International Guidelines for the Management of Septic Shock & Sepsis-Associated Organ Dysfunction in Children (SSCGC)

National Implementation Plan

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The National Implementation Plan (NIP) for the SSCGC was developed, by the HSE National Sepsis Programme (NSP), to support the implementation of the SSCGC recommendations in the Irish context.

Using this Implementation Plan

- The SSCGC has been adopted by the HSE NSP for use in Ireland and applies to children (including infants, school-aged children and adolescents) with septic shock and other sepsis-associated organ dysfunction in all clinical settings in the acute sector. While the SSCGC recommendations apply to all patients from greater than or equal to 37 weeks gestation at birth to 18 years old with severe sepsis or septic shock, the NIP committee recognises that the definition of a child in an Irish Healthcare setting is from birth to 16yrs, neonates defined as under 4 weeks of age (HSE, National Clinical Programme for Critical Care, 2019). The SSCGC included term neonates (0–28 days) born at greater than or equal to 37 weeks gestation within the scope of these guidelines because these infants may be recognized and resuscitated outside of a newborn or neonatal ICU setting. However, neonatal sepsis is recognised as an entity of itself and deserves special attention and a separate guideline in the future.
- There is a separate National Clinical Guideline for adult patients and pregnant women (HSE, 2020).
- This NIP is relevant to all healthcare professionals involved in the care of children with sepsis and suspicion of sepsis, working in the acute healthcare sector in the Republic of Ireland.
- This NIP supports the recommendations of the SSCGC (Weiss et al. 2020) in the acute Irish healthcare system. The wording of the recommendations has not been changed from the SSCGC publication with the exception of units of measurement applicable to the Irish context.
- The NIP provides **Implementation Points** after the SSCGC recommendations to aid the implementation of the guideline within the acute Irish healthcare system and are aimed, primarily, at the pre and post-critical care setting.
- National Implementation Plan References are listed alphabetically.

Follow link to the SSCGC

Date	Version	Details
December 2020	1	National Implementation Plan (NIP) for the SSCGC February 2020

This NIP is relevant to all healthcare professionals involved in the care of children with sepsis and those with suspicion of sepsis, working in the acute healthcare sector in the Republic of Ireland.

The SSCGC and the NIP are also relevant to:

- The HSE to provide appropriate structured support and adequate resources for the governance, operationalisation, audit and data reporting 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, audit and data reporting. 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.

Disclaimer

NSP: **The SSCGC and NIP 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/parent/guardian declines a recommendation as a course of action in their child's/their ward's 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 this NIP must ensure they have the current version (hardcopy or softcopy) by checking the relevant section in the HSE National Sepsis Programme website: https://www.hse.ie/eng/about/who/cspd/ncps/sepsis/resources/

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Foreword

Sepsis is a leading cause of morbidity, mortality and healthcare utilisation for children worldwide (Weiss, et al., 2020). This NIP is intended to be relevant to all healthcare staff involved in the care of children 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 Septic Shock and Sepsis-Associated Organ Dysfunction in Children in 2020 (SSCGC). A panel of 49 international experts representing 12 international organisations, as well as three methodologists and three public members was convened. The SSCGC panel provided 77 statements on early management and resuscitation of children with septic shock and sepsis-associated organ dysfunction.

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

We also wish to acknowledge all the members of the National Sepsis Steering Committee (Appendix 2), the NIPDG (Appendix 3) and the paediatric sepsis form development group who gave freely of their time and expertise (Appendix 4).

Dr Martina Healy, Clinical Lead for the National Sepsis Programme

Signed by the National Clinical Lead: Date: 9/8/21

Martina Healy

Dr Fidelma Fitzpatrick, Chair, National Sepsis Steering Committee.

Signed by the Chair:  Date: 9/8/21

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

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This National Implementation Plan (NIP) for the International Guidelines for the Management of Septic Shock & Sepsis-Associated Organ Dysfunction in Children (SSCGC) has been developed by the National Implementation Plan Development Group (NIPDG), within the HSE National Sepsis Programme (NSP), and approved by the CCO Clinical Forum, HSE on 16/08/2021.

Implementing Clinical Guidelines

Providing standardised clinical care to patients in healthcare is challenging. This is due to a number of factors, among them diversity 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.

Implementing 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 SSCGC 2020 are international evidence-based recommendations intended to guide "best practice" rather than to establish a treatment algorithm or to define a standard of care. In the Irish healthcare setting this NIP gives further direction to some of the SSCGC recommendations where relevant, while acknowledging that each acute care setting will need to adapt this document to local needs.

Contents

List of Tables PAGE

List of Figures PAGE

Section 1. SSCGC Recommendations

1.1 Summary of recommendations

Table 1. The Surviving Sepsis Campaign (SSC) recommendations

Section	Recommendation	Quality of Evidence	Strength of Recommen-dation	National Implementation Points
SCREENING, DIAGNOSIS, AND SYSTEMATIC MANAGEMENT OF SEPSIS	1. In children who present as acutely unwell, we suggest implementing systematic screening for timely recognition of septic shock and other sepsis-associated organ dysfunction.	Very low	Weak	➢ National Sepsis Programme will implement a system wide process to support sepsis screening and monitor sepsis performance improvement.
	2. We were **unable to** issue a recommendation about using blood lactate values to stratify children with suspected septic shock or other sepsis-associated organ dysfunction into low- versus high-risk of having septic shock or sepsis. However, in our practice, if lactate levels can be rapidly obtained, we often measure blood lactate in children when evaluating for septic shock and other sepsis-associated organ dysfunction.			➢ Persistently elevated lactate levels of >4 mmol/L after 20mLs/kg fluid therapy is indicative of organ dysfunction. ➢ Healthcare providers should be aware of their institutions POC accessibility and usage. ➢ Hospitals should be aware of the requirement for Point of care (POC) lactate availability and should support, where appropriate, applications for additional equipment.
	3. We recommend implementing a protocol/guideline for management of children with septic shock or other sepsis-associated organ dysfunction.		BPS	➢ The NSP provides a paediatric sepsis form which incorporates an early recognition, treatment and referral algorithm for the management of children with septic shock or other sepsis-associated organ dysfunction. ➢ Strategies for the utilisation and implementation of the Sepsis NIP and Sepsis form should be initiated by each institution. ➢ Education on form use is part of national education rollout.

	4. We recommend obtaining blood cultures before initiating antimicrobial therapy in situations where this does not substantially delay antimicrobial administration.		BPS	➢ If obtaining blood cultures is difficult, it should not impede antibiotic initiation within the first hour.
ANTIMICROBIAL THERAPY	5. In children with septic shock, we recommend starting antimicrobial therapy as soon as possible, within 1 hour of recognition.	very low	Strong	➢ Initiate the Sepsis 6 bundle within 1 hour of recognition of septic shock.
	6. In children with sepsis-associated organ dysfunction but without shock, we suggest starting antimicrobial therapy as soon as possible after appropriate evaluation, within 3 hours of recognition.	Very low	Weak	➢ Initiate the Sepsis 6 bundle within 3 hours of recognition of sepsis.
	7. We recommend empiric broad-spectrum therapy with one or more antimicrobials to cover all likely pathogens.		BPS	➢ Empiric broad-spectrum therapy until the causative organism and its antimicrobial susceptibilities are defined, as per local antimicrobial guidelines.
	8. Once the pathogen(s) and sensitivities are available, we recommend narrowing empiric antimicrobial therapy coverage.		BPS	➢ Recommendations (8-14) ➢ Start Smart then Focus strategy for all antimicrobial recommendations.
	9. If no pathogen is identified, we recommend narrowing or stopping empiric antimicrobial therapy according to clinical presentation, site of infection, host risk factors, and adequacy of clinical improvement in discussion with infectious disease and/or microbiological expert advice.		BPS	
	10. In children without immune compromise and without high risk for multidrug-resistant pathogens, we suggest against the routine use of empiric multiple antimicrobials directed against the same pathogen for the purpose of synergy.	Very low	Weak	

	11. In children with immune compromise and/or at high risk for multidrug-resistant pathogens, we suggest using empiric multi-drug therapy when septic shock or other sepsis-associated organ dysfunction is present/suspected.	Very low	Weak	➢ Antifungal and antiviral agents should be considered as part of the initial regimen for susceptible patients e.g. oncology/haematology patients.
	12. We recommend using antimicrobial dosing strategies that have been optimized based on published pharmacokinetic/pharmacodynamics principles and with consideration of specific drug properties.		BPS	
	13. In children with septic shock or sepsis-associated organ dysfunction who are receiving antimicrobials, we recommend daily assessment (e.g., clinical, laboratory assessment) for de-escalation of antimicrobial therapy.		BPS	
	14. We recommend determining the duration of antimicrobial therapy according to the site of infection, microbial etiology, response to treatment, and ability to achieve source control.		BPS	
SOURCE CONTROL	15. We recommend that emergent source control intervention be implemented as soon possible after a diagnosis of an infection amenable to a source control procedure is made.		BPS	Recommendations (15-16) ➢ Patients whose infection is not settling on appropriate antimicrobials need to be re-assessed for source control.
	16. We recommend removal of intravascular access devices that are confirmed to be the source of sepsis or septic shock after other vascular access has been established and depending on the pathogen and the risks/benefits of a surgical procedure.	Low	Strong	➢ Patients whose infection is not settling on appropriate antimicrobials need to be re-assessed for source control including reviewing implanted devices and catheters as potential sources.
FLUID THERAPY	17. In healthcare systems with availability of intensive care, we suggest administering up to 40–60 mL/kg in bolus fluid (10–20 mL/kg per	Low	Weak	➢ In acute care settings with access to intensive care capability/support, fluid management is based on the principle of fluid administration of up to 40-60mL/kg

	bolus) over the first hour, titrated to clinical markers of cardiac output and discontinued if signs of fluid overload develop, for the initial resuscitation of children with septic shock or other sepsis-associated organ dysfunction.			over the first hour where the response to each bolus of 10-20mL/kg is assessed. Fluid volume should be calculated based upon ideal body weight.
	18. In healthcare systems with **no** availability of intensive care and in the absence of hypotension, we recommend against bolus fluid administration while starting maintenance fluids.	High	Strong	
	19. In healthcare systems with **no** availability of intensive care, if hypotension is present, we suggest administering up to 40 mL/kg in bolus fluid (10–20 mL/kg per bolus) over the first hour with titration to clinical markers of cardiac output and discontinued if signs of fluid overload develop.	Low	Weak	
	20. We suggest using crystalloids, rather than albumin, for the initial resuscitation of children with septic shock or other sepsis-associated organ dysfunction.	Moderate	Weak	
	21. We suggest using balanced/buffered crystalloids, rather than 0.9% saline, for the initial resuscitation of children with septic shock or other sepsis-associated organ dysfunction.	Very low	Weak	➢ For children with septic shock treated in settings with access to acute intensive care capability, patients **without** signs of fluid overload should receive 10mL/kg to 20mL/kg boluses of balanced crystalloid solution such as lactated Ringer's solution (Hartmann's solution); 0.9% Normal Saline is an acceptable alternative if lactated Ringer's solution is not available.
	22. We recommend **against** using starches in the acute resuscitation of children with septic shock or other sepsis associated organ dysfunction.	Moderate	Strong	

	23. We suggest **against** using gelatin in the resuscitation of children with septic shock or other sepsis-associated organ dysfunction.	Low	Weak	
HEMODYNAMIC MONITORING	24. We were **unable** to issue a recommendation about whether to target mean arterial blood pressure (MAP) at the 5th or 50th percentile for age in children with septic shock and other sepsis-associated organ dysfunction. However, in our practice, we target MAP to between the 5th and 50th percentile or greater than 50th percentile for age.			
	25. We suggest **not** using bedside clinical signs in isolation to categorize septic shock in children as "warm" or "cold".	Very low	Weak	
	26. We suggest using advanced hemodynamic variables, when available, in addition to bedside clinical variables to guide the resuscitation of children with septic shock or other sepsis-associated organ dysfunction.	Low	Weak	➢ It is the responsibility of clinicians to be familiar with the procedures and to know the advantages and limitations of any advanced haemodynamic monitoring equipment deployed.
	27. We suggest using trends in blood lactate levels, in addition to clinical assessment, to guide resuscitation of children with septic shock and other sepsis-associated organ dysfunction.	Very Low	Weak	➢ Elevation of blood lactate >2.0 mmol/L suggests hypoperfusion.
VASOACTIVE MEDICATIONS	28. We suggest using epinephrine, rather than dopamine, in children with septic shock.	Low	Weak	
	29. We suggest using norepinephrine, rather than dopamine, in children with septic shock	Very low	Weak	
	30. We were **unable to** issue a recommendation for a specific first-line vasoactive infusion for children with septic shock. However, in our practice, we select either epinephrine or norepinephrine as			➢ If vasoactive medication is warranted, seek PICU support.

	the first-line vasoactive infusion guided by clinician preference, individual patient physiology, and local system factors.			➢ If there is no PICU support on site, seek advice on national 24-hour hotline.
	31. We were **unable to** issue a recommendation about initiating vasoactive agents through peripheral access in children with septic shock. However, in our practice, we often or sometimes administer a dilute concentration of the initial vasoactive medication through a peripheral vein if central venous access is not readily accessible.			➢ Vasopressors and inotropes are most usually prescribed by critical care and unless familiar with them, it is prudent to obtain critical care support when starting them. ➢ If central venous access is not readily available, consider administering peripheral vasoactive medications with senior clinical support, until central access can be obtained.
	32. We suggest either adding vasopressin or further titrating catecholamines in children with septic shock who require high-dose catecholamines.	Low	Weak	
	33. We were **unable to** issue a recommendation about adding an inodilator in children with septic shock and cardiac dysfunction despite other vasoactive agents. However, in our practice, we sometimes use inodilators in children with septic shock and evidence of persistent hypoperfusion and cardiac dysfunction despite other vasoactive agents.			➢ The decision to introduce an inodilator is based on the child's cardiovascular response to sepsis management protocols. It is recommended that critical care personnel are responsible for its administration, using the paediatric critical care standard concentration infusion protocols.
VENTILATION	34. We were **unable to** issue a recommendation about whether to intubate children with fluid-refractory, catecholamine-resistant septic shock. However, in our practice, we commonly intubate children with fluid-refractory, catecholamine-resistant septic shock without respiratory failure.			➢ Early intubation and mechanical ventilation is considered if the child is critically ill and is unresponsive to initial resuscitation, in order to facilitate procedures and to decrease work of breathing/ oxygen consumption.
	35. We suggest **not** to use etomidate when intubating children with septic shock or other sepsis-associated organ dysfunction.	Low	Weak	

	36. We suggest a trial of noninvasive mechanical ventilation (over invasive mechanical ventilation) in children with sepsis induced pediatric ARDS (PARDS) without a clear indication for intubation and who are responding to initial resuscitation	Very low	Weak	➢ A trial of non-invasive mechanical ventilation (over invasive mechanical ventilation) in children with hypoxemia and normal ability to protect their airway who do not have overt respiratory failure and who are responding to initial resuscitation is reasonable.
	37. We suggest using high positive end-expiratory pressure (PEEP) in children with sepsis-induced PARDS.	Very low	Weak	
	38. We **cannot suggest** for or against the use of recruitment manoeuvres in children with sepsis induced PARDS and refractory hypoxemia.			
	39. We suggest a trial of prone positioning in children with sepsis and severe PARDS	Low	Weak	
	40. We recommend **against** the routine use of inhaled nitric oxide (iNO) in all children with sepsis induced PARDS.	Low	Strong	
	41. We suggest using iNO as a rescue therapy in children with sepsis induced PARDS and refractory hypoxemia after other oxygenation strategies have been optimized.	Moderate	Weak	
	42. We were **unable to** issue a recommendation to use high frequency oscillatory ventilation (HFOV) versus conventional ventilation in children with sepsis induced PARDS. However, in our practice, there is no preference to use or not use HFOV in patients with severe PARDS and refractory hypoxia.			

	43. We suggest using neuromuscular blockade in children with sepsis and severe PARDS.	Very low	Weak	
CORTICOSTE-ROIDS	44. We suggest against using IV hydrocortisone to treat children with septic shock if fluid resuscitation and vasopressor therapy are able to restore hemodynamic stability.	Low	Weak	
	45. We suggest that either IV hydrocortisone or no hydrocortisone may be used if adequate fluid resuscitation and vasopressor therapy are not able to restore hemodynamic stability.	Low	Weak	➢ Hydrocortisone is most usually given in a critical care setting
ENDOCRINE AND METABOLIC	46. We recommend against insulin therapy to maintain a blood glucose target at or below 140 mg/dL (7.8 mmol/L).	Moderate	Strong	
	47. We were unable to issue a recommendation regarding what blood glucose range to target for children with septic shock or other sepsis-associated organ dysfunction. However, in our practice, there was consensus to target blood glucose levels below 180 mg/dL (10 mmol/L) but there was not consensus about the lower limit of the target range.			➢ Hyperglycaemic control should only be considered in the ICU setting.
	48. We were **unable** to issue a recommendation as to whether to target normal blood calcium levels in children with septic shock or sepsis-associated organ dysfunction. However, in our practice, we often target normal calcium levels for children with septic shock requiring vasoactive infusion support.			

	49. We **suggest against** the routine use of levothyroxine in children with septic shock and other sepsis-associated organ dysfunction in a sick euthyroid state.	Low	Weak	
	50. We suggest either antipyretic therapy or a permissive approach to fever in children with septic shock or other sepsis-associated organ dysfunction.	Moderate	Weak	➢ The decision to administer antipyretics is based on senior clinician advice, degree of pyrexia and the overall condition of child.
NUTRITION	51. We were **unable** to issue a recommendation regarding early hypocaloric/trophic enteral feeding followed by slow increase to full enteral feeding versus early full enteral feeding in children with septic shock or sepsis-associated organ dysfunction without contraindications to enteral feeding. However, in our practice, there is a preference to commence early enteral nutrition within 48 hours of admission in children with septic shock or sepsis-associated organ dysfunction who have no contraindications to enteral nutrition and to increase enteral nutrition in a stepwise fashion until nutritional goals are met.			➢ Enteral nutrition should be initiated in all critically ill children, unless it is contraindicated, within 24-48 hours. Feeds should be advanced according to institutional guidelines and stepwise algorithms.
	52. We suggest not withholding enteral feeding solely on the basis of vasoactive-inotropic medication administration.	Low	Weak	
	53. We suggest enteral nutrition as the preferred method of feeding and that parenteral nutrition may be withheld in the first 7 days of PICU admission in children with septic shock or other sepsis-associated organ dysfunction.	Moderate	Weak	➢ Individual assessment is required to determine whether parenteral nutrition is a) indicated b) viable and c) beneficial. PICU should have access to a dedicated dietitian or nutrition support team. Care should be taken to ensure that nutrition support is not entirely withheld from extremely vulnerable children. Any decision to withhold nutrition support should be revisited daily.

