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# Utility of the Modified Early Warning System Score in Early Sepsis Identification

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Utility of the Modified Early Warning System Score in Early Sepsis Identification

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Submitted in Partial Fulfillment of the Requirements

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## **Dedication**

I dedicate this project to my mom and dad, Debbi and Mark Julian, for being my constant source of support and love throughout my life. My mom was unable to see me fulfill this dream, however all that she taught me led me to this point. Her constant devotion, love and dedication to our family were more than anyone could ask. To my dad, thank you for supporting me every step of the way through this journey and constantly offering your love and support. Next, I would like to send my utmost love and thanks to my loving and dedicated husband, Aaron Hart. I would not have completed this journey without you standing next to me and being my constant motivator, friend and husband. Words cannot express how grateful I am to have you walk this journey with me and stand next to me at the finish line. Finally I would like to give thanks to God, in which none of this would be possible.

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## **Abstract**

The purpose of this quality improvement project is to improve outcomes for patients presenting to the emergency department with sepsis, realizing that time is a key factor. The appraised evidence indicates that early recognition and prompt treatment improve outcomes and decrease mortality. The evidence further highlights that use of an early warning system, like the Modified Early Warning Score, can assist nurses and providers with recognizing deterioration more quickly and lead to a reduction in time to interventions. Between January 2016 and March 2017, the author conducted a retrospective chart review to compare time to antibiotic administration and lactate measurement and blood cultures before and after implementation of the MEWS in an urban emergency department. The author randomly selected a total of (n=130) patients to conduct a retrospective chart review. There were demographic differences between the pre-implementation group and post-implementation group in regards to patients with CHF, diabetes and hypertension with fewer patients having CHF, diabetes and hypertension. In the pre-implementation group 14.06% of patients had CHF, 73.44% had hypertension, and 43.75% had diabetes. In the post-implementation group only 1.52% had a history of CHF; 62.12% with hypertension; and 30.30% with diabetes. There were differences between the two groups in regards to disposition status. The pre-implementation group had more deaths (19.35%) compared with the post-implementation group (12.5%) and more patients were discharged home in the post-implementation group (41.94% vs. 64.06%), which was a statistically significant difference between the

two groups. Lactate measurements were obtained in 81.25% of patients in the pre-implementation group compared with 87.88% in the post-implementation group. Blood cultures were drawn in 81.25% of patients in the pre-implementation group compared with 71.21% in the post-implementation group. The mean age for the pre-implementation group was 61.68 with standard deviation of 17.11 (95% CI: 57.41, 65.96) and for post-implementation the mean age was 55.93 with standard deviation of 15.25 (95% CI 52.19, 59.68). There was no statistically significant difference in means in minutes between the two groups. The mean in minutes for antibiotic administration was 353.10 for the pre-implementation group and 363.20 for the post-implementation group. This project did not demonstrate statistically significant differences after implementation of the MEWS score as supported by the literature, however clinical significance was identified with improvements in time in minutes to antibiotic administration at the 3-hour, 6-hour and greater than 8-hour marks.

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## **Chapter 1 Introduction**

### **1.1 The Description of the Clinical Problem**

Sepsis is the 12<sup>th</sup> leading cause of death according to the CDC (CDC, 2015). Estimates show that there are 750,000 cases of sepsis annually, with a 28%-50% mortality rate (Picard, O'Donoghue, Young-Kershaw, & Russell, 2006; Turi & Von Ah, 2013). In 2013, mortality for septicemia rose by 17% while mortality for other diseases including heart disease, respiratory failure and stroke decreased (Schorr, 2016). Emanuel Rivers, vice chairman and research director at Henry Ford's Hospital states, "even the most recent studies continue to show that one in four to five patients admitted with sepsis still die in the hospital. This is the highest mortality of any disease admitted to the hospital" (Frieden, 2015).

Although healthcare professionals agree on improving treatment protocols, disagreement on interventions and implementation barriers have prevented widespread reforms. Early recognition and treatment of severe sepsis greatly improves patients' survivability of sepsis (Vanzant & Schmelzer, 2010). However, despite continued evidence to support improved outcomes, compliance to established evidence-based guidelines and resistance to implementation remains a problem (Vanzant & Schmelzer, 2010; Turi & Von Ah, 2013; Tromp et al, 2010). The literature shows that a primary barrier to early goal directed therapy for sepsis was the healthcare professional's ability to identify signs and symptoms and, therefore, protocols and sepsis bundles are not initiated timely (Turi & Von Ah, 2013; Stoneking, Denninghoff, DeLuca, Keim, &

Munger, 2011; Bruce et al., 2015; Tromp et al., 2010). The Surviving Sepsis Campaign as well as numerous studies point to early recognition and intervention as the key to improved outcomes, reduced mortality and prevention of complications (SSC, 2015; Birriel, 2013; Wira, Dodge, Sather, & Dziura, 2014; Turi & Von Ah, 2013; Wawrzeniak, Loss, Moraes, De La Vega, & Victorino, 2015). In an evolving healthcare climate, using evidence-based research and guidelines is imperative to improve sepsis management. The purpose of this quality improvement project is to improve outcomes for patients presenting to the Emergency Department with sepsis, realizing that time is a key factor. The project will compare the time for initiating the Sepsis Bundle using the Modified Early Warning Score (MEWS) versus the current method of triaging the patient for sepsis without using a MEWS score. (See Appendix B). Measure outcomes include time in minutes as well as actual blood levels for obtaining lactate levels and blood cultures and time in minutes for the administration of antibiotics. The guidelines recommend initiating the Sepsis Protocol within three hours of presentation to the Emergency Department any patient with a MEWS score of  $> 4$ .

## **1.2 Scope of the Clinical Problem**

Sepsis continues to yield high mortality rates and poor outcomes despite treatment advances. Sepsis is the number one cause of death in non-coronary intensive care units, and mortality is greater than lung cancer, breast cancer, and colon cancer combined (AACN, 2016). Sepsis is the sixth most common reason for hospitalizations each year and incidence of sepsis continues to rise each year and is expected to increase 8%-13% annually (Consortiums of Universities for Global Health, 2015). While hospitalizations from myocardial infarction and stroke continue to decline since 2001, sepsis

hospitalizations have risen each year (Consortiums of Universities for Global Health, 2015). Patients discharged from the hospital after treatment of sepsis have poorer outcomes post-hospitalization. The one-year post-discharge mortality rate for septic patients remains 7%-43% and patients that survive continue to have impaired cognitive function, poor pulmonary function and functional disabilities (Gauer, 2013; Consortiums of Universities for Global Health, 2015).

Notwithstanding the human costs of sepsis, the financial burden is crippling as well. Sepsis remains the most expensive hospital problem totaling \$15-\$20 billion in hospital costs each year, and Medicare is the primary payer covering 58.1% of septic patients (Elixhauser, Friedman, & Stranges, 2011). As a result, the Centers for Medicare and Medicaid (CMS) and The Joint Commission began monitoring sepsis measures and outcomes in 2015 (Schorr, 2016). In April 2015, CMS instituted the Sepsis Bundle Project: Early Management Bundle, Severe Sepsis/Septic Shock (“SEP-1”) measures focusing on early recognition and treatment of sepsis in an effort to reduce mortality (Joint Commission, 2015). In October 2015, CMS required all hospitals to utilize and report SEP-1 measures (Schorr, 2016). These reporting measures include measurement of lactate levels, obtaining blood cultures, administration of broad spectrum antibiotics, fluid resuscitation, vasopressor administration for persistent hypotension, reassessment of volume status and perfusion and repeat lactate measurement (The Joint Commission, 2015). The first four measures should be implemented within the first three hours of presentation with the last measures occurring within six hours of presentation. The purpose of these measures “is to support the efficient, effective and timely delivery of

high quality sepsis care in support of the Institute of Medicine’s aims for quality improvement” (AHRQ, 2014).

In 2017, non-compliance with these measures will result in a reduction in reimbursement. With the evolving changes in the healthcare reform, reimbursement, and regulatory compliance changes from CMS, this should be an incentive for all hospitals and organizations to utilize quality measures. According to CMS (2015), to avoid a reduction in Annual Payment Determination in 2017, it is a federal requirement for all hospitals to collect and report data on the SEP-1 measures.

### **1.3 Discussion of Practice Innovation/Best Practices to Address the Problem**

The treatment of sepsis and septic shock has seen drastic advancements in the last fifteen years due to initiation of protocols based on early goal-directed therapy or “EGDT”. In 2001, Rivers et al. (2001) published a study, which examined the use of EGDT in severe sepsis and septic shock patients in the emergency department. Investigators focused on hemodynamic support and improved oxygen delivery (Rivers et al., 2001). The results indicated that early treatment improved mortality (Rivers et al., 2001). Burney et al. (2012) found similar results. Moreover, others found that early recognition and initiating EGDT reduced sepsis mortality (Wira, Dodge, Sather, & Dziura, 2014; Turi & Von Ah, 2013; Wawrzeniak, Loss, Moraes, De La Vega, & Victorino, 2015).

In 2002, a group of international experts including the Society of Critical Care Medicine, European Society of Critical Care Medicine and the International Sepsis Forum created the “Surviving Sepsis Campaign” (SSC) in order to “reduce mortality from sepsis by 25% in 5 years” (SSC, 2015). In order to reach this goal, the SSC adopted

the definitions on sepsis, severe sepsis and septic shock, which were established during a sepsis definitions conference (SSC, 2015). The SSC created bundles to assist clinicians in earlier recognition and treatment based on EGDT guideline criteria, such as early fluid resuscitation, lactate measurement and antibiotic therapy (Birriel, 2013). The SSC also developed a screening tool to improve early sepsis recognition, which they claim is the hallmark for reducing mortality (Birriel, 2013). Since the conception of the SSC guidelines, studies demonstrate that the SSC guidelines reduce sepsis mortality (Nguyen et al., 2007; Westphal et al., 2011; Wawrzoniak et al., 2015; Wira et al., 2014).

In 2016, The Third International Consensus Definitions Task Force for Sepsis and Septic Shock developed new sepsis recommendations, definitions for sepsis, management, and identification tools (Society for Critical Care Medicine, 2016, Seymour et al., 2016). The Surviving Sepsis Campaign adopted the new definitions but added that redefining sepsis does not change the primary focus of early recognition and early treatment (SSC, 2016).

Based on the Rivers et al. (2001) study, the updated SSC guidelines, and mandatory reporting requirement of SEP-1 measures, many hospitals have implemented treatment protocols and bundles aimed at decreasing mortality and costs and improve overall outcomes (Turi & Von Ah, 2013).

However, compliance with the bundles remains sporadic across institutions due to multiple barriers, with early recognition being a primary barrier (Turi & Von ah, 2013; Stoneking, Denninghoff, DeLuca, Keim, & Munger, 2011). The Institute of Medicine (IOM), the Surviving Sepsis Campaign and the Department of Health of Human Services recognize the benefits of early recognition and treatment in reducing mortality, morbidity

and costs (Department of Health and Human Services, 2014). Other studies found similar results (Bruce, Maiden, Fedullo, & Kim, 2015; Gaieski, Edwards, Kallan, & Carr, 2014). In an effort to improve recognition and early intervention, hospitals have implemented screening tools and warning systems to improve assessment of septic patients. Studies have shown that use of a triage-based warning system can reduce time to interventions and improve outcomes (Hayden et al., 2016). Physiological deterioration precedes clinical deterioration in sepsis and early warning systems have been shown to be effective in identifying physiological deterioration earlier (Corfield, Lees, Houston, Dickie, Ward, & McGuffie, 2014). The Institute for Healthcare Improvement reports the use of early warning systems allows nurses to identify changes and potential life-threatening events more quickly and activate the rapid response team for earlier intervention (IHI, 2016). The Modified Early Warning System (“MEWS”) assigns a numerical value to certain physiological components including heart rate, respiratory rate, temperature and level of consciousness, allowing earlier identification of patient deterioration (Corfield, Lees, Zeally, Houston, Dickie, Ward, & McGuffie, 2014; Race, 2015). Studies suggest early warning systems like MEWS improve early recognition in septic patients (Corfield, Lees, Zeally, Houston, Dickie, Ward, & McGuffie, 2014; Race, 2015).

#### **1.4 Statement of the Problem**

Sepsis can occur at any point during a hospital stay, however the emergency department is the entry point for more than half of all severe sepsis patients (Rivers, McIntyre, Morro, & Rivers, 2005; Wira et al., 2014). Studies show that sepsis patients entering the emergency department are not treated as aggressively, thereby increasing mortality due to delays in recognition and early interventions (Wang et al., 2007).



The purpose of this quality improvement project is to improve outcomes for patients presenting to the Emergency Department with sepsis, realizing that time is a key factor. The project compared the time for initiating the Sepsis Bundle using the MEWS score versus the current method of triaging the patient for sepsis. Measure outcomes included time in minutes as well as actual blood levels for obtaining lactate levels and blood cultures and time in minutes for the administration of antibiotics.

The population (P) are adults 18 years and older that present to emergency departments. The intervention (I) is utilizing the MEWS score to help assess acuity of patients presenting to the emergency department with sepsis. The comparison (C) is the current system of triaging patients without the use of the MEWS score system. The outcome (O) is earlier identification and treatment of patients that present to the emergency department with sepsis. The goal is to improve door to intervention time for patients with a MEWS score of > 4.

**Table 1.1 Evidence Based Practice Clinical Question**

Population	Intervention	Comparison	Outcome	Timing
Patients 18 years and older diagnosed with sepsis, severe sepsis or septic shock in the Emergency Department	Assessment using the MEWS score > 4 on patients entering the emergency department that are initially or subsequently diagnosed with sepsis, severe sepsis or septic shock	Current system of triaging patients without using the MEWS score	Within 3 hours of door to intervention for patients with a MEWS Score of > 4 as measured by: Levels for 1. Lactate measurement levels 2. Blood culture draws Time in minutes for Administration of appropriate broad-spectrum antibiotics.	3 months prior to MEWS implementation and 3 months post-implementation

## **1.5 Project Questions**

This project was guided by the following clinical questions:

Does the use of the modified early warning system improve intervention times for lactate measurement, blood cultures and antibiotic administration?

Can decreasing time to intervention for sepsis patients improve outcomes for sepsis patients?

Does the Modified Early Warning System Score (MEWS) improve recognition of sepsis patients and improve outcomes of sepsis patients?

