018** (HSE, 2019)

No. of in-patients	Cost per day €	Average Length of Stay (AvLOS) Days	Total Cost (No x Cost x AvLOS)
12005 - Sepsis	878	17.1	€180 Million
12005 – Other infection	878	10.3	€108 Million
		Differential	€72 Million

Economic and Social Burden:

Silva and Araujo (2009) performed a review to standardise the concepts related to health economic analysis and provide guidelines for reporting economic analyses that were largely based on the US Public Health Service Panel on Cost Effectiveness in Health and Medicine (PCEHM) for the conduct and reporting of economic analyses. This guidance and the methodology deployed by Schmidt were in sufficient detail and used data points available for the Irish Health Care System to allow them to do a short analysis on the costs incurred by current sepsis management and potentially saved with performance and quality improvement. The analysis is for descriptive purposes only.

The costs of sepsis to the economy can be divided into direct costs (28%), loss of productivity due to mortality (56%), loss of productivity due to morbidity (12%) and loss of productivity due to temporary morbidity (4%) (Silva and Araujo, 2009).

Direct	€19,667 (28%)
Loss of productivity due to mortality	€39,334 (56%)
Loss of productivity due to morbidity	€8,429 (12%)
Temporary loss of productivity	€2,810 (4%)

Total costs = €70,240 per patient or €1.03 billion loss to the Irish Economy per annum.

'Loss of wages' method (Mitchell and Bates, 2011)

An alternative method to estimate the loss of productivity due to mortality, is to use the 'Loss of wages' method (Mitchell and Bates, 2011). This is the most frequently used measure of productivity loss; using a retirement age of 65 years, there were a total of 12,600 years lost amongst 1,892 patients who died below the age of 65. It does not include direct costs or productivity loss due to morbidity.

The average annual earnings in 2016 were €36,919, making a total loss of earnings of €465.2million, with an estimated income tax loss to the exchequer of €93million. This is lower than the estimated €583.6million using the previous method above and would result in a total cost of €924 million to the Irish economy per annum.

Comparisons:
Direct costs in ICU versus Non-ICU:
In the U.S., Angus et al (2009), using the claims databases, estimated the ICU septic patient cost $29,900, *(€25,652)** with an AvLOS 23.3 days versus the non-ICU septic patient $13,900 *(€11,928)**, with an AvLOS of 15.6 days (Shen et al., 2016). In the same population, the calculated cost differential between survivors and non-survivors was $38,304 *(€32,870)** versus $49,182 *(€42,202)** (Chalfin et al., 1995).

In France, costs were reported from €26,256 to €35,185 depending on the severity of illness (Brun-Buisson et al., 2003). Other European studies have given lower cost estimates, ranging from €23,000 to €29,000 (Burchardi and Schneider, 2004). In Ireland, a prospective micro-costing of ICU treatment was performed (not limited to sepsis), with mean total ICU costs of €20,487, (McLaughlin et al., 2009).
In Brazil, a micro-costing analysis of ICU sepsis care showed a median total cost of $9,773 *(€8,386)** ($4,643-$19,221) *(€3985-€16,499)** (Sogayar et al., 2008). In China, an analysis showed a mean hospital cost $11,390 - $11,455 *(€ 9,777 -9831)** per sepsis case (Cheng et al., 2007).

Thus, it can be seen that the hospital costs calculated for Ireland are not out of sync with other high-income countries, although direct comparisons cannot be made due to the difference in methodology.
**(Currency conversion as of 25th September 2020 by XE Currency Converter)*

Economic and social burden:
In Germany in 2002, using the administrative and other databases, Schmidt et al. did an assessment of the economic and social burden of sepsis (Schmidt et al., 2002). He identified the ratios used in the analysis for Ireland.
His results include:

- Productivity loss due to temporary morbidity €3,431 to 7,409 depending on severity (calculated at €2,810 in Ireland).
- Productivity loss due to mortality €46,000 per case (calculated at €39,334 in Ireland).
- Total burden of illness €82,886 to €178,954 (calculated at €70,240 per patient in Ireland).

Economic impact of the National Sepsis Programme
An economic impact of the sepsis protocol in an academic, tertiary care hospital in the United States found median total hospital costs were reduced from $21,985 to $16,103, (€18,866 - €13,818)** mainly due to a shorter length of stay (Shorr et al., 2007).
***(Currency conversion as of 25th September 2020 by XE currency converter)*

This has also been seen in Ireland where the AvLOS for patients with sepsis causing or complicating their hospital admission in 2011-2015 was 25.9 with estimated direct costs of €21,437, as this AvLOS fell in 2016/17 to 20.9 this has resulted in a reduction of €3,583 per patient with an estimated direct cost of €17,890 per hospital stay.

Table 9. Cost per bed day according to year (€)

Year	Cost per bed day*
2017	€878
2016	€856
2015	€839
2014	€839
2013	€815
2012	€825
2011	€820

**Average costs, across all nights, all hospitals, and all types of in-patient cases. This figure is a fully absorbed cost which means it includes treatment and care costs (such as diagnostics, theatres etc.) as well as hotel costs but excludes capital and depreciation. It excludes day case, outpatient and emergency department costs. (Healthcare Pricing Office, 2017)*

In the overall sepsis population, two changes occurred as a consequence of the implementation programme, improved recognition and improved treatment. In the non-critical care population changes over time will reflect improved recognition as well as changes due to improved treatment and as such, analysis of trends in this population are problematic. However, in the critical care population lower acuity would have no impact on critical care admission due to the limited number of such beds; indeed, there was a decrease in capacity over the study period suggesting a potential increase in acuity amongst the critical care population.

- Mean sepsis-associated mortality 2011-2015 in patients admitted to a critical care area: 34%,
- Mean sepsis-associated mortality 2016-2018 in patients admitted to a critical care area: 31.4%

An absolute decrease of 2.6% and a relative decrease of 8%.

In 2018, 4,002 patients admitted to ICU had a sepsis code on their hospital discharge.
The mortality decrease suggests an additional 302 lives saved over the 3 years post implementation from this subpopulation.
The hospital AvLOS for this subgroup decreased from 36.72 days in 2011-15 to 33.7 days in 2016-18, a gain of 12,086 bed days and a reduction in direct costs from €30,808 to €29,589 per patient. This represents a saving of €10.6million.

2.3 Rationale for this National Clinical Guideline

Sepsis is a common time-dependent medical emergency. Whilst it can affect a person of any age, from any social background and can strike irrespective of underlying good health, 90% of adults and 70% of children who develop sepsis have underlying risk factors (CDC, 2016) . 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 are associated with an increased compliance with sepsis bundles and a decrease in mortality (Odds Ratio 0.6) (Damiani et al., 2015)

In 2016, the Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3) were developed by a taskforce at the request of the Society of Critical Care Medicine (SCCM) and the European Society of Intensive Care Medicine (ESICM), (Singer et al., 2016).

Sepsis-3 provides a welcome rationalization of the sepsis syndrome with sepsis only being diagnosed when infection has led to acute organ dysfunction and the presence of a systemic inflammatory response no longer being a requirement. A systemic inflammatory response may be caused by infective and non-infective conditions and represents an adaptive response to an insult. It is present in about 85% of sepsis cases and many more cases that are not sepsis. Thus, although its presence can alert a clinician that a patient may have a problem it is not sufficiently discriminatory to identify the cause of the problem.

These changes go a good way to reduce concerns about over diagnosis leading to overuse of antibiotics in a climate of increasing concern about multi-drug resistant organisms by identifying a subset of patients with infection who have a high mortality risk.

2.4 Aim and objectives

Aims

1. To ensure that all acute hospitals give patients with sepsis the best opportunity to survive.
2. To maximize the health-related quality of life in survivors of sepsis.
3. To minimize the burden of sepsis to the healthcare system by reducing the acuity and the chronic sequelae of sepsis.

The National Clinical Guideline for Sepsis Management was published in November 2014 (NCEC, 2014) and the implementation process started in 2015 with an education and awareness campaign. Hospital-based education was delivered by the National Sepsis Programme in all acute hospitals and clinical decision support tools and other educational aids and materials were rolled-out.

