

SEPSIS

Prevention, Early Identification and Response



Getting Started Kit

Effective March 14, 2019, the Canadian Patient Safety Institute has archived the Sepsis intervention. For additional inquiries, please contact info@cpsi-icsp.ca

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This Getting Started Kit has been written to help engage your inter-professional/interdisciplinary teams in a dynamic approach for improving quality and safety while providing a basis for getting started. The Getting Started Kit represents the most current evidence, knowledge and practice, as of the date of publication and includes what has been learned since the first kits were released in 2005. We remain open to working consultatively to update the content as more evidence emerges, as together we make healthcare safer in Canada.

Note:

The Getting Started Kits for all *Safer Healthcare Now!* interventions are available in both French and English.

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Introductory Remarks

In this *Getting Started Kit*, we have chosen to emphasize an approach to sepsis which can be used in hospital inpatient units and emergency departments. Although specifically trained providers (e.g. Critical Care/ and/or Rapid Response Teams, Emergency Department, etc.) should be consulted early on, the initial response to early sepsis is often initiated by the affected patients' treating clinical team. The information provided can also be applied to the pre-hospital setting.

We have included sections on pediatric sepsis and maternal sepsis (sepsis in pregnant or recently delivered women) as it has become a leading cause of maternal mortality in the developed world. We have omitted discussion of neonatal sepsis, the topic being outside the scope of this GSK.

Goal

To decrease the morbidity and mortality from sepsis in hospitalized patients through a structured approach to prevention, early identification and response to sepsis.

The Case for Prevention, Early Identification and Response to Sepsis

Sepsis is a systemic, deleterious host response to infection. It presents a continuum of events starting as an uncomplicated infection which can progress to severe sepsis (acute organ dysfunction secondary to documented or suspected infection) and septic shock (severe sepsis plus hypotension not reversed with fluid resuscitation) with multiple organ dysfunction and failure.

Severe sepsis and septic shock, together defined as "*septic illness*" (see [Glossary of terms](#)) represent one of the oldest and most pressing problems in medicine.

Sepsis is a growing health concern in Canada as well as in the rest of the world.^{1, 2} There are an estimated 19 million cases of sepsis in the world every year² and over 750,000 cases of septic illness are diagnosed yearly in the United States alone.³

In Canada, more than 30,000 patients are hospitalized in Canada each year due to sepsis (CIHI 2009) of whom 30 per cent will die from related complications. Furthermore, the one year overall mortality after a bout of septic illness has been reported as greater than 50 per cent⁴ with a high incidence of residual functional impairment in survivors.⁵ Patients with sepsis stay in hospital eight days longer than an average patient and often require an expensive Intensive Care Unit (ICU) admission.^{1,3} While sepsis carries a significant risk of morbidity and mortality, adequate initial therapy is initiated in septic patients in fewer than 58 per cent of cases.⁶

In addition, as more patients survive sepsis, concern mounts over the lingering sequelae of what was previously a lethal event.⁷ Sepsis survivors remain at increased risk for death in the following months and years, often with impaired neurocognitive impairment and functional disability.⁵ Indeed an additional 18 per cent mortality was observed between the first and third month after a septic illness. This was associated with age, poor preadmission functional status, comorbidities, and nosocomial infection.⁸

The incidence of septic illness continues to rise despite a decline in the associated mortality rate.^{7, 9, 10, 11, 12, 13, 14} Indeed, advances in training, better surveillance and monitoring, and prompt initiation of therapy to treat the underlying infection and support failing organs have all contributed to reducing the mortality from septic illness from greater than 80 per cent to 20-30 per cent in these studies.

Despite these advances, there is still much room for improvement as sepsis remains one of the most deadly emergency department arrival or hospital-acquired conditions.¹⁵ In two independent hospital cohorts where sepsis contributed to one in every two to three deaths, not only was sepsis already identifiable at the time of hospital admission but the sepsis was initially less severe. These features suggest the opportunity for earlier recognition and management of sepsis in improving the outcomes of these patients.¹⁶ Similar to other time-sensitive disorders such as polytrauma, acute myocardial infarction or stroke, the speed and appropriateness of therapy administered in the initial hours after septic illness develops are likely to influence outcome. Reade and Huang qualified initial sepsis care as often still “uneven and ...sluggish”.¹⁷ This is supported by at least two studies documenting low rates of initiation of adequate sepsis management and of completion in those who did initiate it - in the order of 40 to 58 per cent and 10 to 43 per cent respectively.^{6,18}

The Canadian ICU Collaborative and Canadian Patient Safety Institute believe, as others have expressed,¹⁹ that the greatest outcome improvement for septic illness can be made through education and process change for those caring for septic illness patients in the ICU and non-ICU settings across the spectrum of acute care.

In the light of current evidence, many hospitals have demonstrated that early identification and treatment can significantly impact sepsis morbidity, mortality rates and health-care costs. Simple interventions administered early include:^{19, 20}

1. Early administration of broad spectrum antibiotics;
2. Early, aggressive administration of IV fluids;
3. Blood cultures drawn before IV antibiotics are administered;
4. Early and repeated lactate measurements.

Words of Caution

The purpose of this initiative, as for all Canadian Patient Safety Institute interventions, is to improve patient outcomes through self-improvement. It is to be noted, however, that despite remarkable strides in our understanding of sepsis, there are still important limitations in its diagnosis, surveillance and treatment. As an example, epidemiologic estimates of pediatric septic illness can vary up to sevenfold depending on the strategy used for case ascertainment.²¹ The impact of these limitations is currently unknown, but they may nevertheless affect outcomes. This should not prevent us from applying the lessons learned from scientific and experiential evidence, but we, as others, advise caution before mandating sepsis bundles and benchmarking hospitals on their adherence rates.²²

Rigorous implementation of sepsis guidelines will save many lives, but the broad definition of sepsis makes it likely that the number of adults and children exposed to potentially unnecessary treatments will also increase. An informed and targeted approach to the diagnosis and management of the diseases initially categorized as “sepsis” (infections and non-infectious) remains essential and will help to optimize the outcomes of these sick patients. This requires our ongoing commitment to making the best use of the information made available from the medical history, bedside physical examination, available validated rapid diagnostic tests, and the appropriate and timely de-escalation or cessation of antibiotics according to diagnosis and clinical evolution.

Prevention, Early Identification and Response to Sepsis

Sepsis is defined as the presence (probable or documented) of infection together systemic manifestations of infection (see [Table 1](#)).

Severe sepsis is defined as sepsis plus sepsis-induced organ dysfunction or tissue hypoperfusion (see [Table 1](#)).

Septic shock is defined as sepsis-induced hypotension persisting despite adequate fluid resuscitation.

We chose to define the term septic illness as the grouping of the two syndromes of severe sepsis and septic shock because they constitute a continuum of severity and share the same pathophysiology and clinical challenges.

Table 1: Septic Illness

Septic illness is operationally defined as requiring:

A. Some of the following systemic manifestations[¶]

- **General**
 - Core Temperature > 38.3°C or < 36°C
 - Heart rate > 90/min⁻¹ or > 2 SD above the normal value for age
 - Tachypnea
 - Altered mental status
 - Significant edema or positive fluid balance (> 20 mL/kg over 24 hr)
 - Hyperglycemia (plasma glucose >7.7 mmol/L) in the absence of diabetes
- **Inflammatory**[†]
 - WBC > 12,000 μL^{-1} , < 4000 μL^{-1} or normal but with >10% immature forms
 - Plasma C-reactive protein > 2 SD above the normal value
 - Plasma procalcitonin > 2SD above the normal value

AND

B. Any of the following signs of acute organ dysfunction or tissue hypoperfusion

- **Organ dysfunction**
 - Cardiovascular:
 - Hypotension(SBP < 90 mm Hg, MAP < 70 mm Hg,
 - or an SBP decrease > 40 mm Hg in adults or < 2SD below normal for age
 - Pulmonary[‡]:
 - Pao₂/Fio₂<250 in the absence of pneumonia as infection source
 - or < 200 in the presence of pneumonia as infection source
 - Renal:
 - Urine output < 0.5 mL/kg/hr for at least 2hrs despite adequate fluid resuscitation
 - Creatinine[†] > 178 $\mu\text{mol/L}$ or increase by > 45 $\mu\text{mol/L}$
 - Gastrointestinal:
 - Bilirubin[†] (plasma total)> 70 $\mu\text{mol/L}$ or increase by >35 $\mu\text{mol/L}$
 - Hematological:
 - INR[†] > 1.5 or aPTT> 60 sec.
 - Platelet count[†] < 100,000 μL^{-1}
- **Tissue hypoperfusion**
 - Lactate[†] \geq 4mmol/L
 - Decreased capillary refill or mottling

[§] Two or more

[¶] Acute and thought to be due to infection*

[†] Draw blood for CBC, Creatinine, Bilirubin, INR and lactate if infection is suspected either by history, physical examination or two or more "General" criteria are identified. Alternatively, reserve lactate measurement only if in addition the patient has any of the following: looks unwell, age > 65 years, recent surgery, immunocompromised (AIDS, chemotherapy, neutropenia, asplenia, transplant, chronic steroids) or chronic illness (diabetes, renal failure, hepatic failure, cancer, alcoholism, IV drug use)

[‡] Obtain arterial blood gas if Fio₂ > 0.5 (by full face mask) is required to maintain Spo₂ > 90%

Adapted from Dellinger et al.¹⁹

*The term *systemic manifestations* is preferred over the more restrictive term *systemic inflammatory response syndrome*, or SIRS,²³ the latter requiring 2 or more criteria from elevated or decreased temperature or white blood cell count, tachycardia or tachypnea. Indeed a recent study¹⁴ suggests that caution should be exercised in applying uniquely SIRS criteria for the diagnosis of septic illness. This retrospective review of over 1 million ICU admissions over a 10-year period in Australia and New-Zealand found that 1 in 8 (12 per cent) patients diagnosed with septic illness within the first 24hrs of ICU admission but did not meet the conventional criteria for septic illness, i.e. had less than 2 SIRS criteria. These “SIRS-negative” patients were defined as having septic illness by an APACHE III diagnosis of infection and at least 1 organ system failure, OR and APACHE III diagnosis of septic illness. Although these patients were less ill than “SIRS-positive” patients (lower APACHE scores, less shock or kidney injury, length of stay and mortality), the mortality trend followed the same 10-year decrease, suggesting the two groups share a common pathophysiology and/or response to treatment. Limiting the diagnosis of septic illness to conventional “SIRS-positive” criteria may have limited sensitivity and specificity for the diagnosis of septic illness.

Prevention

Prevention involves all health-care providers, as sepsis occurs in the community as well as in healthcare settings. Two ways to prevent septic syndromes are:

- To identify and treat early *infections* before they have met the criteria defining them as sepsis. Examples of infections evolving to sepsis are a community-acquired pneumonia that worsens and requires hospitalisation, or a urinary tract infection that evolves into frank urosepsis.
- To identify, mitigate or prevent, when possible, *risk factors* related either to the patient or as a result of *unintended consequences* from the care delivered to them.
 - age: higher risk in infants and elderly persons than in other age groups³
 - chronic diseases with/without severe organ dysfunction (e.g., chronic obstructive pulmonary disease, cirrhosis, end-stage renal disease, cardiomyopathy, diabetes mellitus, malnutrition, many cancers,^{24, 25} autoimmune disorders, the acquired immunodeficiency syndrome)
 - splenectomy
 - pregnancy is associated with an immunocompromised state, with the result that an infection in a pregnant woman is more likely to evolve to a septic syndrome. In addition physiologic changes during pregnancy can mimic early sepsis.
 - the use of immunosuppressive agents (chemotherapeutic agents, monoclonal antibodies, systemic corticosteroids etc.)
 - the inappropriate use of antibiotics
 - the presence of implanted medical devices (various intravascular (e.g. catheters, grafts, prosthetic heart valves, pacemakers etc.), neurosurgical, orthopedic, urological, gynecological, otolaryngological, ophthalmologic, dental devices)
 - pregnancy (see [Maternal Sepsis](#) on page 17)
 - premature babies and neonates (not discussed in this GSK) have underdeveloped immune systems making it difficult for them to fight infections.

These factors can interact and produce an additive effect on the risk of infection and/or progression to sepsis and acute organ dysfunction. Risk factors specific for sepsis-associated organ dysfunction are less well studied but probably include: the causative organism and the patient's genetic composition, underlying health status and pre-existing organ function, timeliness of therapeutic interventions (e.g. antibiotics,²⁶ age (infants and elderly persons).

Below are some examples:

- In the elderly, dementia may impair the patients' ability to communicate the illness and chronic disease may further impair their immune systems. As well, the effectiveness of the immune system begins to decrease with age making it more difficult for the elderly to fight infections before they spread throughout the body.
- When the normal anatomy is altered by a process that either:
 - Obstructs a normal passage, infection is more likely. This may occur with benign processes (stone(s) in the gallbladder or common bile duct (cholecystitis or cholangitis, respectively), in the renal pelvis or ureter (pyelonephritis), prostatic hypertrophy (prostatitis or cystitis) or malignancy (e.g. cancer of the lung, bile ducts, ureters, bowel, etc.).
 - Breaks a barrier that normally maintains a sterile environment (skin breakdown by trauma, dermatological conditions, etc. leading to soft tissue and joint infections). This may also be due to benign or malignant processes.
- Aspiration of upper digestive contents into the lungs can cause pneumonia leading to sepsis.
- Surgical procedures with known risk of postoperative anastomotic leak or fistulae (e.g. intestinal, pancreatic), e.g. Hartmann's or Whipple's procedure, bowel resection for Crohn's disease, or previously irradiated surgical site.
- Risk factors for and/or inadequate compliance to preventive measures for specific nosocomial events (e.g. ventilator-associated pneumonia, central line, surgical site and urinary tract infections. See Get Started Kits)
<http://www.saferhealthcarenow.ca/EN/Interventions/VAP/Pages/default.aspx>
<http://www.saferhealthcarenow.ca/EN/Interventions/CLI/Pages/default.aspx>
<http://www.saferhealthcarenow.ca/EN/Interventions/RRT/Pages/default.aspx>
- Lack of appropriate vaccination or similar preventive measures for the elderly or people with chronic illnesses or splenectomy.
- In patients with indications for prophylactic antibiotics prior to travel or procedures.