## **1.6 Definitions**

Sepsis mortality can range from 25% to 30% for severe sepsis to as much as 70% for septic shock (Gauer, 2013). Early recognition and intervention within the first six hours of presentation can greatly reduce mortality (Gauer, 2013). Numerous studies indicate that early, broad-spectrum antibiotic therapy improves outcomes in sepsis patients (Vanzant & Schmelzer, 2010). According to Vanzant and Schmelzer (2010), early antibiotic administration is key to decreasing mortality, however, assessing fluid status and perfusion are vital components. Lactate measurement is a good indicator of tissue hypoxia and impaired perfusion in septic patients (Levinson, Casserly, & Levy, 2011). The obtainment of blood cultures assists clinicians in prescribing appropriate antibiotics based on infectious cause. Gaieski et al. (2010) found that decreasing time from presentation to administration of appropriate antibiotics improves outcomes and decreases mortality. In order to expedite antibiotic administration, the literature recognizes the ED nurse is in the optimum position to assess and recognize signs of

sepsis (Turi & Von Ah, 2013; Bruce et al., 2015; Tromp et al., 2010). Using the MEWS score can assist the triage nurse in recognizing sepsis earlier and alerting the provider.

1. Adults are eighteen years of age or older.
2. Broad-spectrum antibiotics are those antibiotic medications used to treat both gram-positive and gram-negative bacteria.
3. Blood culture draws are diagnostic tests used to determine if a patient has bacteremia and, if so, conduct susceptibility testing for narrowing antibiotic therapy.
4. Bundle is a group of care practices that when utilized together have a greater effect on outcomes than if the practices were utilized individually (SSC, 2015).
5. Emergency Department is a point of entry for patients in the hospital.
6. Lactate Measurement is a diagnostic test used to diagnose sepsis-induced hypoperfusion. A lactic level greater than 2mmol is elevated and indicative of early tissue hypoperfusion with a level greater than 4mmol suggestive of septic shock (SSC, 2016).
7. Modified Early Warning System (MEWS) is a physiological score monitored by nurses and used to prevent delay in interventions of critically ill patients (AHRQ, 2016).
8. Mortality rate is defined as the number of deaths per 1,000 people that die from sepsis, septic shock, and/or severe sepsis.
9. Protocols are sets of guidelines that can be customized by organizations that are implemented to improve outcomes. Protocols must follow the standards set by the bundle (SSC, 2015).

10. Provider is defined as a doctor of medicine (M.D.), doctor of osteopathic medicine (D.O), advanced practice registered nurse (APRN) or physician assistant (P.A).
11. Sepsis is “the presence (probable or documented) of infection together with systemic manifestations of infection” (Dellinger et al., 2012)
12. Severe Sepsis is “sepsis plus sepsis-induced organ dysfunction or tissue hypoperfusion” (Dellinger et al., 2012).
13. Septic shock is “sepsis-induced hypotension persisting despite adequate fluid resuscitation” (Dellinger et al., 2012).
14. Sepsis-induced hypoperfusion is “infection-induced hypoperfusion, elevated lactate or oliguria” (Dellinger et al., 2012).
15. Sepsis-induced hypotension is systolic blood pressure less than 90mmHg or a MAP less than 70mmHg, or a systolic blood pressure drop of greater than 40mmHg from baseline
16. Staff is defined as licensed healthcare employee within the emergency department that is involved in direct patient care including physicians, advanced practice registered nurses, physician assistants, nurse managers, registered nurses and licensed practical nurses.
17. Systemic inflammatory response syndrome (SIRS)” is presence of the temperature lower than 36° C (97°F) or higher than 38°C (100°F); heart rate over 120 beats per minute; respiratory rate over 20 breaths per minute; arterial CO<sub>2</sub> less than 32mm Hg; white blood cell lower than 4,000 or higher than 10,000 (Dellinger et al., 2012).

18. Time is defined as the time from documentation by APRN/PA/Physician of severe sepsis or septic shock or when clinical criteria are met for diagnosis to a specific intervention.
19. Triage is defined as the process of sorting patients into the following care categories: immediate, urgent, and non-urgent (Merriem-Webster, 2016). The process is completed routinely upon entry to the emergency department and consists of a brief clinical assessment, including vital signs, to determine a time and sequence in which patients should be seen (Robertson-Steele, 2006).

## **1.7 Chapter Summary**

Although significant gains have been achieved in sepsis treatment, sepsis remains a deadly and expensive problem plaguing the healthcare system. Guidelines from the SSC provide evidence-based recommendations for improved recognition and treatment of sepsis through the use of three and six hour bundles (Schorr, 2016). Studies suggest early recognition and intervention is key to reducing mortality and improving outcomes. The emergency department remains a primary access point for patients with sepsis and therefore, emergency room healthcare providers are pivotal in identifying signs and symptoms of sepsis. In order to improve recognition, the use of early warning systems such as the modified early warning system (MEWS) can assist healthcare professionals such as nurses and advanced practice registered nurses (APRNs) to assess and initiate early intervention of sepsis. The MEWS score has been shown to improve recognition of sepsis. With earlier recognition, providers can reduce time in minutes for lactate measurement, blood culture draws and antibiotic administration. The purpose of this

quality improvement project is to improve outcomes for patients who present to the emergency department with sepsis.

## **Chapter 2 Literature Review**

### **2.1 Introduction**

Mortality rates for sepsis have continued to increase despite current medical advances. Early, goal-directed therapy has been utilized in ICU settings since 2001; however, mortality rates remained high, equaling the rates of the 1970s (Jones, Focht, Horton & Kline, 2007). Prior to 2001, research primarily focused on treatment of sepsis in intensive care units (ICU), yet it is estimated that as much as 50% of sepsis patients initially present to the emergency department (Jones, Focht, Horton & Kline, 2007). In reviewing this data, researchers began to study the impact of early treatment beginning at presentation to the emergency department. This literature review encompasses current and past research focused on the impact of early treatment of sepsis initiated in the emergency department and the use of early warning scores in sepsis patients. The purpose of this chapter is to analyze and synthesize the literature for the efficacy of early onset assessment and treatment for sepsis in the emergency department.

### **2.2 Search Methodology**

Evidence-based research is essential to optimize patient outcomes and ensure care processes and treatments advance with the continuous evolution of healthcare. To that end, healthcare clinicians must possess the skills to critically appraise evidence and differentiate between reliable and unreliable evidence (Melnik & Fineout-Overholt, 2011). A literature search was conducted to review current and past literature regarding severe sepsis, utilization and impact of early-warning systems, implementation of

protocols and early recognition and treatment of sepsis in emergency departments. The purpose of this quality improvement project is to improve outcomes for patients who present to the Emergency Department with sepsis.

A systematic literature review was conducted to identify evidence that supports utilization of the MEWS score or other early-warning systems, use of sepsis bundles using early, goal-directed therapy in septic patients, and early recognition. This study used a comprehensive search of databases accessed through the University of South Carolina's online databases to identify evidence.

The following databases were utilized: CINAHL, PUBMED, Cochrane Library, Joanna Briggs Institute EBP Database as well as Google Scholar Internet search. These databases were searched to identify studies focused on sepsis bundles, early recognition, improved outcomes with early-warning systems, and early, goal-directed therapy and other interventions. The following search terms were utilized: *sepsis* or *septic shock* or *severe sepsis* and *early goal directed therapy* and *bundles* or *protocols* and *emergency department* or *emergency services* or *early-warning systems* or *modified early-warning systems* and *emergency services* or *emergency department* or *early recognition* and *sepsis* or *septic shock* or *severe sepsis* or *barriers to implementation of protocols* and *sepsis* and *resuscitation* The Google Scholar search focused on *early-warning systems and sepsis*", to focus on the use of warning systems specifically with sepsis. Google search also included keywords *sepsis*, *severe sepsis* and *protocols*; *sepsis bundle*; *early goal-directed therapy*; *antibiotics* and *sepsis* and *severe sepsis*. Exclusion criteria included those studies not utilizing early, goal-directed therapy, studies involving patients under 18 years of age, and studies prior to 2001. These limitations were applied to generate current evidence-



based studies on sepsis bundles and early recognition and treatment after the creation of the Surviving Sepsis Campaign (“SSC”). The database search and search engine results generated significant data from articles listed in the evidence table (see Appendix D).

The foundation for evidence-based practice and research is the use of a hierarchical system for classifying evidence (Burns, Rohrich, & Chung, 2011). For this review, studies are rated using the Johns Hopkins Evidence Level and Quality Guide (See Appendix A). The studies included are all of good to high quality based on the guide, which indicates they have reasonably consistent generalizable results with sufficient sample size, clear aims and objectives, definitive conclusions, and consistent recommendations with a basis in scientific evidence as described in the evidence table (Dearholt & Dang, 2014). Levels of evidence are ranked from highest to lowest as follows: experimental study/randomized controlled trial (RCT) or meta-analysis of RCT; quasi-experimental study; non-experimental study, qualitative study, or meta-synthesis; opinion of nationally recognized experts based on research evidence or expert consensus panel (systematic review, clinical practice guidelines); and opinion of individual expert based on non-research evidence. This evidence includes case studies; literature review; organizational experience, e.g., quality improvement and financial data; clinical expertise, or personal experience (Johns Hopkins Medicine, 2016).

### **2.3 Analysis**

The research has been analyzed to identify improved outcomes with early, goal-directed therapy; sepsis bundle and protocols; improved outcomes with early recognition; use of early-warning systems in sepsis identification and early interventions outlined in current guidelines.

## **2.4 Early, Goal-Directed Therapy**

In 2001, Rivers et al. (2001) published a landmark study evaluating the efficacy of early, goal-directed therapy in the emergency department. Rivers and colleagues (2001) state imbalances between systemic oxygen delivery and demand cause global tissue hypoxia leading to septic shock. They further state “transition to serious illness occurs during the ‘golden hours’ when definitive recognition and treatment provide maximal benefit in terms of outcome” (Rivers et al., 2001, pg. 1368). The researchers conducted a randomized, controlled trial wherein patients who entered an urban emergency department with severe sepsis or septic shock were randomly assigned to receive either the six-hour, early, goal-directed therapy or standard therapy (Rivers et al., 2001).

A total of 288 patients were evaluated, with N=263 patients enrolled in the study and 236 completed the initial six-hour period (Rivers et al., 2001). The authors found the mean arterial pressure was lower in the standard therapy group; however, all patients met the goal MAP of greater than 65 mmHg (Rivers et al., 2001). Results indicated mixed venous oxygen saturation (SvO<sub>2</sub>) greater than 70% was met by 60.2% of patients in the control group compared with 94.9% in the early therapy group. Hemodynamic goals, including MAP, central venous pressure and urine output, were met by 86.1% of the standard group versus 99.2% of the early therapy group (Rivers et al., 2001). Those in the standard group were found to have lower SvO<sub>2</sub>, greater base deficit, increased heart rate, and lower MAP (Rivers et al., 2001). Rivers et al. (2001) looked at the Acute Physiology and Chronic Health Evaluation (APACHE II) and Multiple Organ Dysfunction Score (MODS) of patients in the standard group. Clinicians utilize these tools to assess acuity

levels of patients in the ICU. The APACHE II and MODS scores, those assigned to the standard therapy group, had significantly higher scores compared with those in the early therapy group (Rivers et al., 2001). In-hospital mortality rates showed a significant increase in the standard therapy group as well as the 28-day and 60-day mortality rates (Rivers et al., 2001). There were no significant differences overall between the groups in total fluid volume, use of inotropic agents and use of healthcare resources (Rivers et al., 2001). The authors concluded that the use of early, goal-directed therapy improved short and long-term outcomes in patients with severe sepsis and septic shock and they recommended future studies on quality and timing of treatment earlier in the disease process (Rivers et al., 2001). This study was limited by its partially blinded design creating bias among the standard therapy group (Rivers et al., 2001). Rivers and colleagues were rated a level A based on their level of quality through application of the Johns Hopkins Evidence-Based Practice Scale criteria (see Appendix A).

Following the Rivers and colleagues (2001) study, others continued to examine the efficacy of EGDT. Jones, Focht, Horton and Kline (2007) sought to examine the effectiveness of EGDT on mortality and morbidity in patients presenting to the emergency department. The authors assert, “an effectiveness trial determines if a treatment does more good than harm when delivered under real world conditions” (Jones, Focht, Horton, & Kline, 2007, pg. 430). The authors performed a prospective before-and-after study to assess a change in mortality after EGDT intervention was implemented in an emergency department compared with mortality rates prior to implementation (Jones, Focht, Horton & Kline, 2007).

The authors included N=157 patients, 79 in the before phase and 77 in the after phase between August 1, 2004 and October 31, 2006 (Jones, Focht, Horton & Kline, 2007). The authors found a 9% absolute reduction in mortality and 33% relative reduction between the two groups; however, the difference in the Kaplan-Meier survival estimate ( $p=0.13$ ) was not significant for the two groups (Jones, Focht, Horton & Kline, 2007). Intensive care unit length of stays and hospital length of stays were longer in the after group at 1.8 days and 1.2 days, respectively (Jones, Focht, Horton & Kline, 2007). The post-intervention group received higher volumes of crystalloid infusions and vasopressors, but there was no significant increase ( $p=0.21$ ) in packed red blood cell transfusions or dobutamine administration (0.61) between the two groups (Jones, Focht, Horton & Kline, 2007).

The authors acknowledge the patients in the before phase had a lower severity of illness and the study does not allow extrapolation of the data to determine the effectiveness of specific protocol components (Jones, Focht, Horton & Kline, 2007). The authors also acknowledge a possible Hawthorne effect triggering increased awareness by clinical staff resulting in earlier response to physiological changes (Jones, Focht, Horton & Kline, 2007). Antibiotic administration times decreased significantly in the intervention group from 142 minutes to 99 minutes and patients received corticosteroids 40% of the time as opposed to 6% in the before phase (Jones, Focht, Horton & Kline, 2007). Other limitations are present in this study. First, the design was not random, although the aim was not to replicate the original EGDT study (Jones, Focht, Horton & Kline, 2007). Secondly, the small sample size does not allow for inferences about statistical differences in mortality rates between the two groups (Jones, Focht, Horton &

Kline, 2007). Furthermore, the authors stipulate inclusion bias may be present in both groups, either from being misdiagnosed or not treated with EGDT in the after-phase (Jones, Focht, Horton & Kline, 2007). Other treatments not studied as part of EGDT, such as antibiotic treatment and steroids may have an effect on overall improved outcomes (Jones, Focht, Horton & Kline, 2007). Jones and colleagues (2007) were rated a level B based on their level of quality through application of the Johns Hopkins Evidence-Based Practice Scale criteria (see Appendix A).

Rusconi et al. (2015) analyzed current research to evaluate the effectiveness of early, goal-directed therapy in reducing mortality of severe sepsis and septic shock. Five studies with a total of N=4,033 patients were included in the review (Rusconi et al., 2015). The reviewers reduced the risk of bias by including only randomized controlled trials in their review (Rusconi et al., 2015).