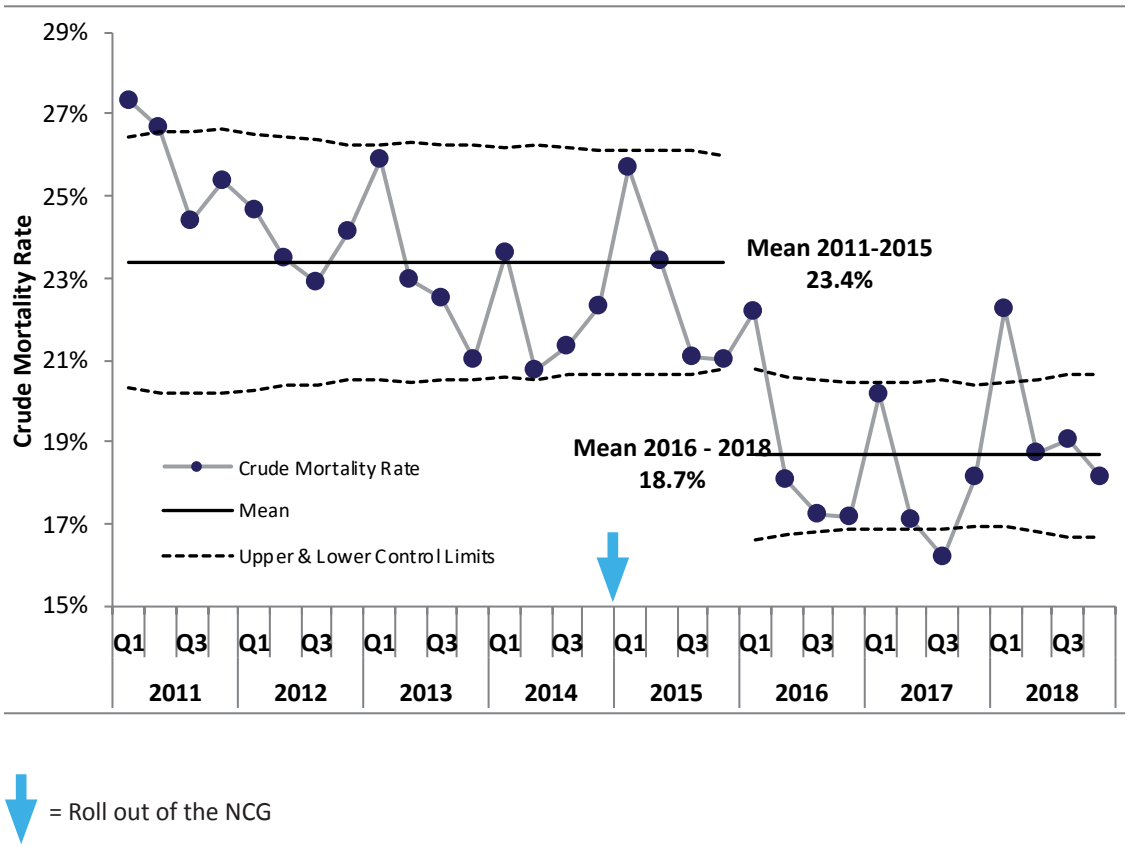


Figure 1. Impact of the National Clinical Guideline Implementation in Ireland; sepsis-associated hospital mortality in all inpatients with a discharge code of Sepsis & SIRS of Infectious origin. (HSE, 2019b)

Quarterly data, 2011 – 2018 (Statistical Process Control Chart)

Quarterly rates of in-hospital mortality for inpatients with a diagnosis of sepsis from 2011 to 2018 were analysed using Statistical Process Control (SPC) methods (Figure 1). The use of SPC methods allows us to see whether the changes made resulted in improvements and allow us to distinguish between variation that may have happened by chance alone and variation that indicates a real improvement in mortality rates. There is an important caveat and that is that the education and awareness campaign will have led to the improved documentation of lower acuity sepsis cases that bring with them a lower mortality rate and this will have impact.

This figure demonstrates that the National Sepsis Programme had a statistically significant impact on the recognition and management of sepsis in Ireland. Between 2011 and 2015, the average in-hospital mortality for inpatients with a diagnosis of sepsis was 23.4%. Using control limits based on SPC methods it was expected during this period that the quarterly mortality rate would vary from around 20 to 26% by chance alone. Since 2016 the quarterly mortality rate has averaged 18.7% which is below this lower control limit of 20% indicating a significant improvement in mortality rates that is not explained by chance alone.

The control limits in the statistical process control chart have been re-calculated to reflect this reduction. We now anticipate that this improvement will be sustained, and mortality will remain below 20% (with some variation due to seasonal effects) (HSE, 2019b).

It is not possible to distinguish what portion of improvement is due to improved recognition and what is due to improved management, however, a 7.95% decrease in mortality is also observed in the critical care patient cohort (Figure 2), where capacity not recognition limits access and where there was a decrease in per capita bed stock. These effects are consistent with those found in other jurisdictions where sepsis quality improvement programmes were implemented (Rhodes et al., 2017).

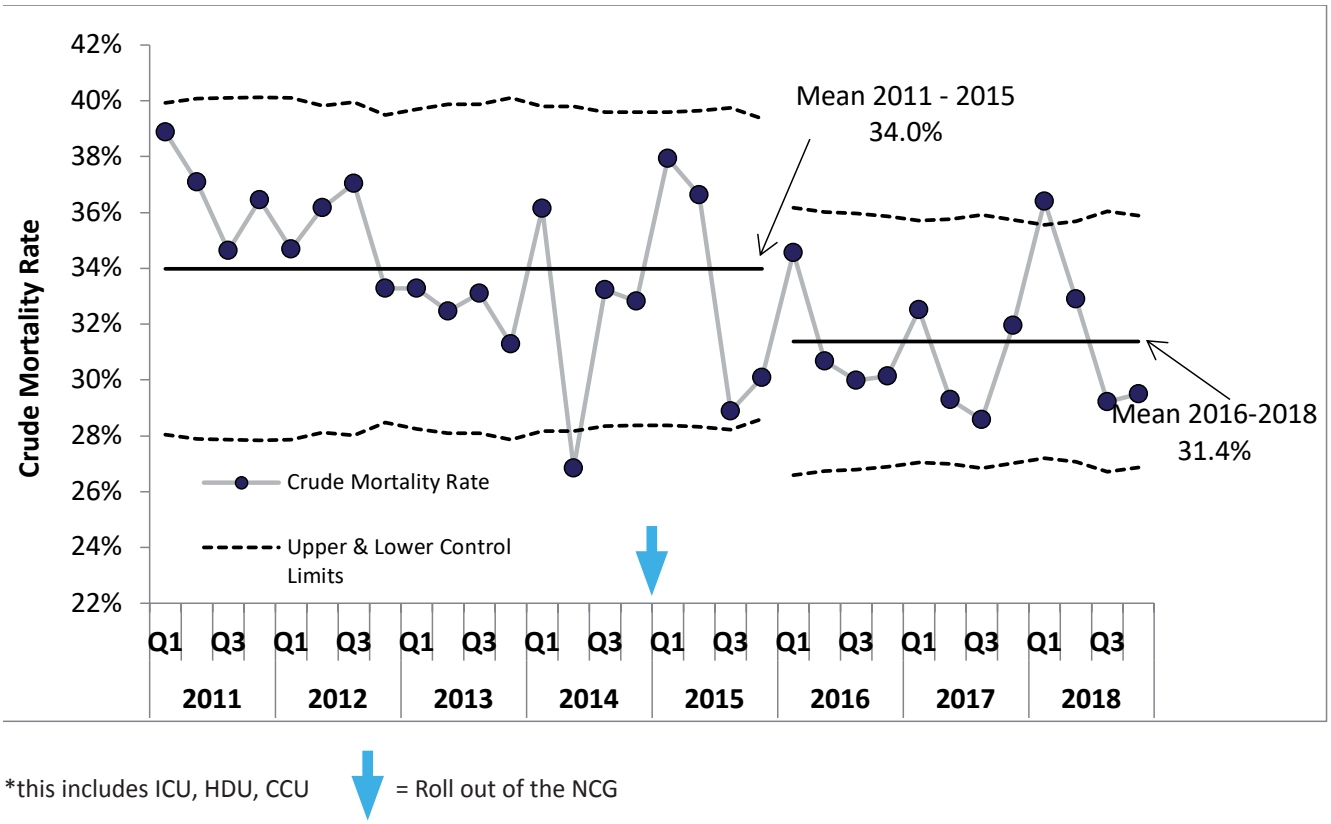


Figure 2. Impact of the Sepsis Guideline Implementation in Ireland; sepsis-associated hospital mortality in inpatients admitted to a critical care area* with a discharge code of Sepsis & SIRS of Infectious origin.

SPC analysis does not identify which changes resulted in the demonstrated improvement. It is acknowledged that improved recognition and documentation of lower acuity sepsis cases, as well as improved management will have contributed to this effect. However, the average mortality rates can be benchmarked against other jurisdictions that have published (Seymour et al., 2017, Martin et al., 2003, Angus et al., 2001) and this indicates that Ireland is performing as well as other high-income countries in terms of sepsis-associated mortality rates.

Objectives

1. That all healthcare professionals have an understanding of the diagnostic criteria for sepsis and its basic pathophysiology.
2. That all medical, nursing and midwifery staff working in the acute sector, recognise patients at high risk of mortality from sepsis.
3. That all medical, nursing and midwifery staff working in the acute sector are:
    i. Familiar with the initial management of patients with a high risk of mortality from sepsis
    ii. Able to use the sepsis form which is a clinical decision support tool and forms part of the patient's clinical notes.
    iii. Able to take a team approach to implementing the Sepsis 6 bundle (Daniels et al., 2011) and the sepsis management algorithms.