Early Identification

Common sources of sepsis are pneumonia, accounting for about half of all cases, followed by intra-abdominal and urinary tract infections.¹⁹

Symptoms and signs can be helpful in localizing the source of infection. The physical examination may alert the clinician to how sick the patient is and thus the timeline required for successful management. For example, a patient suffering from an infection that has a fever but is in no apparent distress and appears to be comfortable with no other systemic manifestations may have an infection that does not meet the definition of sepsis.

On the other hand, if the patient is described as “looking unwell” or “ill-looking” and has two or more systemic manifestations of infection, he is presumed as having sepsis. If, in addition, the extremities are mottled or display poor capillary refill, or oliguria, hypotension or other signs of hypo perfusion or organ dysfunction, this patient meets the definition criteria for septic illness. In these cases, the septic syndrome remains a working diagnosis until either confirmed by a documented source of infection or better explained by another process in the absence of documentable infection and these patients should be treated accordingly.

Although fever is the most common symptom in sepsis, many other symptoms are also present but are commonly mistaken for other conditions. They include: chills and shaking, arthralgias and myalgias (“body aches”), nausea and vomiting, light-headedness and other flu-like symptoms. Occasionally, there are mild mental status changes, such as confusion, as well as increased fatigue and lethargy. Note that elderly or immunocompromised patients (e.g. neutropenia, immunosuppressive drugs, including systemic steroids, certain malignancies or immune diseases) require more caution (specifically a greater index of suspicion) in identifying and treating sepsis as they may not display this graded clinical response to infection, and may present with features not typical for sepsis, e.g. malaise, increasing fatigue, confusion/delirium, and decreased appetite.

Identifying patients who deteriorate within the hospital secondary to sepsis presents an additional challenge. These populations often have concurrent medical or surgical conditions that confound the diagnosis, making early recognition difficult. The widespread introduction of rapid response systems, by virtue of promoting early identification and initiation of acute interventions, has been a significant adjunct to the care of hospitalized patients with sepsis.²⁷

Screening for sepsis improves early identification and when combined with a management approach as parts of a performance improvement process it decreases sepsis-related mortality.

Response

Whenever sepsis detected, efforts should focus on rapidly managing its manifestations and minimizing the impact of factors that could sustain or worsen it. In the Surviving Sepsis Campaign,¹⁹ the following are recommended:

- early quantitative resuscitation* of the septic patient during the first six hours after recognition , timely administration of antibiotics preceded by blood cultures (see below)
- imaging studies performed promptly to confirm a potential source of infection
- infection source control with attention to the balance of risks and benefits of the chosen method within six to 12 hours of diagnosis²⁸
- reassessment of antimicrobial therapy daily for de-escalation, when appropriate

***Early quantitative resuscitation of the septic patient during the first 6 hours after recognition: has Early Goal-directed Therapy (EGDT) gone out of fashion?**

Since the landmark 2001 trial by Rivers²⁹ early goal-directed therapy (EGDT) for septic illness had become the standard of care. However three recent multicentre trials (ARISE,³⁰ ProCESS,³¹ ProMISe³²) showed no survival advantage with early goal-directed resuscitation in patients presenting to the Emergency Department with septic illness/septic illness, despite good study methodology and protocol adherence but was associated with increased utilization of ICU resources. This conclusion was confirmed in two subsequent meta-analyses.^{33, 34} Specifically these trials did not demonstrate superiority of required use of a central venous catheter (CVC) to monitor central venous pressure (CVP) and central venous oxygen saturation (ScvO2) in all patients with septic illness who have received timely antibiotics and fluid resuscitation compared with controls or in all patients with lactate >4 mmol/L. Thankfully there was no suggestion of harm with the use of a central line in any of the trials. It is believed that early resuscitation and antibiotic administration had already become "usual care" and may have had a significant impact before study randomization in participating centres.

The Surviving Sepsis Campaign was created in 2001 with a main goal to reduce mortality from sepsis by 25 per cent within five years of publication of its first guideline (2009) via a seven-point agenda³⁵ including:

- 1) Building awareness of sepsis;
- 2) Improving diagnosis;
- 3) Increasing the use of appropriate treatment;
- 4) Educating health-care professionals;
- 5) Improving post-ICU care;
- 6) Developing guidelines of care; and
- 7) Implementing a performance improvement program.

It espoused the EGDT (early goal-directed therapy) practice as a central part of care.

At the same time Levy²⁰ published the results of a collaborative change intervention among over 200 hospitals during their first four years as participants in the adoption and implementation of the Surviving Sepsis Campaign (SSC) performance bundles. Increased compliance with SSC bundles was associated with a 25 per cent relative risk reduction in mortality rate. Every 10 per cent increase in compliance and additional quarter of participation in the SSC initiative was associated with a significant decrease in the odds ratio for hospital mortality. Hospital and ICU length of stay decreased four per cent for every 10 per cent increase in site compliance with the resuscitation bundle. These results demonstrated that change interventions could improve clinical behavior, quality of care and decrease mortality in patients with SEPTIC ILLNESS.

When taken together these studies share a common perspective for the management of patients with SEPTIC ILLNESS, i.e. 1) that early recognition, resuscitation, antibiotic administration and source control have become "usual care"; and 2) that dynamic bedside reassessment of perfusion (systemic/organ) in these patients is ensured by repeated clinical examination, evaluation and testing rather than by a mandated catheter or prescriptive approach.

In the light of this new information, the Surviving Sepsis Campaign leadership recently released an updated sepsis management statement³⁶ in which their original three-hour bundle is maintained but the six-hour bundle is revised to reflect the most appropriate approach at this time:

TO BE COMPLETED WITHIN THREE HOURS OF TIME OF PRESENTATION*:

1. Measure lactate level;
2. Obtain blood cultures prior to administration of antibiotics;
3. Administer broad spectrum antibiotics;[§]
4. Administer 30ml/kg crystalloid for hypotension or lactate ≥ 4 mmol/L.

* "Time of presentation" is defined as the time of triage in the emergency department or, if presenting from another care venue, from the earliest chart annotation consistent with all elements of septic illness ascertained through chart review.³⁷

TO BE COMPLETED WITHIN SIX HOURS OF TIME OF PRESENTATION:

5. Apply vasopressors[¶] (for hypotension that does not respond to initial fluid resuscitation) to maintain a mean arterial pressure (MAP) ≥ 65 mmHg;
6. In the event of persistent hypotension after initial fluid administration (MAP < 65 mm Hg) or if initial lactate was ≥ 4 mmol/L, reassess volume status and tissue perfusion and document findings;[□]
7. Re-measure lactate if initial lactate elevated.

[§]administer antibiotics as soon as possible, preferably within the first hour of recognition of septic illness

[¶]norepinephrine is the first-choice vasopressor to maintain mean arterial pressure ≥ 65 mm Hg

†document reassessment of volume status and tissue perfusion with:

Either

- Repeat focused exam (after initial fluid resuscitation) by licensed independent practitioner including vital signs, cardiopulmonary, capillary refill, pulse, and skin findings.

/or two of the following:

- Measure CVP
- Measure ScvO₂
- Bedside cardiovascular ultrasound
- Dynamic assessment of fluid responsiveness with passive leg raise or fluid challenge

Other recommendations:

- Do not wait for intensive care unit transfer to initiate resuscitation measures³⁸
- Seek infection source identification and control early according to the clinical situation
- Reassess antimicrobial therapy daily for de-escalation, when appropriate

Additional Evidence-Based Components of Care

The 2012 Surviving Sepsis Campaign also includes a large number of practice interventions to complement the initial management of septic illness, such as specific aspects of resuscitation fluids, antimicrobials, source and infection control, hemodynamic support and adjunctive therapies and other supportive therapies.¹⁹

The World Federation of Critical Care Nurses developed evidence-based strategies for integrating the Surviving Sepsis Campaign guidelines in nursing practice. These address certain aspects not covered in the Surviving Sepsis publication, such as certain site-specific infection prevention considerations, infection control issues, clinical recognition of the deteriorating septic patient, communication skills, and use of the UK's "Sepsis Six"³⁹ action items: (1-administer high flow oxygen, 2-take blood cultures, 3-give broad spectrum antibiotics, 4-give intravenous fluid challenges, 5-measure serum lactate and hemoglobin, 6-measure hourly urine output).

Pediatric Sepsis

Overwhelming infection is the major cause of death in children worldwide.⁴⁰ Neonates and young infants are at highest risk because their immature immune systems are less able to ward off severe pathogens.⁴¹ Pediatric septic illness remains an important cause for PICU admission and mortality and leads to a substantial burden in healthcare costs.^{42, 43} In two recent reports of US pediatric septic illness^{21, 44} a steady increase in prevalence was observed from 2004 to 2012, which was associated with decreased mortality rates. Age, cardiovascular comorbidity, and organ dysfunction were significant prognostic factors. It was however noted chronically ill children are overrepresented in incidence and mortality rates,⁴⁵ where the US hospital mortality rate for septic illness is two per cent in previously healthy children and eight per cent in chronically ill children.

The importance of the burden of illness caused by pediatric and neonatal sepsis makes its recognition and management a global priority. It is hoped that the inclusion of known strategies in coordinated and thoughtful processes will reduce the global burden of sepsis.^{46, 47}

Consensus guidelines have been developed for pediatric and neonatal sepsis definitions⁴⁸ and practice parameters.^{49,50} Definitions of sepsis, septic illness, and multiple organ dysfunction/failure syndromes are similar to adult definitions but depend on age-specific heart rate, respiratory rate, white blood cell count and blood pressure cut-off values.⁴⁸

Management recommendations specific to pediatric septic illness include: therapy with face mask oxygen, high-flow nasal cannula oxygen, or nasopharyngeal continuous PEEP in the presence of respiratory distress and hypoxemia, use of physical examination therapeutic endpoints such as capillary refill for septic illness associated with hypovolemia, the use of crystalloids or albumin to deliver a bolus of 20 mL/kg of crystalloids (or albumin equivalent) over five to 10 minutes; more common use of inotropes and vasodilators for low-cardiac output septic illness associated with elevated systemic vascular resistance; and use of hydrocortisone only in children with suspected or proven “absolute” adrenal insufficiency.⁵¹ The reader is also directed to the paper “Clinical practice parameters for hemodynamic support of pediatric and neonatal septic illness” for the additional components of pediatric SEPTIC ILLNESS care.⁴⁸ It outlines the American College of Critical Care Medicine-Pediatric Life Support guidelines for the management of pediatric septic illness. As for adults, the approach is stepwise, time-sensitive, and goal-directed.

Despite these guidelines, only a minority of newborns and children receive the standard of care^{52, 53} even in industrialized resource-rich settings with full access to intensive care facilities. Suboptimal care for children with septic illness includes delayed recognition and vascular access¹⁹ inadequate fluid resuscitation,⁵⁴ and delayed antibiotics.⁵⁵

Many barriers to timely resuscitation exist in busy emergency departments (EDs).^{56, 57} Burney noted variability between doctors and nurses in perceived barriers, which perhaps provides opportunities for multidisciplinary collaboration to improve sepsis management.⁵⁸ Cruz et al⁵⁹ reported their results of the implementation of a quality-improvement (QI) intervention to improve early recognition and management of children with septic illness. The protocol

consisted of creating an automated triage tool to recognize vital-sign abnormalities, a shock-team response, a physiologic flow sheet, preprinted order sheets for labs and antibiotics.

When compared with pre-implementation, the protocol resulted in earlier recognition of suspected sepsis, reductions in median time from triage to first bolus and triage to first antibiotics – from 56 to 22 minutes ($P < .001$), and from 130 to 38 minutes ($P < .001$) respectively, and decrement in treatment variation. In a quality improvement project to improve overall sepsis bundle compliance, Paul et al.⁶⁰ demonstrated that by performing rapid cycles of improvement with specific processes, bundle compliance reached 100 per cent and a reduction in mortality. Implementation of these interventions as care bundles with audit and feedback can optimize clinician compliance and prevent nosocomial sepsis from central line-associated bloodstream infections.

Maternal Sepsis

The term *maternal sepsis* refers to sepsis occurring during pregnancy, childbirth and puerperium. It encompasses a complicated clinical scenario due to the presence of an additional patient (the fetus) and significant pregnancy-related alterations in cardiorespiratory, immunological and metabolic functions. Indeed when physiological changes associated with sepsis are superimposed on these normal pregnancy-related changes (elevated cardiac output, resting tachycardia, limited reserve to changes in oxygen delivery, coagulopathy and multi-organ dysfunction), sepsis can become life-threatening, especially for patients with pre-existing cardiorespiratory disease. This is compounded by the relative immune deficiency accompanying normal pregnancy. Although an infrequent complication, maternal sepsis results in significant maternal and fetal morbidity and mortality worldwide. Its reported prevalence in developed countries varies between 0.1 and one per 1000 deliveries, and an estimated one to eight per cent of all obstetric ICU admissions are due to sepsis. These observed differences should be interpreted with caution due to the small numbers of cases and differences in definitions, data collection and clinical management. Nevertheless, a 2005-2007 California database reported that over 50 per cent of cases of maternal sepsis with known risk factors (see below) progressed to severe sepsis and three to four per cent to septic shock.⁶¹

Globally maternal sepsis is the cause of approximately 11 per cent maternal deaths annually, the vast majority occurring in developing regions,^{62, 63, 64} in developed countries it accounts for 2.1 per cent of maternal deaths. The Royal College of Obstetricians and Gynaecologists (RCOG) reported from the 2009-2012 UK registry that one-quarter maternal deaths occurring within the six weeks after pregnancy were due to sepsis;⁶⁵ this was despite a greater than 50 per cent decrease in maternal mortality from genital tract sepsis in the two years preceding the dataset. As a result of these findings the RCOG produced a national guideline on bacterial sepsis in pregnancy in 2012.⁶⁶

Despite a sustained fall in maternal deaths in the last century due to improved socioeconomic conditions and the introduction of antisepsis and antibiotics, there remains a high prevalence of serious acute maternal morbidity as a result of sepsis, even in western countries, in the

order of 0.1 to 0.6 per 1000 deliveries.⁶⁷ These can result either directly to the source of infection (e.g. Genitourinary pelvic pain, acute or chronic pelvic inflammatory disease, bilateral tubal occlusion, secondary infertility, etc.), or to the critical illness and multi-organ dysfunction caused by the septic process itself. In addition to maternal complications, maternal sepsis can result in perinatal complications such as preterm labor and delivery, neonatal sepsis, perinatal hypoxia/acidosis or fetal/neonatal death.⁶⁸

According to the Institute for Health Improvement (IHI) *“seven in 10 maternal septic deaths show evidence of substandard care. And for each death, there are dozens of severe morbidities. Many of these ill effects are preventable...”*⁶⁹

Prevention

Maternal infections can be classified into 1) pregnancy-related infections (e.g. chorioamnionitis, endometritis, mastitis), 2) non-pregnancy-related infections (e.g. urinary tract infection, viral pneumonia), 3) infections incidental to pregnancy (e.g. HIV, appendicitis) and 4) nosocomial infections (e.g. urinary tract infection due to catheterization, pneumonia).⁷⁰

Prevention strategies include hand hygiene, intravaginal application of antiseptics, preoperative skin preparations and appropriate immunizations. Regarding prophylactic antibiotics, further studies are needed to identify the most appropriate type and dosage of their routine use.