The five studies included in the review were assessed for heterogeneity using the *I<sup>2</sup>* statistic based on criteria in the *Cochrane Handbook for Systematic Reviews of Interventions* version 5.1.0 (Rusconi et al., 2015). Data were analyzed using Review Manager 5.3 software and DerSimonian and Laird random effects method was used to pool the data (Rusconi et al., 2015). The authors used risk ratio (RR) with 95% confidence intervals for reporting dichotomous data (Rusconi et al., 2015).

The studies represented data from various countries including the United States, China, New Zealand, Finland, England and Republic of Ireland (Rusconi et al., 2015). The settings ranged from single-academic-tertiary-level care emergency departments to multicenter trials across tertiary and non-tertiary urban and rural hospitals (Rusconi et al., 2015). There was wide variation in inclusion criteria related to septic shock for patients

amongst the five studies reviewed (Rusconi et al., 2015). All of the studies included compared EGDT with usual care, and all purported to use the original EGDT protocol outlined in the Rivers' study (Rusconi et al., 2015). In-hospital mortality was significantly lower in two of the studies reviewed, with one study finding a 16-point decrease in mortality (Rusconi et al., 2013). The other three did not find a significant difference in mortality between the EGDT group versus the usual care group (Rusconi et al., 2015). These studies found a three point or less percentage difference between the two groups regarding mortality. Overall, the authors did not find a reduction in mortality between the two groups with RR 0.93, 95% CI (0.77 - 1.11), P=0.42 and moderate heterogeneity between studies ( $I^2=48\%$ ) (Rusconi et al., 2015).

The results preclude drawing any definitive conclusions regarding EGDT effectiveness and the authors noted that treatments varied widely among the five studies and between the two groups (Rusconi et al., 2015). It is possible that "usual care" has incorporated some aspects of EGDT in the 14 years separating some of the studies (Rusconi et al., 2015). The authors also noted that in original EGDT studies, the patients were older with more co-morbidities and higher lactate levels (Rusconi et al., 2015). The authors concluded that EGDT has positive effects on outcomes of septic patients but further research is needed on which elements of the treatment protocol are more effective. Like trauma, acute myocardial infarction and stroke, sepsis should be recognized and treated quickly in order to improve outcomes (Rusconi et al., 2015). Rusconi et al. (2015) concluded that rapid identification and early intervention are shown to be key in the treatment of sepsis, especially in at-risk patients. Rusconi et al. (2015) were rated a

level B based on their level of quality through application of the Johns Hopkins Evidence-Based Practice Scale criteria (See Appendix A).

Wira, Dodge, Sather and Dziura (2014) performed a meta-analysis of studies in which protocolized hemodynamic optimization was administered in the emergency department to determine if there is a significant reduction in mortality. To reduce publication bias, the authors also searched for published abstracts related to *sepsis* and among critical care and emergency medicine (Wira, Dodge, Sather, & Dziura, 2014). The authors structured the analysis on QUOROM and MOOSE recommendations for scientific reviews (Wira, Dodge, Sather, & Dziura, 2014). A total of twenty five studies and abstracts were identified, representing N=9597 from various emergency departments (Wira, Dodge, Sather, & Dziura, 2014).

The studies were analyzed using Fisher's exact test and two-tailed p-value for statistical significance of the primary outcome of short-term mortality with a p-value <0.05 being significant (Wira, Dodge, Sather, & Dziura, 2014). The reviewers used the Comprehensive Meta-Analysis version 2.0 for meta-analysis (Wira, Dodge, Sather, & Dziura, 2014). All of the studies analyzed used "hemodynamic optimization pathways" with MAP thresholds for vasopressor initiation and all but one study used mixed central or venous oxygen saturation monitoring (Wira, Dodge, Sather, & Dziura, 2014). Of the fifteen published studies, N=1795, the mortality rate amongst those patients who received protocolized hemodynamic optimization was 25.7% compared with 44.3% of those in control groups (Wira, Dodge, Sather, & Dziura, 2014). Among the ten abstracts, N=4236, analyzed, the mortality rate was 25.8% for patients receiving protocolized hemodynamic monitoring and 39.7% for control group (Wira, Dodge, Sather, & Dziura, 2014). Each

study reviewed found a lower mortality rate in those patients that received goal-directed therapy when compared to control groups, and the pooled data from the 25 studies of 9,597 patients found a 15.8% reduction in mortality (Wira, Dodge, Sather, & Dziura, 2014).

This review had a number of limitations, with one being heterogeneity. The studies included did not all have clear, identifiable strategies of which patients to target for EGDT, and it is unclear whether those with severe sepsis benefited from EGDT or a reduction in mortality was seen only in those with septic shock (Wira, Dodge, Sather, & Dziura, 2014). Another limitation to this analysis was that only one study was a randomized control trial; the others were before-after designs, which subjects them to selection bias, patient variability, and incomplete data (Wira, Dodge, Sather, & Dziura, 2014). Wira, Dodge, Sather, and Dziura (2014) were rated a level B based on their level of quality through application of the Johns Hopkins Evidence-Based Practice Scale criteria (see Appendix A).

## **2.5 Sepsis Bundles**

With the continued evidence supporting EGDT therapy, focus shifts to implementation of the Surviving Sepsis Campaign's (SSC) recommended 6-hour resuscitation bundle, focusing on early management of sepsis. Current research illustrates a reduction in mortality post-implementation of protocols and bundles. Westphal et al. (2011) conducted research focusing specifically on mortality rates post-implementation of an early detection protocol. Westphal and colleagues (2011) highlighted the fact that "there was a great delay in detection of the first signs of sepsis and in the proper management of the septic patient" across hospitals. The authors conducted a retrospective



study design of two hospitals in Brazil (Westphal et al., 2011, pg. 77). Analysis was conducted using the Number Cruncher Statistical System version 2000 and Power Analysis Software, version 2000 or Statistical Package for Social Sciences, version 13.0 (Westphal et al., 2011). A total of N=102 patients were found to meet inclusion criteria in phase I, before implementation, and N=115 met criteria in phase II, after implementation (Westphal et al., 2011). The authors found that the time to identification of first signs of sepsis and detection of sepsis was longer in phase I than phase II (34 hours vs. 11 hours, respectively) (Westphal et al., 2011). The 28-day mortality rates were significantly lower in phase II (48% vs. 24.3%) (Westphal et al., 2011).

The authors also found in-hospital mortality decreased from 61.7% to 36.5% post-implementation and they found those who did not survive had a longer time between first signs of sepsis and detection by staff (Westphal et al., 2011). Westphal and colleagues (2011) concluded: “active, systematic surveillance for sepsis-related clinical signs can result in early suspicion and diagnosis...leading to prompt treatment and, most impressively, to reduced mortality.” (pg. 78). This study supports the idea that an early-warning system focused on early identification promotes effective management of severe sepsis and septic shock (Westphal et al., 2011).

This study was limited by the small sample size and the biases present between the two groups may reduce the degree of certainty of the results (Westphal et al., 2011). The authors did not control for confounding variables in the two groups and selection bias may be present in phase II due to the active surveillance technique utilized (Westphal et al., 2011). Westphal et al. (2011) were rated a level B based on their level of

quality through application of the Johns Hopkins Evidence-Based Practice Scale criteria (See Appendix A).

Other studies illustrating the utility of sepsis bundles and protocols point out the impact nurses can have on improving time to treatment and reducing mortality. Bruce, Maiden, Fedullo, and Kim (2015) conducted a retrospective chart review of adult patients admitted to two emergency departments with severe sepsis or septic shock. The study evaluated the impact of a nurse-initiated bundle in the emergency department on time to antibiotics, compliance with 3-hour SSC bundle outcomes and in-hospital mortality rate (Bruce, Maiden, Fedullo, & Kim, 2015). Patients included in the study were 18 years and older with an ICD-9 code for severe sepsis and septic shock between September 2011 and May 2012 for a sample size N=195 (Bruce, Maiden, Fedullo, & Kim, 2015). Analysis was conducted using SPSS software, version 21.0 (Bruce, Maiden, Fedullo, & Kim, 2015).

The study found no statistically significant differences in the pre-and post-protocol groups regarding patient characteristics, with the exception of lower systolic blood pressure (< 90mmHg) in the pre-protocol group compared with post-protocol (47.5% vs. 22.4%, respectively,  $p=0.003$ ,) (Bruce, Maiden, Fedullo, & Kim, 2015). Regarding compliance, there was high compliance with lactate measurement, blood culture draws and antibiotic administration, with lactate measurement having a statistically significant improvement between pre-and post-protocol groups (83.9% vs. 98.7%,  $p=0.003$ ). Antibiotic administration was relatively unchanged between the two groups; however, time to initial administration decreased between pre-and post-protocol by 27 minutes (135 minutes vs. 108 minutes). There was not a statistically significant

difference in compliance with fluid resuscitation ( $p=0.139$ ), hospital length of stay ( $p=0.762$ ), or in-hospital mortality rates ( $p=0.838$ ) (Bruce, Maiden, Fedullo, & Kim, 2015). The authors found five predictors of increased in-hospital mortality: 1) respiratory dysfunction, 2) CNS dysfunction, 3) UTI, 4) vasopressor administration, 5) body weight (Bruce, Maiden, Fedullo, & Kim, 2015).

Emergency nurses are critical in triaging and identifying patients with sepsis and using a nurse-initiated bundle, with standard orders, can reduce time to antibiotic administration and fluid resuscitation (Bruce, Maiden, Fedullo, & Kim, 2015). Close collaboration with the multidisciplinary team is crucial in ensuring timely initiation of medical interventions (Bruce, Maiden, Fedullo, & Kim, 2015).

This study had several limitations. First, a power analysis was not completed for sample size, and the sample size was relatively small, therefore, small changes in mortality rate could not be determined and generalizability would be difficult for this study (Bruce, Maiden, Fedullo, & Kim, 2015). Nurses' understanding of the education was not evaluated and it is unknown to what extent the education altered behaviors. Selection bias was a concern as well as it is unknown how many patients without sepsis triggered the protocol and conversely how many patients with severe sepsis and septic shock did not trigger the protocol (Bruce, Maiden, Fedullo, & Kim, 2015). Lastly, the study was based on the SSC 2008 guidelines instead of 2012, which affected the fluid resuscitation recommendation for patients with lactate measurement greater than 4mmol/L and those with hypotension (Bruce, Maiden, Fedullo, & Kim, 2015). Bruce, Maiden, Fedullo, & Kim (2015) were rated a level B based on their level of quality

through application of the Johns Hopkins Evidence-Based Practice Scale criteria (see Appendix A).

Another study, focusing on nurses' role in recognition and treatment of septic patients, illustrated similar results with compliance with the 6-hour sepsis bundle (Tromp et al., 2010). The authors focused on identifying the importance of nurses in implementing SSC bundles. Tromp and colleagues (2010) noted "nurses are often the first to triage a patient, and they have an important role in recognizing patients' signs and symptoms." (pg. 1465). However, the role of nurses is not mentioned in the SSC guidelines nor has it been fully utilized (Tromp et al., 2010).

For this study, the authors conducted a prospective before- and- after intervention study, where they reviewed a newly developed nurse-driven bundle (Tromp et al., 2010). Training was provided to the staff about sepsis and feedback about staffs' performance was given before and after the protocol was introduced (Tromp et al., 2010). The primary outcome measure was compliance with the bundle and completion of individual elements. "The theory behind care bundles is that when several evidence-based interventions are grouped together in a single protocol, it will improve patient outcomes." (Tromp et al., 2010, pg. 1468). The study was not powered to show significance on length of stay and mortality rate; however, these were secondary outcome measures (Tromp et al., 2010).

The study included N=825 patients presenting with sepsis to the emergency department with no statistically significant difference in patient characteristics. In 731 cases, information on six elements was available, with increases in compliance in all six seen across periods one to three (3.5% to 10.8% to 12.4%; 95% CI, 3.6 (1.4-9.0) (Tromp

et al., 2010). There was a significant improvement in completion of three of the six elements after period two and a significant improvement in four of six elements in period three. Lactate measurement improved from 23% to 80% (95% CI, 3.9 (3.0-5.2), chest x-ray improved from 67% to 83% (95% CI, 1.9 (1.3-2.7), urinalysis and culture improved 49% to 67% (95% CI, 1.5 (1.2-1.9) and antibiotic administration within three hours improved from 38% to 56% (95% CI, 1.4 (1.2-1.7)(Tromp et al., 2010). Appropriate inclusion of patients into the bundle improved from period two to period three from 71% to 82%, respectively, and the compliance rate was 88% for all six elements in patients included in the bundle. The mortality rate decreased from 6.3% to 5.5%, but the decrease was not statistically significant and there was no change in hospital length of stay (Tromp et al., 2010).

The study suggests that use of a nurse-driven bundle accompanied with training and feedback improves early recognition and treatment (Tromp et al., 2010). Tromp and colleagues (2010) state the use of a simple and inexpensive implementation program can improve quality of care. The ability to recognize sepsis with the use of bundle elements results in better compliance and better outcomes (Tromp et al., 2007). The authors point out “giving the nurses a greater responsibility in the recognition and treatment of patients with sepsis, the care for these patients obtained a more multidisciplinary character and our study demonstrates that this was associated with an improvement in quality of care” (Tromp et al., 2010, pg. 1465).

This study had several limitations. The study was uncontrolled and in a single center which decreases its generalizability. The implementation program was also specific to this institution, so results cannot be extrapolated (Tromp et al., 2010). The

sepsis screening criteria are sensitive but not specific which leads to over-diagnosis and treatment; however, 82% of patients were diagnosed with an infection, indicating a lower rate of false-positives (Tromp et al., 2010). Tromp et al. (2010) were rated a level B based on their level of quality through application of the Johns Hopkins Evidence-Based Practice Scale criteria (see Appendix A).

Vanzant and Schmelzer (2011) focused on research identifying bundle components and early detection tools to help initiate treatment earlier in severe sepsis and septic shock. Vanzant and Schmelzer (2011) acknowledged early recognition and treatment greatly improve survival rates of severe sepsis and administration of broad-spectrum antibiotics within one hour of recognition is paramount to survival. They further state, “early initiation of medical interventions (e.g. fluid resuscitation) is essential for maintaining blood flow through the microcirculation to prevent organ damage”. The authors highlight that “early sepsis detection also has implications for triage, because triage is used to categorize a patient’s acuity level and resource requirements, to determine treatment priorities” (Vanzant & Schmelzer, 2011). The authors reviewed current research focusing on detection of sepsis and found multiple strategies to be used for early detection. Vanzant and Schmelzer (2011) noted that research illustrates the use of serum lactate measure as a strong indicator of the degree of hypoperfusion and a strong predictor of progression of septic shock, allowing earlier identification of deterioration in patients. They found that mortality rate increased as serum lactate measurements increased and that those in which lactate measurement decreased within the first 24 hours of recognition had significantly lower mortality rates than those in which the elevation persisted. The research emphasized the use of screening tools to

assist in earlier detection and treatment (Vanzant & Schmelzer, 2011). The research illustrated the use of screening tools improves early detection and earlier initiation of evidence-based treatment to improve outcomes. The authors concluded emergency nurses are in a vital position to assess and recognize sepsis timely and therefore improve outcomes (Vanzant & Schmelzer, 2011). Vanzant and Schmelzer (2011) were rated a level B based on their level of quality through application of the Johns Hopkins Evidence-Based Practice Scale criteria (see Appendix A).