	54. We **suggest against** supplementation with specialized lipid emulsions in children with septic shock or other sepsis associated organ dysfunction.	Very low	Weak	
	55. We **suggest against** the routine measurements of gastric residual volumes (GRVs) in children with septic shock or other sepsis-associated organ dysfunction.	Low	Weak	
	56. We suggest administering enteral feeds through a gastric tube, rather than a postpyloric feeding tube, to children with septic shock or other sepsis-associated organ dysfunction who have no contraindications to enteral feeding.	Low	Weak	
	57. We **suggest against** the routine use of prokinetic agents for the treatment of feeding intolerance in children with septic shock or other sepsis-associated organ dysfunction.	Low	Weak	
	58. We **suggest against** the use of selenium in children with septic shock or other sepsis-associated organ dysfunction.	Low	Weak	
	59. We **suggest against** the use of glutamine supplementation in children with septic shock or other sepsis-associated organ dysfunction.	Low	Weak	
	60. We **suggest against** the use of arginine in the treatment of children with septic shock or other sepsis-associated organ dysfunction.	Very low	Weak	
	61. We **suggest against** using zinc supplementation in children with septic shock and other sepsis-associated organ dysfunction.	Very low	Weak	

	62. We **suggest against** the use of ascorbic acid (vitamin C) in the treatment of children with septic shock or other sepsis associated organ dysfunction.	Very low	Weak	
	63. We **suggest against** the use of thiamine to treat children with sepsis-associated organ dysfunction.	Low	Weak	
	64. We **suggest against** the acute repletion of vitamin D deficiency (VDD) for treatment of septic shock or other sepsis-associated organ dysfunction.	Very low	Weak	
BLOOD PRODUCTS	65. We **suggest against** transfusion of RBCs if the blood hemoglobin concentration is greater than or equal to 7 g/dL in hemodynamically stabilized children with septic shock or other sepsis-associated organ dysfunction.	Low	Weak	
	66. We **cannot** make a recommendation regarding hemoglobin transfusion thresholds for critically ill children with unstable septic shock.			➢ Follow TAXI (Transfusion and Anemia Expertise Initiative) guidelines.
	67. We **suggest against** prophylactic platelet transfusion based solely on platelet levels in nonbleeding children with septic shock or other sepsis-associated organ dysfunction and thrombocytopenia.	Very low	Weak	
	68. We **suggest against** prophylactic plasma transfusion in nonbleeding children with septic shock or other sepsis associated organ dysfunction and coagulation abnormalities.	Very low	Weak	

PLASMA EXCHANGE, RENAL REPLACEMENT, AND EXTRACORPOREAL SUPPORT	69. We **suggest against** using plasma exchange (PLEX) in children with septic shock or other sepsis-associated organ dysfunction without thrombocytopenia-associated multiple organ failure (TAMOF).	Very low	Weak	
	70. We **cannot suggest** for or against the use of PLEX in children with septic shock or other sepsis-associated organ dysfunction with TAMOF.			
	71. We suggest using renal replacement therapy to prevent or treat fluid overload in children with septic shock or other sepsis-associated organ dysfunction who are unresponsive to fluid restriction and diuretic therapy.	Very low	Weak	
	72. We **suggest against** high-volume hemofiltration (HVHF) over standard hemofiltration in children with septic shock or other sepsis-associated organ dysfunction who are treated with renal replacement therapy.	Low	Weak	
	73. We suggest using venovenous ECMO in children with sepsis induced PARDS and refractory hypoxia.	Very low	Weak	
	74. We suggest using venoarterial ECMO as a rescue therapy in children with septic shock only if refractory to all other treatments.	Very low	Weak	
IMMUNO-GLOBULINS	75. We **suggest against** the routine use of IV immune globulin (IVIG) in children with septic shock or other sepsis associated organ dysfunction.	Low	Weak	

PROPHYLAXIS	76. We **suggest against** the routine use of stress ulcer prophylaxis in critically ill children with septic shock or other sepsis-associated organ dysfunction, except for high-risk patients.	Very low	Weak	
	77. We **suggest against** routine deep vein thrombosis (DVT) prophylaxis (mechanical or pharmacologic) in critically ill children with septic shock or other sepsis-associated organ dysfunction, but potential benefits may outweigh risks and costs in specific populations.	Low	Weak	

The SSCGC provides explanation on grading of recommendations and levels of evidence (Weiss et al., 2020).

Section 2. Development of the National Implementation Plan (NIP)

The glossary of terms and abbreviations used throughout this document are explained in (Appendix 5).

2.1 Background

2.1.1 Impact of Sepsis in the paediatric population

Globally, an estimated 22 cases of childhood sepsis per 100,000 person-years and 2202 cases of neonatal sepsis per 100,000 live births occur, translating into 1.2 million cases of childhood sepsis per year (Weiss, et al., 2020). 2015 SPROUT (Sepsis Prevalence, Outcomes, and Therapies) study demonstrated that the prevalence of severe sepsis (defined by 2005 criteria) was 8.2% among children in ICU (<18 years old) with the associated hospital mortality of 25%, which was not different by age and between developed and developing countries (Weiss, et al., 2015).

In Ireland, the Hospital Inpatient Enquiry (HIPE) database is used to extract data on the burden of sepsis in the acute hospital sectors, but has its limitations, namely sepsis may be a direct or indirect contributor to morbidity and mortality. The crude sepsis data for 2019 documented a diagnosis of sepsis or septic shock in 642 children and these patients had a mortality rate of 3.7% (HSE, 2019) Table 1.

Table 1. Paediatric sepsis associated incidence and crude mortality rates 2011 - 2019

Year	Children aged 0-15 Years with a Diagnosis of Sepsis	
	Number of Inpatients	Crude Mortality Rate
2011	737	3.0%
2012	763	3.9%
2013	763	3.8%
2014	746	4.0%
2015	765	2.1%
2016	791	3.5%
2017	820	3.9%
2018	746	4.4%
2019	642	3.7%

Providing standardised clinical care to patients in healthcare is challenging. This is due to a number of factors, among them diversity 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.

Implementing 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 SSC published guidelines for Managing Septic Shock and Sepsis-Associated Organ Dysfunction in Children in 2020 (SSCGC).

The SSCGC focuses on the management of sepsis and septic shock in children and underwent a robust process to identify the evidence relating to five areas of practice: 1) recognition and management of infection, 2) haemodynamics and resuscitation, 3) ventilation, 4) endocrine and metabolic therapies and 5) adjunctive therapies. A sixth

subgroup was added to review research priorities in paediatric sepsis. 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 for Children (Weiss, et al., 2020). The SSCGC provides recommendations for good practice that are based on the best available clinical and cost effectiveness evidence.

Before a decision was made to adopt these guidelines for use in Ireland, a literature search was undertaken by the NSP to identify if any other published paediatric sepsis clinical guidelines were available that could be adopted or adapted for use in the Irish Healthcare setting. The search strategy is outlined in Tables 2 and 3.

The literature search identified the SSCGC guideline as the only available guideline for the management of Paediatric Sepsis. In this context, the National Sepsis Programme (NSP) decided to fully adopt the SSCGC and to provide a NIP to support the implementation of the SSCGC recommendations within the acute paediatric healthcare setting in Ireland.

Table 2. Databases searched

Date	Database
September 2020	NICE (National Institute Clinical Effectiveness) GINN (Guidelines International network) TRIP (Turning Research into Practice), American Clearing House Web of Science, PubMed, Scopus, Embase, Google Scholar

Table 3. Search Terms Strategy for Paediatric Sepsis Management

Search
Sepsis OR blood poisoning OR septicaemia OR SIRS OR systemic inflammatory response system OR Septic shock OR severe sepsis. Filters: Guideline, Meta-analysis, Practice Guideline, Systematic review.
Paediatric OR Childhood OR Neonates OR Infants
Excluding foreign language, specific types of Sepsis e.g. acute meningitis, meningococcal Sepsis

2.2 Aims and Objectives of NIP

Aim

To implement the SSCGC evidence-based recommendations in a format that applies to the structures and functions of the acute healthcare setting for children in Ireland.

Objectives

1. To reduce unnecessary variations in practice and provide an evidence base for the most appropriate healthcare to optimize children's survival from sepsis.
2. That all healthcare professionals have an understanding of the diagnostic criteria for sepsis and its basic pathophysiology.
3. That all healthcare professionals recognise children at high risk of mortality from sepsis.
4. That all healthcare professionals are:
    i. Familiar with the initial management of children with a high risk of mortality from sepsis.
    ii. Able to use the Paediatric Sepsis Form (Appendix 9), a clinical decision support tool that forms part of the child's clinical notes.

Why is the pre-critical care setting important?

It is recognised that the presentation of sepsis is variable in symptoms, signs and time course. Thus, sepsis may not be present or not 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 Paediatric Early Warning System (2016) (PEWS) combined with clinical judgment should be deployed to recognise and respond to a deterioration in a child's condition, once admitted to an acute paediatric care setting, outside of ICU (HSE, 2016a).

In 2016, the Centres for Disease Control (CDC) in the U.S. performed a medical record review of paediatric presentations and found 57% were community-associated sepsis cases without health care factors i.e. (≥2 days in long-term or other acute care hospital, receipt of intravenous antimicrobials, peritoneal or haemodialysis, surgery, total parenteral nutrition, chemotherapy, wound therapy, or presence of a central venous

catheter) (Novasad, et al., 2016). The remaining 43% of patients had sepsis with health care factors.

In Ireland, these patients present to the acute hospital sector via the Paediatric Emergency Dept. (PED), Mixed Emergency Departments, the Paediatric Observation Department (POD), Paediatric Assessment Units (PAUs), the Urgent Care Centres (UCC) and to a lesser extent the Outpatient Department (OPD).

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.
In September 2020, the NSP launched a public awareness campaign to promote awareness of the signs and symptoms of sepsis in children, adults, and maternal care. The campaign aims to educate patients and families about early warning signs of sepsis, to empower patient and families to seek urgent medical attention and ask, “could this be sepsis?” and to highlight preventative measures to reduce the risk of infection.

Available resources at www.hse.ie/eng/about/who/cspd/ncps/sepsis/ include videos on paediatric sepsis that can be shared on social media platforms, in community health centres and in GP practices. Patient information leaflets and sepsis awareness posters / cards are also available to download from this site (Appendix 7).

2.3 Definitions

The concept of sepsis as life-threatening organ dysfunction caused by a dysregulated response to infection has face validity for children, but the most appropriate criteria for operationalizing organ dysfunction and the utility of lactate in paediatric sepsis have not yet been established. Nevertheless, studies support using a stratified scoring system for organ dysfunction over Systemic Inflammatory Response Syndrome (SIRS) criteria in children [12], and efforts to update the definition and clinical criteria for paediatric sepsis are currently underway.

Until revised data-driven clinical criteria are determined to better describe paediatric sepsis and septic shock, existing consensus criteria should continue to be used to define paediatric sepsis (Weiss & Pomerantz, Septic shock in children: Rapid recognition and initial resuscitation (first hour), 2020) i.e. 2005 definitions (Goldstein, Giroir, & Randolph, 2005) [1]. The Society of Critical Care Medicine's (SCCM) Paediatric Sepsis Definition Taskforce are currently conducting a systematic review to collate evidence on individual factors, clinical criteria, and/or illness severity scores for the recognition of possible sepsis, sepsis, septicaemia, and septic shock in children. (Menon, et al., 2020)

Table 4. Definitions of Sepsis

Infection	As per 2005 (International Consensus Conference on Paediatric Sepsis) definition, infection is defined as a suspected or proven (by positive culture, tissue stain, or polymerase chain reaction test) infection caused by any pathogen OR a clinical syndrome associated with a high probability of infection. Evidence of infection includes positive findings on clinical exam, imaging, or laboratory tests (e.g. white blood cells in a normally sterile body fluid, perforated viscus, chest radiograph consistent with pneumonia, petechial or purpuric rash, or purpura fulminans).
Sepsis	As per 2005 (International Consensus Conference on Paediatric Sepsis) definition, sepsis is defined as Systemic Inflammatory Response Syndrome (SIRS) in the presence of or as a result of suspected or proven infection. **SIRS criteria** The presence of at least two of the following four criteria, one of which must be abnormal temperature or leukocyte count: ● Core temperature of >38.5°C or <36°C. ● Leukocyte count elevated or depressed for age (not secondary to chemotherapy-induced leukopenia) or 10% immature neutrophils. ● Tachycardia, defined as a mean heart rate 2 SD above normal for age in the absence of external stimulus, chronic drugs, or painful stimuli; or otherwise unexplained persistent elevation over

	a 0.5- to 4-hr time period OR for children <1 yr old: bradycardia, defined as a mean heart rate <10th percentile for age in the absence of external vagal stimulus, beta-blocker drugs, or congenital heart disease; or otherwise unexplained persistent depression over a 0.5-hr time period. ● Mean respiratory rate 2 SD above normal for age or mechanical ventilation for an acute process not related to underlying neuromuscular disease or the receipt of general anaesthesia.
Septic shock	For the purpose of the SSCGC 2020, septic shock in children is defined as severe infection leading to cardiovascular dysfunction (including hypotension, need for treatment with a vasoactive medication or impaired perfusion).
Sepsis-associated organ dysfunction	For the purpose of the SSCGC 2020, sepsis-associated organ dysfunction in children is defined as severe infection leading to cardiovascular and/or noncardiovascular organ dysfunction. **NOTE** Because several methods to identify acute organ dysfunction in children are currently available (17, 19, 20, 22, 23), SSCGC chose not to require a specific definition or scheme for this purpose.

2.4 Process

A NIP Development group was convened to oversee the development of this plan. The NIPDG was chaired by Dr Martina Healy, National Clinical Lead for Sepsis. This NIP is supported by HSE Clinical Strategy and Programmes Division.

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 healthcare sector. NIPDG members included those involved in clinical practice, education, administration, research methodology and persons representing patients and the public.

A NIP Development group was convened to oversee the development of this plan. Membership detailed in (Appendix 3).

The NIP is structured as follows:

i. **SSCGC Recommendations and remarks (if present).**

ii. **NIP - Implementation Points (where relevant)** Implementation points are included to guide implementation of the SSCGC 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, in particular, in emergency departments (EDs) and paediatric hospitals and 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 the National Paediatric Sepsis Form Development Group and the forms amended based on this feedback and re-piloted. Thus, the implementation programme is informed by end-users and by multidisciplinary specialist input.

References that have been incorporated through this document are listed **alphabetically** under **National Implementation Plan References** (Appendix 17). In addition, some **SSCGC references** are cited in this document and are **numbered** as per the SSCGC document (Appendix 16).

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

The recommendations of the SSCGC are included so that it can be read as a standalone document. However, it is recommended that clinicians familiarise themselves with the 2020 SSCGC, https://www.sccm.org/SurvivingSepsisCampaign/Guidelines/Pediatric-Patients

2.5 Consultation summary

The NIPDG sought to ensure that all stakeholders had an opportunity to review and contribute to the development of a National Implementation Plan for Sepsis in children. The NIPDG gratefully acknowledges the contribution made by all those who contributed from professional, academic and patient groups.

2.6 Monitoring and audit

Implementing the SSCGC aims to reduce unnecessary variations in practice and provide an evidence base for the most appropriate healthcare to optimise children's survival from sepsis.

The aims and objectives of the NIP will be monitored by the NSP in two ways:

(1) Audit of implementation of the SSCGC (**Clinical audit/Process audit**); and

(2) Audit of outcomes resulting from implementation of the SSCGC (**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. 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 out 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.

Audit of outcomes:

The primary aim of optimising 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 children's 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 NSP suggests that the annual sepsis outcome report 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 and
- 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 prioritisation. However, for every patient prioritised 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.

The National Sepsis 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 utilisation 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, Tseng, & Shapiro, 2015) and should be reported where possible. The assessment of healthcare utilisation is important as a monitor of the effectiveness of the sepsis quality improvement programme and also provides data for resource planning.

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 audit committee (Appendix 1). 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 NSP, 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 collaboration from hospital sepsis committees and the Hospital Group Leadership Team to ensure any identified issues are addressed.

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, *Clostridioides difficile* infection) and of public health concern (increased rates of multidrug resistant organisms, MDRO) (Department of Health, 2017).

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

1. Children who have deteriorated but have no evidence of potential infective source/sepsis are commenced inappropriately on antimicrobial therapy.
2. Children with sepsis are commenced on inappropriate antimicrobial therapy that is not in line with local /national guidelines, with due consideration of the clinical circumstances.
3. Empiric antimicrobial therapy that has been commenced in a child with suspected sepsis is not reviewed at 24-48 hours as recommended by the Start Smart, then Focus Antimicrobial Care bundle (RCPI , 2012) Appendix 10.

All hospitals should have antimicrobial stewardship programmes in place as outlined in National Guidelines (Department of Health, 2017) (HSE, 2020) that monitor process and outcome measures to ensure that antimicrobials are not being prescribed unnecessarily due to inappropriate application of Sepsis 6. Ensuring antimicrobials are used appropriately for all infections, not just those associated with sepsis, will maximise clinical cure and minimise harm, for the individual patient.

Practical guidance

The NSP suggests that a tool be developed to risk adjust sepsis-associated hospital mortality (direct and in-direct) based on the Hospital In-patient Enquiry (HIPE) database and that each acute hospital, on this database, have annual risk-adjusted sepsis-associated mortality rates benchmarked against the national average.

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 it supports improvement processes.

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.

2.7 Financial impact of the National Implementation Plan

A performance improvement programme for hospitals at both group and local level is provided by the National Sepsis Programme with the provision of audits and education to improve performance in the recognition and management of sepsis. Support for the implementation of this NIP and associated costs are included in the National Clinical Guideline No. 6 (2020 Update) – Sepsis Management for Adults (including maternity), available on the NCEC website.

Specifically, for this NIP, the NIPDG systematically reviewed all 77 SSCGC recommendations to determine if any had an additional budget impact for implementation in Ireland. Each recommendation statement was discussed and determined as either having no budget impact if the recommendation was currently practiced, or as having a requirement for a budget resource. The costs were then determined for the latter.

Key findings relating to costs

Only 2 of 77 recommendations was determined to have a potential budgetary impact.

SSCGC Recommendation 1 In children who present as acutely unwell, we suggest implementing systematic screening for timely recognition of septic shock and other sepsis-associated organ dysfunction.

SSCGC Recommendation 3 We recommend implementing a protocol/guideline for management of children with septic shock or other sepsis-associated organ dysfunction.

Educational methodologies to address paediatric sepsis screening tools and implementation of sepsis protocols will need to be developed. A similar programme to that of the National Sepsis Programme E-learning education “Introduction to the Sepsis Management for Adults including Maternity “to optimise sepsis recognition and treatment, will be essential to ensure widespread adoption of this NIP.

Table 5. Costings related to the development of an e-learning paediatric sepsis component

Potential costings	
Education: E-Learning programme on HSEland, approximate costing based on Adult programme	€54,000
Sepsis form development and colour printing	€356.70 per 1000

2.8 Plan to update this National Implementation Plan

This NIP will be updated in line with the SSC plan to review every 4 years or sooner if breaking and relevant evidence becomes available.

Section 3. SSCGC recommendations incorporating the NIP

Recommendations from the Surviving Sepsis Campaign International Guidelines for the Management of Septic Shock and Sepsis-Associated Organ Dysfunction in Children 2020 (SSCGC) are adopted in total for use in Ireland. Recommendations are labelled 1-77 and are divided into sections with each one pertaining to a different aspect of patient care. Additionally, National Implementation Points are provided and are for the purpose of implementing the SSCGC, in the Irish context, particularly in the non-critical care environment.

The following guidance is based on the best available evidence. The Surviving Sepsis Campaign Guideline for the Management of Septic Shock and Sepsis-Associated Organ Dysfunction in Children 2020 (SSCGC) can be found in the *Intensive Care Medicine journal*, 46 (Suppl 1):S10–S67 at this link giving details of the methods and the evidence used to formulate the recommendations.

3.1 SSCGC recommendations

3.1.1 Screening, diagnosis, and systematic management of sepsis (SSCGC Recommendations 1-4)

SSCGC Recommendation 1
In children who present as acutely unwell, we suggest implementing systematic screening for timely recognition of septic shock and other sepsis-associated organ dysfunction
Quality/level of evidence: Very low + Strength of recommendation: Weak
SSCGC Remarks Systematic screening needs to be tailored to the type of patients, resources, and procedures within each institution. Evaluation for the effectiveness and sustainability of screening should be incorporated as part of this process.

SSCGC Recommendation 2
We were unable to issue a recommendation about using blood lactate values to stratify children with suspected septic shock or other sepsis-associated organ dysfunction into low- versus high-risk of having septic shock or sepsis. However, in our practice, if lactate levels can be rapidly obtained, we often measure blood lactate in children when evaluating for septic shock and other sepsis-associated organ dysfunction.