How should the aims and objectives be supported in the community?

70-80% of sepsis cases arise in the community thus a quality improvement campaign needs to have a 2-fold approach (CDC, 2016).

1. Address sepsis recognition and management by healthcare professionals who work in the community and
2. Improve Sepsis awareness in the public domain.

There is limited evidence-based data to guide recognition, management and escalation in the community and any such programme needs to have robust antimicrobial stewardship to support healthcare professionals in avoiding inappropriate usage (www.antibioticprescribing.ie) (HSE) and to prevent 'protocol-driven' inappropriate emergency department, medical or surgical assessment unit referrals. It needs to be developed with the end users and tested within its context to ensure that it fulfils its purpose without unintended consequences.

Awareness of sepsis and its symptoms and signs is an important part of public health education. Such a programme should be embedded in a strategy to promote prevention of infection, antimicrobial stewardship and the recognition of signs and symptoms of deterioration that should prompt urgent medical review.

Public information is available from https://www.hse.ie/eng/about/who/cspd/ncps/sepsis/resources/

Infection and sepsis in the older population

Infections in the elderly are different from infections in a younger population due to age-related alterations in immunology and concomitant medical diseases – multimorbidity is the norm.

They are more likely to:

- have decreased gag and cough reflex – predisposing them to respiratory tract infections (RTIs).
- be colonised by multi-resistant organisms.
- have poor response to neoantigens and vaccines due to immunosenescence.
- be less mobile than their younger counterparts and more prone to skin breakdown and decubiti.
- have poor urinary bladder emptying, prostate enlargement and neurogenic bladder - predisposing them to urinary tract infections (UTIs).
- have a high risk of falls and injuries predisposing them to skin and wound infections.
- Sepsis is more common and has a higher mortality when it occurs in patients with co-morbidities and as we get older, we accumulate co-morbidities.

This population often presents with:

- cognitive impairment – but there is a danger in normalising the abnormal.
- diminished cardiopulmonary reflexes and physiological reserve,
- malnutrition, endocrine deficiency, chronic inflammatory and prothrombotic effects of aging that weaken the immune system.

A lower threshold and higher index of suspicion is required to recognise sepsis in this population.

2.5 Guideline Scope

2.5.1 Target Population

This NCG applies to adult patients with confirmed or suspected sepsis, including pregnant women in all clinical settings in the acute sector.

The majority of recommendations and implementation points apply to both Adult non-pregnant patients and women pregnant and in the postnatal period up to 42 days. Recognition in the maternity patient is slightly different; therefore, maternity specific implementation points are signposted as such. All maternity specific information is highlighted using purple text. Treatment and escalation are generally the same for both groups. See maternity section for more details on the pregnant woman/post parturient.

2.5.2 Purpose

The purpose of this guideline is to implement the Surviving Sepsis Campaign Guideline (SSCG) in the management of the adult patient in the acute hospital sector in Ireland. It takes these international evidence-based recommendations and implements them in a format that applies to the structures and functions of the Irish Acute Health Care Sector. The National Sepsis Programme would like to thank the Surviving Sepsis Campaign for permission to do this.

The recommendations in the guideline are structured as follows:

i. SSCG - Key Questions
ii. SSCG - Surviving Sepsis Campaign Guideline Rationale
iii. SSCG - Recommendations
iv. NCG - Implementation Points (where relevant)

All **SSCG references are numbered** are extracted directly from the SSCG document. Additional references that have been incorporated into the implementation aspects are in a separate list called **National Clinical Guideline References** and are listed **alphabetically**.

The recommendations of the SSCG are included so that it can be read as a standalone document. However, it is recommended that clinicians familiarise themselves with the SSCG, and is endorsed by the Critical Care Programme, the Joint Faculty of Intensive Care Medicine in Ireland and the Intensive Care Society of Ireland. An important guideline for those dealing with maternity is the 'Critically ill women in obstetrics' (HSE, 2014).

Implementation has been divided into three phases,
1. Recognition
2. Treatment
3. Escalation

Implementation points included after SSCG recommendations are aimed, primarily, at the pre and post-critical care setting, recognizing that much of the research that informed the SSCG occurred in the critical care setting and thus the SSCG can be more directly applied in that setting.

The NCG is designed to guide clinical judgement but not replace it. In individual cases a healthcare professional may, after careful consideration, decide not to follow guideline recommendations if it is deemed to be in the best interests of the patient and is in line with best practice. Clinical decisions and therapeutic options should be discussed with a senior clinician on a case-by-case basis as necessary and documented in the clinical notes.

The Surviving Sepsis Campaign International Guidelines for the Management of Septic Shock and Sepsis-Associated Organ Dysfunction in Children were published in February 2020. The HSE is adopting these guidelines directly as a HSE protocol. The National Sepsis Programme will provide an implementation plan to enable the application of the recommendations in the Irish health care setting.

The recommendations align with the aims of the National Sepsis Programme. 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.

2.5.3 Target Users

This guideline is relevant to all healthcare professionals involved in the care of adult and maternity patients with sepsis and suspicion of sepsis, working in the acute hospital sector in the Republic of Ireland.

The guideline is also relevant to:

- Department of Health (DoH) to support the development, implementation and audit of this National Clinical Guideline.
- The HSE to provide appropriate structured support and adequate resources for the governance, operationalization, and audit of sepsis management.
- The Hospital Group Leadership Team, Hospital Management and Clinical Directors to support sepsis quality improvement and to foster and facilitate the implementation process and audit. They are also responsible for effecting and monitoring change arising from outlier intervention.

- Pre-Hospital Emergency Care to inform their clinical practice guidelines.
- The public as an information resource.

2.6 Conflict of interest statement

The guideline development process followed the conflict of interest policy set out by the NCEC. All members of the Sepsis Management GDG were required to complete a conflict of interest declaration which was managed by the National Sepsis Programme Manager. There were no conflicts of interest stated.

2.7 Sources of funding

There was no external funding, commercial input or resource provided for this guideline by any service or organisation, and as such no potential for influence on editorial independence. The GDG sought and were granted permission to adopt the Surviving Sepsis Campaign Guideline for which no cost was incurred.

2.8 Guideline methodology

In order to update the 2014 Sepsis National Clinical Guideline (NCG) the National Sepsis Programme convened a Guideline Development Group (GDG) consisting of key stakeholders, recognised experts in sepsis management and patient advocates.

A literature search was undertaken by the HSE Library Service to identify any national and international sepsis clinical guidelines published since the previous Sepsis NCG was published in 2014 which could be adopted or adapted for use in the Irish Healthcare setting.

The search strategy included a search of Medline and PubMed using search terms related to the management of sepsis and septic shock (Appendix 6). The websites of key organisations were also searched. The search identified 11 documents, the majority of which were excluded immediately as they related to pre-hospital care, non-acute care settings, paediatrics or were related to a specific type of sepsis, e.g. acute meningitis and meningococcal sepsis.

When the exclusion criteria were applied only three guidelines were eligible for consideration:

- NICE Sepsis: recognition, assessment and early management (NICE, 2017)
- Surviving Sepsis Campaign (SSC): International Guidelines for Management of Sepsis and Septic Shock (Rhodes et al., 2017)
- The Japanese Clinical Practice Guidelines for the Management of Sepsis and Septic Shock (Nishida et al., 2018)

The Prisma flow diagram illustrates the process undertaken in narrowing down the guidelines for appraisal. (Figure 17. Appendix 6)

In order to assess which guideline was relevant for the Irish Healthcare system and to appraise the quality of the guidelines, including the rigour and transparency in which the guidelines were developed a quality assessment was undertaken by two of the GDG Members using the Appraisal of Guidelines for Research and Evaluation II (AGREE II) tool, (Brouwers et al., 2010). The SSC Guideline was the only guideline that scored >70% in all domains and was ranked highest in all domains by both appraisers with overall domain percentages ranging 71-100%. In addition, the appraisers noted that although the Japanese Guideline was an adaption of the SSC Guideline, it was tailored for the Japanese healthcare system with some recommendations that were not widely available within the Irish Healthcare system and the NICE Guideline although well researched and written, was tailored to the UK health service and focused on many elements beyond the scope of the Irish NCG e.g. pre-hospital care and paediatrics. Both appraisers agreed that based on the AGREE II process and the points noted previously that the SSC Guideline should be adopted for use in the Irish Healthcare system.

The SSC Guideline which focuses on early management of sepsis and septic shock, underwent a robust process to identify the evidence relating to five areas of practice (haemodynamics, infection, adjunctive therapies, metabolic, and ventilation). An extensive search was performed for each PICO and the Grading of Recommendations Assessment, Development and Evaluation (GRADE) system principles were used to guide the assessment of the quality of evidence and to determine the strength of the recommendations. Both of these are fully described in the SSC Guideline (Rhodes et al., 2017) and are summarised in Tables 10 and 11. Table 12 identifies the grading terminology used in the 2016 guideline. All of these terms are referred to within the recommendations section of this document.