Turi and Von Ah (2013) conducted a systematic review focused on implementation of early, goal-directed therapy bundles using the guidelines outlined in the *Surviving Sepsis Campaign: For Septic Patients in Emergency Departments*. The review noted that the Surviving Sepsis Campaign has incorporated elements of early goal-directed therapy in order to reduce mortality and morbidity of sepsis patients (Turi & Von Ah, 2013).

The authors focused their review on two distinct subheadings: “Operational and System Issues” and “Implementation of Specific Components of the SSC Guidelines” (Turi & Von Ah, 2013). The authors noted that identification of sepsis is a major barrier to implementing guidelines in the emergency department (Turi & Von Ah, 2013) Three of the seven studies included in this review found recognition of sepsis either delayed or prevented treatment of sepsis among patients entering the emergency departments (Turi & Von Ah, 2013). Sepsis can be difficult to identify and noticeable vital sign changes often accompany a swift decline in patient status (Baldwin et al., 2008 as cited in Turi & Von Ah, 2013). Turi and Von Ah (2013) state the studies acknowledge that nurses and

physicians in emergency departments do not initially recognize sepsis and therefore diagnosis is made late in disease progression, leading to delays in treatment.

Secondly, the authors focused on specific components of the guidelines. The authors found five of the seven studies reported the use of central venous catheter insertion for hemodynamic monitoring and four of the seven studies found monitoring occurred 43.8%-82.9% of the time (Turi & Von Ah, 2013). Mean arterial pressure was monitored in five of the studies and blood cultures were obtained in three of the seven studies, and three of the seven studies found improvement in time to antibiotic administration (Turi & Von Ah, 2013). None of the studies noted antibiotic administration within the first hour, which is a key component of the SSC guidelines (Turi & Von Ah, 2013). Five of the seven studies reported lactate measurements; but, they were not obtained the majority of the time (Turi & Von Ah, 2013).

The authors found collaboration, preplanning, and education between emergency department and intensive care staff improved implementation of early, goal-directed guidelines (Turi & Von Ah, 2013). Further, the literature noted higher success rates in emergency departments utilizing physician and nurse education and training prior to implementation (Turi & Von Ah, 2013). The review found sepsis identification remains a significant barrier to timely therapy and prompt diagnosis (Turi & Von Ah, 2013). Therefore it is recommended that nurses and physicians are educated on early signs and symptoms of sepsis in order to prevent treatment delays (Turi & Von Ah, 2013). Turi and Von Ah (2013) were rated a level B based on their level of quality through application of the Johns Hopkins Evidence-Based Practice Scale criteria (see Appendix A).



Burney et al. (2012) assessed and identified barriers to implementation of sepsis bundles. The authors provided clear and convincing evidence through other studies of the benefits of early treatment and recognition through the use of sepsis bundles (Burney et al., 2012). The authors noted that “time of initiation, rather than choice of monitoring modalities, played the biggest role in improving outcomes. The benefit of bundles appeared to be lost if they were initiated late in the course of the disease” (Burney et al., 2012, pg. 513). The purpose of this study was to implement a sepsis quality improvement project in an emergency department aimed at reducing mortality, improving time to recognition and treatment, and enhancing communication (Burney et al., 2012). The authors used a cross-sectional design to survey full-time staff nurses and physicians in a single, urban emergency department from November 1, 2010, to December 31, 2010 (Burney et al., 2012). The data was analyzed using the PASW/SPSS version 18.0 software, using descriptive statistics for baseline knowledge and attitudes (Burney et al., 2012).

A total of N=85 of nurses and physicians responded to the survey, with a response rate of 43% among all nurses, 57% among attending physicians, and 38% among residents (Burney et al., 2012). The authors found delays in diagnosis, delays in treatment, and poor recognition at triage were the greatest barriers identified (Burney et al., 2012). Other barriers noted were lack of access to central venous pressure and oxygen saturation measurement, lack of space in ER, and an insufficient number of nursing staff needed to carry out protocol (Burney et al., 2012). It was noted that 89.5% of nurses and 86% of physicians stated a written protocol similar to those for acute coronary syndrome and pneumonia would be beneficial (Burney et al., 2012). The authors also found only

15.8% of nurses acknowledged timely reporting of abnormal vital signs and 85% of nurses were “somewhat” or “not at all” familiar with SIRS criteria (Burney et al., 2012). Less than half of physicians surveyed (43.2%) reported they “hardly ever” ordered a lactate measurement and the nurses surveyed reported a lactate greater than 8.3mmol/L instead of 4mmol/L, was significant for sepsis (Burney et al., 2012, pg. 515). Surveyed nurses also reported a lack of knowledge regarding the correlation between lactate measures and sepsis (Burney et al., 2012).

The authors noted the importance of focusing education for nurses on prompt identification of sepsis and the need to take swift action to initiate treatment (Burney et al., 2012). The authors underscored the importance that nurses are essential in recognizing sepsis and alerting physicians to initiate early treatment (Burney et al., 2012). Burney and colleagues (2012) discovered identifying patients with sepsis was a significant obstacle to implementation of sepsis bundles. Furthermore, previous literature noted missed recognition of patient deterioration at triage and delays in diagnosis were commonly cited barriers to bundle implementation (Burney et al., 2012).

A few limitations to this study were present. First, the study utilized a voluntary survey design, leading to selection bias. Second, the survey tool was not validated and was developed solely for this study and therefore the results may not be reproduced. Burney et al. (2012) were rated a level B based on their level of quality through application of the Johns Hopkins Evidence-Based Practice Scale criteria (see Appendix A).

Burrell, McLaws, Fullick, Sullivan, and Sindhusake (2016) conducted a study on recognition, resuscitation, and early treatment using standardized tools to decrease

mortality and improve outcomes in New South Wales. The authors discovered 34% of clinical units did not have guidelines or protocols for sepsis management and failure to recognize and report sepsis has been regularly reported (Burrell et al., 2016). The study promoted a SEPSIS KILLS bundle emphasizing blood culture draws, lactate measurement, antibiotic administration within an hour of triage, and a fluid bolus of 20ml/kg (Burrell et al., 2016). The authors discovered utilizing guidelines for early recognition and treatment can improve outcomes and expedite treatment recommendations in emergency departments, especially if assessed at triage (Burrell et al., 2016).

A total of 97 emergency departments participated in this study. Data was obtained using an online sepsis database to include age, triage time, date, triage category, vital signs, serum lactate, time and date of antibiotic administration, and time of fluid resuscitation (Burrell et al., 2016). A prospective and retrospective chart review was conducted to collect data, allowing emergency departments to monitor time to antibiotics and fluid resuscitation in real time (Burrell et al., 2016).

A total of 13,657 patient records were analyzed for in-hospital mortality and sepsis severity and patients were classified using the Australian Triage Scale (ATS) (Burrell et al., 2016). There was a significant reduction in age of patients from 2009 to 2013 (67.3 to 64.8 years;  $p < 0.0001$ ). During the same time period, the authors found an increase in patients categorized as ATS 1 “see immediately” and ATS 2 “see within 10 minutes” from 2.3% to 4.2% for ATS 1 ( $p < 0.001$ ) and 40.7% to 60.7% for ATS 2 ( $p < 0.001$ ) (Burrell et al., 2016). Antibiotic administration within one hour increased from 29.3% to 52.2% ( $p < 0.001$ ) and patients receiving their second liter of fluid within the

first hour improved from 10.3% to 27.5% ( $p < 0.001$ ) (Burrell et al., 2016). Mortality decreased from 19.3% to 14.1% ( $p < 0.0001$ ) over the four-year study period (Burrell et al., 2016). The authors discovered mortality for patients with severe sepsis (lactate  $> 4$ mmol/L or systolic blood pressure  $< 90$ mmHg) was 19.7% ( $p < 0.0001$ ) and these patients were more likely to die than those with uncomplicated sepsis (lactate  $< 4$ mmol/L and systolic blood pressure  $> 90$ mmHg) (Burrell et al., 2016). In patients with lactate level of  $> 4$ mmol/L, the mortality rate was 24.9% and in those with normal blood pressure and elevated lactate, the mortality rate was 21.2% (Burrell et al., 2016). The authors found an increase in mortality in patients with uncomplicated sepsis admitted to the ward (3.2% in 2009-2011 to 6.2% in 2013,  $p = 0.047$ ) (Burrell et al., 2016). There was no significant change in mortality for patients with severe sepsis admitted to the ICU (23.4% to 16%,  $p = 0.145$ ) (Burrell et al., 2016). Although the authors encountered problems with high turnover in the emergency department and management of antibiotic regimens, the study found improvement in time to treatment and reduced mortality when utilizing a sepsis toolkit based on the SSC guidelines (Burrell et al., 2012).

The authors noted several limitations to the study including the prolonged run-in period. The authors noted difficulty with the voluntary nature of data collection, resulting in inconsistent submission and lack of strict diagnostic criteria (Burrell et al., 2016). Limited resources across emergency departments led to implementation of pathways but lack of data submission (Burrell et al., 2016). Burrell et al. (2016) were rated a level B based on their level of quality through application of the Johns Hopkins Evidence-Based Practice Scale criteria (see Appendix A).

## 2.6 Early-Warning Systems

Early detection of patient deterioration improves patient outcomes, reduces intensive care admissions, and decreases mortality (Race, 2015). By assigning numerical values to certain physiological parameters, identification of patients at risk for critical illness and increased mortality can be made earlier before patient deterioration occurs (Corfield et al., 2014). The idea that physiological decline precedes clinical decline led to the development of early-warning scores and tools to improve recognition (Corfield et al., 2014).

Despite the limited data on the accuracy and reliability of early-warning scores, specifically the Modified Early-Warning Score (MEWS), research on the use, accuracy and reliability of these tools has increased over the last ten years.

In 2014, Corfield et al., conducted a prospective, observational study to evaluate the utility of the National Early Warning Score (NEWS) in 20 Scottish emergency departments. The authors sought to “determine whether a single NEWS on ED arrival is a predictor of outcome, either in-hospital death within 30 days or intensive care admission within 2 days, in patients with sepsis” (Corfield et al., 2014). This study provides evidence that an EWS can help predict necessity for hospital admission and mortality risk (Corfield et al., 2014). Complete data was obtained on 3,890 patients and of those patients, only those who presented with or developed signs of sepsis prior to leaving the ER were included; patients without a full set of initial observations were excluded leaving a final sample size of N=2003 (Corfield et al., 2014). The primary outcomes evaluated were ICU admission within 2 days of presentation and 30-day

mortality (Corfield et al., 2014). Data was analyzed using SPSS V.17.0 for MS Windows (Corfield et al., 2014).

There was no significant difference between men and women in the study and the median age of patients was 72. The median early-warning score for all patients was 7 and there was no significant difference in scores between men and women (Corfield et al., 2014). Those patients admitted to the ICU had higher NEWS than the non-ICU patients (9 vs. 6, respectively,  $p < 0.05$ ) and those patients that died within 30 days were older and had higher NEWS (9 vs. 6,  $p < 0.05$ ) (Corfield et al., 2014). Corfield and colleagues (2014) discovered a one-point rise in NEWS was associated with an increase in mortality (1.95, 95% CI 1.21 to 3.14) and those patients with a NEWS  $> 7$  had a positive predictive value of 27% for ICU admission or mortality within 30 days. For a NEWS  $> 9$ , that number rose to 35% (Corfield et al., 2014).

The authors conclude that the use of an EWS in the emergency department can improve outcomes in patients with sepsis (Corfield et al., 2014). The authors also conclude that use of the EWS can help determine the need for review by senior clinician or critical care team (Corfield et al., 2014).

This study has several limitations. The sample size was limited due to missing observations in patient records. The study also excluded patients discharged within two days; although, it can be hypothesized that those patients had a much lower risk of severe illness (Corfield et al., 2014). There was no follow up after discharge therefore, who were discharged and died within 30 days were not included (Corfield et al., 2014). This study only assessed sepsis patients, and results cannot be generalized to patients with other illnesses (Corfield et al., 2014). Corfield et al., (2014) were rated a level B based on their

level of quality through application of the Johns Hopkins Evidence-Based Practice Scale criteria (see Appendix A).

So, Ong, Wong, Chung, and Graham (2015) discovered use of the Modified Early Warning Score (MEWS) assisted new or inexperienced nurses in identifying patient deterioration. The authors found limited studies proving the accuracy of an early-warning system in the emergency department. The authors note “nurses detect and respond to patient deterioration by vital signs checking and individual nurses’ clinical judgment. There are various factors that may affect nurses’ decision making such as clinical experience, manpower, and workload” (So et al., 2015). Therefore, the purpose of this study was to assess the effectiveness and accuracy of identifying patient deterioration using the MEWS score (So et al., 2015). The authors conducted an observational study in an ED in Hong Kong between January and March 2013 (So et al., 2015). Data analysis was performed using Microsoft Excel, version 14.0. Sensitivity and specificity with 95% confidence intervals were calculated (So et al., 2015).

Sample size was N=544, with 269 patients in the MEWS group and 275 in the usual observation group (So et al., 2015). The authors found an 11.5% pathway activation response in the MEWS group compared with 5.1% in the usual observation group and a change in management plan in 10% of MEWS patients compared with 4.7% of those in the usual observation group (So et al., 2015). The authors found IV fluid and priority admission were the most common intervention in the MEWS group with priority admission representing the most common intervention in the usual observation group (So et al., 2015). The authors found one adverse event in both the MEWS group and the usual observation group, with both patients dying within the first 24 hours of admission

(So et al., 2015). Sensitivity was 100% in both groups in predicting patient deterioration and specificity increased slightly in the MEWS group - from 97.8% in the usual observation group to 98.3% in the MEWS group (So et al., 2015). The authors revealed the MEWS score was a strong predictor in detecting deterioration in high-risk patients (MEWS > 5) (So et al., 2015). The authors noted nurses' clinical judgment is accurate in predicting and recognizing clinical deterioration and combining clinical judgment with the MEWS score enhances the nurses' ability to identify decline promptly, and provide objective evidence of deterioration (So et al., 2015).