The most important causes of septic illness in pregnancy are pyelonephritis, chorioamnionitis and endometritis. The causative microorganisms in severe maternal sepsis are generally polymicrobial, reflecting the vaginal colonization.⁶³ In severe cases of puerperal fever, infection is often caused by Group A Streptococcal (GAS) infection where, in the postpartum period, is often invasive causing necrotizing fasciitis and fulminant streptococcal toxic shock syndrome. In a U.K. national study of severe maternal sepsis 75 per cent of women with a Group A Streptococcal infection had an interval of less than nine hours between the first signs of sepsis and the diagnosis of septic illness; and in 50 per cent of these women, this interval was less than two hours.⁷¹

The incidence of acute medical and surgical emergencies in pregnancy and postpartum leading to septic illness has increased during the past decade and is expected to continue to increase in the future in view of the increasing prevalence of greater maternal age and associated comorbidities (e.g. obesity, diabetes mellitus, placenta previa, and abruptio placenta) and multifetal gestation.

Risk factors for the development of maternal sepsis include all those described earlier for sepsis in non-maternal settings, as well as factors affecting the pregnancy itself, i.e. home birth in unhygienic conditions, low socioeconomic status, history of pelvic infection or of group B streptococcal infection, poor nutrition, diabetes, anemia, primiparity, prolonged rupture of membranes, prolonged labour, multiple pregnancy, pregnancy-related genital manipulation/procedures (multiple (>5) vaginal examinations in labour, cervical cerclage, amniocentesis, artificial reproductive techniques, obstetrical manoeuvres).⁶³

While caesarean section is the single most important risk factor for postpartum infection, unassisted vaginal delivery is an important risk factor in the development of Group A Streptococcal infection, particularly septic illness (see below). In a retrospective cohort study of live births in California⁶¹ of the 1:1,000 live births developing maternal sepsis, Acosta et al observed a significantly increased adjusted odds of progressing to septic illness if mothers were Black (aOR=2.09), Asian (aOR=1.59), Hispanic (aOR=1.42), had public/no-insurance (aOR=1.52), delivered in hospitals with <1,000 births/year (aOR=1.93), were primiparous (aOR=2.03), had a multiple birth (aOR=3.5), diabetes (aOR=1.47), or chronic hypertension (aOR=8.51). Preeclampsia and postpartum hemorrhage were also significantly associated with progression to septic illness (aOR=3.72; aOR=4.18). In this same report, the predominant causes of maternal sepsis varied according to the timing of infection; antenatally, infections of the urinary tract made up about one-third of all cases of maternal sepsis, whereas postnatally, one-third of sepsis was due to genital tract infections.

There is also good evidence that pregnant women are at higher risk of complications of certain specific infections, for example, influenza, varicella zoster, and listeria.

Early identification and initial response

Maternal sepsis can develop very quickly. Early recognition of symptoms and signs, correct diagnosing and coding according to an international classification system and the timely application of evidence-based management can reduce the overall progression of maternal sepsis to the feared complications of septic illness to mother and fetus. This is expected to apply to high-income as well as low-income countries.

The recognition of sepsis during pregnancy is challenging. First, pregnant women are for the most part young and fit and able to physiologically compensate in the presence of infection. Second, it may be difficult to discern simultaneously the effects of fetal/maternal physiologic changes - which vary with the stages of pregnancy - from the effects of sepsis on the clinical presentation. This unique behaviour may explain why pregnant women respond differently to infection.⁷² As examples, sepsis onset in pregnancy can be insidious, and patients may appear deceptively well before rapidly deteriorating with the development of septic illness, multiple organ dysfunction syndrome, or death.⁶⁸

Symptoms such as severe abdominal pain, breathlessness, and diarrhea may be associated with postpartum sepsis. Genital tract sepsis may present with constant severe abdominal pain and tenderness unrelieved by usual analgesia, toxic shock syndrome (staphylococcal or streptococcal) present with nausea, vomiting and diarrhea, exquisite severe pain out of proportion to clinical signs due to necrotizing fasciitis, or a watery vaginal discharge, generalized rash and conjunctival suffusion.⁶⁶

Although little direct evidence exists to validate the extrapolation of some sepsis treatment modalities from other non-pregnant patient populations, approaches like the Surviving Sepsis Campaign guidelines, although unproven, seem reasonable and practical.

As effective maternal resuscitation is the cornerstone for optimizing fetal well-being, the focus should be on the mother. Specific approaches to source identification and choice of antibiotics have been proposed.⁶⁸ The decision for delivery in the setting of antepartum septic

illness can be challenging, although beyond the scope of this starting kit and discussed elsewhere^{65, 70} one should remember the importance of stabilizing the mother first.

The Institute for Healthcare Improvement created an improvement initiative called *Treating Maternal Sepsis*. Created as a web-based, two-session Program, it “...aims to help participants learn how to identify and treat maternal sepsis by sharing screening techniques and treatment protocols geared toward maternal populations...”, and strives to help organizations “...learn the methods to reduce the risk of death and morbidity from this rare but devastating condition.”⁶⁹

Implementing the Strategies

Implementation of sepsis programs involving the Surviving Sepsis Campaign elements of screening, resuscitation and management elements have produced demonstrable improvements in bundle compliance as well as in hospital and 28-day mortality.

In 2005, an implementation study in two British ICUs observed that non-compliance with the six-hour “surviving sepsis” bundle was associated with a more than twofold increase in hospital mortality.⁷³ Non-compliance with the 24-hour bundle resulted in a 76 per cent increase in risk for hospital death. Their conclusion was that the use of sepsis bundles was critical in the care of patients with septic illness.

Since then, several studies observed similar results, showing that in tertiary care and community hospitals alike, improvement programs aimed at adopting practices of early detection and treatment of septic illness reduced hospital mortality.^{74, 75, 76, 77}

In 2010, an implementation of the Surviving Sepsis Campaign guidelines in Spain was associated with significant bundle compliance and decrease in mortality. The six-hour (resuscitation) bundle showed the greatest compliance and effectiveness.⁷⁸ Qualitatively similar results were also observed in a group of septuagenarians with septic illness.⁷⁹

Schramm⁷⁵ showed that in medical ICU patients with septic illness, weekly feedback to clinicians and the activation of a sepsis response team improved both compliance to their sepsis resuscitation bundle (13 per cent to 54 per cent) and hospital mortality (30 per cent to 22 per cent). The sepsis response team was associated with reduced risk of hospital death (odds ratio = 0.66). Of note, bundle compliance was defined as addressing each element through early recognition and a specific therapeutic intervention independent from whether normalization of that parameter was achieved.

In 2013, the multicenter GENESIS project⁸⁰ (GENeralized Early Sepsis Intervention Strategies) demonstrated that patients with septic illness who received the resuscitation bundle had a 14 per cent in-hospital mortality reduction and a 5.1 day decrease in hospital length of stay compared to those who did not. These strategies were associated with one life being saved for every seven treated. These improvements were seen in both the community and tertiary care settings.

During the same year Miller⁷⁶ noted that marked improvements in septic illness bundle compliance were associated with marked reduction in hospital mortality after adjustment for age, severity of illness, and comorbidities in a multicenter ICU cohort. Van Zanten⁷⁷ implemented a national sepsis program in the Netherlands to screen patients for septic illness and implement both Surviving Sepsis Campaign bundles after ICU admission. Over a 3.5 year period they observed small (23.6 per cent), but significant improvements in bundle compliance and a 16.7 per cent relative reduction in mortality (5.8 per cent adjusted absolute mortality reduction) only in participating ICUs, suggesting direct impact of sepsis screening and bundle application on in-hospital mortality. Over the same period a small but significant mortality reduction of 1.9 per cent was observed in screened patients with other diagnoses but not in non-screened patients neither in participating ICUs, nor in patients with sepsis or other diagnoses in non-participating ICUs.

Jones⁸¹ found that the implementation of early goal-directed therapy in the emergency department care of their patients with septic illness was cost-effective (cost of \$5,397 per quality-adjusted life-years gained).

Recently, Barsuk⁸² showed that the dissemination of a simulation-based mastery learning curriculum in central venous catheter insertion at a community hospital significantly improved trainee skills (from 35 per cent to 93 per cent) and decreased CLABSI rates (from 3.82 to 1.29 infections per 1000 catheter-days).

The Surviving Sepsis Campaign (SSC) partnered with the Institute for Healthcare Improvement (IHI) to develop an implementation guide:

<http://www.survivingsepsis.org/Guidelines/Pages/default.aspx>

<http://www.survivingsepsis.org/Improvement/Pages/Implementation-Kit.aspx>

It provides how-to guidance regarding teams, establishing process and outcome measures, setting aims, creating a protocol, educating users, and a detailed description of sepsis bundles and other supportive therapies. For example, it suggests successful SSC adoption requires a hospital champion who can coordinate the LEADER steps outlined below:

- Learn about sepsis and quality improvement by attending local and national sepsis meetings.
- Establish a baseline in order to convince others that improvement is necessary and to make your measurements relevant.
- Ask for buy-in from institutional leadership and seek initial support from the emergency department (ED) and ICU staff and directors, quality improvement personnel, nursing staff, and others.
- Develop an institution-specific SSC protocol comprising all bundle elements.
- Educate stakeholders in the ED and ICU and floors according to shift schedules.
- Remediate errors and anticipate obstacles along the way.

Similarly, the British Columbia Patient Safety and Quality Council (BCPSQC) produced an evidence-based 'Getting Started Kit' for sepsis improvement.⁸³

Forming the Team

One important success factor for a team is its commitment to work together toward a shared aim. Determine what areas of the system and disciplines should participate. Ensure that team members can meet frequently, and work efficiently and effectively to institute change.

Three different types of expertise are required:

- day-to-day leadership
- technical expertise
- system leadership

There may be one or more individuals who represent these areas or one individual may represent more than one type of expertise.

Day-to-Day Leadership

The team needs front-line people who work in and on the process on a daily basis and who will understand the effects of the planned changes. These people have the desire and ability to drive the project to its aim. Day-to-day leadership includes a team leader (often called a “Champion”) who provides an understanding of expectations and scope, and leads activities to accomplish the desired results.

Technical Expertise

The team needs a subject-matter expert who understands the targeted topic and process of care. Additional support may be provided in using the Model for Improvement, designing and testing changes, facilitating meetings, collecting and interpreting data, and preparing presentations.

System Leadership

The team needs a sponsor with enough influence within the organization to implement and sustain the changes. The sponsor must be able to support the team with time and resources to achieve the aim and remove any barriers to success.

Membership on most teams includes an administrator, a physician, a nurse and allied health professionals who work on the process of care under consideration (e.g. respiratory therapists, laboratory personnel). The size of effective teams usually ranges from three to eight members. Others may participate as extended or ad hoc team members by providing input into plans and participating in tests of change.

An Improvement Charter can be used to help teams to document membership, roles and responsibilities, and principles for working together. This document may help provide a base for communication within the team and to sponsors and other stake-holders. The Charter may prevent problems down the road.

Some suggestions to attract and retain excellent team members include:

- engage team members in the overall goal;
- find champions and opinion leaders within the hospital to lend the effort immediate credibility;

- use data and stories to define and solve the problem;
- work with those who want to work on the project, rather than trying to convince those who do not;
- schedule meetings in advance with dates/times that are friendly to all;
- ensure that meetings are purposeful and structured (agenda and minutes);
- ensure meetings are managed effectively (attention to time allocation);
- ensure that there is clarity about task delegation and timelines.

Using the Model for Improvement

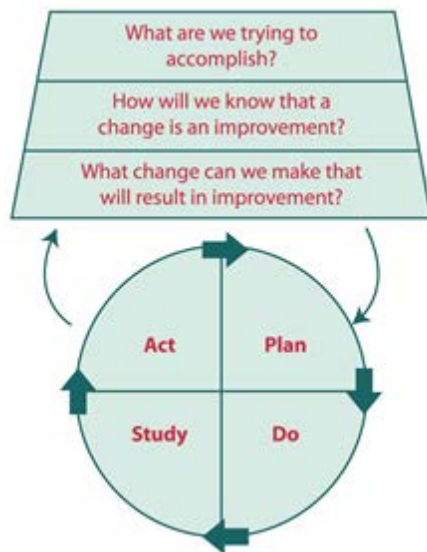
In order to move this work forward, *Safer Healthcare Now!* and the Institute for Healthcare Improvement (IHI) recommend using the Model for Improvement.⁸⁴ Developed by Associates in Process Improvement, the Model for Improvement is a simple yet powerful tool for accelerating improvement that has been used successfully by hundreds of health-care organizations to improve many different health-care processes and outcomes.

The model has two parts:

- Three fundamental questions that guide improvement teams to:
 - 1) set clear aims;
 - 2) establish measures that will tell if changes are leading to improvement; and
 - 3) identify changes that are likely to lead to improvement.
- The Plan-Do-Study-Act (PDSA) cycle to conduct small-scale tests of change in real work settings — by planning a test, trying it, observing the results, and acting on what is learned. This is the scientific method, used for action-oriented learning. After testing a change on a small scale, learning from each test, and refining the change through several PDSA cycles, the team can implement the change on a broader scale — for example, for an entire pilot population or on an entire unit.

After successful implementation of a change or package of changes for a pilot population or an entire unit, the team can spread the changes to other parts of the organization or to other organizations.

Summary: The Model for Improvement



Setting Aims

They should be time-specific and measurable; and also define the specific population of patients or other system that will be affected.

Establishing Measures

Teams use quantitative measures to determine if a specific change actually leads to an improvement.

Selecting Changes

Ideas for change may come from the insights of those who work in the system, from change concepts or other creative thinking techniques, or by borrowing from the experience of others who have successfully improved.