SSCGC Recommendation 3
We recommend implementing a protocol/guideline for management of children with septic shock or other sepsis-associated organ dysfunction.
Quality/level of evidence: ungraded + Strength of recommendation: BPS

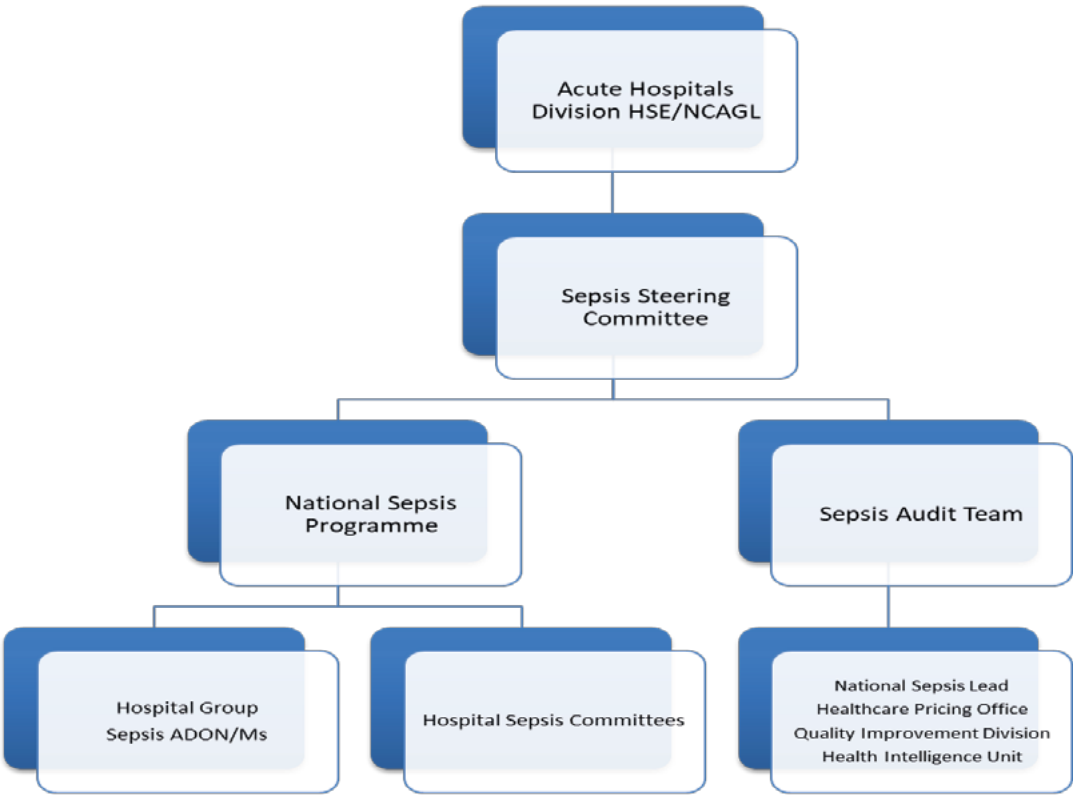
SSCGC Recommendation 4
We recommend obtaining blood cultures before initiating antimicrobial therapy in situations where this does not substantially delay antimicrobial administration.
Quality/level of evidence: ungraded + Strength of recommendation: BPS

National Implementation point 1 (SSCGC Recommendation 1)

The National Sepsis Programme will implement a system wide process to support sepsis screening and monitor sepsis performance improvement in the paediatric population, promoting safe and high-quality sepsis care.

The National Sepsis Programme follows the governance structure outlined in Figure 1. to coordinate the implementation and audit of the NIP.

Figure 1. The National Sepsis Programme Governance Structure



The **National Sepsis Steering Committee** is a multi-disciplinary committee recognising that sepsis affects all specialties and services. Its membership is listed in Appendix 1.

The **National Sepsis Team** reports to the steering committee and the office of the National Clinical Advisor and Group Lead for Acute Hospitals, Health Services Executive (HSE) and works with the National Clinical Effectiveness Committee for the

scheduled updates of the National Clinical Guideline and advises the Department of Health on issues related to sepsis. Its membership is listed in Appendix 2.

Hospital Sepsis Committee

All paediatric hospitals and acute hospitals with paediatric units are required to have a Sepsis Committee whose role is to guide the implementation of the SSCGC recommendations and this NIP in their hospital. This committee oversees the coordination of sepsis education, introduction and utilisation of the sepsis form and reviews audit feedback to inform this process.

The sepsis committee, together with Hospital Management and the Clinical Directors, has responsibility for effecting and monitoring the improvements identified as audit outlier interventions. This committee is multi-disciplinary with a named medical and nursing lead, and should include nursing; NCHDs; clinical microbiology; pharmacy (e.g. antimicrobial pharmacist); coding; practice facilitators and educators and may invite other specialties as required.

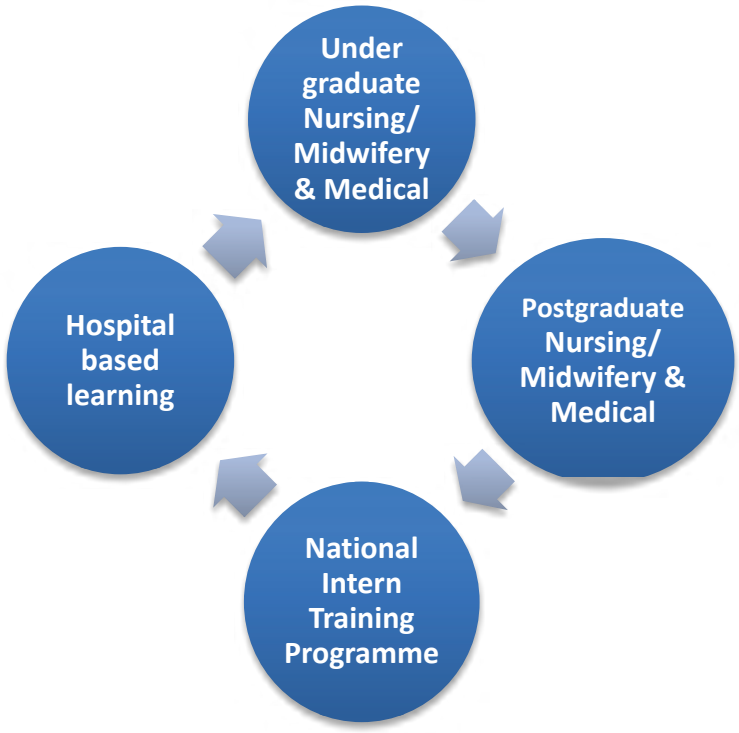
The committees liaise with their Group Sepsis Assistant Director of Nursing (ADON) and the National Team. This is a two-way relationship with the sepsis committees feeding back to the programme on the usefulness of aids and algorithms, suggestions to improve sepsis management and suggesting specific audits. Ideally, there should be a Hospital Group Sepsis ADON as a member of each hospital committee in their group.

In turn the National Team provides tools to assist education, implementation and audit feedback. Should outlier intervention be required, the National Team can advise the Hospital Sepsis Committee and Management and offer further education and audit support. The Hospital Group Sepsis ADON works with the hospital, the Hospital Group Leadership Team and the National Sepsis Team to support sepsis quality improvement.

Sepsis Education

This guideline recognises that the responsibility for sepsis education falls under a number of domains and recommends that education providers ensure that their education curricula are consistent with the SSCGC recommendations and this NIP. (Fig.2)

Figure 2. Sepsis Education Overview



Roles and Responsibilities

It is the responsibility of the HSE to provide appropriate structured support and adequate resources for the governance, operationalisation, and audit of sepsis management in the acute healthcare sector for children.

It is the responsibility of the Sepsis Steering Committee to provide clinical expertise and guidance for the National Sepsis Programme.

It is the responsibility of the National Sepsis Team to ensure that clinical guidance is in line with best international practice, to provide clinical advice and decision support tools to local hospital sepsis committees and to oversee process and outcome audit, provide feedback and to advise on outlier intervention when required.

It is the responsibility of 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.

It is the responsibility of hospital sepsis committees to co-ordinate SSCGC recommendations and NIP implementation in their hospital and to work with the Hospital Group Sepsis Assistant Directors of Nursing (ADON) and the National Sepsis Team with the aim of optimising sepsis recognition and treatment (Appendix 11).

Figure 3. Flowchart for the Implementation of the SSCGC recommendations.

It is the responsibility of the Sepsis ADON to help support the local hospital sepsis committees' aims by performing audit and feedback on the sepsis care in their institution and by liaising with the National Sepsis Programme to ensure effective communication between the Programme, the Hospital Group Leadership and Local

Hospitals. The Sepsis ADONs also have a role in fostering new sepsis initiatives and international benchmarking.

It is the responsibility of Nursing/Midwifery and Medical Colleges, Under and Post-Graduate to ensure that their sepsis curricula are consistent with the SSCGC recommendations and NIP and to provide their graduates with the appropriate knowledge and skillset to be able to comply with the recommendations therein.

Healthcare professionals are responsible for undertaking relevant education as often as they deem necessary to develop their professional practice and maintain their professional competence.

Implementation point 2 (SSCGC Recommendation 2)

Lactate levels should be monitored as part of the ongoing assessment of cardiovascular dysfunction. In Ireland, persistently elevated lactate levels of >4 mmol/L after 20mLs/kg fluid therapy is indicative of organ dysfunction. The target therapeutic lactate level is < 2mmol/L.

Although blood lactate may be affected by the conditions of the blood draw (e.g. use of a tourniquet), both elevated venous and arterial lactate measurements have been shown to be associated with increased risk of organ dysfunction, resuscitative therapies and critical illness (Scott, Donoghue, Gaieski, Marchese, & Mistry, 2012). There is evidence from a number of studies that agreement between peripheral venous and arterial lactate is satisfactory at normal lactate concentration ≤ 2.0 mmol/L, but declines as lactate concentration increases (Samaraweera, Gibbons, Gour, & Sedgwick, 2017).
Blood tests must be sent marked urgent and must be reviewed and acted upon in a timely fashion.

Roles and Responsibilities

To undertake venepuncture and obtain blood samples, healthcare practitioners must have completed appropriate training and maintain best practice when undertaking these procedures. Hospitals should be aware of the requirement for Point of care (POC) lactate availability and should support, where appropriate, applications for additional equipment.

Healthcare providers should be aware of their institutions POC accessibility and usage. It is the responsibility of the hospital and laboratory management to ensure that all point of care equipment is subjected to laboratory governance including internal quality control and external quality assurance.

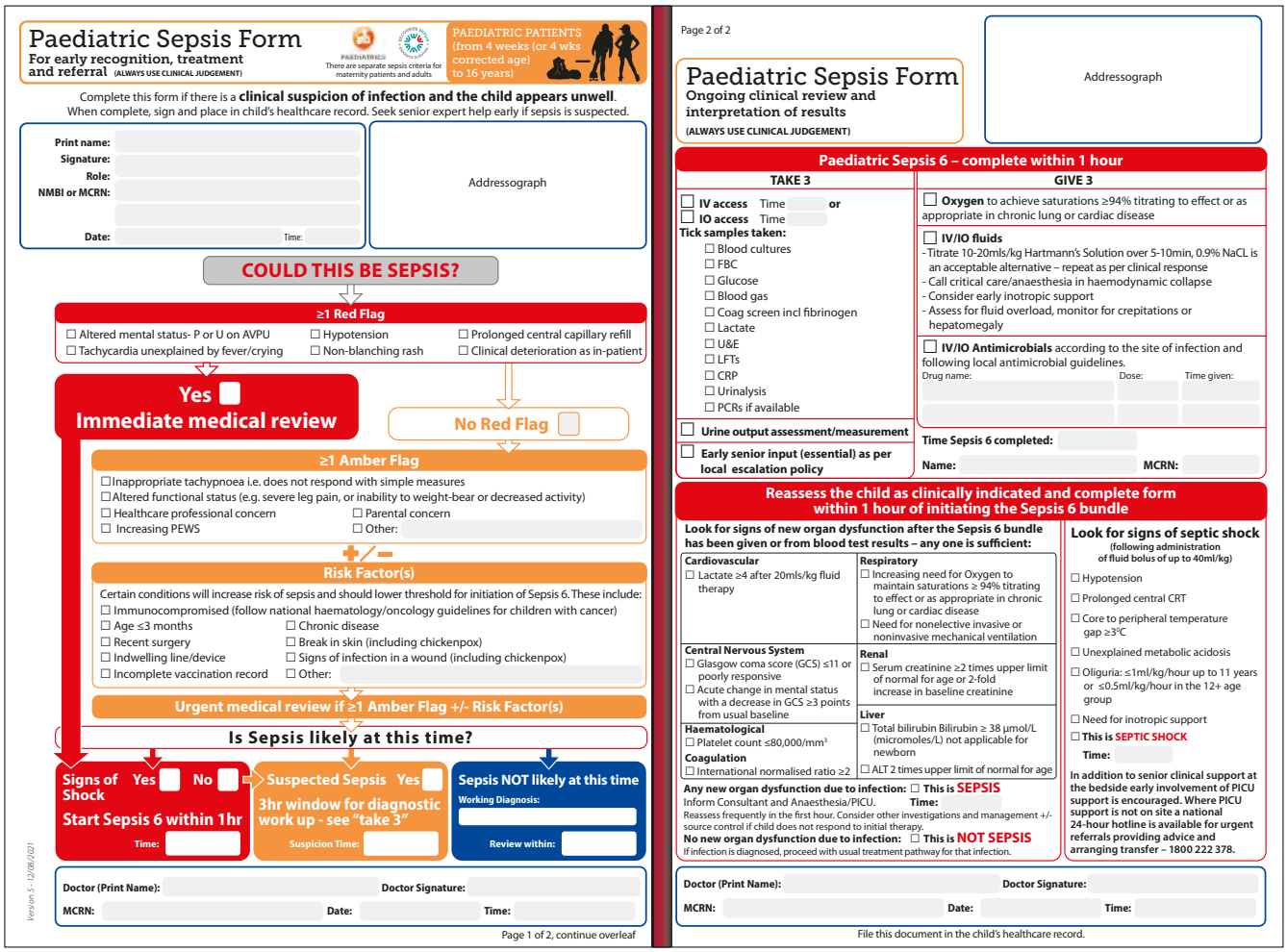
Implementation point 3 (SSCGC Recommendation 3)

The NSP provides a paediatric sepsis form which incorporates an early recognition, treatment and referral algorithm for the management of children with septic shock or other sepsis-associated organ dysfunction (Fig. 3).

The paediatric sepsis form is a clinical decision support tool (Appendix 9) (Fig.4) designed by the Paediatric Sepsis Working Group and is aimed at providing guidance for clinicians to recognise and treat sepsis in a timely manner. It does not replace clinical judgement but it does ensure that all criteria are considered when treating a child who may have sepsis.

Clinical decision support tools help clinicians to identify high-risk patients, consider sepsis as a differential diagnosis during examination and initiate timely treatment if required. Such protocols have been shown to improve the speed and reliability of care for children with septic shock or other sepsis-associated organ dysfunction (Weiss, et al., 2020)

Figure 4. Paediatric Sepsis Form



Paediatric Sepsis Form
For early recognition, treatment and referral (ALWAYS USE CLINICAL JUDGEMENT)
PAEDIATRIC PATIENTS (from 4 weeks (or 4 wks corrected age) to 16 years)
There are separate sepsis criteria for maternity patients and adults
Complete this form if there is a clinical suspicion of infection and the child appears unwell.
When complete, sign and place in child's healthcare record. Seek senior expert help early if sepsis is suspected.
Print name: Signature: Role: NMBI or MCRN: Date: Time:
Addressograph
COULD THIS BE SEPSIS?
≥1 Red Flag
☐ Altered mental status- P or U on AVPU ☐ Hypotension ☐ Prolonged central capillary refill
☐ Tachycardia unexplained by fever/crying ☐ Non-blanching rash ☐ Clinical deterioration as in-patient
Yes Immediate medical review
No Red Flag
≥1 Amber Flag
☐ Inappropriate tachypnoea i.e. does not respond with simple measures
☐ Altered functional status (e.g. severe leg pain, or inability to weight-bear or decreased activity)
☐ Healthcare professional concern ☐ Parental concern
☐ Increasing PEWS ☐ Other:
+/−
Risk Factor(s)
Certain conditions will increase risk of sepsis and should lower threshold for initiation of Sepsis 6. These include:
☐ Immunocompromised (follow national haematology/oncology guidelines for children with cancer)
☐ Age ≤3 months ☐ Chronic disease
☐ Recent surgery ☐ Break in skin (including chickenpox)
☐ Indwelling line/device ☐ Signs of infection in a wound (including chickenpox)
☐ Incomplete vaccination record ☐ Other:
Urgent medical review if ≥1 Amber Flag +/- Risk Factor(s)
Is Sepsis likely at this time?
Signs of Shock Yes ☐ No ☐ Start Sepsis 6 within 1hr Time:
Suspected Sepsis Yes ☐ 3hr window for diagnostic work up - see "take 3" Suspicion Time:
Sepsis NOT likely at this time Working Diagnosis: Review within:
Doctor (Print Name): Doctor Signature: MCRN: Date: Time:
Page 1 of 2, continue overleaf
Version 5 - 12/08/2021

Page 2 of 2
Paediatric Sepsis Form
Ongoing clinical review and interpretation of results
(ALWAYS USE CLINICAL JUDGEMENT)
Addressograph
Paediatric Sepsis 6 – complete within 1 hour
TAKE 3
☐ IV access Time or ☐ IO access Time
Tick samples taken:
☐ Blood cultures ☐ FBC ☐ Glucose ☐ Blood gas ☐ Coag screen incl fibrinogen ☐ Lactate ☐ U&E ☐ LFTs ☐ CRP ☐ Urinalysis ☐ PCRs if available
☐ Urine output assessment/measurement
☐ Early senior input (essential) as per local escalation policy
GIVE 3
☐ Oxygen to achieve saturations ≥94% titrating to effect or as appropriate in chronic lung or cardiac disease
☐ IV/IO fluids
- Titrate 10-20mls/kg Hartmann's Solution over 5-10min, 0.9% NaCL is an acceptable alternative – repeat as per clinical response
- Call critical care/anaesthesia in haemodynamic collapse
- Consider early inotropic support
- Assess for fluid overload, monitor for crepitations or hepatomegaly
☐ IV/IO Antimicrobials according to the site of infection and following local antimicrobial guidelines.
Drug name: Dose: Time given:
Time Sepsis 6 completed:
Name: MCRN:
Reassess the child as clinically indicated and complete form within 1 hour of initiating the Sepsis 6 bundle
Look for signs of new organ dysfunction after the Sepsis 6 bundle has been given or from blood test results – any one is sufficient:
Cardiovascular
☐ Lactate ≥4 after 20mls/kg fluid therapy
Respiratory
☐ Increasing need for Oxygen to maintain saturations ≥ 94% titrating to effect or as appropriate in chronic lung or cardiac disease
☐ Need for nonelective invasive or noninvasive mechanical ventilation
Central Nervous System
☐ Glasgow coma score (GCS) ≤11 or poorly responsive
☐ Acute change in mental status with a decrease in GCS ≥3 points from usual baseline
Renal
☐ Serum creatinine ≥2 times upper limit of normal for age or 2-fold increase in baseline creatinine
Haematological
☐ Platelet count ≤80,000/mm³
Liver
☐ Total bilirubin Bilirubin ≥ 38 µmol/L (micromoles/L) not applicable for newborn
Coagulation
☐ International normalised ratio ≥2
☐ ALT 2 times upper limit of normal for age
Any new organ dysfunction due to infection: ☐ This is SEPSIS
Inform Consultant and Anaesthesia/PICU. Time:
Reassess frequently in the first hour. Consider other investigations and management +/- source control if child does not respond to initial therapy.
No new organ dysfunction due to infection: ☐ This is NOT SEPSIS
If infection is diagnosed, proceed with usual treatment pathway for that infection.
Look for signs of septic shock (following administration of fluid bolus of up to 40ml/kg)
☐ Hypotension
☐ Prolonged central CRT
☐ Core to peripheral temperature gap ≥3°C
☐ Unexplained metabolic acidosis
☐ Oliguria: ≤1ml/kg/hour up to 11 years or ≤0.5ml/kg/hour in the 12+ age group
☐ Need for inotropic support
☐ This is SEPTIC SHOCK
Time:
In addition to senior clinical support at the bedside early involvement of PICU support is encouraged. Where PICU support is not on site a national 24-hour hotline is available for urgent referrals providing advice and arranging transfer – 1800 222 378.
Doctor (Print Name): Doctor Signature: MCRN: Date: Time:
File this document in the child's healthcare record.