There were several limitations to this study. The sample size was small, which, along with patient deterioration and adverse events, led to difficulty in finding causal effects for study outcomes (So et al., 2015). The MEWS performance was difficult to ascertain, as it was incorporated with nursing judgment and the patients were not randomly chosen, leading to an uneven baseline condition between the two groups (So et al., 2015). Lastly, nursing experience ranged from 6-9 years, and therefore MEWS performance can only reflect accuracy among this experienced group. Generalization of results is difficult for this study due to the single center setting and small sample size (So et al., 2015). So et al. (2015) were rated a level B based on their level of quality through application of the Johns Hopkins Evidence-Based Practice Scale criteria (see Appendix A).

Delgado-Hurtado, Berger, and Bansal (2016) found incorporating MEWS into an electronic health record (EHR) can be used in triage to categorize patient acuity. Delgado-Hurtado, Berger, and Bansal (2016) state a higher MEWS score has been associated with increased rate of admission and mortality and MEWS can be used as a



reliable tool to identify patients requiring more intensive care due to increased risk of death. The purpose of this study was to assess whether use of the MEWS in the ER is associated with hospital admission, admission disposition, in-hospital mortality, and length of stay (Delgado-Hurtado, Berger, & Bansal, 2016). The authors retrospectively reviewed patient data from January 1, 2014, to May 31, 2015, and randomly sampled N=3,000 patients for this study (Delgado-Hurtado, Berger, & Bansal, 2016). Analysis was performed using different statistical tests appropriate for each measure (Delgado-Hurtado, Berger, & Bansal, 2016).

The authors found 80.7% of patients were not admitted and 19.3% were admitted to a general medicine or critical care unit (Delgado-Hurtado, Berger, & Bansal, 2016). Of the 3,000 patients, 2,147 had MEWS automatically calculated. The authors found patients admitted to the hospital were older, arrived by ambulance; and had a higher mean, maximum and median MEWS than patients not admitted (medians of 1.1 vs. 0.2, 2 vs. 1, and 1 vs. 0, respectively,  $p < 0.0001$ ) (Delgado-Hurtado, Berger, Bansal, 2016). Those patients admitted to the ICU had higher MEWS than those admitted to a general floor ( $p < 0.0001$ ) (Delgado-Hurtado, Berger, & Bansal, 2016). Furthermore, it was found that patients who died had higher MEWS and there was a significant relationship between length of stay and mean, maximum, and median MEWS (medians of 2.6 vs 0.3, 4 vs. 1, 3 vs. 1, respectively;  $p < 0.0001$ ) (Delgado-Hurtado, Berger, & Bansal, 2016).

The authors found the results support the use of the MEWS during triage in identifying higher patient acuity and it was further noted the results were similar to previous studies in which higher MEWS were associated with admission (Delgado-Hurtado, Berger, & Bansal, 2016). Delgado-Hurtado, Berger and Bansal (2016) further

note in a recent study that “for every 1 point increase in the MEWS, patients were 33% more likely to be admitted to the hospital,” and other studies indicate in-hospital mortality is associated with higher MEWS.

The study has some limitations. First, physicians were not blinded to the MEWS and may have used the score in their decision on admission (Delgado-Hurtado, Berger, & Bansal, 2016). Second the study was retrospective in nature and therefore some patients were excluded, introducing selection bias (Delgado-Hurtado, Berger, & Bansal, 2016). The authors note that the sample size was large; most of the patients without MEWS were not admitted to the hospital; and with very few exclusion criteria, the results can be generalized (Delgado-Hurtado, Berger, & Bansal, 2016).

In conclusion, the authors state, “to have the impact on quality of care and mortality that has been described in the past, the MEWS has to be implemented and used in a systematic and protocolized way” (Delgado-Hurtado, Berger, & Bansal, 2016, pg. 4). Berger, and Bansal (2016) were rated a level B based on their level of quality through application of the Johns Hopkins Evidence-Based Practice Scale criteria (see Appendix A).

In order to ascertain the impact of use of the Early Warning Score (EWS), Alam, Hobbelink, van Tienhoven, van de Ven, Janema, and Nanayakkara (2014) conducted a systematic review to evaluate the impact of the MEWS in the early recognition of patient deterioration. The authors state patient deterioration is precipitated by subtle changes in vital signs and level of consciousness and use of the EWS can assist in recognizing these changes earlier, preventing poor patient outcomes, increases in morbidity and mortality (Alam et al., 2014). The authors highlight the fact that preventable serious adverse events

are often missed due to “poor clinical monitoring, inadequate interpretation of changes in physiological parameters and inability to undertake appropriate action” (Alam et al., 2014). Many studies looking at the use of Early Warning Scores and Modified Early Warning Scores are observational studies, lacking control groups and therefore are usually not generalizable. The authors sought to evaluate the use of the EWS and MEWS and their effects on in-hospital mortality, ICU admissions, length of stay, cardiac arrests and serious adverse events in emergency departments and general wards (Alam et al., 2014).

The authors identified relevant publications using a search of databases including PubMed, EMBASE.com, and The Cochrane Library from inception to April 8, 2013 (Alam et al., 2014). The search generated 637 articles and after excluding duplicates and those not meeting inclusion criteria, seven articles remained for analysis (Alam et al., 2014).

With regards to mortality, the authors found six of the articles evaluated mortality, with two of the articles finding significant reduction in mortality when the EWS was combined with staff education programs (Alam et al., 2014). Alam and colleagues (2014) report that Paterson et al. (2006) found a 2.8% reduction in mortality ( $p=0.046$ ) after implementation of the EWS and Moon et al. found a 0.2% reduction ( $p<0.0001$ ) in mortality. Paterson et al. (2006) also found an eight-fold increase in mortality with  $MEWS > 4$  (15.3%; 95% CI 3.7-26.9) (Alam et al., 2014). One study investigated the impact of the MEWS in a trauma ER, finding a reduction in mortality across both men and women in pre- and –post MEWS mortality (0.4% males, 1.5% females, 0.9% in total;  $p=0.092$ ). Other studies reviewed found reductions in mortality but they were not

statistically significant (Alam et al., 2014). Only one study looked at mortality in the ICU, finding a reduction in mortality after introduction of the EWS, although it was not statistically significant (67% vs. 33%;  $p=0.21$ ) (Alam et al., 2014). Admission data was investigated in two studies, finding increases in admission rates to general units (14% to 21%;  $p=0.0008$ ) after initiation of the EWS, but noted decreases in admission to ICU (11% to 5%;  $p=0.0010$ ) (Alam et al., 2014). One study discovered an EWS  $> 4$  had a higher predictive value for serious adverse events in the five-day period after ICU discharge; nonetheless, they did not find a substantial decrease in adverse events after initiation of the EWS (Alam et al., 2014). One study showed an increase in cardio-pulmonary arrest after introduction of the EWS (2.3% vs. 0.6%;  $p=0.03$ ), but a second study found a reduction in arrests after implementation of EWS (Alam et al., 2014). One study found a significant correlation in length of stay with higher EWS, but others did not find significant reductions in length of stays, still, there were trends to shorter length of stays ( $p=0.001$ )(Alam et al., 2014).

The authors note conflicting conclusions concerning length of stay and cardiac arrests, though the authors generally note a positive trend towards improved outcomes after introduction of EWS (Alam et al., 2014). Alam and colleagues (2014) conclude that “recognizing patients in need of higher care can be quite challenging and is indeed dependent on many factors, such as work experience of the healthcare provider, as well as conscientious use of the given tools such as the EWS.” (Alam et al., 2014, pg. 593).

There were several limitations to this review. Differences in methodology and lack of description of methodology prevented the authors from noting positive outcomes in all areas of hospitals (Alam et al., 2014). Several studies also had small sample sizes

and patient characteristics, including age, may have influenced outcomes (Alam et al., 2014). Alam and colleagues (2014) conclude use of a simple warning system, such as EWS, can lead to improved patient outcomes and early detection of patient deterioration. Alam et al. (2014) were rated a level B based on their level of quality through application of the Johns Hopkins Evidence-Based Practice Scale criteria (see Appendix A).

Kyriacos, Jelsma, and Jordan (2011) conducted a systematic literature review of the use of EWS on adult inpatients. The aim of this review was to evaluate the use of an EWS on adult inpatient, outside of critical care and emergency departments (Kyriacos, Jelsma, & Jordan, 2011). The authors found 16 articles meeting their criteria of English articles of adult inpatients outside of critical care and emergency departments between 1998 and 2010 (Kyriacos, Jelsma, & Jordan, 2011).

The authors found MEWS are “deemed necessary” however little research exists to establish validity and effectiveness (Kyriacos, Jelsma, & Jordan, 2011). The authors note that patients on general wards are not monitored as closely and that lack of monitoring and suboptimal care is associated with poorer outcomes (Kyriacos, Jelsma, & Jordan, 2011). With infrequent monitoring of vital signs, early identification of deterioration is prevented and therefore there is rapid decline in patient condition and delay in transfer to higher care units (Kyriacos, Jelsma, & Jordan, 2011). The authors reveal the literature indicates misrepresentation of data and lack of multidisciplinary teamwork has led to poor outcomes along with delays in reporting (Kyriacos, Jelsma, & Jordan, 2011). The authors determined patient survival is dependent on nurses’ decisions to alert providers for help: 11.3% of patients were delayed up to one hour and 8.9% of patients experienced a delay greater than three hours (Kyriacos, Jelsma, & Jordan, 2011).

Furthermore, only 2.8% of Australian nurses would call a medical emergency team for change in vital signs. This lack of action can be attributed to lack of critical care skills and inexperience among nurses as well as junior doctors, according to the research (Kyriacos, Jelsma, & Jordan, 2011). The literature also notes nurses report lack of confidence in knowledge of certain medical terms and conditions, leading to delays in reporting (Kyriacos, Jelsma, & Jordan, 2011). Kyriacos, Jelsma, & Jordan (2011) point out their review of the research revealed standardized communication systems, like EWS and MEWS, can assist clinicians in reporting changes in condition and vital signs and use of the early-warning systems can be “track and trigger” systems to identify at-risk patients earlier. The authors report their search revealed no research to assess validity of EWS/MEWS charts and it is difficult to obtain results on validity and reliability of these systems due to the human error component (Kyriacos, Jelsma, & Jordan, 2011). There were seven observational studies that looked at validity of the MEWS, but the studies are unable to be generalized due to small sample size, single center studies, differing cut off parameters on the MEWS scale, and sample bias along with incomplete reporting (Kyriacos, Jelsma, & Jordan, 2011). All the studies measured heart rate and respiratory rate; six of the studies measured blood pressure, urine output and consciousness as well; four measured temperature; and two measured oxygen saturation in addition to other parameters (Kyriacos, Jelsma, & Jordan, 2011). One study specifically looked at validity, reliability and utility of MEWS outside of critical care areas, finding a lack of evidence for sensitivity, specificity, and predictive validity of MEWS, noting clinical judgment remains an essential aspect of patient care (Kyriacos, Jelsma, & Jordan, 2011).

The authors point out limitations in their review, including, a lack of randomized controlled trials of EWS/MEWS, leaving research void of evidence to ascertain utility of MEWS (Kyriacos, Jelsma, & Jordan, 2011). The authors point out that the “complexity of introducing an EWS system with an accompanying education program and audit, might suggest that a single RCT of an early-warning scoring system might be almost impossible” (Kyriacos, Jelsma, & Jordan, 2011, pg. 324). They further note the impracticality of randomizing patients in the same unit/ward who would receive differing monitoring parameters (Kyriacos, Jelsma, & Jordan, 2011). Only one study met all inclusion criteria and only observational studies on MEWS/EWS were located (Kyriacos, Jelsma, & Jordan, 2011). The authors found considerable variation in vital sign parameters in the track and trigger systems and the evidence shows abnormal vital signs, such as blood pressure, alteration in mental status, oxygenation and respiratory rate, are associated with serious adverse events, (Kyriacos, Jelsma, & Jordan, 2011).

The authors conclude increased monitoring improves care, but scoring systems have yet to be studied in large, randomized trials. Despite the lack of evidence validating the systems and lack of evidence of utility, MEWS/EWS show sufficient evidence of benefit in early recognition of deterioration (Kyriacos, Jelsma, & Jordan, 2011).

The use of MEWS can be an important patient predictor of risk and studies show that an EWS or MEWS score > 4 is more effective in identifying at-risk patients (Kyriacos, Jelsma, & Jordan, 2011). These simple tools can serve as trigger systems by recognizing abnormalities and allowing clinicians to intervene earlier to improve outcomes. Kyriacos, Jelsma, and Jordan (2011) were rated a level B based on their level

of quality through application of the Johns Hopkins Evidence-Based Practice Scale criteria (See Appendix).

## **2.7 Antibiotic Administration**

The relevance of early recognition is to initiate timely interventions in order to improve outcomes and decrease mortality. Timely antibiotic administration is a key factor in decreasing mortality and improving outcomes in septic patients (Vanzant & Schmelzer, 2010).

Puskarich et al., (2011) examined the association between time to initial antibiotics and mortality of septic shock patients in an emergency department based on an early therapy protocol. The researchers used a cohort of a recently completed prospective, non-blinded randomized clinical trial cohort (Puskarich et al., 2011). A total of N=300 patients were included in the study, with 291 receiving antibiotics.

The primary outcome was that in-hospital mortality and outcomes were compared for patients who received an initial dose of antibiotics at hourly increments up to six hours (Puskarich et al., 2011). Before and after outcomes were also compared at hourly increments of patients receiving antibiotics after shock recognition (Puskarich et al., 2011). Data was analyzed using StatsDirect 2.7.7 and STATA 10.0.

The authors discovered that 59% of patients received the initial dose of antibiotics after shock recognition, with positive blood cultures obtained in 34.4% of the patients (Puskarich et al., 2011). The overall mortality rate was 18.9%, and the mortality rate for positive blood culture septic shock was 26% versus 15.2% for negative blood culture shock ( $p=0.03$ ) (Puskarich et al., 2011). Of the 100 patients with positive cultures, ninety-one received antibiotics to which the causative organism was susceptible and of the nine



patients not treated with appropriate antibiotics, seven received antibiotics to which the organism was resistant and two had fungemia, untreated in ER (Puskarich et al., 2011). The mortality rate for those treated with appropriate antibiotics was 25.3% versus 33.3% ( $p=0.69$ ) for those treated inappropriately (Puskarich et al., 2011). The median time frame was 115 minutes, with no association found between mortality and time from ED triage to antibiotics (Puskarich et al., 2011). The authors found the median time to shock recognition was 89 minutes, and they discovered those receiving antibiotics after shock recognition had a significant increase in odds of death (OR 2.4, 95% CI 1.1 to 4.5). The authors also revealed no increase in mortality associated with delay in antibiotic administration after shock recognition (Puskarich et al., 2011). Puskarich et al. (2011) controlled for potential cofounders using a multivariate, logistic regression model and the adjusted odds ratio showed no changes when compared with unadjusted odds ratio.