Table 10. Determination of the quality of evidence

Underlying Methodology 1. High: RCTs 2. Moderate: Downgraded RCTs or upgraded observational studies. 3. Low: Well-done observational studies with RCTs. 4. Very Low: Downgraded controlled studies or expert opinion or other evidence.
Factors that may decrease the strength of evidence 1. Methodologic features of available RCTs suggesting high likelihood of bias. 2. Inconsistency of results, including problems with subgroup analyses. 3. Indirectness of evidence (differing population, intervention, control, outcomes, comparison) 4. Imprecision of results. 5. High likelihood of reporting bias.
Main factors that may increase the strength of evidence 1. Large magnitude of effect (direct evidence, relative risk >2 with no plausible confounders) 2. Very large magnitude of effect with relative risk >5 and no threats to validity (by two level). 3. Dose-response gradient.

RCT = Randomised controlled trials

Table 11. Factors determining strong versus weak recommendations

What should be considered	Recommendation Process
High or moderate evidence (Is there high, or moderate, quality evidence?)	The higher the quality of evidence, the more likely a strong recommendation.
Certainty about the balance of benefits versus harms and burdens (Is there certainty?)	The larger the difference between the desirable and the undesirable consequences and the certainty around the difference, the more likely a strong recommendation. The smaller the net benefit and the lower the certainty for that benefit, the more likely a weak recommendation.
Certainty in, or similar, values (Is there certainty or similarity?)	The more certainty or similarity in values and preferences, the more likely a strong recommendation.
Resource implications (Are resources worth expected benefits?)	The lower the cost of an intervention compared to the alternative and other costs related to the decision (i.e. fewer resources consumed), the more likely a strong recommendation.

Table 12. Grading terminology

	2016 Descriptor
Strength	Strong Weak
Quality	High Moderate Low Very low
Ungraded strong recommendation	Best practice statement (BPS)

The guideline provides recommendations for good practice that are based on the best available clinical and cost effectiveness evidence.

It was agreed by the GDG to fully adopt the SSC Guideline with the addition of implementation points to aid the implementation of the guideline within the Irish Healthcare System in both pregnant and non-pregnant adults. It was also agreed by the GDG to limit the NCG to adults, non-pregnant and pregnant, and to exclude paediatrics from the scope of the guideline as the SSC Guideline refers to adults only. In addition, the Surviving Sepsis Campaign International Guidelines for the Management of Septic Shock and Sepsis-Associated Organ Dysfunction in Children were published in February 2020. The HSE is adopting these guidelines directly as a HSE protocol. The National Sepsis Programme will provide an implementation plan to enable the application of the recommendations in the Irish health care setting.

2.9 Consultation summary

The GDG sought to ensure that all stakeholders had an opportunity to review and contribute to the update of the National Clinical Guideline for Sepsis. The guideline and feedback form were placed on the HSE public website under the clinical programmes and the link was circulated to those listed in Appendix 7 with an invitation to review and provide feedback. The GDG gratefully acknowledges the contribution made by all those who contributed from professional, academic and patient groups.
The stakeholders are listed in Appendix 7.

2.10 External review

Two international experts were invited to review and provide feedback on an early draft of the guideline. These experts were independent from the Guideline Development Group and selected based on their contribution to academic literature and clinical practice:

1. Professor Kevin Rooney is a Consultant Anesthetist and Professor of Care Improvement at University of the West of Scotland. He is the Clinical Lead for the Acute Adult Workstream of the Scottish Patient Safety Program for Healthcare Improvement Scotland and led their breakthrough series collaborative on sepsis, which resulted in a sustained relative risk reduction of 21% in sepsis mortality across Scotland.
2. Dr John Bates, Galway University Hospital, Department of Anaesthesia and Intensive Care, Dean of Joint faculty of Intensive Care Medicine.

The GDG are very grateful to these reviewers for their time, expertise and contribution to this guideline.

2.11 Implementation

These guidelines are divided into sections with each one pertaining to a different aspect of patient care. Recommendations from the Surviving Sepsis Campaign Guideline Update 2016 are labelled 'SSCG Recommendation' and 'SSCG Rationale'.

Implementation points are included to guide implementation of the SSCG recommendations in Ireland, particularly in the non-critical care environment. The implementation points arise from piloting clinical decision support tools in the acute hospital sector, particularly in emergency departments (EDs) and maternity units to ensure that the implementation recommendations could be affected within the resources of our healthcare system and had the support of end-users. The feedback from these pilots was overviewed by multidisciplinary committees (the National Steering Committee and the Maternity Working Group) and the forms amended based on this feedback and re-piloted, if required. Thus, the implementation programme is informed by end-users and by multidisciplinary specialist input.

Appendix 8 identifies the enablers and barriers to implementing the recommendations along with the responsibilities and timelines.

Funding for guideline implementation is subject to service planning and the estimates process.

2.12 Monitoring and audit

The aim of this National Clinical Guideline is to reduce unnecessary variations in practice and provide an evidence base for the most appropriate healthcare to optimize patient survival from sepsis.
The National Sepsis Programme (NSP) will monitor this aim in two ways:
(1) Audit of implementation of the NCG (Clinical audit/Process audit)
(2) Audit of outcomes resulting from implementation of the NCG (National Sepsis Report).

Clinical audit/Process audit is the systematic review and evaluation of current practice against research-based standards with a view to improving clinical care for service users and is an important part of any quality improvement programme. It takes a snapshot of performance and benchmarks it against the guideline and thus identifies areas that may benefit from improvement. Since process audit does not contextualize the decisions made during a patient's care episode, it is not designed to assess the quality of an individual care episode. However, should an area of concern be identified it should be brought to the attention of the local hospital sepsis committee for their consideration.

Outcomes: The primary aim of optimizing patient survival should be audited by the publication of age and co-morbidity adjusted sepsis-associated (direct and in-direct) hospital mortality rates for each acute hospital and benchmarked against the national average. International benchmarking of the national sepsis-associated hospital mortality rate should be done against other high-income jurisdictions that publish such mortality rates.

The National Sepsis Report is published annually and describes the burden of sepsis, in terms of the number of cases and the associated age adjusted mortality, to our healthcare system. The report (HSE 2019) recommends the development of a sepsis mortality prediction model and scoring system to compare age and co-morbidity adjusted hospital sepsis-associated mortality rates nationally and internationally.

Secondary outcome aims include healthcare utilization assessment such as the total number of bed days, average length of stay, critical care admission rates and average length of stay, and hospital readmission rates within three months (Chang et al., 2015) and should be reported where possible. The assessment of healthcare utilization is important as a monitor of the effectiveness of the sepsis quality improvement programme and also provides data for resource planning. As sepsis incidence increases with age with an ageing population it can be expected that healthcare provision for sepsis care will increase. An effective programme can modulate this increase.

Maternity

Sepsis outcome audits are carried out by The Confidential Enquiry into Maternal Deaths (CEMD) in the UK and Ireland. Since June 2012, these audits have been carried out by the MBRRACE-UK (Mothers and Babies: Reducing Risk through Audits and Confidential Enquiries) collaboration and Maternal Death Enquiry (MDE) in the National Perinatal Epidemiology Centre-Ireland. They are published on the National Perinatal Epidemiology Unit (NPEU) website: https://www.npeu.ox.ac.uk/mbrrace-uk/reports. Each topic-specific/sepsis confidential enquiry chapter now appears in an annual report once every three years on a cyclical basis, in contrast to the past when a single report was produced every three years.

Practical guidance A:

The GDG suggests that a tool be developed to risk adjust sepsis-associated hospital mortality (direct and in-direct) based on the Hospital In-patient Enquiry database and that each acute hospital, on this database, have annual risk-adjusted sepsis-associated mortality rates benchmarked against the national average. When operational, this tool will facilitate the development of Key Performance Indicators (KPI's) for sepsis.

Rationale:

Optimising survival from sepsis depends on the hospital system working efficiently and effectively as a whole. It requires effective communication, adequate resources and capacity both in infrastructure and staffing. Sepsis management and risk-adjusted sepsis-associated hospital mortality are robust markers of the quality of acute health care delivery.

Monitoring and acting on outcome audit ensures improvement occurs throughout the acute healthcare system and is not sporadic. It informs the population a hospital serves and its staff on the effectiveness of its sepsis management and supports improvement processes.