Testing Changes

The Plan-Do-Study-Act (PDSA) cycle is shorthand for testing a change in the real work setting — by planning it, trying it, observing the results, and acting on what is action-oriented learning.

Setting Aims

“The first step in improving the care of patients with septic illness is making a solid commitment to improving that care. This commitment includes a strong and well-worded aim statement that sets an aggressive global aim. It is critical that the overall aim has a measurable objective and a specified time frame” (Surviving Sepsis Campaign).

Improvement requires setting aims. An organization will not improve without a clear and firm intention to do so. Teams are more successful when they have unambiguous, focused aims. The aim should be time-specific and measurable; it should also define the specific population of patients that will be affected. You may choose to target a particularly high-risk patient population, say all medical CTU patients, or all patients receiving immunosuppressive/chemotherapeutic medications etc. Agreeing on the aim is crucial, as is allocating the people and resources necessary to accomplish the aim.

Setting numerical goals clarifies the aim, helps to create tension for change, directs measurement and focuses initial changes. Once the aim has been set, the team needs to be careful not to back away from it deliberately or “drift” away from it unconsciously.

- For sepsis, the “global” aim is to decrease incidence of sepsis by a certain proportion over a specified timeframe. In addition, below are several examples of “sub-aims” or “specific objectives” that could contribute to achieving the global aim, such as: Improve percentage of patients screened for sepsis to 100 per cent for all patients admitted to the unit.

- Reduce time from clinical presentation* to presumptive diagnosis of septic illness to less than two hours.
- Reduce time from clinical presentation* to all patients' meeting septic illness criteria having a serum lactate to less than three hours.
- Reduce time from clinical presentation* to appropriate antibiotics administered to less than one hour.
- Improve the percentage of patients with septic illness and hypotension refractory to fluid resuscitation who receive vasopressors within six hours from time of presentation.*

*Time of (clinical) presentation is defined as the time of triage in the emergency department or, if presenting from another care venue (e.g. wards, ICU etc.), from the earliest chart annotation consistent with all elements of septic illness ascertained through chart review.³⁶

Establishing Measures

It is important to know whether changes are leading to improvement and when goals have been achieved. It is recommended that teams collect data for two to six useful measures.

Below are some examples of measures that could be useful:

1. 28 Day In-Hospital Mortality Rate from Septic Illness
2. Percentage of Patients Having Received IV Antibiotics within 3 Hours of Time of Presentation
3. Percentage of Patients Having Had Blood Cultures Taken before IV Antibiotics were Initiated
4. Percentage of Patients Having Had an Appropriate Fluid Challenge within the Appropriate Time
5. Percentage of Patients with Appropriate Initial Lactate Measurement
6. Percentage of Patients with Appropriate Repeat Lactate Measurement

See [Appendix A](#) for Technical Descriptions of Measures.

Please note, although we have chosen to use the term "*septic illness*", which as described earlier groups the definitions of *severe sepsis* and *septic shock*, in establishing our clinical indicators, this does not prevent teams who so desire to monitor their rate or outcomes from severe sepsis or septic shock separately.

Use a data collection form, such as the worksheets in [Appendix A](#). Using a data collection form makes it easier to create run charts each month.

Improvement takes place over time. Determining if improvement has really occurred and if it is a lasting effect requires observing patterns over time. Run charts are graphs of data over time and are one of the single most important tools in performance improvement. Using run charts has a variety of benefits:

- They help improvement teams formulate aims by depicting how well (or poorly) a process is performing;
- They help in determining when changes are truly improvements by displaying a pattern of data that you can observe as you make changes;
- They give direction as you work on improvement and information about the value of particular changes.

Developing, Testing and Implementing Changes

Hospitals will not successfully test and implement changes overnight. A successful program involves careful planning, testing to determine if the process is successful, making modifications as needed, re-testing, and careful implementation. Once a team has prepared the way for change by studying the current process and educating the key stakeholders, the next step is to begin testing Sepsis change ideas. Teams that are just starting can begin by testing and implementing one component at a time, working towards consistently implementing all components of the Sepsis Change Package:

- Make sure that the approach is carried over from shift to shift, to eliminate gaps in teaching and utilization;
- Process feedback and incorporate suggestions for improvement;
- Begin using the Sepsis Change Ideas with one patient, for one day with one provider;
- Use PDSA cycles to introduce elements of the change package. Engage in subsequent PDSA cycles to refine the process and make it more reliable.

Barriers That May Be Encountered

- **Fear of change**
All change is difficult. The antidote to fear is knowledge about the deficiencies of the present process and optimism about the potential benefits of a new process.
- **Communication breakdown**
Organizations have not been successful when they failed to communicate with staff about the importance of ventilator care, as well as when they failed to provide ongoing teaching as new staff become involved in the process.
- **Physician & staff “partial buy-in”** (e.g., “Just another flavour of the week”). In order to enlist support and engage staff, it is important to share current baseline data on sepsis rates and to share the results of improvement efforts. If the run charts suggest a large increase in rates percentage of patients screened for sepsis screening or in percent compliance with sepsis preventive strategies compared to baseline, issues surrounding “buy-in” tend to fade. Often a story of a recent patient, including the perspective of the patient’s perceptions of the clinical team/environment will support the need to change practice.

Appendix A: Technical Descriptions and Data Screens

Technical Description of the Measurement Worksheets:

Implementation Stages - Definitions apply to all interventions and measures

Baseline Stage (Pre-intervention) - Data collected for Baseline should be collected prior to implementing small tests of change and reflect the current process.

Early (Partial) Implementation Stage - The team has set a clear aim(s) for the Sepsis intervention, identified which measures will indicate if the changes will lead to improvement, and started to implement small tests of change (PDSA) to identify and refine processes, procedures and practices which will lead to improvement and achieving the aim. When the team is close to goal they are ready to move to Full Implementation.

Full Implementation Stage (At Goal) - The processes, procedures and practices are finalized and have led to significant improvement. These practices on the selected unit are being consistently applied and monitored, showing a sustained performance at or close to goal. The team has achieved (and sustained) their aim(s) and is ready to spread to other areas.

The measurement methodology and recommendations regarding sampling size referenced in this GSK, is based on The Model for Improvement and is designed to accelerate the pace of improvement using the PDSA cycle; a "trial and learn" approach to improvement based on the scientific method.¹

It is not intended to provide the same rigor that might be applied in a research study, but rather offers an efficient way to help a team understand how a system is performing. When choosing a sample size for your intervention, it is important to consider the purposes and uses of the data and to acknowledge when reporting that the findings are based on an "x" sample as determined by the team.

The scope or scale² (amount of sampling, testing, or time required) of a test should be decided according to:

1. The team's degree of belief that the change will result in improvement
2. The risks from a failed test
3. Readiness of those who will have to make the change

Please refer to the [Improvement Frameworks GSK \(2015\)](#) for additional information.

¹ Langley, G., Nolan, K., Nolan, T., Norman, C., Provost, L. The Improvement Guide: A Practical Approach to Enhancing Organizational Performance. San Francisco, Second Edition, CA. Jossey-Bass Publishers. 2009

² Provost, Lloyd P; Murray, Sandra (2011-08-26). The Health Care Data Guide: Learning from Data for Improvement (Kindle Locations 1906-1909). Wiley. Kindle Edition

Definitions

The following definitions apply to all SEPSIS measures:

Septic Illness: Refer to [Table 1](#) for operational definition. As mentioned earlier, improvement teams may choose in addition to monitor their rate or outcomes from severe sepsis or septic shock separately.

Age Groups: The clinical variables used to define systemic inflammatory response syndrome (SIRS) and organ dysfunction are greatly affected by the normal physiologic changes that occur as children age.⁴⁷ Therefore, definitions of the sepsis continuum in children rely on age specific norms of vital sign and laboratory data. Six clinically and physiologically meaningful age groups for age-specific vital sign and laboratory variables to meet SIRS criteria are proposed: newborn, neonate, infant, toddler and preschool, school-aged child, adolescent, and young adult.⁴⁷ The SHN Sepsis faculty recommends that Sepsis data are collected and analysed separately for pediatrics and adults as follows:

Newborn	0 days to 1 week
Neonate	1 week to 1 month
Infant	1 month to 1 year
Toddler and preschool	2-5 years
School age child	6-12 years
Adolescent and young adult	13 to <18 years
Adult	> 18 years

Blood culture: a microbiological culture of blood used to detect infections that are spreading through the bloodstream (such as bacteremia, septicemia etc.). Obtaining multiple sets of cultures increases the probability of discovering a pathogenic organism in the blood and reduces the probability of having a positive culture due to skin contaminants.

Hypotension: Systolic Blood Pressure < 90 mm Hg, MAP < 70 mm Hg, or an SBP decrease > 40 mm Hg in adults or < 2SD below normal for age

Patient Population: is defined as all patients identified, through screening at Time of Presentation, as meeting criteria for septic illness. Adult and Pediatric patients (age 18 cut-off) should be tabulated separately.

Time of Presentation: is defined as the time of triage in the emergency department or, if presenting from another care venue, from the earliest chart annotation consistent with all elements of septic illness ascertained through chart review.

1.0 Percentage of 28 day in-hospital mortality rate from septic illness - Sample Worksheet

Sepsis 1 - Percentage of 28 day in-hospital mortality rate from septic illness (In Patient, Adult, DEMO)

Year Month

The number of in-hospital deaths within 28 days of time of presentation in the patient population identified with septic illness. Septic illness includes severe sepsis and septic shock (see definitions). Reported as mortality rate in percent for the identified sepsis population.

Denominator1 Count of all patients identified, through screening at time of presentation, as meeting criteria for septic illness. **Numerator**2 Mortality – the number of patients identified with septic illness that died in-hospital within 28 days of the time of presentation. **Your Result**

3 Numerator / Denominator x 100

Your Result Goal 25% or less

1.0 Percentage of 28 day in-hospital mortality rate from septic illness - Technical Description

Intervention(s): Sepsis - Prevention, Early Identification and Response

Definition: The number of in-hospital deaths within 28 days of time of presentation in the patient population identified with septic illness. Septic illness includes severe sepsis and septic shock (see [Definitions](#)). Reported as mortality rate in percent for the identified sepsis population.

Significance: Septic illness increases morbidity, mortality and costs. This can be managed using evidence-based interventions. This measure can be used to detect changes related to implementation or lack of adherence to these best practices.

Standard Goal: 25 per cent ^{28, 29, 30}

Note: Sustain the mortality rate at 25 per cent or less among septic patients over time

CALCULATION DETAILS:

Numerator Definition: Mortality - the number of patients identified with septic illness that died in-hospital within 28 days of the time of presentation.

Note: The 'time of presentation' is defined in '[Definitions](#)' section page 28

Numerator Exclusions:

- Same exclusions as for denominator

Denominator Definition: Count of all patients identified, through screening at time of presentation, as meeting criteria for septic illness (defined in '[Definitions](#)' section page 28).

Denominator Exclusions:

- Age group defined (see '[Definitions](#)' section page 28)

Data Collection Method:

Data is to be collected through a surveillance process that includes monitoring patients for mortality at 28 days post presentation, including those patients who may be transferred from the intensive care unit. A process to record and tabulate the total number of patients identified in the patient population is also required.

Measurement Period: Monthly

Definition of Terms: see '[Definitions](#)' section page 28

Calculate as: (numerator / denominator) expressed as a percentage rate

<p>Example of the Calculation:</p> <p>No. of patients identified with septic illness that died in-hospital within 28 days of the time of presentation</p> <p>-----</p> <p>Total no. of patients identified with septic illness at the time of presentation</p>	<p>X 100 =</p>	<p>Percentage 28 day in-hospital mortality rate from septic illness</p>
<p>Comments:</p> <ul style="list-style-type: none"> In addition to factors related to individual caregiver or systemic factors affecting care delivery, this rate may also vary according to patient case mix (proportion of patients with septic shock, risk factors for clinical deterioration from sepsis) and to pre-hospital factors. 		
<p>COLLECTION STRATEGY:</p> <p><i>Safer Healthcare Now!</i> recommends that teams complete concurrent or “real time” data collection as much as possible. The ability to sustain data collection is higher if you integrate data collection into day-to-day work. However, if a team decides to collect their data using retrospective chart reviews then a hospital information system may be able to identify the patients from all discharges by sorting based on these elements. Another alternative is to work with the coding or medical records department to identify the patients at the time of coding and prepare a list or set aside records for review.</p>		
<p>SAMPLING STRATEGY:</p> <p><i>Safer Healthcare Now!</i> recommends that you monitor all patients identified as having septic illness at time of presentation either for the entire facility or specific unit e.g. ICU.</p>		

2.0 Percentage of patients with septic illness who received IV antibiotics within three hours of time of presentation - Sample Worksheet

— Sepsis 2 - Percentage of patients with septic illness who received IV antibiotics within 3 hours of time of presentation (In Patient, Adult, DEMO)

Year Month

The number of patients with septic illness who received IV antibiotics within 3 hours of time of presentation. Timing should be sooner (e.g. within 1 hour) according to the severity of clinical presentation (unstable vital signs/hemodynamics), the abnormalities in tissue perfusion and/or organ dysfunction and to propensity of deterioration.

Denominator

1 Total number of patients identified, through screening at time of presentation, as meeting criteria for septic illness.

Numerator

2 The number of patients identified as meeting criteria for septic illness at the time of presentation who received IV antibiotics within 3 hours of presentation.

Your Result

3 Numerator / Denominator x 100

Your Result

Goal 95%

2.0 Percentage of patients with septic illness who received IV antibiotics within three hours of time of presentation - Technical Description

Intervention: Sepsis - Prevention, Early Identification and Response

Definition: The number of patients with septic illness who received IV antibiotics within three hours of time of presentation. Timing should be sooner (e.g. within one hour) according to the severity of clinical presentation (unstable vital signs/hemodynamics), the abnormalities in tissue perfusion and/or organ dysfunction (see definition of septic illness) and to propensity of deterioration (see risk factors).

Significance: The timing of IV antibiotic delivery for septic illness patients is an important consideration to decrease morbidity, mortality and costs

Standard Goal: 95 per cent or higher^{28, 29, 30}

Note: Sustain the percentage of septic patients receiving antibiotic within three hours at 95 per cent or higher

CALCULATION DETAILS:

Numerator Definition: The number of patients identified as meeting criteria for septic illness at the time of presentation who received IV antibiotics within three hours of presentation.