Familiarity with the paediatric sepsis form is required, if early detection of sepsis is to be successful. Bedside identification and severity assessment for sepsis can be instigated using the tool, in conjunction with clinical judgement.

If there is a **clinical suspicion of infection and the child appears unwell** – you need to ask – **COULD THIS BE SEPSIS**.

Broad categorisations of high risk criteria (red flags) and intermediate risk criteria (amber flags & risk factors) are displayed algorithmically, to empower the clinician to act promptly. Following screening for sepsis with the paediatric form, patients who trigger a "red flag" require immediate medical review, patients with an amber flag +/- risk factors, have an increased risk of deterioration from sepsis and need to be reviewed promptly.

The outcome of screening is NOT the Sepsis 6 bundle but rather an early thorough medical review to develop a differential diagnosis for the patient's presentation.

SEPSIS 6 BUNDLE: Initial treatment

For children with septic shock, for whom clinical recognition of abnormal perfusion or hypotension is evident, without the need for additional laboratory testing, the Sepsis 6 bundle should be completed within **one hour** of recognition, (i.e. **TIME ZERO**) (Weiss & Pomerantz, Septic shock in children: Rapid recognition and initial resuscitation (first hour), 2020).

For children with suspected sepsis but without clinical evidence of shock, the same management steps are recommended if additional laboratory and clinical testing to assess for infection and organ dysfunction support the diagnosis of sepsis. Initiation of the Sepsis 6 bundle should occur within **three hours** of initial suspicion of sepsis (but start as soon as sepsis is evident) (Weiss & Pomerantz, Septic shock in children: Rapid recognition and initial resuscitation (first hour), 2020).
The SSCGC Initial Resuscitation Algorithm for Children illustrates this clearly (Appendix 13).

Antimicrobials are the primary medical therapy that directly targets the underlying cause of sepsis, and there is strong biologic rationale for rapid delivery of antimicrobials in patients with sepsis (Weiss, et al., 2020)

Figure 5. Sepsis 6 Bundle

Paediatric Sepsis 6 – complete within 1 hour

TAKE 3	GIVE 3
☐ **IV access** Time ____ **or** ☐ **IO access** Time ____ **Tick samples taken:** ☐ Blood cultures ☐ FBC ☐ Glucose ☐ Blood gas ☐ Coag screen incl fibrinogen ☐ Lactate ☐ U&E ☐ LFTs ☐ CRP ☐ Urinalysis ☐ PCRs if available	☐ **Oxygen** to achieve saturations ≥94% titrating to effect or as appropriate in chronic lung or cardiac disease ☐ **IV/IO fluids** - Titrate 10-20mls/kg Hartmann's Solution over 5-10min, 0.9% NaCL is an acceptable alternative – repeat as per clinical response - Call critical care/anaesthesia in haemodynamic collapse - Consider early inotropic support - Assess for fluid overload, monitor for crepitations or hepatomegaly ☐ **IV/IO Antimicrobials** according to the site of infection and following local antimicrobial guidelines. Drug name: Dose: Time given:
☐ **Urine output assessment/measurement**	**Time Sepsis 6 completed:** ____
☐ **Early senior input (essential) as per local escalation policy**	**Name:** ____ **MCRN:** ____

Having administered the Sepsis 6 bundle, the patient should be reviewed with the results of the tests and investigations sent as a consequence of their medical review. This provides the first opportunity to review the working diagnosis and treatment. If a non-infective aetiology for the patients' presentation has been identified, stop antimicrobials.

If the investigations have localised the site of infection, review antimicrobial prescription using local antimicrobial guidelines to ensure it is the most appropriate choice. If not already reviewed when empiric antimicrobial therapy was prescribed, review patients past microbiology results, as a previous history of multi-drug resistant organisms may influence choice of antimicrobial. Complex cases may benefit from Clinical Microbiology/ Infectious Disease speciality review.

In general terms, if discharging a child or infant from an acute care setting, ensure that verbal and preferably written safety net advice has been given. If the diagnosis is uncertain, that uncertainty should be communicated to the patient (or parent/carer) so that they are empowered to re-consult if necessary (Roland, Jones, Neill, Thompson, & Lakhanpaul, 2014).

In the context of possible sepsis, safety net advice should include the specific clinical features that the patient (or parent/carer) should look out for and when they should seek medical help. Parent information leaflets are a useful aide memoire for parents/carers (HSE parent leaflet Appendix 7).

Roles and Responsibilities

All clinicians (medical and nursing) should be familiar with the Sepsis 6 treatment bundle; they should work together to ensure that patients, who on history and examination have a suspicion of infection and are identified by screening as high risk of mortality from sepsis, receive the components of the Sepsis 6 bundle within the recommended timeframe.

Sepsis diagnosis

Sepsis is diagnosed when acute organ dysfunction consequent to infection occurs. This diagnosis can be made before or after the initiation of the Sepsis 6 bundle depending on whether the organ dysfunction is diagnosed clinically or based on the laboratory results.

Infection, sepsis and septic shock are clinical diagnoses. There is no one test that will confirm the presence of infection, sepsis or septic shock to the exclusion of other diagnoses. Rather, the suite of symptoms and signs together with tests and investigations need to be weighed against the differential diagnoses and a clinical decision made. The presence of positive cultures does much to support an infective aetiology but only occurs in 40-60% of sepsis cases, (Martin, Mannino, Eaton, & Moss, 2003) (Brun-Buisson, et al., 1995) ((Phua, et al., 2003) and has a time lag to positivity (HSE, 2020).

SSCGC defines septic shock as severe infection leading to cardiovascular dysfunction (including hypotension, treatment with a vasoactive medication, or impaired perfusion) and “sepsis-associated organ dysfunction” in children as severe infection leading to cardiovascular and/or noncardiovascular organ dysfunction. New or progressive organ dysfunction is associated with higher mortality in children with suspected infections (Lin, et al., 2017).

Identifying an organ dysfunction scoring system for children, similar to the adult model e.g. SOFA score has proven difficult due to the differences that exist in physiology, immune responses and co- morbidities in the paediatric patient population (Hsu, et al., 2019). Similar organ dysfunction scoring systems for children are currently being explored, primarily in critical care settings, to help define robust organ dysfunction categorisation (Schlapbach, Straney, Bellomo, MacLaren, & Pilcher, 2018).

Implementation point 4 (SSCGC Recommendation 3)

Early escalation to senior support is vital so that early sepsis treatment can be initiated. Use of early warning systems in conjunction with the sepsis form will support this to occur in acute healthcare settings for children.

In-patients:

However, the sepsis form must work well with existing or planned early warning and rapid response systems that may also have inherent limitations (Weiss, et al., 2020).

For example, children can often compensate well during a disease process like sepsis. This means that subtle changes can be missed until they suddenly decompensate and become extremely unwell. Using national paediatric observation charts, it is essential to note any individual outlying parameters, observe trends, and be aware that a child showing no signs of improvement may quickly lose the ability to compensate (HSE, 2016a). The Irish Paediatric Early Warning System (PEWS) is recommended as the system to be used to identify high risk and deteriorating admitted children with infection and sepsis (HSE, 2016a) (HSE, 2018) http://health.gov.ie/wp-content/uploads/2017/02/NCG-12-PEWS-full-report-V21.pdf Sepsis awareness and education should be interlinked with the PEWS programme to ensure consistency and cohesion of the sepsis NIP.

Emergency Department:

Many children with sepsis will present with non-specific signs and symptoms early in their disease course, with the full severity of the illness becoming manifest later. This presents a challenge to clinicians working in an ED regarding when to initiate the Paediatric Sepsis Form for the un-differentiated child. In the paediatric emergency department setting, the Irish Children's Triage System (ICTS) facilitates the prompt recognition of acuity for ill or injured children (HSE, 2016b). The presenting complaint determines how quickly a child will be medically reviewed. Children who present in septic shock must have the Sepsis 6 completed within 1 hour of presentation and children who are at risk of sepsis but do not present in septic shock, should be medically reviewed and have the Sepsis 6 completed within 3 hours if appropriate. The Paediatric Sepsis Form is a clinical decision support tool that will help in this decision-making process.

Implementation point 5 (SSCGC Recommendation 3)

Strategies for the utilisation and implementation of the sepsis form should be initiated by each institution to enable continuous improvement and embedding of good practice. Education on using the sepsis form in a clinical context needs to be consistently driven by each paediatric acute care setting through a variety of methodologies. The development of a virtual learning programme will be a key driver in the education of paediatric sepsis nationally.

Implementation point 6 (SSCGC Recommendation 4)

In children with suspected sepsis or septic shock, blood cultures should be obtained before initiation of antimicrobial therapy if it results in no substantial delay to the start of antimicrobials. The collection of other biological specimens to identify pathogens from nonblood sites (e.g. urine, cerebrospinal fluid, tracheal aspirate, broncho-alveolar lavage, drainage from collections) should also happen as soon as possible, and depending on the suspected site of infection, such specimens may have a higher yield of pathogen identification than blood cultures. Where cultures yield specific target pathogens, these should be sent to relevant reference laboratories for confirmation.

Blood cultures should always be taken using an aseptic (no touch) technique. Care should be taken to prevent contamination when obtaining cultures as this may lead to the initiation of unnecessary antimicrobial therapy and investigations, potential adverse events, as well as lengthening hospital stays and costs (HSE, 2020).

3.1.2 Antimicrobial therapy (SSCG Recommendations 5-14)

SSCGC Recommendation 5
In children with septic shock, we recommend starting antimicrobial therapy as soon as possible, within 1 h of recognition
Quality/level of evidence: very low + Strength of recommendation: Strong

SSCGC Recommendation 6
In children with sepsis-associated organ dysfunction but **without shock**, we suggest starting antimicrobial therapy as soon as possible after appropriate evaluation, within 3 h of recognition
Quality/level of evidence: very low + Strength of recommendation: Weak

SSCGC Recommendation 7
We recommend empiric broad-spectrum therapy with one or more antimicrobials to cover all likely pathogens
Quality/level of evidence: ungraded + Strength of recommendation: BPS

SSCGC Recommendation 8
Once the pathogen(s) and sensitivities are available, we recommend narrowing empiric antimicrobial therapy coverage.
Quality/level of evidence: ungraded + Strength of recommendation: BPS

SSCGC Recommendation 9
If no pathogen is identified, we recommend narrowing or stopping empiric antimicrobial therapy according to clinical presentation, site of infection, host risk factors, and adequacy of clinical improvement in discussion with infectious disease and/or microbiological expert advice.
Quality/level of evidence: ungraded + Strength of recommendation: BPS

SSCGC Recommendation 10
In children without immune compromise and without high risk for multidrug-resistant pathogens, we suggest against the routine use of empiric multiple antimicrobials directed against the same pathogen for the purpose of synergy.
Quality/level of evidence: very low + Strength of recommendation: Weak

***SSCGC Remarks**:* In certain situations, such as confirmed or strongly suspected group B streptococcal sepsis, use of empiric multiple antimicrobials directed against the same pathogen for the purpose of synergy may be indicated

SSCGC Recommendation 11
In children with immune compromise and/or at high risk for multidrug-resistant pathogens, we suggest using empiric multi-drug therapy when septic shock or other sepsis-associated organ dysfunction is present/suspected.
Quality/level of evidence: very low + Strength of recommendation: Weak

SSCGC Recommendation 12
We recommend using antimicrobial dosing strategies that have been optimized based on published pharmacokinetic/pharmacodynamic principles and with consideration of specific drug properties.
Quality/level of evidence: ungraded + Strength of recommendation: BPS

SSCGC Recommendation 13
In children with septic shock or sepsis-associated organ dysfunction who are receiving antimicrobials, we recommend daily assessment (e.g., clinical, laboratory assessment) for de-escalation of antimicrobial therapy.
Quality/level of evidence: ungraded + Strength of recommendation: BPS

SSCGC Remarks: This assessment should include a review of the ongoing indication for empiric antimicrobial therapy after the first 48 h that is guided by microbiologic results and in response to clinical improvement and/or evidence of infection resolution. This recommendation applies to patients being treated with empiric, targeted, and combination therapy.

SSCGC Recommendation 14
We recommend determining the duration of antimicrobial therapy according to the site of infection, microbial aetiology, response to treatment, and ability to achieve source control.
Quality/level of evidence: ungraded + Strength of recommendation: BPS

Implementation point 7 (SSCGC Recommendations 5-6)

Children with sepsis or septic shock generally warrant empiric broad-spectrum therapy until the causative organism and its antimicrobial susceptibilities are defined. At that point, the spectrum of coverage should be narrowed by eliminating unneeded antimicrobials and replacing broad-spectrum agents with more specific agents. However, if relevant cultures are negative, empiric narrowing of coverage based on a good clinical response is appropriate. Collaboration with antimicrobial stewardship programmes is encouraged to ensure appropriate choices and rapid availability of effective antimicrobials for treating septic patients (HSE Health Protection Surveillance Centre, 2009) (HSE, 2020).

Managing sepsis in the era of increasing rates of multi-drug resistant organisms (MDRO) should be tightly linked with antimicrobial stewardship. Coupled with rising rates of MDRO, few new antimicrobials are being developed, therefore, prescribing antimicrobials appropriately is essential for patient safety (to minimise adverse effects and maximise clinical cure) and to minimise the risk of causing antimicrobial resistance in the individual, that may also have an impact for other patients, so that effective antimicrobials are available to manage infection and sepsis. It is recommended that the ‘Start Smart and then Focus’ approach is employed for antimicrobial therapy (Royal College of Physicians of Ireland, 2020) (Appendix 11).

Start Smart

Intravenous antimicrobials are administered as part of the Sepsis 6 bundle within one hour of diagnosis of infection in children with septic shock OR within a three-hour window for those patients with suspected infection without clinical signs of shock or organ dysfunction. All acute hospitals have local antimicrobial age related guidelines for the empiric use of antimicrobials in children that are appropriate for the local MDRO epidemiology. It is recommended that these guidelines be used to choose empiric therapy for patients with infection, taking the following into consideration:

1. Source of the infection
    - Community acquired
    - Health-care associated
    - Hospital acquired.
2. Site of the infection

    Based on the history and the examination of the patient e.g. respiratory, abdominal, genito-urinary, device or catheter-related, cellulitis, central nervous system, bone or joint or unknown.
3. Patient considerations

    Patient factors that need to be taken into consideration and may influence the choice of empiric antimicrobial therapy include:
        - Age: neonates and young infants < 3months, infants >3 months-1 yr and children
        - Vaccination Status
        - Malignancy and immunocompromising medical conditions.
        - Previous infection or colonisation with MDRO such as methicillin resistant Staphylococcus aureus (MRSA), extended-spectrum B-lactamase (ESBL) producing /gram negative organism etc.
        - Recent antimicrobial therapy
        - Current outbreaks
        - Recent infections in close contacts
        - Recent travel or hospitalization and/or residence in another country
        - Allergy status
        - Renal/hepatic impairment
        - Drug interactions
        - Conditions that make some antimicrobials a greater risk

Local/national antimicrobial prescribing guidelines take these principles into account when recommending doses for differing infection severities and infections at particular body sites.
Contact a senior colleague or infection specialist (microbiologist, infectious diseases physician or antimicrobial pharmacist) for advice regarding dose optimisation.

Then Focus

It is important to review the patient daily and to assess the antimicrobial therapy in terms of the patients' clinical response and laboratory results during the acute phase of the illness and to decide on and document the duration of treatment appropriate to the illness. Important determinants of the required duration of antimicrobial therapy include site of infection, ability to drain or remove fixed infectious foci, choice of antimicrobial therapy, time to clearance of positive cultures, the nature of the causative pathogen, and the integrity of the host immune response. (Royal College of Physicians of Ireland, 2020).

For children with septic shock, broad-spectrum IV antimicrobial therapy should commence within one hour of presentation, preferably after obtaining appropriate cultures. Effective delivery of antibiotics usually requires two ports or sites for IV access: one devoted to fluid resuscitation and one for antimicrobial delivery. If obtaining blood cultures is difficult, it should not impede antibiotic initiation within the first hour.

Antifungal and antiviral agents should be considered as part of the initial regimen for susceptible patients e.g. oncology/haematology patients. Contact a senior colleague or infection specialist (microbiologist, infectious diseases physician) for further advice if required. Local/national guidelines may include alternative antibiotics for susceptible patients.

In cases of suspected Toxic Shock Syndrome, seek senior clinician support, consult with microbiology and consider Clindamycin as an adjunctive agent.

3.1.3 Source Control (SSCGC Recommendations 15-16)

SSCGC Recommendation 15
We recommend that emergent source control intervention be implemented as soon possible after a diagnosis of an infection amenable to a source control procedure is made
Quality/level of evidence: ungraded + Strength of recommendation: BPS

SSCGC Remarks: Appropriate diagnostic testing to identify the site of infection and microbial aetiology should be performed, and advice from specialist teams (e.g., infectious diseases, surgery) should be sought, as appropriate, in order to prioritize interventions needed to achieve source control

SSCGC Recommendation 16
We recommend removal of intravascular access devices that are confirmed to be the source of sepsis or septic shock after other vascular access has been established and depending on the pathogen and the risks/ benefits of a surgical procedure
Quality/level of evidence: low + Strength of recommendation: Strong

Implementation point 8 (SSCGC Recommendations 15-16)

In order to achieve compliance with these recommendations a number of steps need to occur:

1. Microbiology or infectious diseases consult and advice
2. Identification of the need for source control
3. Early consultation with appropriate surgical team
4. Access to diagnostics
5. Feasibility of achieving source control
6. Access to interventional radiology/ surgery

Patients whose infection is not settling on appropriate antimicrobials need to be re-assessed for source control including reviewing implanted devices and catheters as potential sources. If such devices are potential sources, they should be removed or treated where possible and sent for culture and antimicrobial susceptibility testing.

3.1.4 Fluid Therapy (SSCGC Recommendations 17-23)

SSCGC Recommendation 17
In healthcare systems with availability of intensive care, we suggest administering up to 40–60 mL/kg in bolus fluid (10–20 mL/kg per bolus) over the first hour, titrated to clinical markers of cardiac output and discontinued if signs of fluid overload develop, for the initial resuscitation of children with septic shock or other sepsis-associated organ dysfunction.
Quality/level of evidence: low + Strength of recommendation: Weak

SSCGC Recommendation 18
In healthcare systems with no availability of intensive care and in the absence of hypotension, we recommend against bolus fluid administration while starting maintenance fluids
Quality/level of evidence: high + Strength of recommendation: Strong

SSCGC Recommendation 19
In healthcare systems with no availability of intensive care, if hypotension is present, we suggest administering up to 40 mL/kg in bolus fluid (10–20 mL/kg per bolus) over the first hour with titration to clinical markers of cardiac output and discontinued if signs of fluid overload develop
Quality/level of evidence: low + Strength of recommendation: Weak

SSCGC Remarks: Clinical markers of cardiac output may include heart rate, blood pressure, capillary refill time, level of consciousness, and urine output. In all settings, the need for fluid administration should be guided by frequent reassessment of clinical markers of cardiac output, serial blood lactate measurement and advanced monitoring, when available. Signs of fluid overload that should limit further fluid bolus therapy may include clinical signs of pulmonary edema or new or worsening hepatomegaly

SSCGC Recommendation 20
We suggest using crystalloids, rather than albumin, for the initial resuscitation of children with septic shock or other sepsis-associated organ dysfunction.
Quality/level of evidence: moderate + Strength of recommendation: Weak

SSCGC Remarks: Although there is no difference in outcomes, this recommendation takes into consideration cost and other barriers of administering albumin compared with crystalloids.