The authors concluded that this study identified a decrease in mortality with administration of susceptible antibiotics; however, in contrast to a previous study, time of administration is less important than is administration during initial resuscitative phase (Puskarich et al., 2011). Administration of antibiotics prior to shock recognition is associated with decreased mortality, further outlining importance of early symptom recognition (Puskarich et al., 2011).

A strength of this study was the use of a “standardized, prescribed early recognition and resuscitation protocol”, which enabled the authors to remove variability of early treatment (Puskarich et al., 2011, pg. 6). Notwithstanding, this study had several weaknesses. First, the three hospitals used had experience with early resuscitation protocols, resulting in increased knowledge and experience dealing with symptom

recognition and interventions. These results may not be generalized to hospitals with limited early therapy protocols (Puskarich et al., 2011). Second, the majority of patients received antibiotics within 3 hours of triage, which creates wide confidence intervals and makes it more difficult to make associations due to longer time points (Puskarich et al., 2011). Difficulty in ascertaining the exact timing of onset of septic shock makes the timing of antibiotics difficult to ascertain (Puskarich et al., 2011). Puskarich et al. (2011) were rated a level A based on their level of quality through application of the Johns Hopkins Evidence-Based Practice Scale criteria (see Appendix A).

In comparison, Gaieski et al. (2010) discovered that the time elapsed from triage to qualification of early, goal-directed therapy (EGDT), including administration of antibiotics, is a primary determinant of mortality in severe sepsis and septic shock. The authors studied the association between the timing of antibiotics and the survival rate of severe sepsis and septic shock (Gaieski et al., 2010). The SSC recommends antimicrobial therapy should be administered within one hour of recognition of severe sepsis, but with the unpredictable nature of the emergency department, that time frame can be difficult to accomplish (Gaieski et al., 2010). The authors conducted a retrospective analysis of severe sepsis and septic shock patients treated with EGDT in a single-center emergency department (Gaieski et al., 2010). Data was collected and recorded in Microsoft Access (Gaieski et al., 2010). Data was analyzed using SAS version 9.1 and STATA, version 10 (Gaieski et al., 2010). A multivariable logistic regression was utilized to adjust for confounding variables regarding the association between time to antibiotics and mortality (Gaieski et al., 2010). A total of N=291 patients were included in the study.

The authors found 47% of patients qualified for EGDT at triage and 53% qualified later in ED stay (Gaieski et al., 2010). Those with cryptic shock (high lactate level without hypotension) comprised 48% of the patients, and those with severe sepsis comprised 52% of the sample population (Gaieski et al., 2010). Gaieski and colleagues (2010) noted all patients received antibiotics during the ED stay and the median length of time to initial administration was 119 minutes from triage and 42 minutes from EGDT qualification. Nevertheless, time to appropriate antibiotic administration was 127 minutes from triage and 47 minutes from EGDT qualification (Gaieski et al., 2010). Cultures were obtained in all patients, with positive cultures occurring in 56.7% of patients (Gaieski et al., 2010). The authors found 85.1% of those with positive cultures received appropriate antibiotics (Gaieski et al., 2010). In-hospital mortality was 31% overall; 35.1% for culture-positive patients, and 25.7% for culture-negative patients ( $p=0.11$ ) (Gaieski et al., 2010). Mortality for culture-positive patients receiving appropriate antibiotics was 32.5%, compared with 50% ( $p=0.15$ ) mortality in patients receiving inappropriate antibiotics (Gaieski et al., 2010). There was no relationship between time from triage to administration of antibiotics and mortality or between time from EGDT to administration of antibiotics ( $p=.13$ ) (Gaieski et al., 2010). Comparatively, mortality was significantly decreased when appropriate antibiotics were given within the first hour from triage (19.5% vs. 33.2%;  $p=0.02$ ) (Gaieski et al., 2010).

The authors discovered treatment for sepsis is “constantly evolving and includes initial resuscitation, rapid diagnosis, timely administration of appropriate antibiotics, source identification and control, and meticulous ED and intensive care unit (ICU) management” (Gaieski et al., 2010). Gaieski and colleagues (2010) revealed three

important factors in antibiotic administration 1) time to patient qualification for EGDT; 2) length of time from triage to appropriate antibiotic administration; and 3) length of time from EGDT qualification to appropriate antibiotic administration. Based on these factors, the authors recommend rapid (within 1 hour of qualification of EGDT) administration of appropriate antibiotics when severe sepsis or septic shock is suspected (Gaieski et al., 2010).

This study has several limitations. First, the small sample size may have hindered ability to discern hour-to-hour increases. The study is a single center study using a specific resuscitation algorithm and therefore may not be generalizable to institutions with differing resources and management strategies (Gaieski et al., 2010). The authors were unable to determine whether sicker patients received antibiotics sooner, confounding the results. The authors acknowledge the possibility that differences in time to EGDT end points may play a role in mortality. The authors acknowledge weekly meetings with data abstractors and an author may have resulted in bias (Gaieski et al., 2010). Gaieski et al. (2010) were rated a level B based on their level of quality through application of the Johns Hopkins Evidence-Based Practice Scale criteria (see Appendix A).

In contrast to the above studies, Kumar et al. (2006) studied the prevalence and impact on mortality of delays on antibiotic administration in severe sepsis and septic shock from onset of hypotension and found “effective antimicrobial administration within the first hour of documented hypotension was associated with increased survival to hospital discharge in adult patients with septic shock.” Kumar and colleagues (2006) noted the lack of research on delays of antibiotic therapy from certain physiological

variables such as hypotension. The authors conducted a retrospective review of three patient cohorts of adults (over the age of 18) with septic shock: the first cohort included all septic shock patients admitted to adult ICUs of all the hospitals in a specific area from May, 1999 to June, 2004 (Kumar et al., 2006). The second cohort included all septic shock cases between June 1989 and April 1999 and the third included all consecutive adult septic shock patients from July 1999 and June 2004. The authors used a logistic regression model to evaluate survival to discharge related to effective antimicrobial administration (Kumar et al., 2006). Another logistic regression model was used to examine the impact of other variables on survival to discharge, including time to effective antimicrobial therapy (Kumar et al., 2006). SAS version 9.0 was used for statistical analysis.

A total of N=2,731 cases from all cohorts fit the criteria for septic shock (Kumar et al., 2006). All cohorts were comparable in demographics, acuity scores, clinical infections, time to antibiotics, and outcome; therefore, all data was combined (Kumar et al., 2006). The authors discovered the overall mortality rate was 56.2% and was similar whether there was a confirmed or suspected infection and whether the organism was identified or not (Kumar et al., 2006). The mortality rate for patients receiving antibiotic therapy after evidence of hypotension was 58% (Kumar et al., 2006). The authors found a 7.6% decrease in survival for every hour of delay in antibiotic therapy during the first 6 hours after the onset of recurrent or persistent hypotension and delay in treatment was a critical determinant in survival to transfer to the ICU ( $p < 0.0001$ ). In comparison, there was an 82.7% survival rate in patients when effective antimicrobial therapy was administered within 30 minutes of initial evidence of hypotension, and a 77.2% survival

rate when effective antimicrobial therapy was administered in the second half hour (Kumar et al., 2006). After six hours, there was a progressive increase in mortality with each hour of delay of antimicrobial therapy, equating to a 12% decreased probability of survival each hour treatment was delayed (Kumar et al., 2006). The median time to implementation of antimicrobial therapy was 6 hours (Kumar et al. 2006). When delays in treatment were assessed as a continuous variable, the adjusted odds ratio was 1.119 for each hour delay ( $p < 0.0001$ ) (Kumar et al., 2006). Kumar and colleagues (2006) further discovered that time to effective therapy was most strongly associated with increased survival, accounting for a 28.1% variance in survival to discharge ( $p < 0.0001$ ). The authors concluded that delay in initial, effective antimicrobial therapy following the onset of recurrent or persistent hypotension is a critical determinant in mortality in septic shock, and administration within the first hour was associated with 79.9% survival rate to discharge (Kumar et al., 2006).

This study had a large sample, thus improving the ability to demonstrate the progressive increase in-hospital mortality associated with delays in antimicrobial therapy and showing that this effect applies to major patient subgroups (Kumar et al., 2006). This case was not a randomized controlled trial, and patients were not randomly selected to the cohorts. The authors report the unlikeliness that other covariant factors were responsible for the association between mortality and time to effective antimicrobial therapy, stating the relationship holds even with multivariate analysis with other variables and prognosis predictors (Kumar et al., 2006). This study was also conducted at multiple centers, making it more able to be generalized, and it included all patients diagnosed with septic shock (Kumar et al., 2006). This study supports other studies finding increased mortality

after onset of persistent hypotension and further supports current guidelines recommending initiation of antimicrobial therapy within one hour of presentation with severe sepsis and septic shock, creating a “golden hour” in which effective antimicrobial therapy should be initiated (Kumar et al., 2006). Kumar et al., (2006) were rated a level B based on their level of quality through application of the Johns Hopkins Evidence-Based Practice Scale criteria (see Appendix A).

Ferrer et al., (2014) studied the relationship between timing of antibiotic therapy and mortality in a large population study. The authors found delays in antibiotic therapy in patients with severe sepsis and septic shock is associated with increased mortality (Ferrer et al., 2014). The study also identified an increase in mortality with each hour administration of antibiotics was delayed (Ferrer et al., 2014). Ferrer and colleagues (2014) conducted a retrospective analysis of N=28,150 patients across 165 intensive care units between January 2005 and February 2010. Data was collected from the Surviving Sepsis Campaign database of patients with severe sepsis and septic shock and analyzed using STATA version 12.1 (Ferrer et al., 2014) The authors utilized a logistic regression to evaluate hospital mortality and a risk factor modeling approach to determine the role of timing antibiotic administration in survival (Ferrer et al., 2014).

Ferrer and colleagues (2014) found a total of 457 patients received no antibiotics, 832 received antibiotics but were lacking information on the time frame, and 8,871 patients received antibiotics prior to suspected sepsis. These patients were removed from the analysis, leaving 17,990 patients included (Ferrer et al., 2014). The study revealed a higher mortality rate (46.6%;  $p < 0.001$ ) when severe sepsis and septic shock were first identified in the ICU (Ferrer et al., 2014). Patients identified with severe sepsis in the

ICU also had higher proportions of respiratory failure (30.8%), nosocomial infections (21.9%), and septic shock (69.9%), along with longer ICU and hospital stays (Ferrer et al., 2014). When sepsis was identified in the ER, the mortality was 26.3%, decreasing to 25.2% when antibiotic administration was completed within the first hour ( $p < 0.001$ ) (Ferrer et al., 2014). The mortality rate of septic patients identified in the ER rose to 31.2% when antibiotic administration was delayed over six hours ( $p < 0.001$ ) (Ferrer et al., 2014). When adjusted for sepsis severity score, ICU admission source (ED, other wards, or ICU), and geographic region, the authors found a significant relationship between hospital mortality and the time to first antibiotic administration ( $p < 0.001$ ) (Ferrer et al., 2014). The results also revealed that the adjusted hospital mortality odds ratio increased from 1.00 to 1.52 with each hour delay of antibiotics (Ferrer et al., 2014). The authors conclude that in a large population study of patients with severe sepsis and septic shock, delay in antibiotic administration was associated with increased in-hospital mortality and there was a linear increase in the risk of mortality for each hour antibiotic was delayed (Ferrer et al., 2014). This study was unique in the population and location of the patients in the hospital and identified that delay in antibiotic administration has a significant negative impact on survival independent of the area of hospital and illness severity (Ferrer et al., 2014). The authors state the “most important finding from our study is the survival benefit associated with prompt antibiotic administration in severe sepsis and septic shock” (Ferrer et al., 2014, pg. 1754).

This study did have several limitations. The retrospective design creates potential for residual confounding even though some confounding variables were adjusted for in their analysis (Ferrer et al., 2014). The authors also did not study the appropriateness of



the antibiotic, which may be a confounding variable. The study did demonstrate adherence to the SSC recommendation of broad-spectrum antibiotics (Ferrer et al., 2014). There was also no analysis or ability to ascertain reason for delay in administration (Ferrer et al., 2014). Ferrer et al., (2014) were rated a level B based on their level of quality through application of the Johns Hopkins Evidence-Based Practice Scale criteria (see Appendix A).

## **2.8 Lactate Measurement**

Lactate measurements have been shown to be the best indicator of tissue hypoxia and can be done quickly and easily in the emergency department (Nguyen et al., 2004). Studies have further shown that lactate measurement  $> 4\text{mmol/L}$  and two or more SIRS criteria significantly increases ICU admission rates and mortality rates (Nguyen et al., 2004). Previous studies show that lactate elevation for more than 24 hours is associated with an 89% mortality rate in severe sepsis patients (Nguyen et al., 2004). Lactate clearance is an indicator of improved tissue hypoxia (Nguyen et al., 2004). Lactate clearance is defined as the percent decrease in lactate level from emergency department presentation to hour six post-presentation. Early lactate clearance has been associated with decreased mortality rates and improved outcomes. Nguyen and colleagues (2004) studied the utility of serial lactate measurements and lactate clearance prior to intensive care admission as an indicator of outcome in severe sepsis and septic shock. The authors conducted a prospective observational study of patients in the emergency department with severe sepsis and septic shock between February 1, 1999 and February 1, 2000 (Nguyen et al., 2004). All patients were managed in the intensive care unit of the emergency department with hemodynamic monitoring capabilities and were managed

according to the Society of Critical Care Medicine parameters for hemodynamic support of sepsis (Nguyen et al., 2004). Data was collected and entered into database software and analyzed using SAS statistical software (Nguyen et al., 2004). All clinicians caring for patients were blinded to the study (Nguyen et al., 2004).