Note: The 'time of presentation' is defined in '[Definitions](#)' section page 28

Numerator Exclusions:

- Same exclusions as for denominator

Denominator Definition: Total number of patients identified, through screening at time of presentation, as meeting criteria for septic illness (defined in '[Definitions](#)' section page 28).

Denominator Exclusions:

- Age group defined (see '[Definitions](#)' section page 28)

Data Collection Method:

A process is required that indicates the total elapsed time between the time of presentation and the first administration of IV antibiotics. A process to record and tabulate the total number of patients identified in the Patient Population is also required.

Measurement Period: Monthly

Definition of Terms: see '[Definitions](#)' section page 28

Calculate as: (numerator / denominator); as a percentage

<p><i>Example of the Calculation:</i></p> <p>No. of pts. identified with septic illness who received IV antibiotics within three hours of time of presentation</p> <p>-----</p> <p>Total no. of pts. identified with septic illness in this reporting period</p>	<p>X 100 =</p>	<p>Percentage of patients who received IV antibiotics within three hours of time of presentation</p>
<p>COLLECTION STRATEGY:</p> <p><i>Safer Healthcare Now!</i> recommends that teams complete concurrent or “real time” data collection as much as possible. The ability to sustain data collection is higher if you integrate data collection into day-to-day work. However, if a team decides to collect their data using retrospective chart reviews then a hospital information system may be able to identify the patients from all discharges by sorting based on these elements. Another alternative is to work with the coding or medical records department to identify the patients at the time of coding and prepare a list or set aside records for review.</p>		
<p>SAMPLING STRATEGY:</p> <p><i>Safer Healthcare Now!</i> recommends that you monitor all patients identified as having septic illness at time of presentation either for the entire facility or specific unit e.g. ICU.</p>		

3.0 Percentage of patients with septic illness who had blood cultures taken before IV Antibiotics were initiated - Sample Worksheet

— Sensus 3 - Percentage of patients with septic illness who had blood cultures taken before IV Antibiotics were initiated (In Patient, Adult, DEMO)

Year Month

The percentage of patients with septic illness who had blood cultures taken prior to the IV Antibiotics being administered.	
Denominator	
1 Total number of patients identified, through screening at time of presentation, as meeting criteria for septic illness who received IV antibiotics.	<input type="text"/>
Numerator	
2 The total number of patients with septic illness who had blood cultures taken before antibiotic administration.	<input type="text"/>
Your Result	
3 Numerator / Denominator x 100	Your Result <input type="text"/>
	Goal 85% <div><div></div></div>

3.0 Percentage of patients with septic illness who had blood cultures taken before IV Antibiotics were initiated - Technical Description

Intervention(s): Sepsis - Prevention, Early Identification and Response

Definition: The percentage of patients with septic illness who had blood cultures taken prior to the IV Antibiotics being administered

Significance: Taking blood cultures prior to IV antibiotic delivery is sound medical practice. It allows to i) identify a pathogenic organism relevant to the septic illness, ii) as a corollary to help identify the source of infection according to the probability of the microorganism's host residence, and iii) adjust the most appropriate antimicrobial coverage according to in vitro susceptibility testing.

Standard Goal: 85 per cent^{17, 75, 77, 78}

Note: Increase the percentage of patients with septic illness who had blood cultures drawn prior to antibiotic administration every year

CALCULATION DETAILS:

Numerator Definition: The total number of patients with septic illness who had blood cultures taken before antibiotic administration

Numerator Exclusions: Same exclusions as for denominator exclusions

Denominator Definition: Total number of patients identified, through screening at time of presentation, as meeting criteria for septic illness (defined in 'Definitions' section page 28) who received IV antibiotics.

Denominator Exclusions:

- Age group defined (see 'Definitions' section page 28)

Data Collection Method:

A process is required to identify the number of patients who had blood cultures taken prior to administration of IV antibiotics and tabulate the total number of patients identified in the patient population who received antibiotics.

Measurement Period: Monthly

Definition of Terms: see 'Definitions' section page 28

Calculate as: (numerator / denominator); as a percentage

<p>Example of the Calculation:</p> <p>No. of patients with septic illness who received antibiotics and who had blood cultures taken before antibiotic administration</p> <p>-----</p> <p>Total no. of pts. identified with septic illness who received IV antibiotics in this reporting period</p>	<p>X 100 =</p>	<p>Percentage of patients with septic illness who had blood cultures taken before IV antibiotics were administered</p>
<p>Comments :</p> <p><i>Safer Healthcare Now!</i> recommends:</p> <ul style="list-style-type: none"> Although this should be considered as a “best” practice, there may be logistical reasons why it was not implemented, i.e. antibiotics were initiated before blood sampling could be performed, not enough blood could be obtained for culture, etc. This would then oblige maintaining a broad empirical antimicrobial coverage until a change is warranted by clinical evolution or new clinical information. 		
<p>COLLECTION STRATEGY:</p> <p><i>Safer Healthcare Now!</i> recommends that teams complete concurrent or “real time” data collection as much as possible. The ability to sustain data collection is higher if you integrate data collection into day-to-day work. However, if a team decides to collect their data using retrospective chart reviews then a hospital information system may be able to identify the patients from all discharges by sorting based on these elements. Another alternative is to work with the coding or medical records department to identify the patients at the time of coding and prepare a list or set aside records for review.</p>		
<p>SAMPLING STRATEGY:</p> <p><i>Safer Healthcare Now!</i> recommends that you monitor all patients identified as having septic illness at time of presentation either for the entire facility or specific unit e.g. ICU.</p>		

4.0 Percentage of Patients with septic illness having had appropriate fluid challenge for hypotension or lactatemia within the appropriate time - Sample Worksheet

— Sepsis 3 - Percentage of patients with septic illness who had blood cultures taken before IV Antibiotics were initiated (In Patient, Adult, DEMO)

Year Month

The percentage of patients with septic illness who had blood cultures taken prior to the IV Antibiotics being administered.	
Denominator	
1 Total number of patients identified, through screening at time of presentation, as meeting criteria for septic illness who received IV antibiotics.	<input type="text"/>
Numerator	
2 The total number of patients with septic illness who had blood cultures taken before antibiotic administration.	<input type="text"/>
Your Result	
3 Numerator / Denominator x 100	Your Result <input type="text"/> Goal 85% <div style="width: 85%; background-color: #4f81bd; height: 10px;"></div>

4.0 Percentage of Patients with septic illness having had appropriate fluid challenge for hypotension or lactatemia within the appropriate time - Technical Description

Intervention(s): Sepsis - Prevention, Early Identification and Response

Definition: The percent of patients with septic illness who had a 30ml/kg infusion of crystalloid initiated within 60 minutes of onset of hypotension or of lactate ≥ 4 mmol/L

Significance: Initiating an appropriate (i.e. timely and adequate) fluid challenge within 60 minutes of hypotension or hypoperfusion indicates ongoing active resuscitation by correcting the deficient cardiovascular preload.

Standard Goal: 95 per cent or higher^{28, 29, 30}

Note: Sustain the percentage of patients with septic illness who had an appropriate infusion of crystalloid initiated within 60 minutes of onset of hypotension or lactate ≥ 4 mmol/L at 95 per cent or higher

CALCULATION DETAILS:

Numerator Definition: Number of patients with septic illness who had a 30ml/kg infusion of crystalloid initiated within 60 minutes of onset of hypotension or lactate ≥ 4 mmol/L.

Numerator Exclusions:

- Same exclusions as for denominator

Denominator Definition: Total number of patients with septic illness who met the criteria for hypotension or had lactate ≥ 4 mmol/L.

Denominator Exclusions:

- Age group defined (see '[Definitions](#)' section page 28)

Data Collection Method:

A process is required for identifying the number of patients with septic illness who

1. were hypotensive or had an elevated lactate ≥ 4 mmol/L and
2. had an appropriate fluid challenge (at least 30ml/kg of crystalloid) initiated within 60 minutes of onset of hypotension or lactate ≥ 4 mmol/L.

Measurement Period: Monthly

Definition of Terms: see '[Definitions](#)' section page 28

Calculate as: (numerator / denominator); as a percentage

<p>Example of the Calculation:</p> <p>No. of pts. with septic illness who had an appropriate infusion of crystalloid (at least 30ml/kg) initiated within 60 minutes of onset of hypotension or lactate \geq 4mmol/L.</p> <p>-----</p> <p>Total no. of pts. identified with septic illness who met the criteria for hypotension or had lactate \geq 4 mmol/L in this reporting period</p>	<p>X 100 =</p>	<p>Percentage of patients with septic illness who had an appropriate fluid challenge initiated within the appropriate time.</p>
<p>Comments :</p> <ul style="list-style-type: none"> This indicator is a surrogate for active fluid resuscitation. It should not overshadow careful bedside reassessment of ongoing volume needs and responsiveness. Although compliance to fluid administration of at least 90 per cent has been documented, the current indicator has not been specifically evaluated in clinical trials. 		
<p>COLLECTION STRATEGY:</p> <p><i>Safer Healthcare Now!</i> recommends that teams complete concurrent or “real time” data collection as much as possible. The ability to sustain data collection is higher if you integrate data collection into day-to-day work. However, if a team decides to collect their data using retrospective chart reviews then a hospital information system may be able to identify the patients from all discharges by sorting based on these elements. Another alternative is to work with the coding or medical records department to identify the patients at the time of coding and prepare a list or set aside records for review.</p>		
<p>SAMPLING STRATEGY:</p> <p><i>Safer Healthcare Now!</i> recommends that you monitor all patients identified as having septic illness at time of presentation either for the entire facility or specific unit e.g. ICU.</p>		

5.0 Percentage of patients with appropriate initial lactate measurement - Sample Worksheet

— Sepsis 5 - Percentage of patients with appropriate initial lactate measurement (In Patient, Adult, DEMO) —

Year Month

The percent of patients with septic illness who had an initial blood sample for serum lactate obtained within 30 minutes from the time of presentation.

Denominator1 Total number of patients with septic illness. **Numerator**2 Number of patients with septic illness who had an initial blood sample for serum lactate obtained within 30 minutes from the time of presentation. **Your Result**

3 Numerator / Denominator x 100

Your Result

Goal 95%

5.0 Percentage of patients with appropriate initial lactate measurement - Technical Description

Intervention(s): Sepsis: Prevention, Early Identification and Response

Definition: The per cent of patients with septic illness who had an initial blood sample for serum lactate obtained within 30 minutes from the time of presentation

Significance: An elevated blood lactate level ($\geq 4\text{mmol/L}$) in the context of sepsis is suggestive of tissue hypo-perfusion and as such carries with it a higher mortality when compared to a normal lactate level. Furthermore, such an abnormal finding helps guide the clinician during resuscitation in order to more rapidly restore perfusion in the midst of sepsis care.

Standard Goal: 95 per cent or higher^{28, 29, 30}

Note: Sustain the percentage of patients with septic illness who had an initial lactate measured at 95 per cent or higher.

CALCULATION DETAILS:

Numerator Definition: Number of patients with septic illness who had an initial blood sample for serum lactate obtained within 30 minutes from the time of presentation.

Numerator Exclusions:

- Same exclusions as for denominator

Denominator Definition: Total number of patients with septic illness.

Denominator Exclusions:

- Age group defined (see '[Definitions](#)' section page 28)

Data Collection Method:

A process is required to identify the number of patients who had an initial lactate taken within 30 minutes from the time of presentation.

A process to record and tabulate the total number of patients with septic illness.

Measurement Period: Monthly

Definition of Terms: see '[Definitions](#)' section page 28

Calculate as: (numerator / denominator); as a percentage

<p>Example of the Calculation:</p> <p>No. of pts. with septic illness who had an initial blood sample for serum lactate obtained within 30 minutes from the time of presentation</p> <p>-----</p> <p>Total number of patients with septic illness in this reporting period</p>	<p>X 100 =</p>	<p>Percentage of patients with appropriate initial lactate measurement</p>
---	----------------	--

Comments:

The simplest way to comply would be to request a lactate level with the initial blood drawn at the time of presentation (see ‘[Definitions](#)’ section page 28). Alternatively, lactate measurement could be reserved to patients meeting two or more “general” criteria of systemic manifestation (see ‘[Definitions](#)’ section page 28) and in addition has any of the following: looks unwell, age > 65 years, recent surgery, immunocompromised (AIDS, chemotherapy, neutropenia, asplenia, transplant, chronic steroids) or chronic illness (diabetes, renal failure, hepatic failure, cancer, alcoholism, IV drug use). Compliance with this intervention has been reported between 91 to 97 per cent in recent trials.^{75, 77}

COLLECTION STRATEGY:

Safer Healthcare Now! recommends that teams complete concurrent or “real time” data collection as much as possible. The ability to sustain data collection is higher if you integrate data collection into day-to-day work. However, if a team decides to collect their data using retrospective chart reviews then a hospital information system may be able to identify the patients from all discharges by sorting based on these elements. Another alternative is to work with the coding or medical records department to identify the patients at the time of coding and prepare a list or set aside records for review.

SAMPLING STRATEGY:

Safer Healthcare Now! recommends that you monitor all patients identified as having septic illness at time of presentation either for the entire facility or specific unit e.g. ICU.

6.0 Percentage of patients with septic illness with appropriate repeat lactate measurement - Sample Worksheet

– Sepsis 6 - Percentage of patients with septic illness with appropriate repeat lactate measurement (In Patient, Adult, DEMO) –

Year Month

Percentage of patients with septic illness who had blood sample for repeat serum lactate obtained within 4 hours of an initially elevated Lactate Measurement.

Denominator

1 Total number of patients with septic illness who had an initial serum lactate value ≥ 4 mmol/L.

Numerator

2 Number of patients with septic illness who had a second lactate measured within 4 hours after the initial elevated lactate measurement.

Your Result

3 Numerator / Denominator x 100

Your Result

Goal 95%

6.0 Percentage of patients with septic illness with appropriate repeat lactate measurement - Technical Description

Intervention(s): Sepsis - Prevention, Early Identification and Response

Definition: Percentage of patients with septic illness who had blood sample for repeat serum lactate obtained within four hours of an initially elevated Lactate Measurement

Significance: A decrease in blood lactate from a previously elevated value in the context of septic illness normally occurs within two to four hours of resuscitative interventions, and is suggestive of tissue reperfusion

Standard Goal: 95 per cent or higher^{28, 29, 30}

Note: Sustain the percentage of patients with septic illness who had a repeat serum lactate measured within four hours of the initially elevated sample at 95 per cent or higher

CALCULATION DETAILS:

Numerator Definition: Number of patients with septic illness who had a second lactate measured within 4 hours after the initial elevated lactate measurement.