Outlier management:
Hospitals whose outcome measures are in excess of the control limits will, in the first instance have their data reviewed by the national sepsis programme working group (Appendix 2). There are 3 possible outcomes from this initial review:

1. No action warranted
2. Monitor pending further review
3. Outlier intervention warranted

Outlier interventions:
1. The National Sepsis Team, including the Hospital Group Sepsis ADON, will discuss the findings and the outcome of the National Audit Committee data review with the Hospital Management and Clinical Director/s.
2. An improvement plan will be formulated by Hospital Management, the Clinical Director/s and the Sepsis/ Deteriorating Patient Committee, with advice from National Sepsis Team.
3. Audit of the improvement plan, its implementation and effect by the Hospital with support from the Hospital Group Sepsis ADON and the Hospital Group Leadership Team to ensure any identified issues are addressed.
4. It is the responsibility of the Hospital Management, Clinical Director/s and Sepsis/ Deteriorating Patient Committee to effect and monitor the findings of the outcome and process audits.

Practical guidance B
The GDG suggest that intermittent process audit be performed to support improvements in sepsis recognition, management and escalation.

Rationale:
The purpose of these audits is to benchmark different areas of practice against these guidelines for the purpose of informing on-going education and performance improvement initiatives.

The National Sepsis Programme will agree the process audit schedule annually and inform Hospital Group leadership of same. The Group Sepsis ADONs will also notify local sepsis committees and plan accordingly.

The process audits will be carried by the Group ADONs in collaboration with appropriate staff in local hospitals.

Process audit does not review the context of decision-making in patient management and as such, cannot comment on the standard of care relating to an individual patient. However, if during the course of an audit, the possibility of a serious patient safety incident is considered this should be brought to the attention of the Sepsis/ Deteriorating Patient Committee. It is the responsibility of the Committee to decide if any further action is warranted.

It is the responsibility of the hospital sepsis committee to inform clinicians of the audit findings and to adjust the hospital's sepsis education programme to improve management and to effect, along with hospital management, any outlier interventions.

Practical guidance C

The GDG suggests that an annual sepsis outcome report be published which includes, but is not limited to:

- the risk-adjusted hospital mortality rates
- the incidence, patient characteristics and healthcare utilization of patients with sepsis during their hospitalization
- hospital group level amalgamated process audit results
- balancing measures.

Rationale:

A culture of openness promotes good practice and confidence in the healthcare system. It is important that the community is aware of the limitations of sepsis care, its high mortality risk and the efforts being made to reduce that risk. Sepsis guidelines are based on the best available information at the time of publication; however, they are just guidelines and cannot anticipate the complexity of an individual case. Data collection on patient characteristics and risk factors allows the identification of high-risk patients for prioritization. However, for every patient prioritized there are others who have been deemed less at risk. When capacity is challenging, getting this right is a vital and difficult component of time-dependent care especially when the clinical scenario is evolving. A hospital working within the control limits of the national average demonstrates that it is providing a service, in terms of sepsis care, that is as good as anywhere else within the state.

Balancing measures:

Audits should also include considerations of potential unintended consequences of the National Sepsis Programme including inappropriate antimicrobial use. Inappropriate antimicrobial use is a patient safety issue (e.g. adverse reactions, Clostridium difficile infection) and of public health concern (increased rates of multidrug resistant organisms, MDRO) (DOH, 2017a).

In relation to antimicrobial use, there are at least three potential unintended consequences of implementing the Sepsis 6 bundle:

1. Patients who have deteriorated but have no evidence of potential infective source/sepsis are commenced inappropriately on antimicrobial therapy.
2. Patients with sepsis are commenced on inappropriate antimicrobial therapy that is not in line with local guidelines.
3. Empiric antimicrobial 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 Antimicrobial Care bundle (RCPI, 2012).

All hospitals should have antimicrobial stewardship programmes in place as outlined in National Guidelines (DOH, 2017a) (HSE, 2019a) that monitor process and outcome measures to ensure that antimicrobials are not being prescribed unnecessarily due to inappropriate application of Sepsis 6/Sepsis 6 + 1. Ensuring antimicrobials are used appropriately for all infections, not just those associated with sepsis, will help to ensure effective antimicrobial therapy is available when cases of sepsis do occur.

Roles and responsibilities:

The National Sepsis Programme is responsible for publishing an annual sepsis outcome report. Working with the Health Pricing Office (HPO), the National Sepsis Programme will provide guidance on what outcomes, processes and patient characteristics to audit and will review audit methodology and results to ensure that they make clinical and statistical sense. It is the responsibility of the Programme to provide outlier support to hospitals when indicated.

It is the responsibility of sepsis committees, Hospital Management and Hospital Group Leadership to effect recommendations arising out of outlier intervention.

It is the responsibility of the Department of Health, the HSE, hospital group leadership and hospital management to support the audit process and to ensure that adequate resources are available to perform the audit and to effect change required based on audit results.

It is the responsibility of the Department of Health and the HSE to resource a risk-adjusted sepsis-associated hospital mortality rate audit tool as the key performance indicator for sepsis in Ireland.

2.13 Legislation and other related policies

On occasion in clinical practice, prescriptions are written for licensed drugs given for unlicensed indications, and/or via an unlicensed route (NCEC, 2015b). Often it is simply a matter of the route or dose being different from those in the manufacturer's SPC (summary of product characteristics). It is of note that the licensing process for drugs regulates the marketing activities of pharmaceutical companies, and not prescribing practice. Unlicensed use of drugs by prescribers is often appropriate and guided by clinical judgment. This practice is safeguarded in legislation in accordance with Medicinal Products (Control of Placing on the Market) Regulations 2007 (S.I 540/2007) as amended, (GOV, 2007). Furthermore, drugs prescribed outside license can be dispensed by pharmacists and administered by nurses or midwives (NCEC, 2015b).

2.14 Plan to update this National Clinical Guideline

This guideline will be scheduled for review 3 years after publication by the National Sepsis Programme. In the event that new relevant evidence comes to light, then a rapid update may be required within the three-year period.

3 Appendices

Only appendices 8,9 and 10 are presented here as they are key to interpreting the recommendations in this summary guideline.

Refer to the full guideline report for the remaining appendices:

Appendix 1: Guideline Development Group Terms of Reference

Appendix 2: Sepsis steering committee/working group membership

Appendix 3: Glossary of terms and abbreviations

Appendix 4: Economic assessment of sepsis management in adults (including maternity)

Appendix 5: The coding process

Appendix 6: Literature search strategy

Appendix 7: Consultation stakeholders

Appendix 11: Sepsis predisposition and recognition in the community

Appendix 12: PHECC practitioner screening and treatment CPG for sepsis

Appendix 13: Fluid resuscitation algorithm for adults with sepsis

Appendix 14: ISBAR communication tool

Appendix 15: Start Smart and Then Focus approach for antimicrobial therapy

Appendix 8: Implementation plan

These guidelines are divided into sections with each one pertaining to a different aspect of patient care. Implementation points are included to guide implementation of the SSCG recommendations in Ireland, particularly in the non-critical care environment.

While the implementation plan is specific to the individual recommendations in the guideline, some actions will assist with guideline implementation as a whole. These include the role of the Sepsis ADONS and engagement with hospital sepsis committees to ensure dissemination and communication of the updated guideline. The National Sepsis Programme will work with HSE communications both internally and externally to inform key stakeholders of the Sepsis Management – National Clinical Guideline No. 26 update and to provide support as appropriate. The Annual Sepsis Summit will also be used as a platform to disseminate the updated guideline. The sepsis e-learning module update further supports the updated National Clinical Guideline and will continue to be available through HSeLanD.

The implementation of the Sepsis Management National Clinical Guideline No. 26 (2021) is dependent on various factors. Table 26 identifies the enablers and barriers to implementing the recommendations along with the responsibilities and timelines. See also the Logic model illustrated in Table 27.