A total of N=111 patients were studied during the one-year period. The authors found 52.3% patients presented with septic shock and in-hospital mortality was 42.3% (Nguyen et al., 2004). Surviving patients had a lactate clearance of  $38.1\% \pm 34.6\%$  compared with  $12\% \pm 51.6\%$  in non-survivors ( $p=0.005$ ) (Nguyen et al., 2004). A multivariate logistic regression modeling was performed: it showed lactate clearance was significantly associated with decreased mortality rate and that there was an 11% decrease in the likelihood of death for every 10% increase in lactate clearance ( $p=0.04$ ) (Nguyen et al., 2004). There was not a statistically significant risk associated with mortality in patients with septic shock ( $p=0.07$ ) (Nguyen et al., 2004). The authors found a 44.7% sensitivity, 84.4% specificity, and 67.6% predictive value for in-hospital mortality in those with a lactate clearance of  $< 10\%$  after 6 hours of intervention (Nguyen et al., 2004). Both groups of patients (high-versus-low lactate clearance) had similar demographics, but the high lactate clearance group had higher platelet counts, lower prothrombin times and had significantly less vasopressor therapy in the first 6 hours compared with the low clearance group ( $p < 0.05$ ) (Nguyen et al., 2004). Both groups had similar APACHE II scores (Nguyen et al., 2004). The high-lactate-clearance group had a mortality rate 52% lower than the low-clearance group ( $p < 0.001$ ) (Nguyen et al., 2004). The high-clearance group required less fluid therapy and blood transfusions; however, this was not statistically significant when compared with the low-clearance group ( $p=0.44$

and 0.18, respectively) (Nguyen et al., 2004). The high-clearance group received significantly less vasopressors ( $p=0.02$ ) (Nguyen et al., 2004). The high-lactate clearance group had significantly more severe sepsis, yet, had a lower mortality rate ( $p=0.01$ ) (Nguyen et al., 2004). Mortality rate for the high-lactate clearance group was 47.2% versus 72.7% for the low-clearance group (Nguyen et al., 2004).

Lactate clearance “represents a useful and clinically obtainable surrogate marker of tissue hypoxia and disease severity, independent of blood pressure” (Nguyen et al., 2004, pg.1640). Persistently elevated lactate has been a better indicator of increased mortality than oxygen delivery, oxygen consumption, and oxygen extraction ratio (Nguyen et al., 2004). The authors further noted non-survivors had significantly higher lactate measurements during the initial and final phases of shock, while survivors demonstrated lower lactate measurements during the course of the disease process (Nguyen et al., 2004). The study demonstrated that lactate clearance within the first 6 hours from presentation is an independent variable associated with decreased mortality (Nguyen et al., 2004). The study found when lactate clearance occurs in the “proximal stages of disease presentation such as the ED stay, it may be associated with improved organ function and suggests decreased mortality rate up to 60 days (Nguyen et al., 2004, pg. 1640).

This study had several limitations, including taking place in a single-center setting with higher acuity patients and ICU admissions than the national average therefore results should be generalized cautiously with other EDs (Nguyen et al., 2004). The small sample size may also reduce generalizability (Nguyen et al., 2004). The study was not randomized, but clinicians were blinded to the data collection (Nguyen et al., 2004).

Nguyen et al., (2004) were rated a level B based on their level of quality through application of the Johns Hopkins Evidence-Based Practice Scale criteria (see Appendix A).

Arnold et al. (2008) focused on lactate clearance effect on survival in emergency department patients as well as the connection between central venous oxygen saturation (ScvO<sub>2</sub>) optimization and lactate clearance during sepsis resuscitation. The authors conducted a prospective observational study of three emergency departments using an ED-based resuscitation protocol for patients with severe sepsis between 2004 and 2007 (Arnold et al., 2008). Initial lactate measurement was taken from all patients, but serial lactate measurements were obtained at the discretion of treating providers. Data from patients was collected and analyzed using SigmaStat version 3.5 (Arnold et al., 2008). The authors determined the necessary sample size to perform multivariate modeling would be 120 patients. A total of N=166 were included in the study from the 3 study centers (Arnold et al., 2008).

Arnold and colleagues (2008) found an overall mortality rate of 23% with no center effect on in-hospital mortality. Lactate clearance occurred in 91% of all patients, with mortality being 19% in the clearance group compared with 60% in the non-clearance group ( $p < 0.001$ ) (Arnold et al., 2008). There was not a significant difference in vasopressor administration and ScvO<sub>2</sub> goals between the two groups, and there was no difference in lactate clearance and ScvO<sub>2</sub> ( $p = 0.39$ ) (Arnold et al., 2008). The authors further determined lactate clearance was a strong independent predictor of in-hospital mortality (OR 4.9; 95% CI, 1.5-15.9) (Arnold et al., 2008). Four factors were significantly different for survivors compared with non-survivors: initial cardiovascular

organ failure ( $p < 0.05$ ); persistent hypotension despite fluid resuscitation ( $p < 0.05$ ); maximum  $ScvO_2 < 70\%$  ( $p < 0.05$ ); and lactate non-clearance ( $p < 0.05$ ) (Arnold et al., 2008).

This study was the first to demonstrate the benefit of lactate clearance on survival combined with protocol-directed resuscitation for patients with severe sepsis (Arnold et al., 2008). The study further determined serial lactate measurements and the assessment of lactate clearance is an “important predictor of mortality independent of achievement of  $ScvO_2$  goals and tracking  $ScvO_2$  does not reliably reflect the effectiveness of lactate clearance during resuscitation” (Arnold et al., 2008, pg. 38).

This study had several limitations including the non-experimental observation design, which can only detect an association between lactate clearance and mortality (Arnold et al., 2008). Serial measurements were done at the discretion of the clinician and were not mandatory, resulting in possible selection bias (Arnold et al., 2008). This cohort had a low lactate non-clearance (9%), which can be attributed to aggressive resuscitation measures at the included centers (Arnold et al., 2008). This study may only be able to be extrapolated to centers utilizing quantitative resuscitation protocols in the ED setting (Arnold et al., 2008). Deviations in protocol may have occurred, though the study was not able to determine such deviations (Arnold et al., 2008). Some patients included may have been classified incorrectly, and mortality may be attributed to other non-sepsis etiologies (Arnold et al., 2008). Arnold et al. (2008) were rated a level B based on their level of quality through application of the Johns Hopkins Evidence-Based Practice Scale criteria (see Appendix A).

Singer, Taylor, LeBlanc, Williams, and Thode Jr (2014) examined the impact emergency department point-of-care (POC) lactate measurements in sepsis patients had on mortality and time to intravenous fluids. The authors hypothesized that POC lactate measurements would reduce time to intravenous fluids and reduce mortality (Singer et al., 2014). Recognizing the importance of early detection of sepsis and early treatment improves outcomes and further recognizing that lactate measurements are strong predictors of outcomes, having these results immediately can result in recognition and treatment earlier in the disease process (Singer et al., 2014). The authors state that “guidelines recommend early measurement of lactate levels in order to identify patients with tissue hypoperfusion who are at the greatest risk of morbidity and mortality, especially in patients with cryptic shock in which hypotension is not yet apparent” (Singer et al., 2014, pg.1120).

The authors conducted a before and after study, with patients identified using an institutional sepsis screening tool (Singer et al., 2014). Patients were chosen for the after group during a prospective period between January and September 2013 and the before group was chosen through a retrospective analysis of patients between January and November 2011(Singer et al., 2014). Data was collected and entered into the Research Electronic Data Capture software (Singer et al., 2014). The primary outcomes include: time from ED triage to IV fluid and antibiotic administration (Singer et al., 2014). Secondary outcomes were: time from ED triage to ordering of antibiotics; total volume of IV fluids given within ED or within first 6 hours; ED length of stay; need for vasoactive agents; admission to ICU; length of stay in ICU; total length of stay; and in-hospital mortality (Singer et al., 2014). A power analysis was conducted to determine adequate

sample size to evaluate outcome measures (Singer et al., 2014). A total of N=160, 80 in the before group and 80 in the after group, were included in the study (Singer et al., 2014).

The authors found baseline demographics and clinical characteristics were similar for both groups, including baseline lactate levels (Singer et al., 2014). POC measurements reduced time to lactate level results by 88 minutes ( $p < 0.001$ ) (Singer et al., 2014). Nevertheless, antibiotic orders and administration times were similar in both groups (62 minutes for the after group vs. 69 minutes for the before group;  $p=0.27$ ) (Singer et al., 2014). The authors did find a significant reduction in time to IV fluid administration between the two groups (55 minutes for the after group vs. 71 minutes for the before group;  $p=0.03$ ) (Singer et al., 2014). The study found a significant reduction in in-hospital mortality (6% vs. 19%;  $p=0.02$ ) and ICU admission between the after and before groups (33% vs. 51%;  $p=0.02$ ) (Singer et al., 2014). The study found no differences in the ED length of stay ( $p=0.50$ ), hospital length of stay ( $p=0.27$ ), and ICU length of stay ( $p=0.9$ ) (Singer et al., 2014). The authors determined the correlation between POC lactate and central lab lactate was 0.94 with 95% confidence interval between 0.91 and 0.97, and the mean difference was  $0.26 \pm 0.43$  mmol/L (Singer et al., 2014). All patients had lactate levels over 2 mmol/L, and only 2 patients had a lactate less than 2 mmol/L on a central lab result (Singer et al., 2014). Serial lactate measures were conducted in 85% of patients in the after group and were significantly lower than the first measure (Singer et al. 2014). It was also determined that 63% of patients saw the second lactate normalize, dropping below 2 mmol/L; of those patients mortality rate was 2%,

compared with 12% in those patients without serial measurements ( $p=0.10$ ) (Singer et al., 2014).

The authors demonstrated “introduction of bedside POC measurements of lactate was associated with significant reduction in time to test results, time to administration of intravenous fluids, ICU admission rates, and in-hospital mortality in ED patients with suspected sepsis “(Singer et al., 2014, pg. 1121). The authors determined bedside POC lactate measures can be an effective tool in providing critical information in a timely manner to ensure rapid recognition and treatment of patients with sepsis in the ED (Singer et al., 2014). The study also determined that POC lactate measures are a reliable and feasible tool to introduce into the care of these patients (Singer et al., 2014).

This study had several limitations. First, the observational design can identify associations but not prove causality. Second, there may have been confounding variables that could have caused the differences in mortality (Singer et al., 2014). The physicians and nurses were aware of the POC testing and could have introduced a Hawthorne effect, which may have biased the after group results (Singer et al., 2014). The sample was also a convenience sample, including patients that entered the ED when the investigators were present, causing possible selection bias (Singer et al., 2014). Finally, the study was a single center study and results may not generalize to all institutions (Singer et al., 2014). Singer et al., (2014) were rated a level B based on their level of quality through application of the Johns Hopkins Evidence-Based Practice Scale criteria (See Appendix).

## **2.9 Blood Culture Draws**

In this review, literature regarding the utility of blood cultures and their effect on outcomes in sepsis patients was extremely limited. Armstrong et al. (2015) state that due



to the absence of guidelines for blood culture draws and the lack of evidence of a correlation between blood cultures and outcomes, clinicians are left to arbitrarily assess the need for blood culture draws. With the high mortality for patients with bloodstream infections (14% to 37%), it is important to isolate the infectious pathogens to determine treatment. However, data suggests only 4% to 7% of patients presenting to the ED with suspected infections had a positive blood culture (Armstrong et al., 2015). The authors conducted a retrospective study of adult patients presenting to the ER in December 2013 who had suspected sepsis with blood cultures drawn (Armstrong et al., 2014).

A total of N=189 patients were included in the study, 135 with blood cultures drawn and 54 diagnosed with sepsis. In the sepsis cohort of 54 patients, Armstrong and colleagues (2015) found 34 patients had positive blood cultures and 20 had negative cultures. The authors found no statistically significant differences in outcomes between patients with positive cultures compared to those with negative cultures (Armstrong et al., 2015). Of those with negative cultures, 73.5% were admitted to ICU compared with 90% of those with positive cultures (Armstrong et al., 2015). Thirty-two percent of those with negative cultures died during their hospital stay compared with 30% of those with positive cultures, showing blood cultures are not predictive of mortality (Armstrong et al., 2015). In the ED cohort, 134 patients were reviewed, finding 93% had negative cultures and 7% had positive cultures (Armstrong et al., 2015). Of those with negative cultures, 25% were admitted to ICU and 75% to a general medical floor (Armstrong et al., 2015). There was no significant difference between ICU admission and patients with positive and negative cultures, but those with positive cultures had longer length of stays (Armstrong et al., 2015).

The authors determined that the presence of SIRS criteria is usually used to determine the need for blood cultures; however, these patients have a history of fever or newly developed fever and there was not an increased incidence of positive cultures among these patients (Armstrong et al., 2015). The authors further highlight that contaminants lead to unnecessary antibiotic treatment and increased hospital costs (Armstrong et al., 2015). The authors note the study did not show a statistically significant increase in mortality, although there was an increase in length of stay in those with positive cultures from the ED (Armstrong et al., 2015). The authors conclude utility of blood culture draws has not been determined but liberal use of blood cultures may not be cost-effective or show any positive outcome (Armstrong et al., 2015).

This study has several limitations. It is a single-center study with a small sample size from a limited time period; therefore, results may not be generalized to other settings (Armstrong et al., 2015). Patients with infections may not have been cultured, resulting in selection bias (Armstrong et al., 2015). Armstrong et al., (2015) were rated a level B based on their level of quality through application of the Johns Hopkins Evidence-Based Practice Scale criteria (see Appendix A).

Blood cultures are necessary in identifying infectious pathogens in order to narrow the antibiotic course to treat the specific causative organism and reduce antibiotic resistance (Flayhart, 2012). Nevertheless, clinicians must be cognizant of when to draw cultures. Flayhart (2012) states volume of blood cultured is important as well as the number of sets of cultures. Two to three sets of aerobic and anaerobic cultures should be obtained, as a study in 2007 identified an increased incidence of anaerobic bacteremia (Flayhart, 2012). Other factors that can improve utility of blood culture testing are

collection methods, limiting contamination and rapid and accurate reporting of results (Flayhart, 2012).

## **2.10 Physiological Deterioration**

Changes in vital signs, mentation, and urine output are all signs of physiological decline in septic patients. Vanzant and Schmelzer (2011) report the ten symptoms of instability to include: temperature changes, heart rate increase, changes in pain, respiratory rate changes, lowered systolic blood pressure and mean arterial pressure, changes in level of consciousness, decreased capillary refill, decreased urinary output, changes central venous oxygen and decreased oxygenation on Spo2 measures. Changes in at least two of these parameters can be indicative of sepsis (Vanzant & Schmelzer, 2011). The MEWS measures systolic blood pressure, pulse, respiratory rate, temperature, and level of consciousness (So et al., 2014). Each documented parameter provides a score, with scores > 4 associated with poorer outcomes (So et al., 2014). With accurate and complete recording of these parameters, using MEWS can help identify high-risk patients and improve care (Corfield et al., 2014; So et al., 2014; Delgado-Hurtado, Berger, & Bansal, 2016).