Numerator Exclusions:

- Same exclusions as for denominator

Denominator Definition: Total number of patients with septic illness who had an initial serum lactate value ≥ 4 mmol/L.

Denominator Exclusions:

- Age group defined (see '[Definitions](#)' section page 28)
- Serum lactate never ≥ 4 mmol/L

Data Collection Method:

A process is required to identify the number of patients with septic illness who had a second lactate taken within 4 hours after the initial lactate measurement.

A process to record and tabulate the total number of patients with septic illness who had an initial lactate measurement ≥ 4 mmol/L.

Measurement Period: Monthly

Definition of Terms: see '[Definitions](#)' section page 28

Calculate as: (numerator / denominator); as a percentage

<p>Example of the Calculation:</p> <p>No. of pts with septic illness who had a second lactate measured within 4 hours after the initial elevated lactate measurement</p> <p>-----</p> <p>Total number of patients with septic illness who had an initial serum lactate value ≥ 4 mmol/L in this reporting period.</p>	<p>$\times 100 =$</p>	<p>Percentage of patients with septic illness with appropriate repeat lactate measurement</p>
<p>Comments:</p> <ul style="list-style-type: none"> Despite the sound physiological and clinical basis for this intervention, compliance to its use has not been specifically evaluated in clinical studies. However, because the value of an initial lactate measurement is well established, that of repeat measurement after therapeutic interventions should be the same. A paradoxical increase in lactate may occasionally be observed after resuscitation (“reperfusion syndrome”) but i) is accompanied by clinical improvement in other parameters (see Definition of septic illness) and ii) is followed by subsequent normalization of lactate level upon re-measurement. 		
<p>COLLECTION STRATEGY:</p> <p><i>Safer Healthcare Now!</i> recommends that teams complete concurrent or “real time” data collection as much as possible. The ability to sustain data collection is higher if you integrate data collection into day-to-day work. However, if a team decides to collect their data using retrospective chart reviews then a hospital information system may be able to identify the patients from all discharges by sorting based on these elements. Another alternative is to work with the coding or medical records department to identify the patients at the time of coding and prepare a list or set aside records for review.</p>		
<p>SAMPLING STRATEGY:</p> <p><i>Safer Healthcare Now!</i> recommends that you monitor all patients identified as having septic illness at time of presentation either for the entire facility or specific unit e.g. ICU.</p>		

Appendix B: Sample Checklists and Other Tools

Cape Breton District Health Authority Order Set 2014

Cape Breton District Health Authority

Severe Sepsis/Septic Shock Physician Order Sheet

Orders will be activated when the order sheets are signed and dated by the physician.
To complete the order form, check the appropriate boxes and/or fill in the required blanks.
To delete an unwanted order the physician is to CROSS OUT AND INITIAL THE DISCONTINUED ORDER.

Allergies: _____

1. RECOGNITION OF SEVERE SEPSIS

SYSTEMIC INFLAMMATORY RESPONSE SYNDROME (SIRS) (≥ 2 OF THE FOLLOWING)

- Temperature greater than 38°C or less than 36°C
- Heart Rate greater than 90/min
- Respiratory Rate greater than 20 /min or PaCO₂ less than 32mmHg
- WBC greater than 12, less than 4 or greater than 10% immature neutrophils

KNOWN OR SUSPECTED INFECTION SUCH AS

- Pneumonia (clinical or radiograph evidence)
- Perforated Viscus
- Abnormally elevated WBC in normally sterile fluid

ACUTE ORGAN DYSFUNCTION (≥ 1 OF THE FOLLOWING)

- Cardiovascular: SBP less than 90mmHg; Respiratory: Sat less than 92%
- Renal: Urine output less than 0.5 mL/kg/hr ; CNS: Altered LOC
- PTT greater than 60 or INR greater than 1.5 without anticoagulant therapy
- Platelet count less than 100

2. Apply 100% O₂ by NRB unless the patient is a chronic CO₂ retainer

If patient is a chronic CO₂ retainer, adjust FiO₂ to maintain Sats between 88-94%

4. If patient recognized with SEVERE SEPSIS & Systolic BP less than 90mmHg IV Normal Saline 30mL/kg Bolus over 30 minutes (use Pressure Bag)

5. INVESTIGATIONS

☐ STAT Labs within first hour of presentation

CBC, Lytes, Urea, Creatinine, Lactic Acid, Glucose, INR, PTT, AST, ALT, LDH, Bilirubin, Alk Phos, Group & Screen

☐ STAT Cultures

- Blood X2 (One from line if in place & one from percutaneous)
- Urine • Sputum for gram stain and C&S
- Wound / Abscess (if applicable)

Additional Labs (check below)

- ☐ Amylase ☐ Lipase ☐ Phosphorus ☐ Magnesium ☐ Calcium ☐ Troponin Protocol
☐ Lactic Acid Q 2-3 hours (if initially elevated) until normal.

Additional Investigations (check below)

- ☐ XRAY _____ ☐ ECG _____ ☐ US _____
☐ SCAN (specify site & Contrast) _____

Physician's Signature: _____ Date & Time: _____ Page 1 of 4

**Cape Breton
District Health
Authority**

**Severe Sepsis/Septic Shock
Physician Order Sheet**

5. ANTIBIOTIC THERAPY

Administer Within 1 Hr of Recognition of Severe Sepsis Dosages may require modification if significant renal or hepatic dysfunction. Physicians to check the desired antibiotic based on suspected source and fill in the dose and dosing interval.

SEPSIS - UNKNOWN SOURCE:

- ☐ Imipenem _____ mg IV q _____ h
OR
☐ Piperacillin/Tazobactam _____ g IV q _____ h
OR
☐ Cefepime _____ g IV q _____ h PLUS Metronidazole 500mg IV q8H
OR
☐ Penicillin allergy Ciprofloxacin _____ mg IV q _____ h
PLUS Clindamycin 900 mg IV q8H

SUSPECTED PNEUMONIA:

- ☐ Piperacillin/Tazobactam _____ g IV q _____ h
Plus Moxifloxacin 400 mg IV q24h
OR
☐ Penicillin allergy Vancomycin _____ mg IV q _____ h
PLUS Ciprofloxacin _____ mg IV q _____ h

SUSPECTED SKIN AND SOFT TISSUE:

- ☐ Cefepime _____ g IV q _____ h
OR
☐ Penicillin allergy Clindamycin 900 mg IV q8h
OR
☐ MRSA suspected Vancomycin _____ mg IV q _____ h

SUSPECTED GU:

- ☐ Imipenem _____ mg IV q _____ h
OR
☐ Ciprofloxacin _____ mg IV q _____ h PLUS Metronidazole 500 mg IV q8H

If risk factors for Enterococcus (Foley, recent hospitalization, recent instrumentation, anatomical tract abnormality)

- Ampicillin _____ g IV q _____ h
OR Vancomycin _____ mg IV q _____ h

Physician's Signature: _____ Date & Time: _____ Page 2 of 4

**Cape Breton
District Health
Authority**

**Severe Sepsis/Septic Shock
Physician Order Sheet**

SUSPECTED CNS:

- ☐ Ceftriaxone _____ g IV q _____ h (give first dose IV push)
PLUS Vancomycin _____ mg IV q _____ h

If risk factors for Listeria (Pregnant, Age > 50; Immunocompromised;
Diabetes; End-Stage Renal Disease) then ADD Ampicillin _____ g IV q _____ h

Dexamethasone 10 mg IV Q6h x 4 days 15-20 mins prior to or
at the same time of first antibiotic infusion. Discontinue if not
bacterial (Pneumococcal) meningitis

SUSPECTED MRSA:

- ☐ Vancomycin _____ mg IV q _____ h

SUSPECTED PSEUDOMONAS:

(Severely Immunocompromised; Elderly; Central Line Antibiotics in last 30 days; Foley)

- ☐ Imipenem _____ mg IV q _____ h
OR
☐ Penicillin allergy Ciprofloxacin _____ mg IV q _____ h

OTHER ANTIBIOTICS:

6. RECOGNITION OF SEPTIC SHOCK

If greater than or equal to 1 of the following is present despite the initial bolus of 20-30 mL/kg of IV Crystalloid Fluid

- Systolic BP less than 90 mmHg
- Mean Arterial BP (MAP) less than or equal to 65 mmHg
- Blood Lactic Acid greater than 4MMOL/L

7. EARLY GOAL DIRECTED THERAPY (EGDT) ORDERS

Treatment Goals to be MET within the first 6hrs.

1. Mean Arterial Pressure (MAP) greater than 65mmHg
2. Central Venous Pressure (CVP) of 8-12 mmHg (12 -15mmHg if mechanical ventilation)
3. Urine output greater than or equal to 0.5 ml/kg/hr
4. Central Venous Oxygen Saturation (ScvO2) greater than or equal to 70%

Physician's Signature: _____ Date & Time: _____ Page 3 of 4

**Cape Breton
District Health
Authority**

**Severe Sepsis/Septic Shock
Physician Order Sheet**

- ☐ Critical Care Consultation
- ☐ Prepare patient for PreSep Central Line Insertion and CVP monitoring
- ☐ Prepare for arterial Line Insertion (recommended if vasopressors are required)

IV FLUIDS

- ☐ NS 500mL over 30 mins. Repeat until CVP 8-12 (12 -15 if mechanical ventilation) Notify MRP when CVP target is in target range and obtain a maintenance IV rate
- ☐ Other _____

TISSUE PERFUSION ASSESSMENT (CHOOSE ONE)

- ☐ Obtain ScvO₂ every 30-60 mins until greater than or equal to 70% (Venous Gas)
- ☐ Continuous ScvO₂ monitoring Using Vigelio Monotoer (target is greater than or equal to 70%)

VASOPRESSORS

If MAP remains less than 65 mmHg despite achieving a CVP of CVP 8-12 mmHg (12-15 mmHg if mechanical ventilation) Initiate vasopressor therapy via central line as follows;

- **Norepinephrine** 0.05 mcg/kg/min IV infusion and titrate to achieve a MAP > 65 mmHg (max 1 mcg/kg/min)
- If **Norepinephrine** max dose is reached and MAP < 65, then add **Epinephrine** 0.01 mcg/kg/min IV infusion and titrate to achieve a target MAP > 65 mmHg (max 0.05 mcg/kg/min)
- If **Norepinephrine** and **Epinephrine** max doses are reached and MAP < 65, then add **Vasopressin** 0.03 Units/min IV infusion and titrate to MAP > 65mmHg (max 0.04 units/min)

TRANSFUSION THERAPY

If ScvO₂ < 70% despite a CVP 8-12 (12-15 if Mechanical ventilation) and the MAP > 65 mmHg, then transfuse 1 unit PRBC's if hematocrit < 30%. Recheck the hematocrit post transfusion to determine if further transfusion is necessary

INOTROPIC THERAPY

If CVP 8-12 mmHg (12 -15mmHg if mechanical ventilation) MAP greater than or equal to 65mmHg and Hematocrit greater than or equal to 30% but ScvO₂ remains less than 70%, then initiate **Dobutamine** 2.5 mcg/kg/min Increase by 2.5mcg/kg/min every 30mins until ScvO₂ greater than or equal to 70% (max dose 20mcg /kg/min)

CORTICOSTEROID THERAPY

If CVP 8-12 (12-15 if MV) but the patient remains hypotensive (ie SBP < 90 mmHg or MAP < 65 mmHg) despite 1 hour of vasopressor therapy, then start **Hydrocortisone** 200 mg IV per day (by continuous infusion) x 3 days then reassess

Physician's Signature: _____ Date & Time: _____ Page 4 of 4

Kingston General Hospital

KGH has a three stage process for screening, antimicrobial management and sepsis management. Used with permission.

1

Adult Sepsis Screening Tool

To be used upon ED triage and when sepsis is suspected

Patient: _____ Initial Screen by: _____

Date: __ / __ / __-__-__ Time: __ / __-
 d d m m y y y y h h : m m

Time Reported to Physician (if applicable): __ / __-
 h h : m m

1 Suspected/Possible Infection

☐ Yes ☐ No

If yes, proceed to #2.

↓

2 Systemic Inflammatory Response Syndrome (SIRS)?

☐ Yes ☐ No

Temp < 36.0°C or > 38.0°C

☐ Yes ☐ No

Resp Rate > 20/min

☐ Yes ☐ No

Heart Rate > 90/min

If at least 2 yes's, proceed to #3.

↓

3 Possible Sepsis!

a) **NOTIFY MD** as soon as possible

b) Consider drawing blood for:

- Lactate
- VBG's
- Other tests

c) Reassess patient frequently

URGENT

Organ Dysfunction!

☐ Yes ☐ No

BP (systolic < 90 or MAP < 65)

☐ Yes ☐ No

Acute mental status change

☐ Yes ☐ No

O₂Sat < 90%

If at least 1 yes
and/or lactate > 2.2
and/or venous pH < 7.31
and/or HCO₃ < 22:

Possible SEVERE Sepsis

Notify MD immediately and
proceed to page **2** :
Antimicrobial Management.

Reassess patient frequently.