SSCGC Recommendation 21
We suggest using balanced/buffered crystalloids, rather than 0.9% saline, for the initial resuscitation of children with septic shock or other sepsis-associated organ dysfunction.
Quality/level of evidence: very low + Strength of recommendation: Weak

SSCGC Recommendation 22
We recommend against using starches in the acute resuscitation of children with septic shock or other sepsis-associated organ dysfunction.
Quality/level of evidence: moderate + Strength of recommendation: Strong

SSCGC Recommendation 23
We suggest against using gelatin in the resuscitation of children with septic shock or other sepsis-associated organ dysfunction.
Quality/level of evidence: low + Strength of recommendation: Weak

Implementation point 9 (Recommendations 17-23)

For children with septic shock treated in settings with access to acute intensive care capability, (either locally or via inter-hospital transfer), patients without signs of fluid overload should receive 10-20mL/kg of balanced crystalloid solution such as lactated Ringer's solution (Hartmann's solution); 0.9% Normal Saline is an acceptable alternative if lactated Ringer's solution is not available. (Advanced Paediatric Life Support Group, 2016). The volume of either 10-20mL/kg of fluid resuscitation acknowledges clinician discretion with regard to the individual patient, considering aetiology, pathophysiology, age, i.e. infants < 3mths, comorbidities, pre-existing cardiac disease. Fluids should be rapidly infused over a 5-10 minute period, either via intravenous (IV) or intraosseous (IO) access. Fluid volume should be calculated based upon ideal body weight.

Caution: Some medications interact with Ringers Lactate/Hartmann's Solution Check local guidelines

If the patient develops signs of fluid overload (e.g., rales, worsening respiratory distress, new or worsening oxygen requirement, gallop rhythm, hepatomegaly, or cardiomegaly or pulmonary oedema on chest X-ray), the fluid bolus should be omitted or reduced. After the initial infusion, the child should be quickly reassessed for signs of inadequate end-organ perfusion to determine if additional fluid is needed and to identify any signs of fluid overload. Further fluid boluses should be titrated according to cardiovascular response. If, following 40mL/kg fluid bolus within the first hour, the child continues to show signs of cardiovascular dysfunction and/or new organ dysfunction and a third bolus is warranted, senior clinical input is required.

Note: Children with fluid-refractory, hypotensive septic shock, warrant initiation of vasoactive medication**.** If there is no PICU support on site, seek advice on national 24-hour hotline **1800 222 378**.

IPATS (Irish Paediatric Acute Transport Service) supports the transfer of critically ill infants and children (aged 4 weeks to 16 years) from a referring hospital to the Paediatric Intensive Care Unit (PICU) in CHI at Crumlin or CHI at Temple Street (Appendix 12).

Services include:

- 24 hour/day PICU referral and advice
- 5 day IPATS Critical Care Transport Team – IPATS transfers critically ill infants and children (aged 4 weeks to 16 years) to the Paediatric Intensive Care unit (PICU) in CHI at Crumlin or CHI at Temple Street
- IPATS website have documents and guidelines to assist a local team transfer outside of IPATS operational hours, to facilitate the safe transfer of children. www.nasccrs.ie/IPATS

NNTP (National Neonatal Transport Programme) is a 24/7 retrieval service for the stabilisation and transportation of premature and sick neonates up to the age of 6 weeks corrected gestational age.

While it is acknowledged that critical care facilities for children are not available in all hospitals that anaesthetise children, facilities for initiating intensive care prior to transfer/retrieval to a designated regional PICU/HDU facility should be available. This may involve the short-term use of adult/general ICU facilities (HSE Model of Care for Paediatric Critical Care, 2019).
Where critically ill children present to the adult critical care service, the care principles are focused on resuscitation and transport/retrieval. (HSE, Critical Care Programme, 2014).
All paediatric facilities where undifferentiated paediatric patients present must retain the equipment and competencies to resuscitate, stabilise and transfer out critically ill children. (HSE, National Clinical Programme for Anaesthesia, 2019).

In centres that do not have an on-site PICU, anaesthesia involvement will also be required in the management of critically ill children who frequently require intubation, resuscitation and initiation of intensive care, before the arrival of the retrieval team or direct transfer to a PICU. (HSE,National Clinical Programme for Anaesthesia, 2015).

In all circumstances, arrangements should be made as soon as possible with the paediatric critical care network for the transfer/retrieval of the critically ill child.

3.1.5 Haemodynamic monitoring (SSCGC Recommendations 24-27)

SSCGC Recommendation 24
We were unable to issue a recommendation about whether to target mean arterial blood pressure (MAP) at the 5th or 50th percentile for age in children with septic shock and other sepsis-associated organ dysfunction. However, in our practice, we target MAP to between the 5th and 50th percentile or greater than 50th percentile for age.

SSCGC Recommendation 25
We suggest not using bedside clinical signs in isolation to categorize septic shock in children as “warm” or “cold”.
Quality/level of evidence: very low + Strength of recommendation: Weak

SSCGC Recommendation 26
We suggest using advanced hemodynamic variables, when available, in addition to bedside clinical variables to guide the resuscitation of children with septic shock or other sepsis-associated organ dysfunction.
Quality/level of evidence: low + Strength of recommendation: Weak

SSCGC Remarks: Advanced hemodynamic monitoring may include cardiac output/cardiac index, systemic vascular resistance, or central venous oxygen saturation (Scvo2).

SSCGC Recommendation 27
We suggest using trends in blood lactate levels, in addition to clinical assessment, to guide resuscitation of children with septic shock and other sepsis-associated organ dysfunction.
Quality/level of evidence: very low + Strength of recommendation: Weak

SSCGC Remarks*:* In children with an elevated blood lactate, repeat testing that reveals a persistent elevation in blood lactate may indicate incomplete hemodynamic resuscitation and should prompt efforts, as needed, to further promote hemodynamic stability.

Implementation point 10 (SSCGC Recommendations 24-27)

Hypotension can be defined as

(1) systolic blood pressure of

- Less than 50 mm Hg in children younger than 12 months old,
- less than 60 mm Hg in children 1–5 years old,
- less than 70 mm Hg in children older than 5 years old [183]

OR

(2) by the WHO criteria of cold extremities “with” prolonged capillary refill greater than 3 secs, accompanied by a weak, fast pulse [14]. (Appendix 14)

The systolic blood pressure reading should be checked against an appropriate BP centile chart to ensure that it is within normal parameters (Advanced Paediatric Life Support Group, 2016). The arm should be used for measuring blood pressure, but if this is not possible in infants, the lower leg can be used ensuring alignment with the artery. If regular BP measurements are being undertaken, the same limb should be used to identify any changes (Royal College of Nursing, 2017).
During ongoing management of septic shock, monitoring of tissue perfusion using physiologic indicators and target goals should continue.

The clinician should determine the need for invasive monitoring via intra-arterial and central venous cannulas. **Non-invasive blood pressure measurement** is acceptable in patients who have markedly improved or had total reversal of septic shock. Efforts to obtain intra-arterial access should **not** interfere with the resuscitation of septic shock. However, automated blood pressures overestimate systolic blood pressure relative to intra-arterial or Doppler ultrasound measurements in hypotensive children and underestimate systolic blood pressure among hypertensive patients. Therefore, insertion of an intra-arterial catheter is suggested if restoration of arterial perfusion pressures is expected to be a protracted process (Weiss & Pomerantz, Septic shock in children: Rapid recognition and initial resuscitation (first hour), 2020).

Central venous access is indicated for patients with fluid-resistant septic shock because these patients frequently are dependent upon uninterrupted vasoactive medication administration to prevent further decompensation. If they also have poor perfusion, then they are at a greatly increased risk of extravasation and significant local tissue damage from peripherally administered vasoactive medications. Furthermore, central venous access permits monitoring of central venous pressures and $ScvO_2$ in these unstable patients, which helps guide ongoing therapy (Weiss & Pomerantz, Septic shock in children: Rapid recognition and initial resuscitation (first hour), 2020).

Serial cardiac ultrasound can also help to identify patients with persistent hypovolaemia, myocardial dysfunction, and/or pericardial effusion that may be contributing to persistent shock. This is especially important for children who do not improve with initial fluid resuscitation or develop signs of fluid overload, for whom direct assessment of cardiac function can more accurately gauge physiologic derangements than physical examination alone.

Blood lactate can be obtained by bedside testing. Limited evidence suggests that serum lactate that decreases with treatment is associated with better outcomes for children with sepsis. The therapeutic target is <2 mmol/L. Elevation of blood lactate >2.0 mmol/L suggests hypoperfusion. Small observational studies in children have demonstrated that lactate can correlate with severity of shock and prognosis in sepsis [11-13]. In one observational study of septic shock in children, normalization of lactate (blood lactate <2 mmol/L) within four hours was associated with reduced organ dysfunction, but lactate clearance (reduction ≥10 percent decrease in lactate level) was not (Weiss & Pomerantz, Septic shock in children: Rapid recognition and initial resuscitation (first hour), 2020). Each site caring for children should have access to point of care testing for Lactate as per local guidelines.
See Recommendation 2

Roles and Responsibilities
It is the responsibility of clinicians to be familiar with the procedures and to know the advantages and limitations of any advanced haemodynamic monitoring equipment deployed.

3.1.6 Vasoactive medications (SSCGC Recommendations 28-33)

SSCGC Recommendation 28
We suggest using epinephrine, rather than dopamine, in children with septic shock.
Quality/level of evidence: low + Strength of recommendation: Weak

SSCGC Recommendation 29
We suggest using norepinephrine, rather than dopamine, in children with septic shock.
Quality/level of evidence: very low + Strength of recommendation: Weak

SSCGC Recommendation 30
We were **unable** to issue a recommendation for a specific first-line vasoactive infusion for children with septic shock. However, in our practice, we select either epinephrine or norepinephrine as the first-line vasoactive infusion guided by clinician preference, individual patient physiology, and local system factors.

SSCGC Recommendation 31
We were **unable** to issue a recommendation about initiating vasoactive agents through peripheral access in children with septic shock. However, in our practice, we often or sometimes administer a dilute concentration of the initial vasoactive medication through a peripheral vein if central venous access is not readily accessible.

SSCGC Remarks (28-31): It is reasonable to begin vasoactive infusions after 40–60 mL/kg of fluid resuscitation if the patient continues to have evidence of abnormal perfusion, or sooner if fluid overload develops or other concerns for fluid administration are present. Either epinephrine or norepinephrine may be administered through a peripheral vein (or intraosseous, if in place) if central venous access is not readily accessible. Dopamine may be substituted as the first-line vasoactive infusion, administered either peripherally or centrally, if epinephrine or norepinephrine is not readily available.

SSCGC Recommendation 32
We suggest either adding vasopressin or further titrating catecholamines in children with septic shock who require high-dose catecholamines.
Quality/level of evidence: very low + Strength of recommendation: Weak

SSCGC Remarks: No consensus was achieved on the optimal threshold for initiating vasopressin. Therefore, this decision should be made according to individual clinician preference.

SSCGC Recommendation 33
We were **unable** to issue a recommendation about adding an inodilator in children with septic shock and cardiac dysfunction despite other vasoactive agents. However, in our practice, we sometimes use inodilators in children with septic shock and evidence of persistent hypoperfusion and cardiac dysfunction despite other vasoactive agents.

Implementation point 11 (Recommendations 28-33)

When treating a child with septic shock, it is wise to pre-empt the need for vasoactive infusions if the child has received 40mL/kg bolus and continues to show signs of cardiovascular dysfunction. In children, it reasonable to begin vasoactive infusions after 40–60 mL/kg of fluid resuscitation if the patient continues to have evidence of abnormal perfusion or sooner if fluid overload develops. Vasopressors and inotropes are most usually prescribed by critical care and unless familiar with them, it is prudent to obtain critical care support when starting them.

Resources to assist with calculations of inotropes and other medications are available on the IPATS website http://www.nasccrs.ie/IPATS/Calculators. Use of drug calculators, especially in a time critical event, is a safety tool that assists in the reduction of medication errors.

Starting vasopressors requires multidisciplinary support for central venous access, constitution and delivery of the vasopressors and aseptic technique. If central venous access is not readily available, consider administering peripheral vasoactive medications, with senior clinical support, until central access can be obtained. All vasoactive agents may be initiated through peripheral venous (or intraosseous, if in place) access if central venous access is not readily available to avoid delays in therapy. In these situations, close monitoring of PIVC site is recommended for early identification of chemical phlebitis.

Inodilators have shown to improve cardiac dysfunction despite an adequate correction of intravascular volume and mean arterial pressure by fluid administration and vasopressor support (Ospina-Tascon & Calderon-Tapia, 2020). The decision to introduce an inodilator e.g. Milrinone is based on the child's cardiovascular response to sepsis management protocols. It is recommended that critical care personnel are responsible for its administration, using the paediatric critical care standard concentration infusion protocols.

Roles and responsibilities

It is the responsibility of hospital management to ensure the appropriate equipment and staff is available to provide this service.

3.1.7 Ventilation (SSCGC Recommendations 34-43)

SSCGC Recommendation 34
We were **unable** to issue a recommendation about whether to intubate children with fluid-refractory, catecholamine-resistant septic shock. However, in our practice, we commonly intubate children with fluid refractory, catecholamine-resistant septic shock without respiratory failure.

SSCGC Recommendation 35
We suggest not to use etomidate when intubating children with septic shock or other sepsis-associated organ dysfunction.
Quality/level of evidence: very low + Strength of recommendation: Weak

SSCGC Recommendation 36
We suggest a trial of non-invasive mechanical ventilation (over invasive mechanical ventilation) in children with sepsis-induced paediatric ARDS (PARDS) without a clear indication for intubation and who are responding to initial resuscitation.

SSCGC Remarks: When non-invasive mechanical ventilation is initiated, clinicians should carefully and frequently re-evaluate the patient's condition
Quality/level of evidence: very low + Strength of recommendation: Weak

SSCGC Recommendation 37
We suggest using high positive end-expiratory pressure (PEEP) in children with sepsis-induced PARDS
Quality/level of evidence: very low + Strength of recommendation: Weak

SSCGC Remarks: The exact level of high PEEP has not been tested or determined in PARDS patients. Some RCTs and observational studies in PARDS have used and advocated for use of the ARDS-network PEEP to Fio2 grid though adverse hemodynamic effects of high PEEP may be more prominent in children with septic shock.

SSCGC Recommendation 38
We cannot suggest for or against the use of recruitment manoeuvres in children with sepsis-induced PARDS and refractory hypoxemia.

SSCGC Remarks: If a recruitment manoeuvre is considered, the use of a stepwise, incremental and decremental PEEP titration manoeuvre is preferred over sustained inflation techniques that have not been optimized through direct testing in PARDS patients. All PARDS patients must be carefully monitored for tolerance of the manoeuvre.

SSCGC Recommendation 39
We suggest a trial of prone positioning in children with sepsis and severe PARDS
Quality/level of evidence: low + Strength of recommendation: Weak

SSCGC Remarks: Research trials in adults with ARDS and children with PARDS have emphasized prone positioning for at least 12 h per day, as tolerated.

SSCGC Recommendation 40
We recommend against the routine use of inhaled nitric oxide (iNO) in all children with sepsis-induced PARDS
Quality/level of evidence: low + Strength of recommendation: Strong

SSCGC Recommendation 41
We suggest using iNO as a rescue therapy in children with sepsis-induced PARDS and refractory hypoxemia after other oxygenation strategies have been optimized
Quality/level of evidence: moderate + Strength of recommendation: Weak

SSCGC Recommendation 42
We were **unable** to issue a recommendation to use high-frequency oscillatory ventilation (HFOV) versus conventional ventilation in children with sepsis induced PARDS. However, in our practice, there is no preference to use or not use HFOV in patients with severe PARDS and refractory hypoxia.

SSCGC Recommendation 43
We suggest using neuromuscular blockade in children with sepsis and severe PARDS (weak recommendation, very low quality of evidence).
Quality/level of evidence: very low + Strength of recommendation: Weak

SSCGC Remarks: The exact duration of neuromuscular blockade to use in severe PARDS patients has not been determined to date. Most of the adult RCT data and paediatric observational data support treatment for 24–48 h after ARDS onset.

Implementation point 12 (Recommendations 34-43)

In an Irish context, early intubation and mechanical ventilation is considered if the child is critically ill and is unresponsive to initial resuscitation, in order to facilitate procedures and to decrease work of breathing/oxygen consumption. Early communication with senior clinical support/critical care personnel within each institution is recommended and early involvement of PICU services is encouraged. Advice and referral to a PICU is available 24/7.

In patients with continued shock, worsening hypoxemia, or progression to PARDS, advanced airway support (i.e. non-invasive or invasive ventilation) is frequently needed. A trial of non-invasive mechanical ventilation (over invasive mechanical ventilation) in children with hypoxemia and normal ability to protect their airway who do not have overt respiratory failure **and** who are responding to initial resuscitation is reasonable. However, for children with high metabolic demand from refractory shock, typically indicated by progressive lactic acidosis and end-organ dysfunction, early intubation and mechanical ventilation prior to overt hypoxemic or hypercarbic

respiratory failure can help to mitigate deficits in systemic oxygen delivery (Weiss & Pomerantz, Septic shock in children: Rapid recognition and initial resuscitation (first hour), 2020).

COVID-19

The SSCGC suggests that systematic screening should be implemented for timely recognition of septic shock and other sepsis-associated organ dysfunction. The underlying rationale for this recommendation is grounded in the often subtle and nonspecific manner in which sepsis and septic shock may present in children. With the advent of Coronavirus disease 2019, there is a high risk of diagnostic fixation or anchoring bias that a child with cardiopulmonary dysfunction must have acute COVID-19 illness. (Weiss, et al., 2020).

Organ dysfunctions triggered by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) should be considered a phenotype of paediatric sepsis or septic shock. More recently, there has been a surge in children presenting with hyper inflammatory shock resembling atypical Kawasaki disease, Kawasaki-shock, and/or toxic shock syndrome. In cases where SARS-CoV-2 is the most likely pathogen or has already been confirmed, patients with COVID-19 are at risk for bacteraemia or other secondary bacterial or viral co-infections (e.g. pneumonia) (Weiss, et al., 2020).

Corticosteroids (SSCGC Recommendations 44-45)

SSCGC Recommendation 44
We suggest against using IV hydrocortisone to treat children with septic shock if fluid resuscitation and vasopressor therapy are able to restore hemodynamic stability
Quality/level of evidence: low + Strength of recommendation: Weak

SSCGC Recommendation 45
We suggest that either IV hydrocortisone or no hydrocortisone may be used if adequate fluid resuscitation and vasopressor therapy are not able to restore hemodynamic stability
Quality/level of evidence: low + Strength of recommendation: Weak

Implementation point 13 (Recommendations 45-46)

Hydrocortisone may be required if adequate fluid resuscitation and vasopressor therapy are not able to restore hemodynamic stability, this is most often provided in a critical care setting not in the immediate resuscitation phase.

If corticosteroids are given, refer to local hospital children's formulary.

3.1.9 Endocrine and Metabolic (SSCGC Recommendations 46-50)

SSCGC Recommendation 46
We recommend against insulin therapy to maintain a blood glucose target at or below 140 mg/dL (7.8 mmol/L)
Quality/level of evidence: moderate + Strength of recommendation: Strong

SSCGC Recommendation 47
We were **unable** to issue a recommendation regarding what blood glucose range to target for children with septic shock or other sepsis-associated organ dysfunction. However, in our practice, there was consensus to target blood glucose levels below 180 mg/dL (10 mmol/L) but there was not consensus about the lower limit of the target range.

SSCGC Recommendation 48
We were **unable** to issue a recommendation as to whether to target normal blood calcium levels in children with septic shock or sepsis-associated organ dysfunction. However, in our practice, we often target normal calcium levels for children with septic shock requiring vasoactive infusion support.

SSCGC Recommendation 49
We suggest against the routine use of levothyroxine in children with septic shock and other sepsis-associated organ dysfunction in a sick euthyroid state.
Quality/level of evidence: low + Strength of recommendation: Weak

SSCGC Recommendation 50
We suggest either antipyretic therapy or a permissive approach to fever in children with septic shock or other sepsis-associated organ dysfunction.
Quality/level of evidence: moderate + Strength of recommendation: Weak

Implementation point 14 (Recommendations 46-47)

Hypoglycaemia:

Children with septic shock are at risk for hypoglycaemia; rapid blood glucose should be measured as IV access is obtained. If present, hypoglycaemia should be corrected by rapid IV infusion 2mLs/kg of Dextrose 10% (ALSG, 2016). A continuous maintenance infusion of dextrose 5% to 10% in addition to resuscitation fluids is a reasonable option to prevent the occurrence of hypoglycaemia (Weiss & Pomerantz, Septic shock in children: Rapid recognition and initial resuscitation (first hour), 2020).