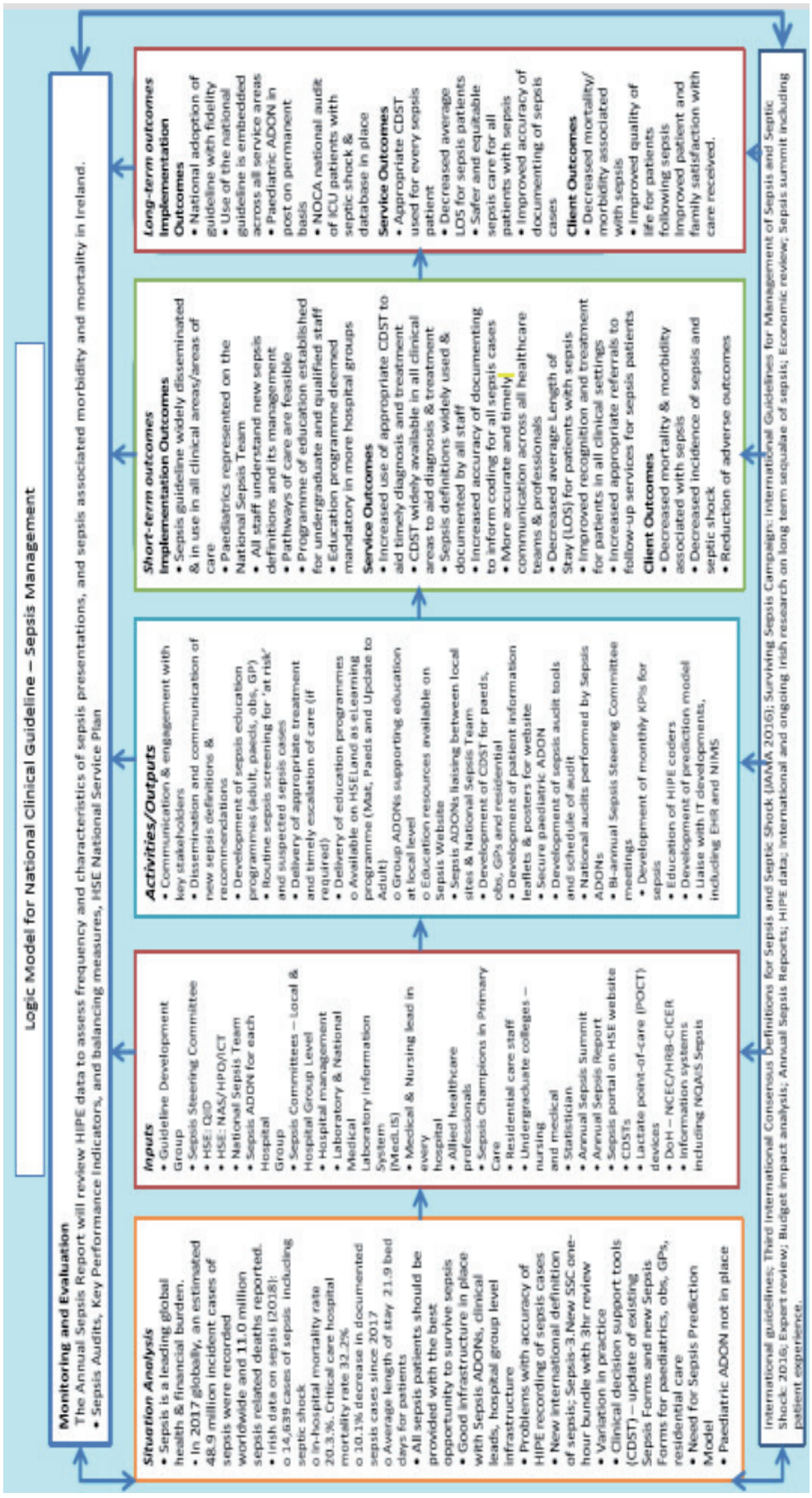
Table 26. Implementation plan for National Clinical Guideline (NCG) on sepsis management

Guideline recommendation or number(s)	Implementation barriers/enablers/gaps	Action/intervention/task to implement recommendation	Lead responsibility for delivery of the action	Timeframe for completion			Expected outcome and verification
				Year 1	Year 2	Year 3	
General	**Enablers** • Current good compliance with many of the recommendations from the Sepsis Summit **Barrier** • Lack of knowledge	Develop communication, dissemination and stakeholder engagement plan, including annual Sepsis Summit.	• Sepsis National Clinical Programme	X			**Outcome** • Improved awareness and knowledge of sepsis guideline **Verification** • Acknowledgement from hospital leads upon receipt of guideline • Monitoring and Audit feedback
Screening for sepsis and performance improvement **Recommendation 1**	**Enablers** • Audit and feedback • Medical and nursing sepsis leads in hospitals • Support from Hospital Senior Management • Local Sepsis Committees • Sepsis ADONs • NQAIS Sepsis currently being tested **Barrier** • Lack of hospital senior management engagement • Lack of medical/nursing sepsis leads in hospitals	Development of network of medical and nursing sepsis leads in hospitals Develop and use audit tools and audit schedules Dissemination of audit findings with hospital management Link with NQAIS Sepsis team re: building of mortality prediction model for sepsis. When operational, this tool will facilitate the development of Key Performance Indicators (KPI's) for sepsis.	• Sepsis ADONs • Hospital Sepsis Committees	X	X	X	**Outcomes** • Greater clarity for role of Clinical Leads • More champions • Improved focus on sepsis by management • Improved compliance with guideline, leading to improved outcomes for patients • Improved support from hospital management • Improved access to sepsis data and hospital comparisons of mortality data **Verification** • Audit and annual reports • Reporting from Sepsis ADONs • Feedback from Hospital Sepsis Committees

							• Feedback from hospital group management • Paediatric ADON in place on permanent
Initial resuscitation **Recommendations (2 – 14)**	**Enabler** • CDST (Sepsis Forms and Algorithms) for early recognition & treatment **Barriers:** • Reluctance to use CDSTs • Lack of knowledge	Ongoing review and update of CDSTs Promote value and importance of CDSTs (use medical/nursing sepsis leads in hospitals) Targeted education on use of clinical decision-making tools – develop scenarios and video/animation	• National Sepsis Team • Hospital Nursing and Clinical Leads • National Sepsis Team	X	X	X	**Outcome** • Improved knowledge of recognising sepsis **Verification** • Audit and Annual report
	Enablers • Sepsis e-learning programme • Mandatory training **Barriers** • Lack of knowledge • Challenges in recognising sepsis early – complex and evolving	Update e-learning sepsis education programme to include the new sepsis definitions and review every three years Advocate for making sepsis e-learning mandatory in all hospital groups Delivery of local education, as required (by ADONs, ANPs, Clinical leads, National Clinical Lead)	• Sepsis National Clinical Programme • Sepsis ADONs • Local Sepsis Committees	X X	X		**Outcome** • Easy access to online Sepsis Education via HSE land which will improve the recognition and management of sepsis in adult and maternity settings **Verification** • HSeLanD e-learning reports
	Barriers • Lack of IT systems to capture information • Lack of integration across IT systems	Addressing the lack of a National IT system is beyond the scope of this National Clinical Guideline however the GDG advocate for liaising with national groups overseeing the development of IT systems to ensure sepsis requirements are appropriately included.	• National Sepsis Team • National Sepsis Team		X	X	**Outcome** • IT systems more fit for purpose – earlier recognition, supporting more effective treatment and monitoring **Verification** • IT systems in place

Antimicrobial therapy **Recommendations (15-33)**	**Enabler** • Local Sepsis Committees • CDSTs • Local antimicrobial guidelines • Consultant Microbiologists • Antimicrobial stewardship **Barriers** • Possible lack of POC equipment to measure lactate • Possible lack of awareness of individual hospital antimicrobial guidelines	Although the requirement for POC Lactate measurement has not changed with the update of the guideline, hospitals should be aware of the requirement for POC Lactate availability and should support, where appropriate, applications for additional equipment. All hospital induction programmes should incorporate training on local antimicrobial guidelines.	• Sepsis ADONs • Hospital Sepsis Committees	X	X		**Outcome** • Improved access to equipment • Improved adherence to local antimicrobial guidelines **Verification** • Review of Hospital Antimicrobial Consumption
Source control Recommendation (34-35) **Vasoactive medication Recommendations (36-41)** **Corticosteroids (Recommendation 42)** **Blood products (Recommendation 43)** **Immunoglobulins (Recommendation 44)** **Blood purification (Recommendation 45)** **Anticoagulants (Recommendation 46-47)** **Mechanical ventilation (Recommendation 48-62)** **Sedation and analgesia (Recommendation 63)** **Glucose control (Recommendation 64-67)** **Renal Replacement Therapy (Recommendation 68-70)** **Bicarbonate Therapy (Recommendation 71)** **Venous Thromboembolism Prophylaxis (Recommendation 72-75)** **Stress Ulcer Prophylaxis (Recommendation 76-78)** **Nutrition (Recommendation 79-90)** **Setting Goals of Care (Recommendation 91-93)**	The GDG have provided implementation points after each recommendation or group of recommendations, to guide implementation of the SSCG recommendations in Ireland.						