2

Adult Sepsis Antimicrobial Management

Use for patients suspected to be severely septic

1 Draw Blood Cultures

2 Prescribe APPROPRIATE Antimicrobial Agents

Consider the following:

- source of infection
- allergies
- appropriate dose
- co-morbidities (e.g. Diabetes)
- immune status (e.g. Neutropenia)
- recent exposure to:
 - hospital/health care institution
 - antibiotics
 - procedures (e.g. surgery, catheter, device)

3 Prescribe Initial Fluid Bolus (20 ml/kg)

4 Communicate Verbally with RN

- Urgent
- Multiple IV access = multiple antibiotics simultaneously (if required)

5 Proceed to the Sepsis Management Flowchart

Suggested Initial Empiric Antibiotics

Community-acquired pneumonia

- Ceftriaxone 2 g IV + azithromycin 500 mg orally or IV
- Moxifloxacin 400 mg orally or IV

Intra-abdominal

- Ceftriaxone 2 g IV + metronidazole 500 mg IV
- Piperacillin-tazobactam 3.375 g IV
- Ciprofloxacin 400 mg IV + metronidazole 500 mg IV

Urinary tract infection

- Ceftriaxone 2 g IV
- Levofloxacin 750 mg IV

Meningitis

- Dexamethasone 10 mg before ceftriaxone 2 g IV

Soft-tissue/bone/joint

- Cefazolin 2 g IV
- Cloxacillin 2 g IV

Necrotizing Fasciitis Type I (Polymicrobial)

- Piperacillin-tazobactam 3.375 g IV

Necrotizing Fasciitis Type II (Group A Strep)

- Clindamycin 900 mg IV + penicillin G 4 million units IV

Infective Endocarditis

- Vancomycin 20 mg/kg IV + gentamicin 1 mg/kg IV

Infected central line

- Vancomycin 20 mg/kg IV + pull the line

Neutropenia

- Ceftazidime 1g IV
- Piperacillin-tazobactam 4.5 g IV

Source unknown

- Ceftriaxone 2 g IV + Cloxacillin 2 g IV

If recent hospitalization within last two months;

- Piperacillin-tazobactam 3.375 g IV + Vancomycin 20 mg/kg IV

3

Sepsis Management Flowchart

Severe Sepsis Collaborative Assessment and Management

Assesment date: / / - - -
 d d m m y y y yTime: / - -
 h h : m m

1	Okay	Not Okay	N/A
Mental Status	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Vital Signs	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Urine Output	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
O ₂ Sat	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
CVP	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Lactate	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
CVO ₂ Sat	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>

2 Is the Patient Improving ?

No ☐ Yes ☐

3 Consider the Following

- Do you need help? (staff/decisions/expertise)
- O₂ Supplement
- IV Fluids
- Vasopressors
- Inotropes
- Central Line / IV access
- Intubation
- Transfusion
- Source control
- Appropriate Antibiotics
- Imaging
- Tests (e.g. serial VBG's, lactate)
- Consults (e.g. ICU)

4 Address Identified Issues

5 Proceed to Physician Orders Form

6 Schedule Next Collaborative Assessment:

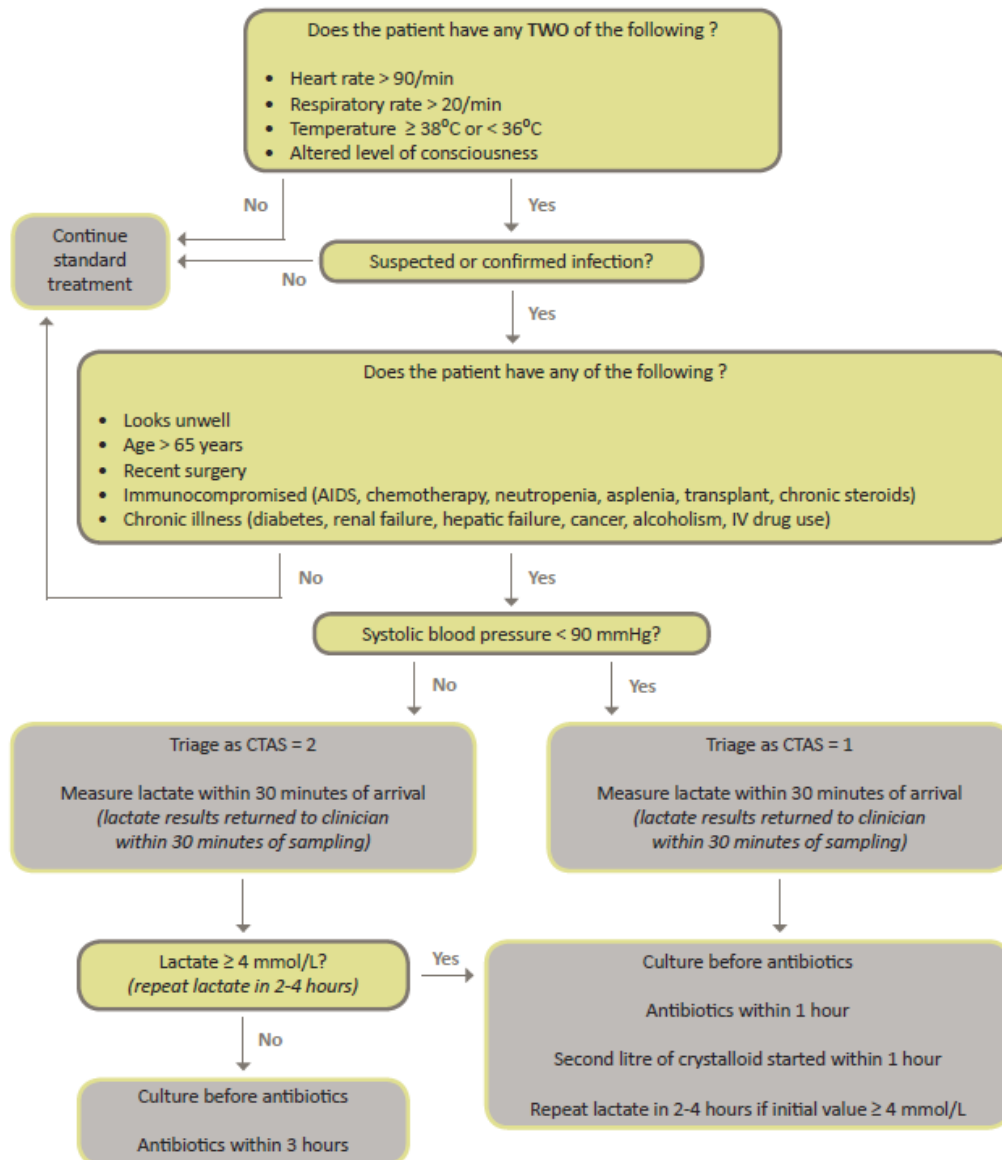
 / - -
h h : m m

BC Patient Safety and Quality Council

Through the BC Sepsis network, an algorithm and driver diagram were developed for use by BC improvement teams. These tools are available at <https://bcpsqc.ca/clinical-improvement/sepsis/guidelines/>