After initial hypoglycaemia is reversed, the clinician should continue to monitor blood glucose levels. Maintaining a blood glucose <180 mg/dL (8.33 mmol/L) is desirable. Hypoglycaemia may also be an indicator of adrenal insufficiency in predisposed

children and those with refractory septic shock (Weiss & Pomerantz, Septic shock in children: Rapid recognition and initial resuscitation (first hour), 2020).

Hyperglycaemia:

Sepsis can induce a hyperglycaemic stress response. Defining hyperglycaemic parameters that may require insulin is based on adult guidelines, however the SSCGC guidelines consider an upper blood glucose target of 180 mg/dL (10 mmol/L) to reasonably require insulin therapy with a caveat of continuous monitoring for hypoglycaemia.

In an Irish context, hyperglycaemic control should only be considered in the ICU setting.

Implementation point 15 (Recommendation 50)

Antipyretics

The decision to administer antipyretics is based on senior clinician advice, degree of pyrexia and the overall condition of child. Refer to local age-related guidelines for antipyretic therapy.

In febrile children, the basal heart rate may be calculated by deducting approximately 10 beats per minute for every 1°C (1.8°F) elevation in temperature. However, tachycardia should resolve when the temperature returns to normal; persistent tachycardia is a sensitive indicator of circulatory dysfunction and should not be overlooked (Weiss & Pomerantz, Septic shock in children: Rapid recognition and initial resuscitation (first hour), 2020).

Fever is a complex physiologic response associated with sepsis, and it remains unclear whether fever is a beneficial or a harmful response to infection. Potential benefits include inhibiting the growth of some pathogens and increased neutrophil production and lymphocyte proliferation. Conversely, fever is associated with an increased metabolic rate (which may or may not have detrimental effects in patients with sepsis) and may impair some components of immune function.

3.1.10 Nutrition (SSCGC Recommendations 51-64)

SSCGC Recommendation 51
We were **unable** to issue a recommendation regarding early hypocaloric/trophic enteral feeding followed by slow increase to full enteral feeding versus early full enteral feeding in children with septic shock or sepsis-associated organ dysfunction without contraindications to enteral feeding. However, in our practice, there is a preference to commence early enteral nutrition within 48 h of admission in children with septic shock or sepsis-associated organ dysfunction who have no contraindications to enteral nutrition and to increase enteral nutrition in a stepwise fashion until nutritional goals are met.

SSCGC Recommendation 52
We suggest not withholding enteral feeding solely on the basis of vasoactive-inotropic medication administration.

SSCGC Remarks: Enteral feeding is not contraindicated in children with septic shock after adequate hemodynamic resuscitation who no longer require escalating doses of vasoactive agents or in whom weaning of vasoactive agents has started.
Quality/level of evidence: low + Strength of recommendation: Weak

SSCGC Recommendation 53
We suggest enteral nutrition as the preferred method of feeding and that parenteral nutrition may be withheld in the first 7 days of PICU admission in children with septic shock or other sepsis-associated organ dysfunction.
Quality/level of evidence: moderate + Strength of recommendation: Weak

SSCGC Recommendation 54
We suggest against supplementation with specialized lipid emulsions in children with septic shock or other sepsis-associated organ dysfunction
Quality/level of evidence: very low + Strength of recommendation: Weak

SSCGC Recommendation 55
We suggest against the routine measurements of gastric residual volumes (GRVs) in children with septic shock or other sepsis-associated organ dysfunction.
Quality/level of evidence: low + Strength of recommendation: Weak

SSCGC Recommendation 56
We suggest administering enteral feeds through a gastric tube, rather than a postpyloric feeding tube, to children with septic shock or other sepsis-associated organ dysfunction who have no contraindications to enteral feeding.
Quality/level of evidence: low + Strength of recommendation: Weak

SSCGC Recommendation 57
We suggest against the routine use of prokinetic agents for the treatment of feeding intolerance in children with septic shock or other sepsis-associated organ dysfunction.
Quality/level of evidence: low + Strength of recommendation: Weak

SSCGC Recommendation 58
We suggest against the use of selenium in children with septic shock or other sepsis-associated organ dysfunction.
Quality/level of evidence: low + Strength of recommendation: Weak

SSCGC Recommendation 59
We suggest against the use of glutamine supplementation in children with septic shock or other sepsis-associated organ dysfunction.
Quality/level of evidence: low + Strength of recommendation: Weak

SSCGC Recommendation 60
We suggest against the use of arginine in the treatment of children with septic shock or other sepsis-associated organ dysfunction.
Quality/level of evidence: very low + Strength of recommendation: Weak

SSCGC Recommendation 61
We suggest against using zinc supplementation in children with septic shock and other sepsis-associated organ dysfunction.
Quality/level of evidence: very low + Strength of recommendation: Weak

SSCGC Recommendation 62
We suggest against the use of ascorbic acid (vitamin C) in the treatment of children with septic shock or other sepsis-associated organ dysfunction.
Quality/level of evidence: very low + Strength of recommendation: Weak

SSCGC Recommendation 63
We suggest against the use of thiamine to treat children with sepsis-associated organ dysfunction.
Quality/level of evidence: low + Strength of recommendation: Weak

SSCGC Recommendation 64
We suggest against the acute repletion of vitamin D deficiency (VDD) for treatment of septic shock or other sepsis-associated organ dysfunction.
Quality/level of evidence: very low + Strength of recommendation: Weak

Implementation point 16 (Recommendation 51-52)

Enteral Nutrition

It is generally recommended that enteral nutrition (EN) be initiated in all critically ill children, unless contraindicated, within 24-48 hours. The use of institutional EN guidelines and stepwise algorithms to advance feeding and optimize progress is also recommended (ASPEN Guidelines, 2020) (Mehta, et al., 2017).

Implementation point 17 (Recommendation 53)

Individual assessment is required to determine whether parenteral nutrition is a) indicated b) viable and c) beneficial. PICU should have access to a dedicated dietitian or nutrition support team (ASPEN Guidelines, 2020) (Mehta, et al., 2017). Care should

be taken to ensure that nutrition support is not entirely withheld from extremely vulnerable children (Koletzko et al, 2017). Any decision to withhold nutrition support should be revisited daily.

3.1.11 Blood Products (SSCGC Recommendations 65-68)

SSCGC Recommendation 65
We suggest against transfusion of RBCs if the blood haemoglobin concentration is greater than or equal to 7 g/dL in hemodynamically stabilized children with septic shock or other sepsis-associated organ dysfunction.
Quality/level of evidence: low + Strength of recommendation: Weak

SSCGC Remarks: According to the 2018 Transfusion and Anemia Expertise Initiative (TAXI) guidelines, for the purposes of RBC transfusion, "hemodynamically stabilized" is defined as a MAP higher than 2 sds below normal for age and no increase in vasoactive medications for at least 2 h.

SSCGC Recommendation 66
We **cannot** make a recommendation regarding haemoglobin transfusion thresholds for critically ill children with unstable septic shock.

SSCGC Recommendation 67
We suggest against prophylactic platelet transfusion based solely on platelet levels in nonbleeding children with septic shock or other sepsis-associated organ dysfunction and thrombocytopenia
Quality/level of evidence: very low + Strength of recommendation: Weak

SSCGC Recommendation 68
We suggest against prophylactic plasma transfusion in nonbleeding children with septic shock or other sepsis-associated organ dysfunction and coagulation
Quality/level of evidence: very low + Strength of recommendation: Weak

SSCGC Remarks: Prophylactic plasma transfusion refers to situations in which there is an abnormality in laboratory coagulation testing but no active bleeding.

Implementation point 18 (Recommendations 65-66)

Haemoglobin is the primary determinant of blood oxygen carrying capacity and, therefore, of tissue oxygen delivery. Thus, maintaining adequate haemoglobin levels is an important aspect of managing children with ongoing septic shock.

The challenge of treating critically ill children with unstable shock is less clear as there is insufficient data available to guide RBC transfusion therapy in these children.

For children with sepsis or septic shock who are hemodynamically stable (defined as mean arterial blood pressure higher than two standard deviations below normal for age and no increase in vasoactive medications for at least two hours), we recommend following the TAXI guidelines.

TAXI (Transfusion and Anemia Expertise Initiative) guidelines state "**not** administering a RBC transfusion if the haemoglobin concentration is greater than or equal to 7 g/dL in haemodynamically stable critically ill children with a diagnosis of severe sepsis or septic shock" (Muszynski JA, (TAXI), & Pediatric Critical Care Blood Research Network (Blood Net), 2018).

3.1.12 Plasma exchange, renal replacement, and extracorporeal support (SSCGC Recommendations 69-74)

SSCGC Recommendation 69
We suggest against using plasma exchange (PLEX) in children with septic shock or other sepsis-associated organ dysfunction without thrombocytopenia-associated multiple organ failure (TAMOF)
Quality/level of evidence: very low + Strength of recommendation: Weak

SSCGC Recommendation 70
We cannot suggest for or against the use of PLEX in children with septic shock or other sepsis-associated organ dysfunction with TAMOF.

SSCGC Recommendation 71
We suggest using renal replacement therapy to prevent or treat fluid overload in children with septic shock or other sepsis-associated organ dysfunction who are unresponsive to fluid restriction and diuretic therapy.
Quality/level of evidence: very low + Strength of recommendation: Weak

SSCGC Recommendation 72
We suggest against high-volume hemofiltration (HVHF) over standard hemofiltration in children with septic shock or other sepsis-associated organ dysfunction who are treated with renal replacement therapy.
Quality/level of evidence: low + Strength of recommendation: Weak

SSCGC Recommendation 73
We suggest using venovenous ECMO in children with sepsis-induced PARDS and refractory hypoxia.
Quality/level of evidence: very low + Strength of recommendation: Weak

SSCGC Recommendation 74
We suggest using venoarterial ECMO as a rescue therapy in children with septic shock only if refractory to all other treatments.
Quality/level of evidence: very low + Strength of recommendation: Weak

3.1.13 Immunoglobulins (SSCGC Recommendation 75)

SSCGC Recommendation 75
We suggest against the routine use of IV immune globulin (IVIG) in children with septic shock or other sepsis-associated organ dysfunction
Quality/level of evidence: low + Strength of recommendation: Weak

SSCGC Remarks: *Although routine use of IVIG is not recommended, select patients may benefit from such treatment.*

3.1.14 Prophylaxis (SSCGC Recommendations 76-77)

Recommendation 76
We suggest against the routine use of stress ulcer prophylaxis in critically ill children with septic shock or other sepsis-associated organ dysfunction, except for high-risk patients
Quality/level of evidence: very low + Strength of recommendation: Weak

Remarks: Although routine stress-ulcer prophylaxis is not recommended, some high-risk patients may benefit from stress ulcer prophylaxis. Studies have supported benefit of stress-ulcer prophylaxis when baseline rate of clinically important bleeding is approximately 13%.

Recommendation 77
We suggest against routine deep vein thrombosis (DVT) prophylaxis (mechanical or pharmacologic) in critically ill children with septic shock or other sepsis-associated organ dysfunction, but potential benefits may outweigh risks and costs in specific populations.
Quality/level of evidence: low + Strength of recommendation: Weak

Implementation point 19 (Recommendation 76)

Rather than routine, universal administration of stress-ulcer prophylaxis, individual patients should be assessed for the presence of risk factors of clinically important gastrointestinal bleeding. These include multiple organ dysfunction, prolonged mechanical ventilation (> 48 hr), coagulopathy, persistent shock, and treatment with corticosteroids and nonsteroidal anti-inflammatory agents. The risk of GI bleeding is also reduced by mucosal protection introduced by gastric feeding. Early enteral nutrition could therefore be a viable alternative to pharmacological stress-ulcer prophylaxis.

Stress ulcer prophylaxis should not be routinely administered to children with septic shock or other sepsis-associated organ dysfunction, as evidence for benefit is lacking and may increase risk of adverse effects, such as pneumonia or C. difficile infection.

Implementation point 20 (Recommendation 77)

Healthcare providers should follow local hospital guidelines regarding CVC care bundles and remain vigilant for the signs and symptoms of an evolving VTE as patients with sepsis and septic shock are likely to have an increased risk of this complication if CVCs are inserted (Radulescu, 2015).

3.2 Rehabilitation and post-discharge care

Survival from sepsis is not without its complications. Some sepsis survivors experience a variety of physical, psychological and emotional problems while recovering. This is known as Post Sepsis Syndrome (PSS) and usually lasts between 6 and 18 months, sometimes longer. In infants, symptoms of post-sepsis syndrome may not be spotted until they reach school age and find themselves academically behind their peers, or until it appears that they are not developing normally. (Als, et al., 2013) One paediatric study by Brooner et al (2009) showed that 44% of the sepsis survivors overall had problems with their cognitive function (Bronner, et al., 2009).

Awareness of the long-term sequelae of sepsis and septic shock should be promoted amongst healthcare providers, patients, parents/carers and teachers.

Mobilisation and physical rehabilitation should start as early as clinically possible during hospital stay, basing rehabilitation goals on the clinical assessment of healthcare professionals experienced in critical care and rehabilitation.

Sepsis information booklets should be made available to the parents/carers and relatives of patients admitted to a critical care area with sepsis.

3.3 Parental considerations

“When a child is suddenly admitted to hospital, parents are in a state of panic and shock. They need to know, in layman's terms, what has happened to their child (potential medical diagnosis) and the required treatment”. Lesley Richards, parent representative.

As healthcare professionals we need to establish standardised practices around these conversations to ensure parents emotional needs are met. With an acute presentation to hospital, the emergency management of the child is the initial priority for healthcare professionals who may not be in a position to provide detailed

information on progress and prognosis immediately. Ideally, identification of a liaison person from the team to communicate with the parents/carers, will facilitate timely conversations at differing stages of diagnosis and treatment. Key to supporting parents during a sudden event, is the ability to establish an open relationship, allowing adequate time to understand, discuss and process the information regarding their child's diagnosis and prognosis.

It is vital that healthcare professionals collaborate with parents in their child's care, as much as possible, which helps relieve both parental and patient anxiety. Being present at the child's bedside gives parents a greater understanding of the severity of illness and the opportunity to advocate for their child.

Acknowledgements:

A special word of thanks to our parent representative, Lesley Richards, who reinforced the integral part a parent plays in their child's care and highlighted the importance of tenderness, compassion and empathy, when caring for sick children and their families.

We gratefully acknowledge the support and endorsement by Prof. Mark Peters, European Co-chair of the Paediatric Surviving Sepsis Campaign, Great Ormond St. Hospital, who externally reviewed this document.

Section 4. Appendices

Appendix 1: National Sepsis Steering Committee membership – 2019 /2020

Name	Name Job Title and Affiliation
Dr Fidelma Fitzpatrick	Chair
Dr Martina Healy	National Sepsis Clinical lead
Ciara Hughes	Programme Manager National Sepsis Programme – Oct 2020
Mary Bedding	Group Sepsis ADoN RCSI Hospital Group
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
Fidelma Gallagher	Group Sepsis ADoN Saolta Hospital Group
Sinead Horgan	Group Sepsis ADoN South/South West Hospital Group
Nuala Clarke	Group Sepsis ADoN CHI Hospital Group
Elaine Browne	Representative from Acute Hospitals Division
Dr Vida Hamilton	Representative from NCAGL office
Ger Shaw	Representative from ONMSD
Jacqui Hurley	Representative from Health Pricing Office
Collette Tully	Representative from National Office Clinical Audit
Dr Gerry McCarthy/Fiona Mc Daid	Representative for Emergency Medicine
Prof Ellen Crushell	Representative for Paediatrics
Prof Gary Courtney	Representative for Acute Medicine
Dr Michael Power	Representative for Critical Care
Avilene Casey	Representative for Deteriorating Patient
Dr Diarmuid Quinlan	Representative for General Practitioner
Brian Power	Representative Pre-Hospital Emergency Care Council
Barbara Egan	Patient representatives x 2
Anne Mc Cabe	Representative for NASCCRS (National Ambulance Service and critical care and retrieval services)

Awaiting confirmation of representatives from the Health Pricing Office, the Integrated Care Programmes, the HSE Health Intelligence Unit, the National HPSC Office, the National Ambulance Service and Public Health Nursing.

Appendix 2: National Sepsis Programme Team (NSP)

Name	Name Job Title and Affiliation
Martina Healy	National Sepsis Clinical lead
Ciara Hughes	Programme Manager National Sepsis Programme – Oct 2020
Mary Bedding	Group Sepsis ADoN RCSI Hospital Group
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
Fidelma Gallagher Ronán O Cathasaigh	Group Sepsis ADoN Saolta Hospital Group – Nov 2020 Group Sepsis ADoN Saolta Hospital Group – Jan 2021
Sinead Horgan	Group Sepsis ADoN South/South West Hospital Group
Nuala Clarke	Group Sepsis ADoN CHI Hospital Group

Appendix 3: National Implementation Plan Development Group (NIPDG)

Name	Name Job Title and Affiliation
Dr Martina Healy	National Sepsis Clinical Lead
Ciara Hughes	Programme Manager National Sepsis to Oct 2020
Nuala Clarke	Group Sepsis ADON CHI
Celine Conroy	Group Sepsis ADON Ireland East Hospital Group
Dr Laura Melody	Consultant, Paediatric Emergency Medicine, CHI @ Crumlin
Dr Regina Cooke	Consultant Paediatrician, Portiuncula
Dr Robert Cunney	Consultant Microbiologist, CHI @ Temple St
Dr Turlough Bolger	Consultant in Paediatric Emergency Medicine, CHI @ Tallaght
Dr Niamh O Sullivan	Consultant Microbiologist
Kara Tedford	Antimicrobial Pharmacist, CHI @ Crumlin
Dr Julie Lucey	Consultant Paediatrician, Waterford
Dr Roisin McNamara	Consultant, Paediatric Emergency Medicine, CHI @ Temple St
Joan Broderick	CNM3, ED, CHI @ Temple St
Helen Flynn	CNM3, UCC, CHI@ Blanchardstown
Susan Keane	Clinical Practice Coordinator, CHI @ Temple St
Linda Farren	RO, CHI @ Crumlin
Experts co opted	
David Menzies & Ricky Ellis	PHECC
Jessica Sheppard	Paediatric Dietitian, PICU , CHI @ Crumlin
External Experts	Prof. Mark Peters, ESICM / SSC GOSH, UK
Lesley Richards	Parent/patient representative

Appendix 4: National Paediatric Sepsis Form Development Group 2019

Name	Name Job Title and Affiliation
Dr Martina Healy	National Sepsis Clinical Lead
Ciara Hughes	Programme Manager National Sepsis to Oct 2020
Nuala Clarke	RO, CHI @ Tallaght Hospital
Celine Conroy	Group Sepsis ADON Ireland East Hospital Group
Dr Roisin McNamara	Consultant in Paediatric Emergency Medicine, CHI @ Temple St
Dr Regina Cooke	Consultant Paediatrician, Portiuncula
Jean Donnelly	Consultant Paediatrician, CHI @ Crumlin
Linda Farren	RO, CHI @ Crumlin
Turlough Bolger	Consultant in Paediatric Emergency Medicine, CHI @ Tallaght
Helen Flynn	CNM3, UCC , CHI@ Blanchardstown
Susan Keane	Clinical practice coordinator , CHI @ Temple St

Appendix 5: Glossary of Terms and Abbreviations

Glossary of Terms

Child/Children: Refers to an infant, child or adolescent admitted to inpatient paediatric services

Clinician: A registered nursing/midwifery, medical or health and social care professional.

Escalation of Care: the point at which a clinician successfully contacts/calls for a more senior clinical review - nursing or medical - of a patient

EWS: Early Warning System

Infant: A child, from birth to one year of age.

PEWS: Paediatric Early Warning System

Sepsis is lifethreatening organ dysfunction caused by a dysregulated host response to infection

Septic Shock defined as severe infection leading to cardiovascular dysfunction (including hypotension, need for treatment with a vasoactive medication, or impaired perfusion)

Sepsis-associated organ dysfunction defined as severe infection leading to cardiovascular and/or noncardiovascular organ dysfunction.