Table 27. Logic model for National Clinical Guideline - Sepsis Management



Appendix 9: Sepsis Forms

SEPSIS FORM - ADULT

For In-patient (IP) and Emergency Department (ED) use

Use Clinical Judgement

Where you see this symbol, there is supporting information on page 2

LIKELY INFECTION?
SCREEN FOR SEPSIS

- INEWS ≥ 4 (or ≥ 5 on Oxygen)
- INEWS < 4 or < 5 if on Oxygen in immunocompromised or older person
- ED Sepsis Screen at Triage

Check for 1,2 or 3

1. Risk of Neutropenia e.g. on chemotherapy/radiotherapy
2. Clinical evidence of NEW ONSET organ dysfunction
3. Systemic Inflammatory Response (≥ 2 SIRS) plus ≥ 1 Comorbidity

If there IS evidence of 1, 2 or 3:

- IP Use INEWS Escalation and Response Protocol - escalate to medical review within 30 mins
- ED Triage Category 2

Continue Sepsis Form and place with chart

If there is NO evidence of either 1, 2 or 3:

- Follow usual management pathway
- IP Use INEWS Escalation and Response Protocol
- ED Triage Category 3 - Reassess if deteriorates

Name:

DOB:

HCRN:

Addressograph Label

Date:

Time of INEWS/Triage:

INEWS: **or Triage Category:**

Signature:

NMBI PIN/MCRN:

A) MEDICAL REVIEW

Site of Infection:

_____

If no clinical suspicion of infection, end form and sign at the bottom ☐

1. **At risk of neutropenia** ☐
2. **New onset organ dysfunction** ☐
3. **≥ 2 SIRS + ≥ 1 Comorbidity** ☐

If 1, 2 or 3 ticked

If 1, 2 or 3 not ticked but infection is present, end the form and sign. Continue usual treatment pathway but review diagnosis if patient deteriorates ☐

Signature:_____

Is there is an end of life care plan in place where the sepsis 6 would not be appropriate

If yes, do not proceed with sepsis pathway and document in clinical notes ☐

IF NO, proceed with Sepsis 6 ☐

NMBI/MCRN:_____:

B) SEPSIS 6 BUNDLE

TIME ZERO: _____ 1 hr to complete

TAKE 3

- **Blood Cultures** ☐ Time:_____
- **Blood Tests** incl. lactate ☐ Time:_____
- **Urine Output Assessment** ☐ Time:_____

GIVE 3

- **IV Antimicrobials** ☐ Time:_____
- **IV Fluids** ☐ Time:_____
- **Oxygen given** ☐ Time:_____

NOTES

C) MEDICAL REVIEW Post Sepsis 6 bundle administration

Evidence of infection and new onset organ dysfunction (including at initial presentation) → This is **SEPSIS**: Seek senior input as per local guideline ☐

Evidence of infection without any new onset organ dysfuntion (including at initial presentation) → This is **NOT SEPSIS**: Proceed with usual treatment for specific infection ☐

Look for signs of Septic Shock

Requires inotropes/pressors to maintain MAP ≥ 65 mmhg ☐

If yes, this is SEPTIC SHOCK ☐

Inform Consultant ☐

Contact CRITICAL CARE ☐

D) Clinical Handover

using ISBAR3

This section only applies when handover occurs before the form is completed which is then signed off by receiving doctor

Doctor's Name:

Doctor's Signature:

MCRN:

Date:

Sections Completed

A ☐

B ☐

Receiving Doctor's Name:

Form Completion *including Section C*

Doctor's Name: **MCRN:**

Doctor's Signature: **Date:** **Time:**

1/12/2020 v3

SEPSIS FORM - ADULT

Page 2

This side of the form provides important information to support the completion of Page 1 of the Sepsis Form

Name:

DOB:

HCRN:

Addressograph Label

Infection Sites

- Respiratory Tract
- Skin
- Central Nervous System
- Intra-abdominal
- Catheter/Device related
- Urinary Tract
- Intra-articular/Bone
- Unknown
- Other

Who needs to get the Sepsis 6 treatment bundle?

***Infection** plus any one of the following:*

1. **Risk of Neutropenia e.g. on chemotherapy/radiotherapy**

   Patients at risk of neutropenia due to bone marrow failure, autoimmune disorder or treatment including but not limited to chemotherapy and radiotherapy who present unwell

2. **Clinical evidence of NEW ONSET organ dysfunction such as any of one of the following:**

   - Acutely altered mental state
   - Oligo or anuria
   - Non-blanching rash
   - Respiratory Rate > 30 rpm
   - Pallor/mottling with prolonged capillary refill
   - Systolic Blood Pressure < 90 mmHg
   - Heart Rate > 130 bpm
   - Oxygen Saturation < 90%
   - Other organ dysfunction

3. **Systemic Inflammatory Response (≥2 SIRS) plus ≥1 Comorbidity**

   SIRS Note - physiological changes should be sustained not transient

   - Respiratory Rate ≥ 20 breaths/min
   - Heart Rate > 90 beats/min
   - WCC < 4 or > 12 x 10^9/L
   - Temperature < 36 or > 38.3°C
   - Acutely altered mental state
   - Bedside glucose > 7.7mmol/L *(in the absence of diabetes mellitus)*

   Co-morbidities associated with increased mortality in sepsis

   - COPD
   - DM
   - Frailty
   - HIV/AIDS
   - Chronic liver disease
   - Immunosuppressant medications
   - Age ≥ 75 years
   - Cancer
   - Recent Surgery/Major trauma
   - Chronic kidney disease

The Sepsis 6 treatment bundle

TAKE 3

Blood Cultures

Take blood cultures using aseptic (no touch) technique prior to giving antimicrobials unless this leads to a delay > 45 minutes. Other cultures as indicated by history and examination.

Blood Tests

Point of care lactate (venous or arterial). Full blood count, Renal Profile, Liver Profile +/- Coagulation screen. Other tests and investigations as indicated.

Urine Output

Assess urinary output as part of volume/perfusion status assessment. For patients with sepsis/septic shock start fluid balance charts. Catheterisation and hourly measurements may be required.

GIVE 3

IV Antimicrobials

Give antimicrobials as per local antimicrobial guideline based on the site and source of infection (community or healthcare acquired) and the patient's allergy status. Assess requirement for source control.

IV Fluids

Patients with hypotension should receive up to 30mls/kg of isotonic crystalloid within 1 hour of presentation. Start vasopressors in patients who are fluid unresponsive. Patients with hypoperfusion should receive fluid to restore perfusion using a bolus and review technique. Give 500ml bolus over 15mins up to 2 litres, reassessing frequently. Boluses may be amended based on clinical context - see fluid resuscitation algorithm.

Call Anaesthesiology/Critical Care if hypotensive or if unresponsive to fluid

Oxygen (only give if needed)

Titrate supplementary oxygen to achieve oxygen saturations 94-96% (88-92% in patients with chronic lung disease).

Evidence of infection and new onset organ dysfunction (Either at Initial presentation or after Sepsis 6 given)

- Lactate ≥ 4 mmol/L after 30mls/kg Intravenous fluid therapy
- Cardiovascular - systolic BP < 90 mmHg or Mean Arterial Pressure (MAP), < 65 mmHg or Systolic BP > 40 mmHg below patients normal
- Respiratory - New need for oxygen to achieve saturation > 90% (note this is a definition not the target)
- Renal - Creatinine > 170 micromol/L OR urine output < 0.5ml/kg for 2 hours - despite adequate fluid resuscitation
- Liver - Bilirubin > 32 micromol/L
- Haematological - Platelets < 100 x 10^9/L
- Central Nervous System - Acutely altered mental status

Any pathway modifications need to be agreed by the Hospital Sepsis Committee and align with the current National Clinical Guideline for Sepsis Management for Adults including maternity

Practical Guidance

- Reassess the patient's clincal response frequently
- Reassess and repeat lactate within 3hrs, or more frequently as indicated, if the first is abnormal
- Achieve source control, if required, at the earliest opportunity
- If the patient is deteriorating despite appropriate treatment, seek senior assistance and reassess antimicrobial therapy
- Use Clinical Judgement

Sepsis Predisposition & Recognition

(ALWAYS USE CLINICAL JUDGEMENT)

There are separate sepsis criteria for non-pregnant adult patients

RECOGNISE SEPSIS • ENHANCE SURVIVAL •

MATERNITY PATIENTS

Complete this form and apply if there is a clinical suspicion of infection.

I

Section 1:

Midwife Name:

Midwife Signature:

NMBI PIN:

IMEWS:

Date: Time:

Patient label here

Maternal Sepsis is a life-threatening condition defined as organ dysfunction resulting from infection during pregnancy, childbirth, post-abortion or postpartum period (WHO 2016).

S

Section 2: Are you concerned that the woman could have infection

- ☐ History of fevers or rigors
- ☐ Cough/sputum/breathlessness
- ☐ Flu like symptoms
- ☐ Unexplained abdominal pain/distension
- ☐ Pelvic pain
- ☐ Vomiting and/or diarrhoea
- ☐ Line associated infection/redness/swelling/pain
- ☐ Possible intrauterine infection
- ☐ Myalgia/back pain/general malaise/headache
- ☐ New onset of confusion
- ☐ Cellulitis/wound infection/perineal infection
- ☐ Possible breast infection
- ☐ Multiple presentation with non-specific malaise
- ☐ Others

B

Section 3: Obstetric History

Para:

Gestation:

Pregnancy related complaints:

Days post-natal:

Delivery:

- ☐ Spontaneous vaginal delivery (SVD)
- ☐ Vacuum assisted delivery
- ☐ Forceps assisted delivery
- ☐ Cesarean section

Risk factors

Pregnancy Related

- ☐ Cerclage
- ☐ Pre-term/prolonged rupture of membranes
- ☐ Retained products
- ☐ History pelvic infection
- ☐ Group A Strep. infection in close contact
- ☐ Recent amniocentesis

Non Pregnancy Related

- ☐ Age > 35 years
- ☐ Minority ethnic group
- ☐ Vulnerable socio-economic background
- ☐ Obesity
- ☐ Diabetes, including gestational diabetes
- ☐ Recent surgery
- ☐ Symptoms of infection in the past week
- ☐ Immunocompromised e.g. Systemic Lupus
- ☐ Chronic renal failure
- ☐ Chronic liver failure
- ☐ Chronic heart failure

Record observations on the Irish Maternity Early Warning (IMEWS) chart.