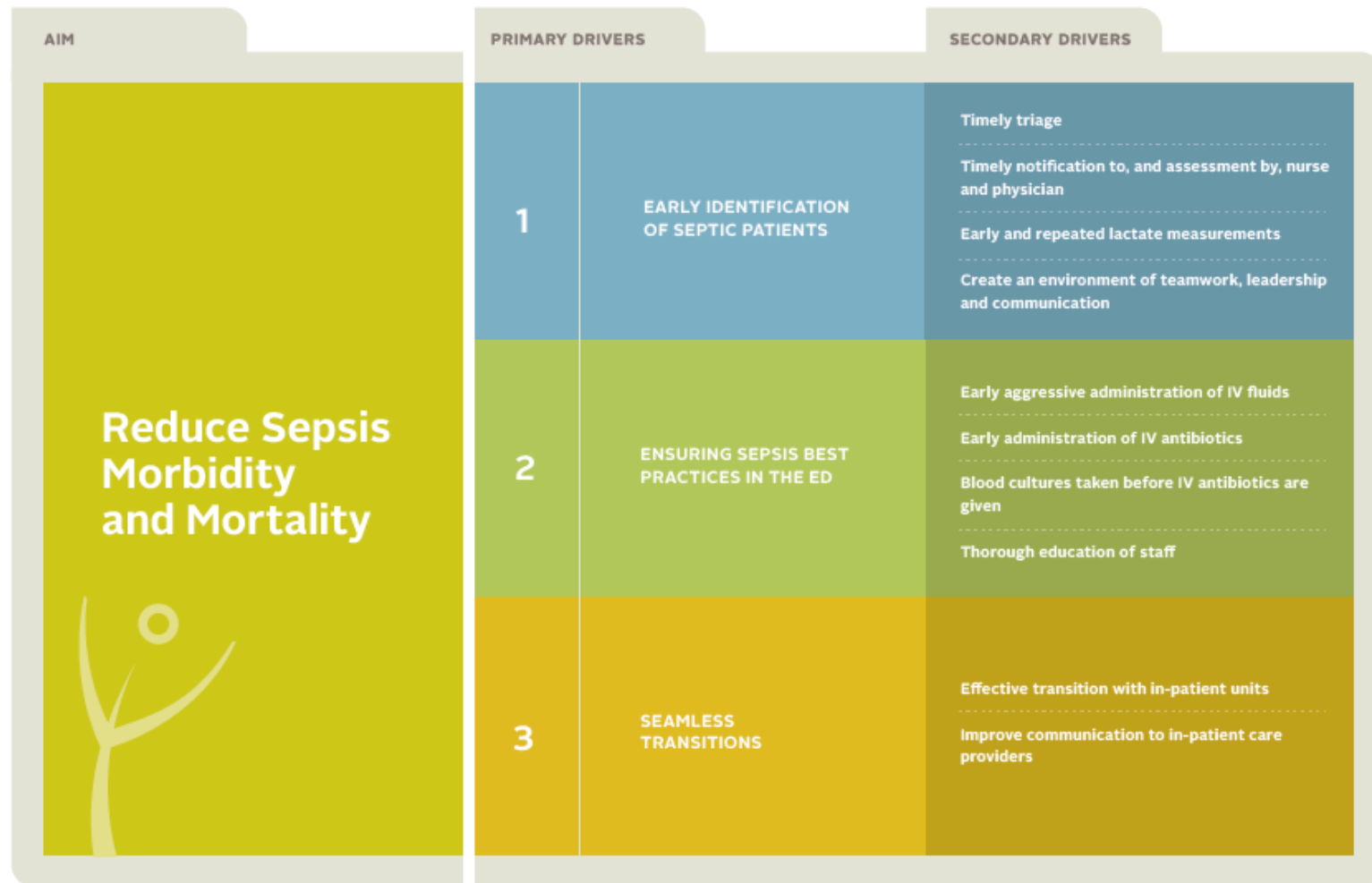


BC Sepsis Guidelines Algorithm



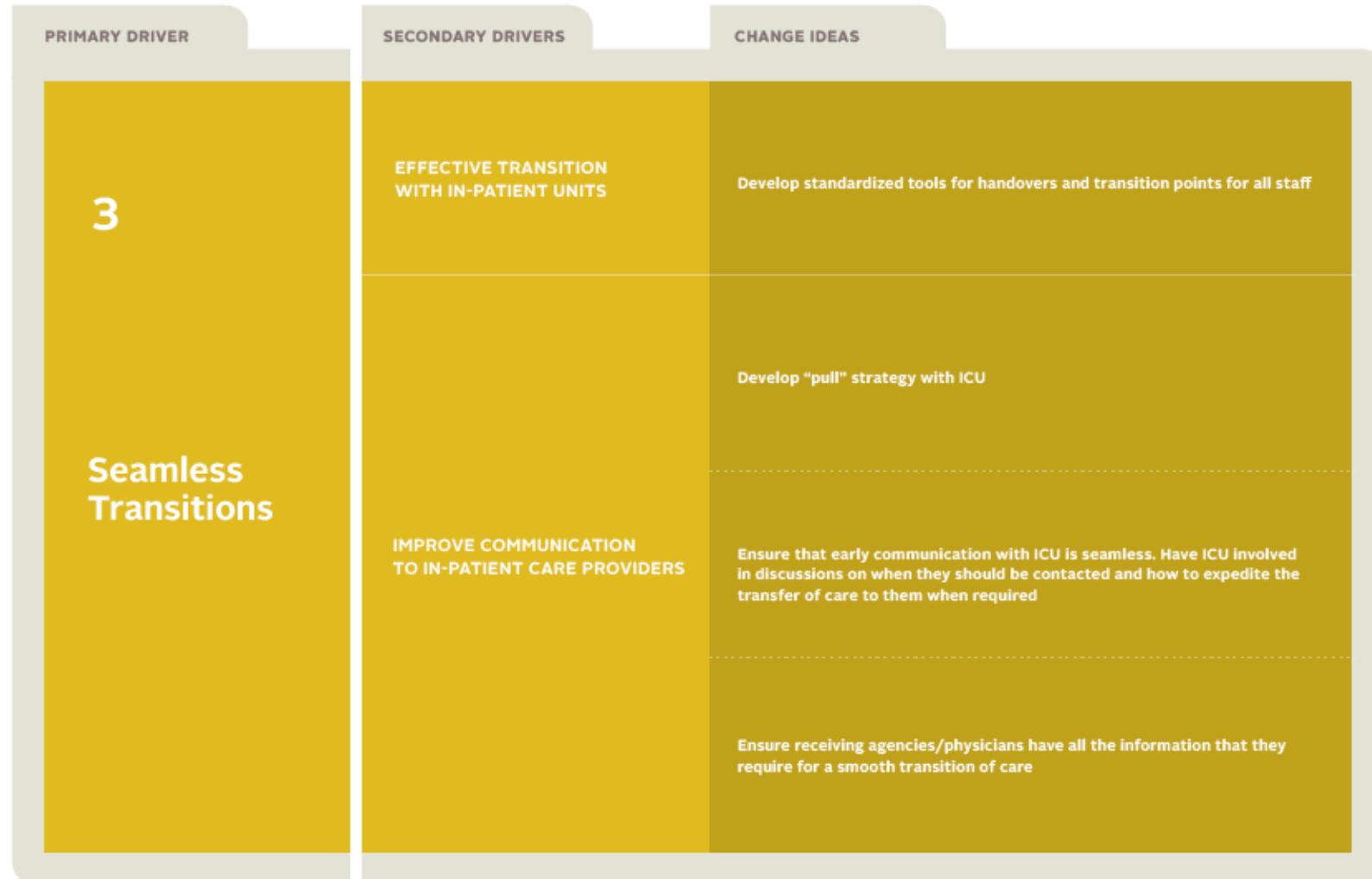
Additional recommendations

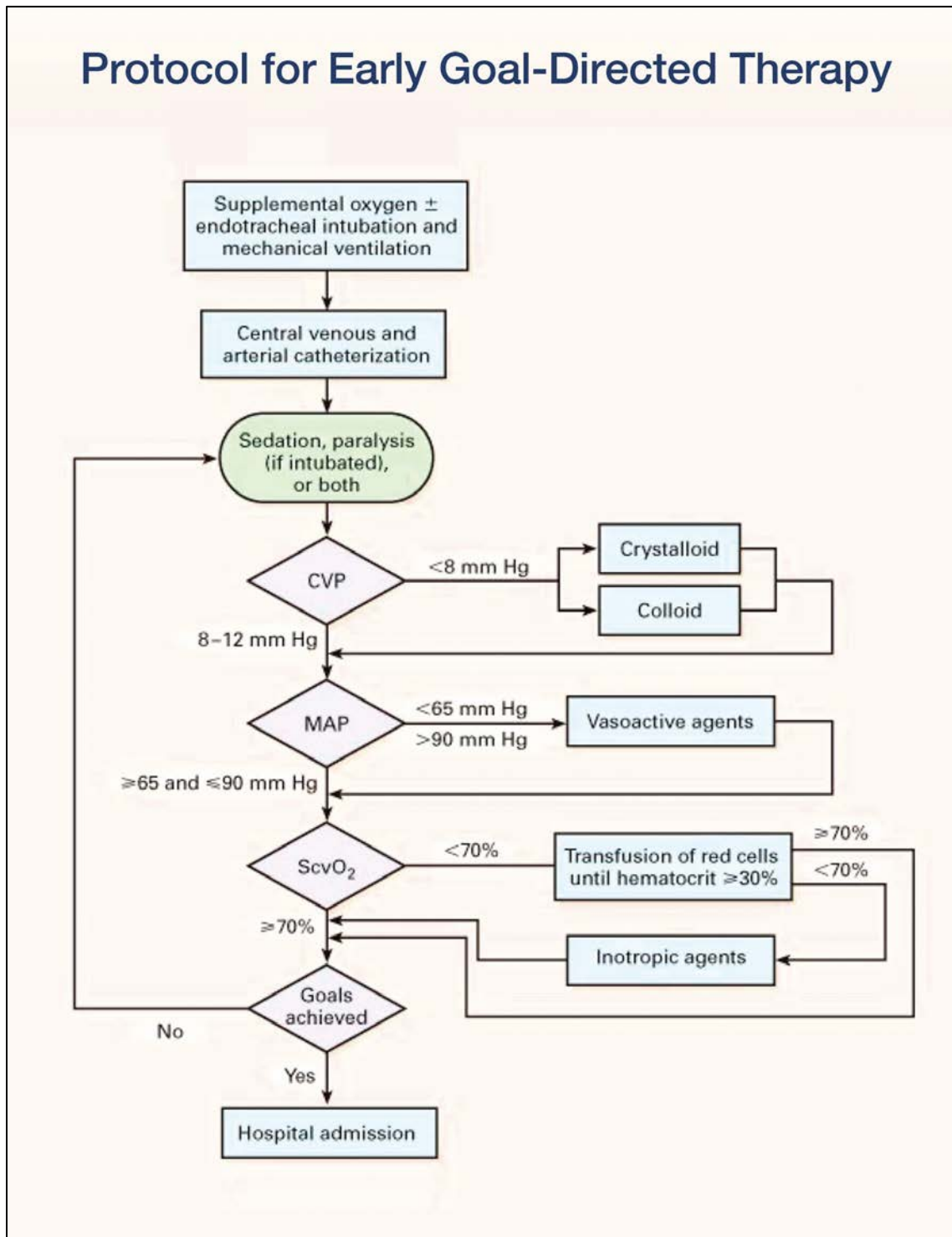
- Early investigations to determine infectious source (radiologic, surgical, other cultures i.e. cerebrospinal fluid, joint aspiration)
- Early source control with appropriate consultation
- Early critical care (ICU) contact or BC Patient Transfer Network (<http://ow.ly/oN248>) contact if early knowledge that patient will need higher level of care
- Encourage a 'culture of lactate' where any nurse, RT, or physician is empowered to check a lactate if concerned. Check early and often (if lactate elevated or patient unwell)
- If hypotensive despite fluid bolus (30ml/kg) or lactate fails to improve by 10% after second measurement (at least 2 hours after initial measurement), consider:
 - Placing central venous catheter and arterial catheter, continue fluid resuscitation and initiate norepinephrine or epinephrine to maintain mean arterial pressure > 65 mmHg. Use inotropes as needed and begin invasive monitoring and quantitative resuscitation.



PRIMARY DRIVER	SECONDARY DRIVERS	CHANGE IDEAS
1 Early Identification of Septic Patients	TIMELY TRIAGE	<p>Review SIRS criteria and the importance of early sepsis identification with all triage nurses</p> <p>Standardize triage screening tool for identification of sepsis</p> <p>Ensure proper documents/references/posters at triage</p>
	TIMELY NOTIFICATION TO, AND ASSESSMENT BY, NURSE AND PHYSICIAN	<p>Develop mechanism to notify physician and nurse of potential sepsis patient; a sticker or other visible clue on their charts, overhead page, direct communication</p> <p>Incorporate the use of communication systems such as "Code Sepsis" paging system, whiteboards, verbal and environmental cues, electronic bed boards</p>
	EARLY AND REPEATED LACTATE MEASUREMENTS	<p>Standardize order set for sepsis and link orders for lab so if blood culture is ordered, a serum lactate is ordered simultaneously (electronic order sets and defaults if possible)</p> <p>Work with lab to ensure that when initial blood work is taken that a venous blood gas is taken to measure lactate and results to clinician within 30 minutes (need access to arterial blood gas machine or point of care lactate device)</p> <p>Encourage a "culture of lactate" where any team member (MD, RN, RT) is empowered to check early and often</p>
	CREATE AN ENVIRONMENT OF TEAMWORK, LEADERSHIP AND COMMUNICATION	<p>Work with lab to ensure that when initial blood work is taken that a venous blood gas is taken to measure lactate and results to clinician within 30 minutes (need access to arterial blood gas machine or point of care lactate device)</p> <p>Encourage a "culture of lactate" where any team member (MD, RN, RT) is empowered to check early and often</p>

PRIMARY DRIVER	SECONDARY DRIVERS	CHANGE IDEAS
<p>2</p> <p>Ensuring Sepsis Best Practices In The ED</p>	EARLY AGGRESSIVE ADMINISTRATION OF IV FLUIDS	<p>Nurse initiated order sets and resuscitation</p> <p>Have sepsis kits including antibiotics, lab draw supplies, IV tubing and fluids for easy access available in the ED</p> <p>Start IV fluids, lab work, antibiotics before getting a bed if no beds available</p> <p>Establish a standard that all potentially septic patients receive a 1 litre crystalloid bolus with emphasis on hanging the second litre and documenting the times these are done</p> <p>Develop a protocol for escalated care for those patients that remain hypotensive despite fluid bolus</p>
	1. BLOOD CULTURES TAKEN BEFORE IV ANTIBIOTICS ARE GIVEN 2. EARLY ADMINISTRATION OF ANTIBIOTICS	<p>Adopt sepsis pre-printed orders for your department and place in patient charts</p> <p>Decide on antibiotic choices according to suspected source of infection (discuss with local infectious disease, pharmacy and microbiology specialists). Ensure there is a trigger system to alert for blood culture draw.</p>
	THOROUGH EDUCATION OF STAFF	<p>Process map the patient's journey and processes relating to sepsis. Use the process map to identify and eliminate bottlenecks in your process</p> <p>Establish educational sessions – consider using E2E educational slide sets and lectures/videos on www.evidence2excellence.ca. Establish on-going education (eg. educational rounds including M&M rounds; newsletter; case examples and report cards; updates on new sepsis issues)</p> <p>Sepsis education in ALL new staff orientation including physicians and students</p> <p>Set up forums for communicating with smaller community hospitals OR to larger hospitals. Consider setting up coordinated rounds with rural sites to discuss management and transfer issues</p>





Source: BC Sepsis Network 2015 <https://bcpsqc.ca/clinical-improvement/sepsis/bc-sepsis-network/>

Canadian Association of Paediatric Health Centres (CAPHC)

The [CAPHC Paediatric Sepsis Screening Tool](#) was developed and piloted by the [CAPHC Sepsis Community of Practice \(CoP\)](#) for use in emergency departments.

CAPHC SEPSIS SCREENING TOOL

Emergency Department

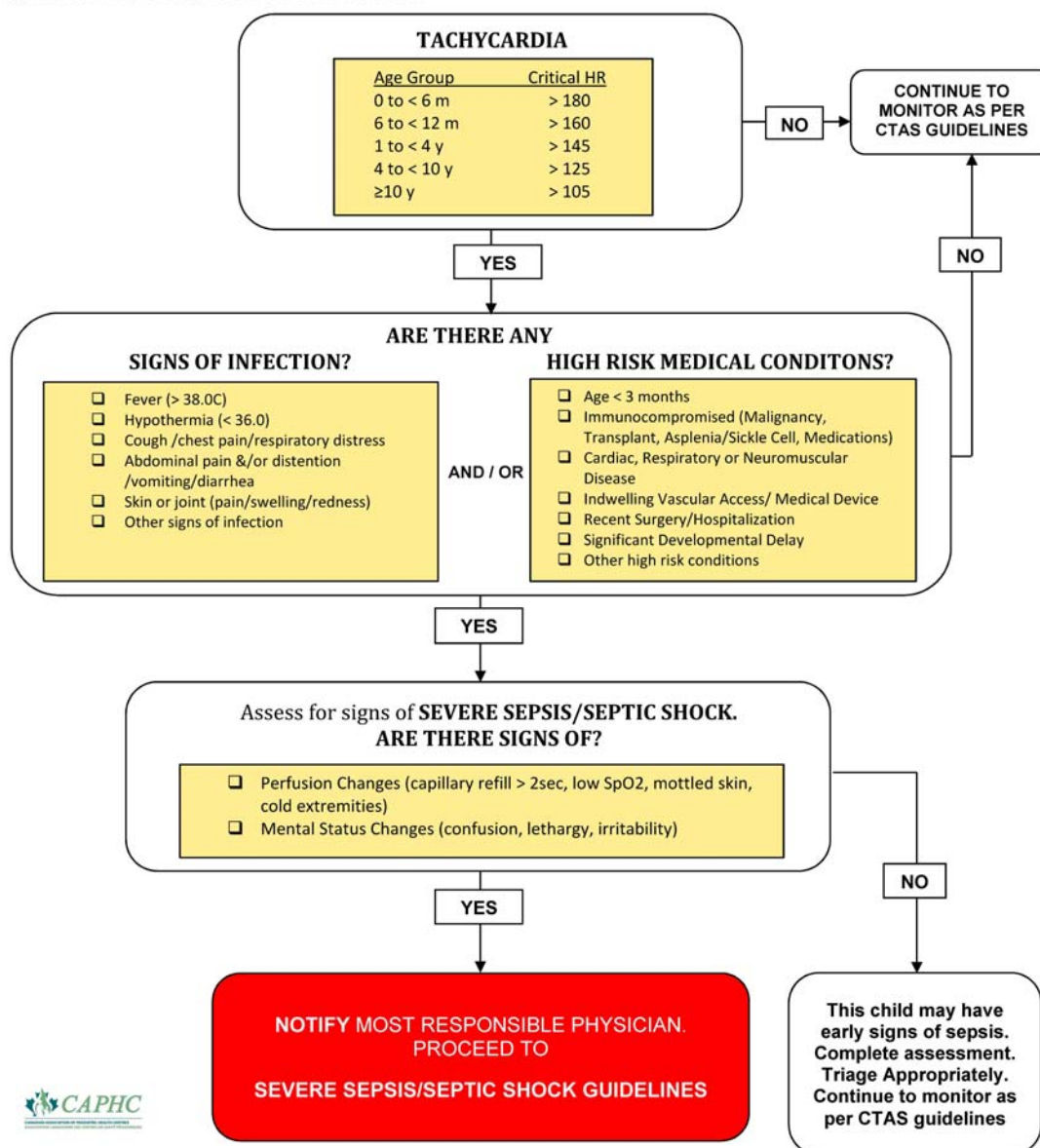
Patient Age: _____ days/months/years

Vital Signs: Temp: _____ HR: _____ RR: _____ BP: _____ SpO2: _____

Date/Time: _____

Patient Identification Label

****This is a screening tool to identify patients with severe sepsis. No screening tool can identify all patients with severe sepsis. If you are concerned that a patient might have severe sepsis or another serious condition, notify the responsible physician immediately regardless of whether they meet the criteria in this tool.**



Additional Resources

Pediatric Sepsis

Child Health BC resources for Pediatric Sepsis. Accessed from: BC Sepsis/Network
<http://childhealthbc.ca/guidelines-reports-and-presentations?drawer=Sepsis%20Guidelines>
(May 31, 2015)

Maternal Sepsis

- Fernandez-Perez ER, Salman S, Pendem S et al. Sepsis during pregnancy. Suppl. Critical Illness of Pregnancy. Crit Care Med. 2005;33(10Supp): S286-S293
- Burke C. Perinatal Sepsis. *J Perinat NeonatNurs* 2009; 23(1): 42-51
- Downs B, Sheffield J. Sepsis in Maternal Healthcare Settings. Webcast slides accessed from <http://www.survivingsepsis.org/Resources/Pages/Media.aspx>

Videos

Associates in Process Improvement (API) Model for Improvement

- Clip 1. <https://www.youtube.com/watch?v=SCYghxtiolY>
- Clip 2. <https://www.youtube.com/watch?v=6MIUqduINwQ>
- Whiteboard: The PDSA Cycle (Institute for Healthcare Improvement (IHI) Open School)
- Part 1. <https://www.youtube.com/watch?v=-ceS9Ta820>
- Part 2. https://www.youtube.com/watch?v=eYoJxjmv_QI

Sepsis stories (YouTube)

- Anyone can get sepsis (<https://www.youtube.com/watch?v=GNz3S3tvYLA>)
- The turning Point - Surviving Sepsis (<https://www.youtube.com/watch?v=tD0RY7saYQI>)
- Howard Hoover: A Sepsis Survival Story
(<https://www.youtube.com/watch?v=DVrFjBNjy0>)
- RSF Sepsis A Hidden Crisis Exposed
(<https://www.youtube.com/watch?v=t4FQrRRTUnY>)

Also on the Web

Sites for public information/awareness about sepsis, personal stories and resources for health professionals including teaching material and patient sepsis stories:

- **National Health Service (UK)**
Sepsis (<http://www.nhs.uk/conditions/Blood-poisoning/Pages/Introduction.aspx>)
Septic illness (<http://www.nhs.uk/conditions/Septic-shock/Pages/Introduction.aspx>)
Basic information for patients and lay public
- www.cdc.gov/sepsis
Basic information, data reports, improving survival, clinical guidelines and tools, bibliography
- **Global Sepsis Alliance** (sepsisalliance.org)
- **World Sepsis Day** (world-sepsis-day.org)
- **Sepsis Trust** (sepsistrust.org)
Tool kits include guidelines and suggested standards for the Emergency Department, General and Acute Medical Wards, and Pediatrics
- **Survive Sepsis** (www.sepsistrust.org)
Educational resource from Sepsis Trust (UK) built around early recognition and immediate management of sepsis - using "Sepsis Six" - for healthcare professionals.

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