SIRS Systemic Inflammatory Response Syndrome

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, Nutbeam, McNamara, & Galvin, 2011) as a practical tool to help healthcare professionals deliver the SSCG 1 hour bundle.

Abbreviations

ALT: Alanine transaminase

ASPEN: American Society for Parenteral and Enteral Nutrition

AvLOS: Average Length of Stay

BIA: Budget Impact Analysis

BPS: Best Practice Statement

CDC: Centre for Disease Control

CDI: Clinical Design and Innovation

CDST: Clinical Decision Support Tool

CNS: Central Nervous System

CPAP: Continuous Positive Airway Pressure

CPG: Clinical Practice Guideline

CRRT: Continuous Renal Replacement Therapy

CVP: Central Venous Pressure

DIC: Disseminated Intravascular Coagulation

DoH: Department of Health

DON: Director of Nursing

DRG: Diagnostic Related Group

DVT: Deep Vein Thrombosis

Dx1: Primary Diagnosis

Dx2: Secondary Diagnosis

ECMO: Extracorporeal membrane oxygenation

ED: Emergency Department

EM: Emergency Medicine

EGDT: Early Goal-Directed Therapy

EMT: Emergency Medicine Technician

ESBL: Extended-Spectrum B- lactamase

ESRI: The Economic and Social Research Institute

FEAST: Fluid expansion As Supportive Therapy

GCS: Glasgow Coma Scale

GI: Gastrointestinal

GP: General practitioner

GRADE: Grading of Recommendations Assessment, Development and Evaluation

GRV: Gastric Residual Volume

HCAI: Healthcare-Associated Infection

HCW: Healthcare Worker/healthcare staff

HDU: High Dependency Unit

HES: Hydroxyethyl starches

HFOV: High Frequency Oscillatory Ventilation

Hg: Mercury

HIPE: Hospital Inpatient Enquiry

HIQA: Health Information and Quality Authority

HPA: Health Protection Agency

HPO: Healthcare Pricing Office

HPSC: Health Protection Surveillance Centre

HSCP: Health and Social Care Professionals

HSE: Health Service Executive

HVHF: High Volume Haemofiltration

ICD: International Classification of Disease

ICU: Intensive Care Unit

ICTS: Irish Children's Triage System

IPATS: Irish Paediatric Acute Transfer service

IVIG: Intravenous Immunoglobulin

IDSA: Infectious Disease Society of America (IDSA)

iNO: inhaled nitric oxide

IO: intraosseous

IPC(T): Infection prevention and control (team)

Abbreviations (continued)

ISBAR: Identify, Situation, Background, Assessment, Recommendation

IV: Intravenous

LMWH: Low Molecular Weight Heparin

LOS: Length of stay

MAP: Mean Arterial Pressure

MDRO: Multidrug Resistant Organisms

MIC: Minimum Inhibitory Concentration

MRSA: Methicillin-Resistant Staphylococcus Aureus

N/A: Not Applicable

NCEC: National Clinical Effectiveness Committee

NCG: National Clinical Guideline:

NSP: National Sepsis Programme

NEWS: National Early Warning System

NICE: National Institute for health and Care Excellence

NIP: National Implementation Plan

NIV: Non-Invasive Ventilation

NNTP: National Neonatal Transport Service

NOCA: National Office Clinical Audit

ONMSD: The Office of the Nursing and Midwifery Services

OPD: Out-patient Department

$PaCO_2$: Partial Pressure of Carbon Dioxide

PARDS: Paediatric Respiratory Distress Syndrome

PDSA: Plan, Do, Study, Act

PE: Pulmonary Embolism

PED: Paediatric Emergency Department

PEEP: Positive End Expiratory Pressure

PEWS: Paediatric Early Warning System

PHECC: Pre- Hospital Emergency Care Council

PICO: Population, Intervention, Comparison and Outcomes.

PICU: Paediatric intensive Care Unit

PIVC: Peripheral Intravenous Catheter

PLEX: Plasma Exchange

POC: Point Of Care

POD: Paediatric Observation Department

PPI's: Proton Pump Inhibitors

PSS; Post Sepsis Syndrome

QA: Quality Assurance

RBC: Red Blood Cell

RCT: Randomised Controlled Trial

RCPI: Royal College of Physicians, Ireland

RRT: Renal Replacement Therapy

SAC: Scientific Advisory Committee

SCCM: Society of Critical Care Medicine

SD: Standard Deviation

ScvO2: Central Venous Oxygen Saturation

SIRS: Systemic Inflammatory Response Syndrome

SOFA: Sequential Organ Failure Assessment

SSC: Surviving Sepsis Campaign

SSCGC: Surviving Sepsis Campaign Guideline for Children

TAMOF: Thrombocytopenia-Associated Multiple Organ Failure

TAXI: Transfusion and Anemia Expertise Initiative

UCC: Urgent Care Centre

UFH: Unfractionated Heparin

UK: United Kingdom

US: United States

VAP: Ventilator Associated Pneumonia

VDD: Vitamin D Deficiency

VTE: Venous Thromboembolism

WHO: World Health Organisation

Appendix 6: Guideline search strategy for Paediatric

Sepsis Guidelines Searched

1. Up To Date – Systemic inflammatory response syndrome (SIRS) and sepsis in children: Definitions, epidemiology, clinical manifestations, and diagnosis

https://www.uptodate.com/contents/systemic-inflammatory-response-syndrome-sirs-and-sepsis-in-children-definitions-epidemiology-clinical-manifestations-and-diagnosis?search=sepsis&source=search_result&selectedTitle=3~150&usage_type=default&display_rank=3#H2892990901

2. BMJ Best Practice – Sepsis in children

https://bestpractice.bmj.com/topics/en-gb/1201/guidelines

3. Other guideline databases searched:
   NICE, (National Institute Clinical Effectiveness);
   GINN, (Guidelines International Network);
   TRIP (Turning Research into Practice) and
   American Clearing House.

Databases Searched (Using the search strategy in table 3)

Web of Science – Hits 9

PubMed – Hits 143

Scopus – Hits 297

Embase – Hits 132

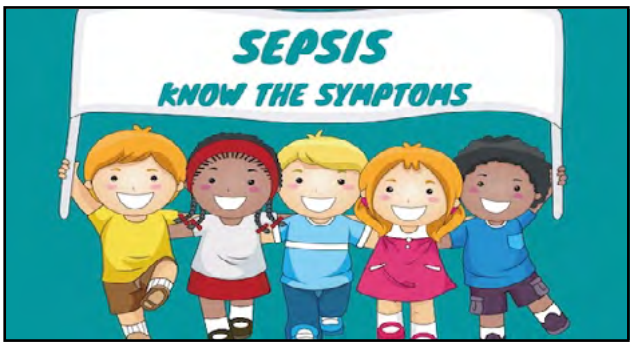
Google Scholar Hits 148

Appendix 7: Paediatric Sepsis Awareness

Leaflets

Video/social media campaign

Posters



Appendix 8: Enablers and Barriers to implementing the NIP

Table 20. (Draft) Implementation Plan for International Clinical Guideline for the management of septic shock and sepsis-associated organ dysfunction in children

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
GENERAL	Enablers • Screening tool piloted 11/20 sites • Public awareness leaflets/pop ups • Train the trainer workshops x 3 Barriers • Challenges in recognising sepsis early- Gaps in knowledge/education • 9 outstanding sites to pilot. • Lack of IT systems to capture information Lack of integration across IT systems	Develop communication, dissemination and stakeholder engagement with 2020 SCC guidelines Dissemination of audit findings with hospital management Education: • Develop an e-learning paediatric sepsis programme • Address current knowledge gaps • Targeted education on use of clinical decision-making tools – develop scenarios Identify requirements from IT systems (EHR) to capture sepsis data Improve data capture with collaboration from IT experts	Sepsis National Clinical Programme Paediatric Working Group Paed Sepsis ADON Education Leads across disciplines ICT engagement	To be decided	**Outcome** Improved awareness and knowledge of paediatric sepsis guideline and accompanying tools. **Verification** Acknowledgement from hospital leads upon receipt of guideline. Monitoring and Audit feedback.
SCREENING, DIAGNOSIS, AND SYSTEMATIC MANAGEMENT OF SEPSIS Recommendations 1-4	Enablers • Audit and feedback Champions identified • Support from Hospital Senior Management • Local Sepsis Committees • Paed Sepsis ADON	Development of network of champions – medical and nursing across all sites Develop and use audit tools and audit schedules	National Sepsis Team Paediatric Working Group ED engagement Paed Sepsis ADON	To be decided	**Outcome** More champions. Engagement with guideline, leading to improved outcomes for patients. Improved access to sepsis data and hospital.

	Barriers • ED specific pathway for screening tool lacking • Lack of clarity regarding medical/nursing champions on some sites	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)	Hospital Sepsis Committees		comparisons of mortality data for children. **Verification** Audit and annual reports. Reporting from Sepsis ADON. Feedback from Hospital Sepsis Committees. Feedback from hospital group.
ANTIMICROBIAL THERAPY Recommendations 5-14 **SOURCE CONTROL** Recommendations 15-16	Enablers • Local Sepsis Committees • Sepsis tools/algorithm • Local antimicrobial guidelines • Consultant Microbiologists • Antimicrobial stewardship • CHI cross site antibiotic guideline Barriers • Lack of knowledge • Lack of equipment to measure lactate	Conduct gap analysis on equipment for point-of-care lactates. Education: e-learning tool Lecture/PPT Simulation IPC involvement Sepsis prevention for devices Feedback from audits: • compliance with tool • source/pathogen identified Involve surgical specialities early for source control.	Sepsis ADONs Hospital Sepsis Committees Antimicrobial pharmacists/ infection Pharmacists	To be decided	**Outcome** Improved access to equipment. Improved adherence to local antimicrobial guideline. **Verification** Review of Hospital Antimicrobial Consumption Review of device related infections.
FLUID THERAPY Recommendations 17-23 **HEMODYNAMIC MONITORING** Recommendations 24-27	The NIP development group have provided implementation points after each recommendation or group of recommendations, to guide implementation of the SSC International Guidelines for children in Ireland.				

VASOACTIVE MEDICATIONS Recommendations 28-33 **VENTILATION** Recommendations 34-43 **CORTICOSTEROIDS** Recommendations 44-45 **ENDOCRINE AND METABOLIC** Recommendations 46-50 **NUTRITION** Recommendations 51-64 **BLOOD PRODUCTS** Recommendations 65-68 **PLASMA EXCHANGE, RENAL REPLACEMENT, AND EXTRACORPOREAL SUPPORT** Recommendations 69-74 **IMMUNOGLOBULINS** Recommendation 75 **PROPHYLAXIS** Recommendation 76	The NIP development group have provided implementation points after each recommendation or group of recommendations, to guide implementation of the SSC International Guidelines for children in Ireland.

Appendix 9: Paediatric Sepsis Form Draft

Paediatric Sepsis Form

For early recognition, treatment and referral (ALWAYS USE CLINICAL JUDGEMENT)

PAEDIATRICS
There are separate sepsis criteria for maternity patients and adults

PAEDIATRIC PATIENTS (from 4 weeks (or 4 wks corrected age) to 16 years)

Complete this form if there is a **clinical suspicion of infection and the child appears unwell**.
When complete, sign and place in child's healthcare record. Seek senior expert help early if sepsis is suspected.

Print name:
Signature:
Role:
NMBI or MCRN:
Date: Time:

Addressograph

COULD THIS BE SEPSIS?

≥1 Red Flag

- ☐ Altered mental status- P or U on AVPU
- ☐ Hypotension
- ☐ Prolonged central capillary refill
- ☐ Tachycardia unexplained by fever/crying
- ☐ Non-blanching rash
- ☐ Clinical deterioration as in-patient

Yes ☐ Immediate medical review

No Red Flag ☐

≥1 Amber Flag

- ☐ Inappropriate tachypnoea i.e. does not respond with simple measures
- ☐ Altered functional status (e.g. severe leg pain, or inability to weight-bear or decreased activity)
- ☐ Healthcare professional concern
- ☐ Parental concern
- ☐ Increasing PEWS
- ☐ Other:

+/−

Risk Factor(s)

Certain conditions will increase risk of sepsis and should lower threshold for initiation of Sepsis 6. These include:

- ☐ Immunocompromised (follow national haematology/oncology guidelines for children with cancer)
- ☐ Age ≤3 months
- ☐ Chronic disease
- ☐ Recent surgery
- ☐ Break in skin (including chickenpox)
- ☐ Indwelling line/device
- ☐ Signs of infection in a wound (including chickenpox)
- ☐ Incomplete vaccination record
- ☐ Other:

Urgent medical review if ≥1 Amber Flag +/- Risk Factor(s)

Is Sepsis likely at this time?

Signs of Shock Yes ☐ No ☐

Start Sepsis 6 within 1hr

Time:

Suspected Sepsis Yes ☐

3hr window for diagnostic work up - see "take 3"

Suspicion Time:

Sepsis NOT likely at this time

Working Diagnosis:

Review within:

Doctor (Print Name): **Doctor Signature:**
MCRN: **Date:** **Time:**

Version 5 - 12/08/2021

Page 1 of 2, continue overleaf

Paediatric Sepsis Form

Ongoing clinical review and interpretation of results

(ALWAYS USE CLINICAL JUDGEMENT)

Addressograph

Paediatric Sepsis 6 – complete within 1 hour

TAKE 3

☐ **IV access** Time _____ **or**
☐ **IO access** Time _____

Tick samples taken:

- ☐ Blood cultures
- ☐ FBC
- ☐ Glucose
- ☐ Blood gas
- ☐ Coag screen incl fibrinogen
- ☐ Lactate
- ☐ U&E
- ☐ LFTs
- ☐ CRP
- ☐ Urinalysis
- ☐ PCRs if available

☐ **Urine output assessment/measurement**

☐ **Early senior input (essential) as per local escalation policy**

GIVE 3

☐ **Oxygen** to achieve saturations ≥94% titrating to effect or as appropriate in chronic lung or cardiac disease

☐ **IV/IO fluids**

- Titrate 10-20mls/kg Hartmann's Solution over 5-10min, 0.9% NaCL is an acceptable alternative – repeat as per clinical response
- Call critical care/anaesthesia in haemodynamic collapse
- Consider early inotropic support
- Assess for fluid overload, monitor for crepitations or hepatomegaly

☐ **IV/IO Antimicrobials** according to the site of infection and following local antimicrobial guidelines.

Drug name:	Dose:	Time given:

Time Sepsis 6 completed: _____

Name: _____ **MCRN:** _____

Reassess the child as clinically indicated and complete form within 1 hour of initiating the Sepsis 6 bundle

Look for signs of new organ dysfunction after the Sepsis 6 bundle has been given or from blood test results – any one is sufficient:

Cardiovascular
☐ Lactate ≥4 after 20mls/kg fluid therapy

Respiratory
☐ Increasing need for Oxygen to maintain saturations ≥ 94% titrating to effect or as appropriate in chronic lung or cardiac disease
☐ Need for nonelective invasive or noninvasive mechanical ventilation

Central Nervous System
☐ Glasgow coma score (GCS) ≤11 or poorly responsive
☐ Acute change in mental status with a decrease in GCS ≥3 points from usual baseline

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

Haematological
☐ Platelet count ≤80,000/mm^3

Coagulation
☐ International normalised ratio ≥2

Liver
☐ Total bilirubin Bilirubin ≥ 38 µmol/L (micromoles/L) not applicable for newborn
☐ ALT 2 times upper limit of normal for age

Any new organ dysfunction due to infection: ☐ **This is SEPSIS**
Inform Consultant and Anaesthesia/PICU. **Time:** _____
Reassess frequently in the first hour. Consider other investigations and management +/- source control if child does not respond to initial therapy.

No new organ dysfunction due to infection: ☐ **This is NOT SEPSIS**
If infection is diagnosed, proceed with usual treatment pathway for that infection.

Look for signs of septic shock

(following administration of fluid bolus of up to 40ml/kg)

- ☐ Hypotension
- ☐ Prolonged central CRT
- ☐ Core to peripheral temperature gap ≥3^{0}C
- ☐ Unexplained metabolic acidosis
- ☐ Oliguria: ≤1ml/kg/hour up to 11 years or ≤0.5ml/kg/hour in the 12+ age group
- ☐ Need for inotropic support
- ☐ **This is SEPTIC SHOCK**

Time: _____

In addition to senior clinical support at the bedside early involvement of PICU support is encouraged. Where PICU support is not on site a national 24-hour hotline is available for urgent referrals providing advice and arranging transfer – 1800 222 378.

Doctor (Print Name): _____ **Doctor Signature:** _____

MCRN: _____ **Date:** _____ **Time:** _____

File this document in the child's healthcare record.

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Appendix 10: Supporting tools

National Sepsis Programme www.hse.ie/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/

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

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

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

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

IPATS drug calculators: http://www.nasccrs.ie/IPATS/Calculators/

Model of care for Adult Critical care: https://www.hse.ie/eng/about/who/cspd/ncps/critical-care/moc/

Conversion websites:

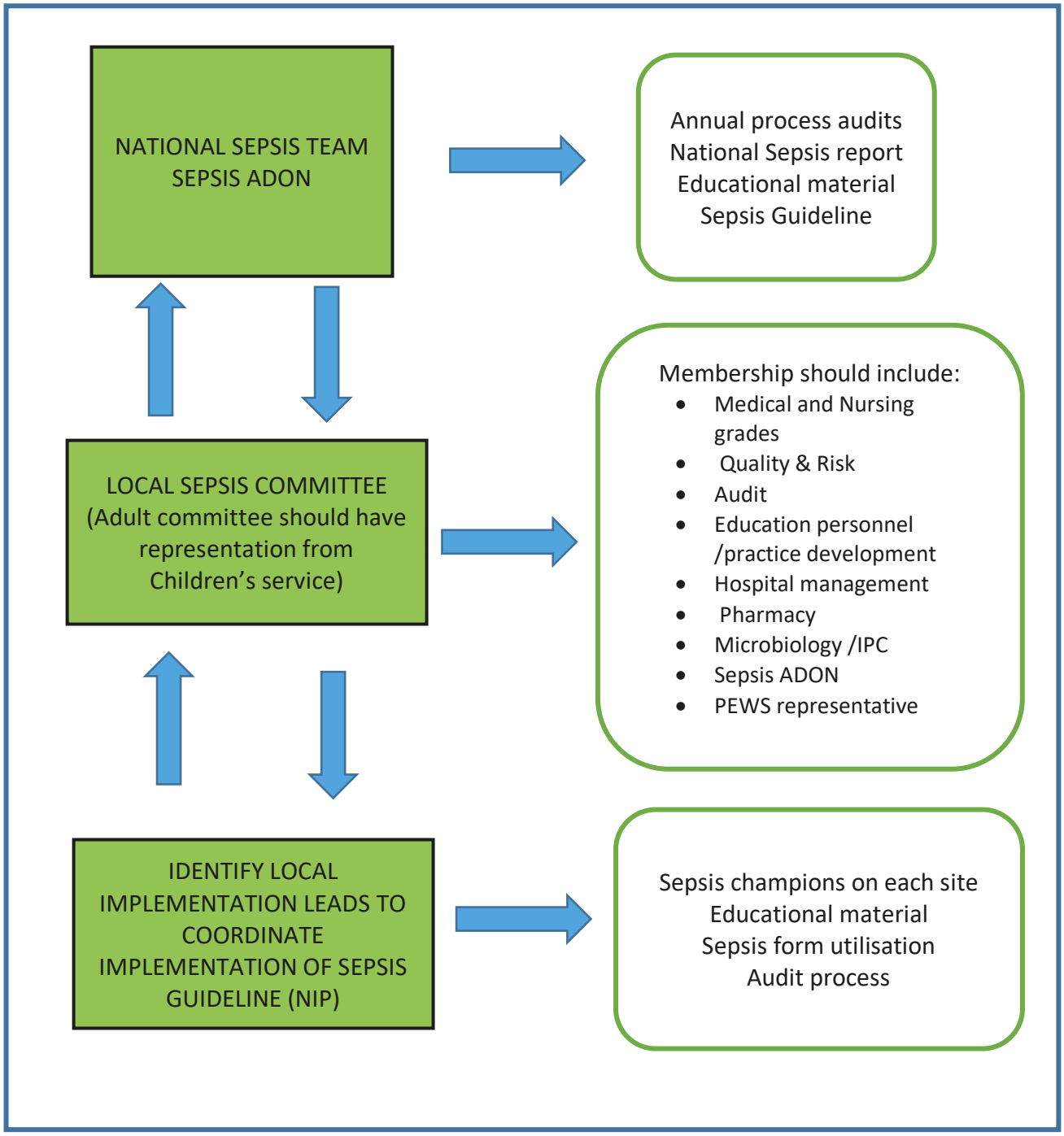
http://www.conversion-website.com/pressure/centimeter-of-water-to-millimeter-of-mercury.html