Request immediate medical review
if you are concerned the woman has INFECTION plus ANY 1 of the following:

A

Section 4:

1. ☐ IMEWS trigger for immediate review, i.e. **>2 YELLOWS** or **>1 PINK**
2. ☐ SIRS Response, i.e. ≥2 SIRS criteria listed below.
   SIRS criteria: Note - physiological changes must be sustained not transient.
   - ☐ Respiratory rate ≥ 20 breaths/min
   - ☐ Heart rate ≥ 100bpm
   - ☐ Fetal heart rate >160bpm
   - ☐ WCC < 4 or > 16.9 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)*
3. ☐ At risk of neutropenia, due to bone marrow failure, autoimmune disorder or treatment including but not limited to, chemotherapy and radiotherapy, who present unwell.

R

Section 5:

If sepsis is suspected following screening, escalate to Medical review. Use ISBAR as outlined.

Doctor's Name: **Time Doctor Contacted:**

Midwife's Signature:

Sepsis 3 Maternity Version 1 - 13/08/2018

Sepsis Form - Maternity

(ALWAYS USE CLINICAL JUDGEMENT)

There are separate sepsis criteria for non-pregnant adult patients

If infection suspected following History and Examination, Doctor to complete and sign sepsis screening form

Section 6: Clinical Suspicion of Infection

Document site:

☐ Genital Tract ☐ Urinary Tract ☐ Skin
☐ Respiratory Tract ☐ Intra-abdominal ☐ Catheter/Device Related
☐ Central Nervous System ☐ Intra-articular/Bone ☐ Unknown
☐ Other suspected site:

☐ **No clinical suspicion of INFECTION**: proceed to section 9.

Section 7: Who needs to get the "Sepsis 6" – infection plus any one of the following:

1. ☐ SIRS Response, i.e. ≥2 SIRS criteria listed on page 1.
2. ☐ Clinically or biochemically apparent new onset organ dysfunction, i.e. any one of the following:
   ☐ Acutely altered mental state ☐ RR > 30 ☐ O_2 sat < 90% ☐ HR > 130
   ☐ Oligo or anuria ☐ Pallor/mottling with prolonged capillary refill ☐ SBP < 90
   ☐ Non-blanching rash ☐ Other organ dysfunction
3. ☐ Patients at risk of neutropenia, due to bone marrow failure, autoimmune disorder or treatment including but not limited to, chemotherapy and radiotherapy, who present unwell.

☐ **YES. Start Maternal Sepsis 6 + 1** Time Zero:

Section 8 **TAKE 3** **SEPSIS 6 + 1* – complete *within 1 hour*** **GIVE 3**

☐ **BLOOD CULTURES:** Take blood cultures before giving antimicrobials (if no significant delay i.e. >45 minutes) and other cultures as per examination.

☐ **BLOODS:** Check point of care lactate & full blood count, U&E +/- LFTs +/- Coag. Other test and investigations as indicated by history and examination.

☐ **URINE OUTPUT:** assess urinary output as part of volume/perfusion status assessment. For patients with sepsis or septic shock start hourly urinary output measurement.

*+1 If Pregnant, Assess Fetal Wellbeing ☐

☐ **OXYGEN:** Titrate O_2 to saturations of 94 -98% or 88-92% in chronic lung disease. **N/A** ☐

☐ **FLUIDS:** Start IV fluid resuscitation if evidence of hypovolaemia. 500ml bolus of isotonic crystalloid over 15mins & give up to 2 litres, reassessing frequently. Call Anaesthesia/Critical Care if hypotensive or not fluid responsive. Caution in pre-eclampsia. **N/A** ☐

☐ **ANTIMICROBIALS:** Give IV antimicrobials according to the site of infection and following local antimicrobial guidelines.

Type: Dose: Time given:
Type: Dose: Time given:
Type: Dose: Time given:

Laboratory tests should be requested as EMERGENCY aiming to have results available and *reviewed within 1 hour*

Section 9 Following history and examination, and in the absence of clinical criteria or signs. Sepsis 6+1 is not commenced. If infection is diagnosed, proceed with usual treatment pathway for that infection.

☐ **NO.** Doctor's Name: Date: Time:

Section 10

Look for signs of new organ dysfunction after the Sepsis 6+1 bundle or from blood tests - any one is sufficient:

☐ Lactate ≥ 4 after 30mls/kg Intravenous therapy
☐ Cardiovascular - Systolic BP < 90 or Mean Arterial Pressure (MAP) < 65 or Systolic BP more than 40 below patient's normal
☐ Respiratory - New or increased need for oxygen to achieve saturation > 90% (note: this is a definition, not the target)
☐ Renal - Creatinine > 170 micromol/L **or** Urine output < 500mls/24 hrs – despite adequate fluid resuscitation
☐ Liver - Bilirubin > 32 micromol/L
☐ Haematological - Platelets < 100 x 10^9/L
☐ Central Nervous System - Acutely altered mental status

One or more new organ dysfunction due to infection:

☐ **This is SEPSIS.** Inform Registrar, Consultant and Anaesthetics immediately. Reassess frequently in 1st hour. Consider other investigations and management +/- source control if patient does not respond to initial therapy as evidenced by haemodynamic stabilisation then improvement.

No new organ dysfunction due to infection:

☐ **This is NOT SEPSIS**: If infection is diagnosed proceed with usual treatment pathway for that infection.

Section 11

Look for signs of septic shock

(following adequate initial fluid resuscitation, typically 2 litres in the first hour unless fluid intolerant)

☐ Requiring inotropes/pressors to maintain MAP ≥ 65

☐ **This is SEPTIC SHOCK**

☐ Inform Consultant
☐ Contact CRITICAL CARE/Anaesthesia

Pathway Modification

All Pathway modifications need to be agreed by the Hospital's Sepsis Steering Committee and be in line with the National Clinical Guideline No 6 Sepsis Management.

Section 12 **Clinical Handover. Use ISBAR$_3$ Communication Tool**

This section only applies when handover occurs before the form is completed and is then signed off by the receiving doctor.

Doctor's Name (PRINT): Doctor's Signature: **Doctor's Initials** **MCRN**

Patient care handed over to: Time: Sections completed:

File this document in patient notes - Document management plan.

Doctor's Name: **Doctor's Signature:** **MCRN:** **Date:** **Time:**

Appendix 10: Supporting tools

National Sepsis Programme: https://www.hse.ie/eng/about/who/cspd/ncps/sepsis/

HSeLanD: https://www.hseland.ie/

Global Sepsis Alliance: https://www.global-sepsis-alliance.org/

Surviving Sepsis Campaign: https://www.sccm.org/SurvivingSepsisCampaign/Home

UK Sepsis Trust: https://sepsistrust.org/

Deteriorating Patient Improvement Programme: https://www.hse.ie/eng/about/who/cspd/ncps/deteriorating-patient-improvement-programme/

National Acute Medicine Programme: https://www.hse.ie/eng/about/who/cspd/ncps/acute-medicine/

National Clinical Programmes: https://www.rcpi.ie/national-clinical-programmes/

NCG No 1 INEWS: https://www.gov.ie/en/collection/cc5faa-national-early-warning-score-news/

NCG No. 4 IMEWS: https://www.gov.ie/en/collection/517f60-irish-maternity-early-warning-system-imews-version-2/

NCG No. 5 Communication (Clinical Handover) in Maternity Services: https://www.gov.ie/en/collection/d3b3bd-clinical-handover-in-maternity-services/

NCG No. 11 Clinical Handover in Acute and Children's Hospital Services: https://www.gov.ie/en/collection/006e63-clinical-handover-in-acute-and-childrens-hospital-services/

NCG No. 12 PEWS: https://www.rcpi.ie/paediatric-early-warning-system/

NCG No. 18 EMEWS: https://www.gov.ie/en/collection/bd79b1-emergency-medicine-early-warning-system-emews/

Conversion websites:

http://www.conversion-website.com/pressure/centimeter-of-water-to-millimeter-of-mercury.html

https://www.sensorsone.com/mmhg-to-kpa-conversion-table/

Glucose measurement conversation chart: https://www.google.com/search?q=convert+mg/dl+to+mmol/l&rlz=1C1GCEU_enIE857IE857&source=lnms&tbm=isch&sa=X&ved=2ahUKEwiS3ISb_PfqAhX5SxUIHW-LALgQ_AUoAXoECA0QAw&biw=1024&bih=488#imgrc=W4Q7ngSpX6Q6FM

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