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

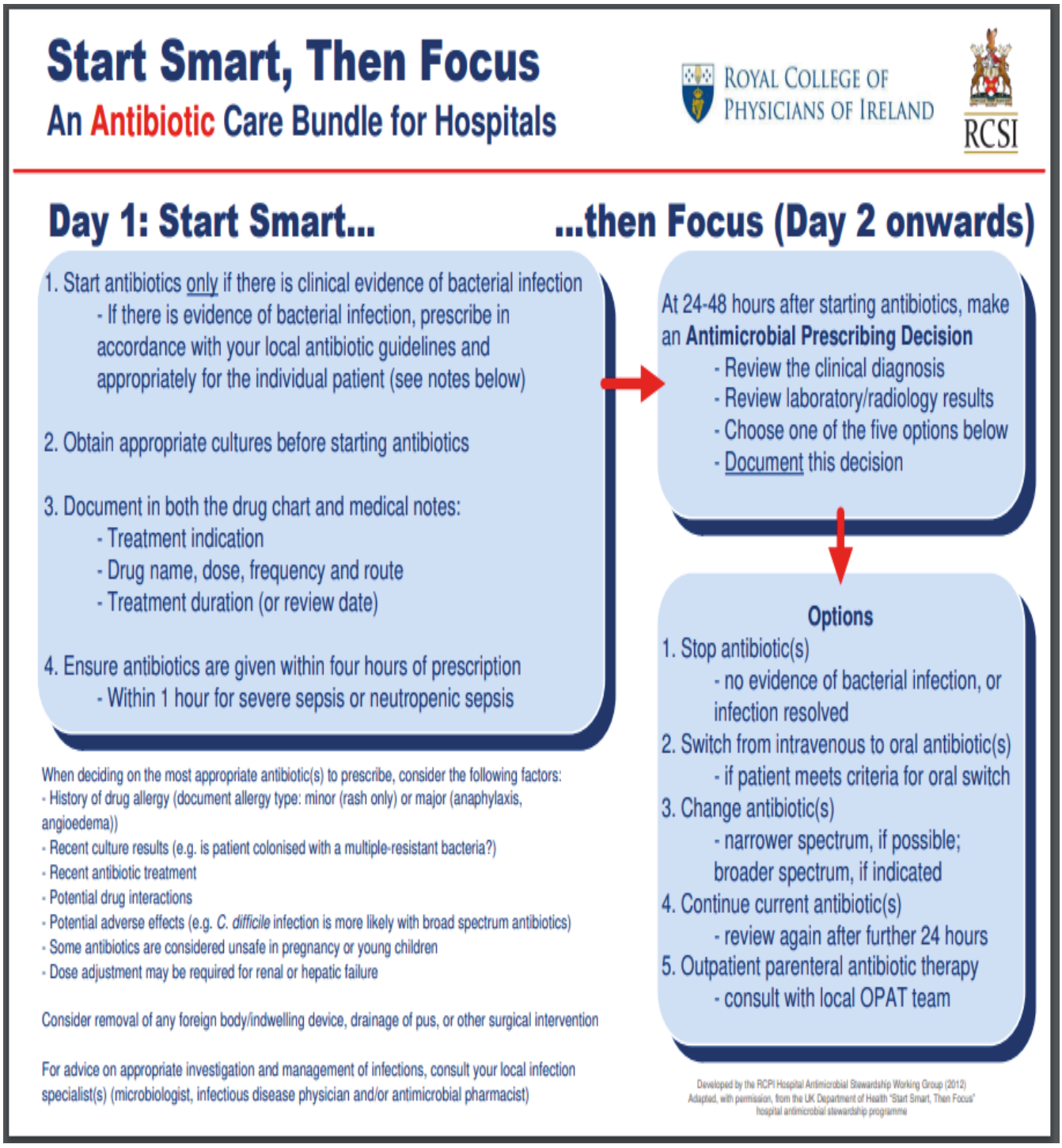
Appendix 11: Flowchart of implementation of SSCGC recommendations within the Irish acute healthcare sector

All paediatric hospitals and acute hospitals with paediatric units are required to have a Sepsis Committee whose role is to guide the implementation of the SSCGC recommendations and this NIP in their hospital. This committee oversees the coordination of sepsis education, introduction and utilisation of the sepsis form and reviews audit feedback to inform this process.

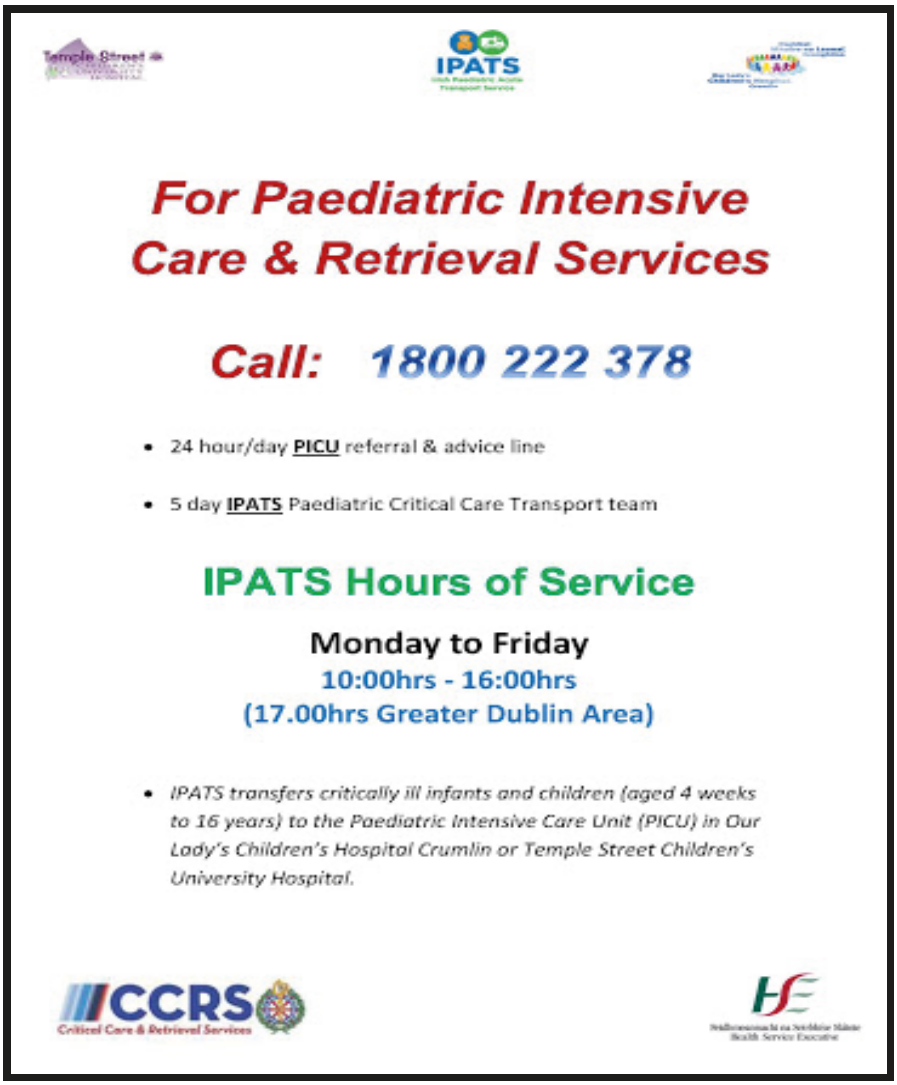
Implementation Plan



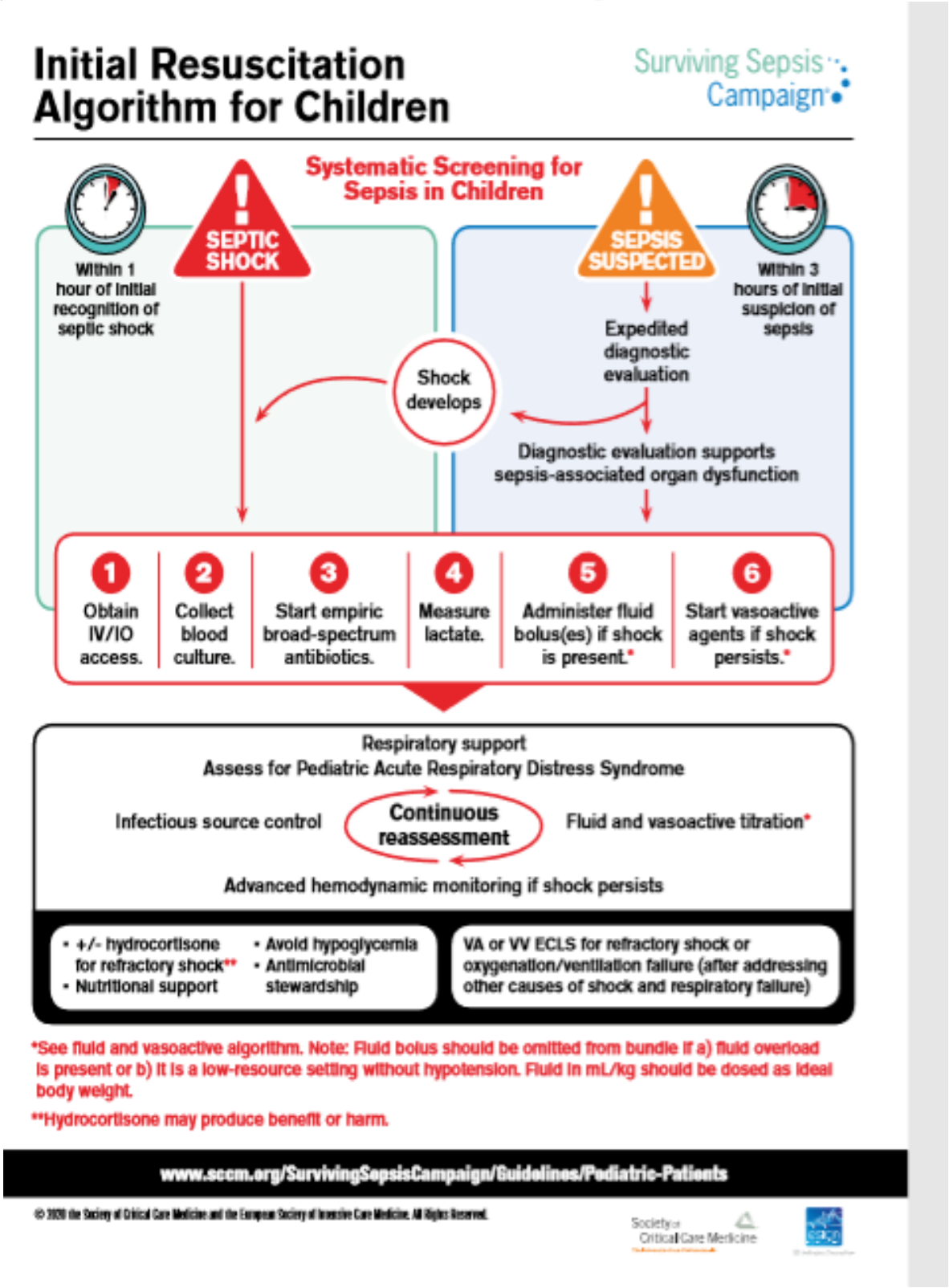
Appendix 12: Start Smart and then Focus' approach for antimicrobial therapy 2012



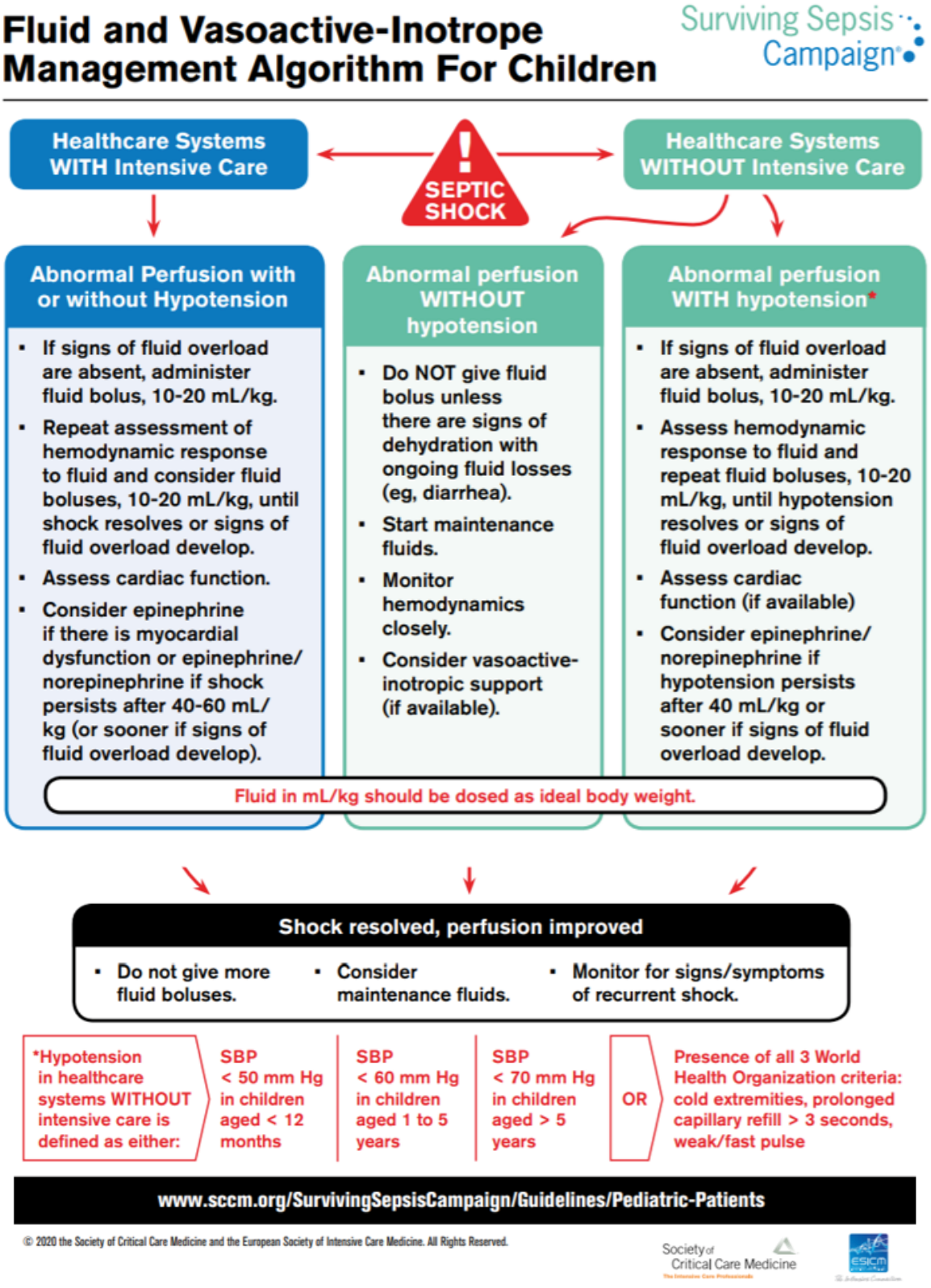
Appendix 13: Irish Paediatric Acute Transport Service (IPATS)



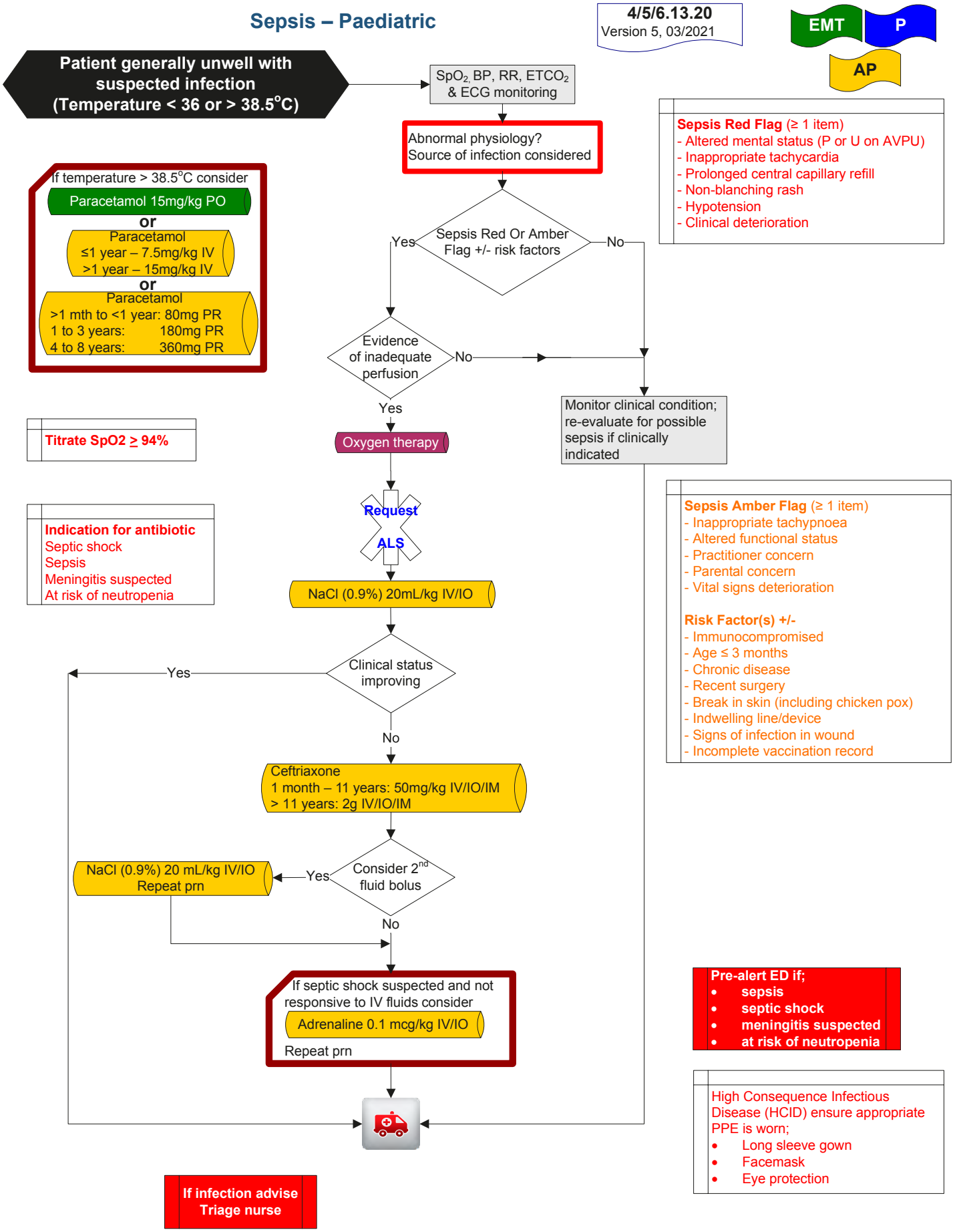
Appendix 14: SSCGC Initial Resuscitation Algorithm for Children



Appendix 15: SSCGC Fluid and Vasoactive-Inotrope Management Algorithm for children



Appendix 16: PHECC CPG for Septic Shock – Paediatric ≤ 15yrs (2021)



Appendix 17: Surviving Sepsis Campaign References

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