## **2.11 Respiratory Rate**

Accurate and frequent monitoring and recording of vital signs is critical to ensuring the MEWS is calculated correctly and provides an accurate source of information for clinicians when assessing physiological deterioration in patients. So et al. (2014) highlight the importance of recording the respiratory rate in patients. The authors found respiratory rate was a significant determinant between stable patients and those at risk of deterioration (So et al., 2014). Kyriacos, Jelsma, and Jordan (2011) found less

than 50% of nurses recorded respiratory rates in patients in the UK. Incomplete and infrequent monitoring can delay recognition of patient deterioration and delay life-saving interventions. Kyriacos, Jelsma, and Jordan (2011) conclude, “respiratory rate is the most sensitive indicator of deterioration, but is poorly recorded” (pg. 326). They found that when using MEWS, recording of vital signs was improved, leading to more accurate signs of decline (Kyriacos, Jelsma, & Jordan, 2011).

## **2.12 Synthesis**

After the analysis of research articles (see Appendix D), this synthesis identified supporting evidence that use of the Modified Early Warning Score (MEWS) can identify sepsis earlier, resulting in early evidence-based treatment proven to improve outcomes. The analyses of the selected articles were pertinent to improving clinical practice of treating septic patients presenting to the emergency department. This synthesis outlined sufficient evidence to support the use of the MEWS at triage in the emergency department in order to improve early recognition and early treatment of severe sepsis and septic shock. Evidence supported the idea that early treatment and early detection is critical to improving outcomes and decreasing mortality in severe sepsis and septic shock (Rivers et al., 2001; Jones, Focht, Horton, & Kline, 2007; Rusconi et al., 2015; Turi & Von Ah, 2013; Wira, Dodge, Sather, & Dziura, 2014). The evidence further found use of sepsis bundles, focused on early antibiotic administration and lactate measurements in ED improve outcomes and assist clinicians in identifying sepsis and initiating early treatment (Westphal et al., 2011; Bruce, Maiden, Fedullo, & Kim, 2015; Tromp et al., 2010; Vanzant & Schmelzer, 2011; Burney et al., 2012; Burrell et al., 2016; Puskarich et al., 2011; Gaieski et al., 2010; Kumar et al., 2006; Ferrer et al., 2014; Nguyen et al.,

2004; Arnold et al., 2008; Singer et al., 2014). Evidence supports the use of an early warning score or modified score in the ED to improve recognition of those patients with acute, physiological deterioration, leading to initiation of treatment earlier in the disease process (So et al., 2015; Kyriacos, Jelsma, & Jordan, 2011; Delgado-Hurtado, Berger, & Bansal, 2016; Corfield et al., 2014; Alam et al., 2014). Complete recording of vital signs, especially respiratory parameters, can detect decline much sooner (Kyriacos, Jelsma, & Jordan, 2011; So et al., 2014). Of the evidence reviewed, the ratings were as follows: two were rated an A and twenty-two were rated a B using the Johns Hopkins Evidence-Based Practice Scale criteria.

### **2.13 Summary**

Mortality and morbidity from severe sepsis and septic shock has been identified as an increasing problem, especially in patients presenting to the ED. The inability of clinicians to recognize and intervene early in disease process has been cited as two of the most prevalent barriers to improved outcomes in septic patients (Burney et al., 2012). Over 500,000 patients annually present to the ED with severe sepsis and septic shock and have a mortality rate of 40%-60% (Burney et al., 2012; Bruce, Maiden, Fedullo, & Kim, 2015).

According to the literature, early, goal-directed therapy improves outcomes and reduces mortality (Rivers et al., 2001; Jones, Focht, Horton, & Kline, 2007; Rusconi et al., 2015; Turi & Von Ah, 2013; Wira, Dodge, Sather, & Dziura, 2014). Furthermore, evidence supports the use of sepsis bundles and guidelines and suggests that their use can improve time to interventions (Westphal et al., 2011; Bruce, Maiden, Fedullo, & Kim,

2015; Tromp et al., 2010; Vanzant & Schmelzer, 2011; Burney et al., 2012; Burrell et al., 2016; Shapiro et al., 2006).

The literature outlined early antibiotic administration as an important component in decreasing mortality in patients with severe sepsis (Puskarich et al., 2011; Ferrer et al., 2014). Evidence further concluded that delays in antibiotic treatment reduced survivability of septic patients, highlighting the importance of prompt recognition and treatment (Gaieski et al., 2010; Kumar et al., 2006).

According to the literature, initial and serial lactate measurement greater than 4 mmol/L is a significant indicator of tissue hypoperfusion, leading to increased mortality (Nguyen et al., 2004; Arnold et al., 2008). Ability to quickly measure and obtain initial and serial measurements in the ED can allow clinicians to intervene earlier, thereby improving tissue hypoperfusion and reducing mortality (Nguyen et al., 2004; Arnold et al., 2008; Singer et al., 2014).

Fluid resuscitation, early antibiotic administration and lactate clearance are critical interventions that must be initiated early in the disease course, preferably prior to signs of clinical deterioration. Studies suggest “existing systems fail to recognize or respond appropriately to early signs of critical illness” (Corfield et al., 2014, pg. 485). Evidence reinforces the use of an early-warning score or modified early-warning score; these scores are able to reliably and accurately detect physiological deterioration of patients early in the disease course before signs of clinical deterioration are present (So et al., 2015; Kyriacos, Jelsma, & Jordan, 2011; Delgado-Hurtado, Berger, & Bansal, 2016; Corfield et al., 2014; Alam et al., 2014).

## 2.14 Recommendations

Based on the evidence illustrated from the selected studies, this review identified the following recommendations to clinicians in recognizing and intervening earlier in patients with sepsis presenting to the emergency department. These recommendations have been graded according to the Michigan Quality Improvement Consortium (2008) system (see Appendix C). They are based on the quality and amount of evidence available to support the recommendation for guidelines, practice constraint, or clinical policy.

1.) **Assess patients at triage using an acuity-screening tool like MEWS to recognize physiological deterioration early in the disease course to allow earlier implementation of treatment. Evidence Grade C.** Assess patients at triage using a screening tool and report high acuity patients to clinicians. It is imperative that nurses and providers are trained to recognize signs and symptoms of deterioration in patients in order to allow for earlier intervention. Nurses must record all vital signs frequently and recognize worsening in patients' clinical presentation (Kyriacos, Jelsma, & Jordan, 2011). Prompt communication of patient decline with providers is imperative in initiating early therapy (Kyriacos, Jelsma, & Jordan, 2011). Further research is necessary to assess validity of screening tools and how best to score patients based on presentation (So et al., 2015; Kyriacos, Jelsma, & Jordan, 2011).

2.) **Use of a bundle based on SSC guidelines to provide early, goal-directed therapy to improve tissue hypoperfusion and treat infectious organisms within the first 6 hours of resuscitation. Evidence Grade B.** Implement and follow bundle guidelines outlined by the SSC in the emergency department. The bundle should include

administration of broad-spectrum antibiotics within one hour of presentation and fluid resuscitation of 20ml/kg of crystalloid fluid to improve tissue hypoperfusion and decreasing of lactate levels to promote lactate clearance. Initial and serial lactate measurements should be obtained to ascertain effectiveness of fluid resuscitation. Further research is needed to determine which elements of the guidelines are the most effective on meeting resuscitation targets and improving outcomes (Rusconi et al., 2015; Vanzant & Schmelzer, 2010; Bruce, Maiden, Fedullo & Kim, 2015; Burney et al., 2012).

3.) **Provide education to the providers and nurses on signs and symptoms of sepsis as well as bundle elements and target goals. Evidence Grade C.** Educating nurses and providers on how to recognize signs and symptoms results in earlier detection of sepsis. Nurses are in a critical position to be able to assess patients early in the disease process and notify providers of abnormalities. Bruce, Maiden, Fedullo, and Kim (2015) recommend utilizing emergency room nurses early in triage to identify patients and initiate diagnostic workup to reduce time to interventions. Burney et al., (2012) found identification of sepsis and recognition of signs and symptoms was a primary barrier to compliance with bundles. Burney et al., (2012) illustrated the need for in-service educational sessions and continuous feedback for nurses and providers on both protocols and physiology of sepsis to improve care. It is imperative that nurses and providers are educated and familiar with signs and symptoms of sepsis as well as bundle guidelines and resuscitation goals in order to achieve intervention timeline goals and improve compliance of bundle components (Bruce, Maiden, Fedullo & Kim, 2015; Burney et al., 2012).



## **2.15 Implications**

This quality improvement project based implications on specific conclusions and suggestions of the research in order to implement the research findings into clinical practice, education, and overall policy (Burns & Grove, 2009). Current evidence has shown that the use of a MEWS helps clinicians recognize physiological deterioration from sepsis earlier and apply interventions based on current guidelines and bundles earlier in disease process. The evidence has shown early recognition and early intervention are critical to reducing mortality from sepsis.

## **2.16 Implications for Practice**

The MEWS can easily be incorporated into the triage assessment and allows clinicians the ability to effectively and accurately utilize an early-warning score with sepsis patients (Corfield et al., 2014). Further research is needed to determine validity and reliability of early-warning scores (Kyriacos, Jelsma, & Jordan, 2011; Corfield et al., 2014). Early-warning scores, in combination with nursing judgment, detects deterioration earlier and are shown to improve outcomes and assist clinicians in seeking higher level care (Corfield et al., 2015). Corfield et al. (2014) highlight current issues and the lack of research regarding standardizing tools for use in the ED in order to improve specificity and sensitivity of warning tools (Corfield et al., 2014).

Another implication for practice is ensuring vital signs are entered correctly and frequently so that scores are calculated correctly and promptly. Kyriacos, Jelsma, and Jordan (2011) highlight that use of the MEWS/EWS with frequent recording of vital signs along with nursing assessments and judgment is critical to recognizing deterioration. Evidence suggests the score can be used to alert clinicians to the need for

immediate assessment (Corfield et al., 2014; Kyriacos, Jelsma, & Jordan, 2011). It was further noted that recording all vital signs, especially respiratory rate improves care (Kyriacos, Jelsma, & Jordan, 2011).

### **2.17 Implications for Clinical Education**

Evidence supports the use of bundles that aid in early detection and treatment and regular in-services and feedback are necessary to ensure compliance with these bundles (Vanzant & Schmelzer, 2011). To ensure clinicians are able to recognize signs and symptoms of sepsis and intervene based on current guidelines, it is critical that all clinicians in the ED are continuously educated on sepsis and current treatments. Clinicians must also recognize the importance of multi-disciplinary teams in treating septic patients. Educating all members of the multi-disciplinary team on sepsis physiology and treatment will improve compliance with bundle targets. An implication noted in the evidence was the lack of access to antibiotics in the ED, causing delays in treatment. It is important that pharmacy, as a member of the multi-disciplinary team, is included in education to ensure access to broad-spectrum antibiotics for prompt administration (Bruce, Maiden, Fedullo, & Kim, 2015). Collaboration with the team in the ED and ICU staff, along with regular education, increases success with bundle implementation (Kuan et al., 2013). Bruce, Maiden, Fedullo, and Kim (2015) suggest performance tracking and regular feedback are necessary to improve compliance.

### **2.18 Implications for Policy**

Implications for policy development include new mandatory reporting and regulations by the Centers for Medicaid and Medicare which requires hospitals to follow certain bundle guidelines modeled after those recommended by the Surviving Sepsis

Campaign. The goal of implementing these guidelines is to reduce mortality from sepsis and decrease morbidity. In April 2015, CMS instituted the Sepsis Bundle Project: Early Management Bundle, Severe Sepsis/Septic Shock (“SEP-1”) measures, which focus on early recognition and treatment of sepsis in an effort to reduce mortality (Joint Commission, 2015). In October 2015, CMS required all hospitals to utilize and report SEP-1 measures (Schorr, 2016). The purpose of these measures “is to support the efficient, effective and timely delivery of high quality sepsis care in support of the Institute of Medicine’s aims for quality improvement” (Department of Health and Human Services, 2014).

To avoid a reduction in Annual Payment Determination in 2017, it is a federal requirement for all hospitals to collect and report data on the SEP-1 measures (CMS, 2015). By utilizing an early-warning score such as MEWS, emergency departments can detect sepsis earlier, thereby improving time to guideline interventions to reduce mortality as well as avoid reductions in reimbursements.

## **2.19 Summary**

Managing patients with severe sepsis and septic shock can be difficult and requires a multidisciplinary team approach, beginning with clinicians in the emergency department. Utilization of the Modified Early Warning Score (MEWS) should be implemented at triage when patients present to the ED in order to recognize patient deterioration early, allowing for prompt intervention based on evidence-based guidelines (So et al., 2014; Corfield et al., 2014; Alam et al., 2014; Kyriacos, Jelsma, & Jordan, 2011; Delgado-Hurtado, Berger, & Bansal, 2016). Research has identified early, goal-directed therapy using bundled interventions reduces mortality in septic patients and early

detection of symptoms is critical to early therapy (Rivers et al., 2001; Jones, Focht, Horton, & Kline, 2007; Wira, Dodge, Sather, & Dziura, 2014; Rusconi et al., 2015).

Research found that using MEWS could detect patient physiological deterioration earlier (Corfield et al., 2014; Alam et al., 2014).

## Chapter 3 Design

### 3.1 Introduction

Sepsis is a devastating condition plaguing hospitals nationwide. Hospitals and healthcare providers continue to strive to decrease mortality and improve outcomes in sepsis patients. Studies and data support using sepsis bundles based on early, goal-directed therapy. Studies demonstrate bundles reduce mortality in septic patients and improve overall outcomes (Rivers et al., 2001; Jones, Focht, Horton, & Kline, 2007; Wira, Dodge, Sather, & Dziura, 2014; Rusconi et al., 2015). It is evident that early recognition is key to implementing early treatment; however, recognition of septic patients entering the emergency department remains a barrier to compliance with early bundle initiatives (Vanzant & Schmelzer, 2011; Burney et al., 2012). Proper assessment and recognition is key to preventing further decline in patients with sepsis. Using the triage nurse to assist with identification of septic patients early in patient presentation has shown to improve time to interventions and initiation of prompt diagnostic work-up (Bruce, Maiden, Fedullo & Kim, 2015). Studies support adding the Modified Early Warning Score (MEWS) into the nurses' assessment at triage, improves recognition of physiological deterioration, leading to decreased time to interventions (Kyriacos, Jelsma, & Jordan, 2011; Corfield et al., 2014; Delgado-Hurtado, Berger, & Bansal, 2016). Best practices suggest implementing tools, such as the MEWS, to assist nurses and other clinicians in quickly identifying patient deterioration related to sepsis and preventing delays in treatment. Beginning in 2017, CMS will begin requiring all hospitals to collect

and report data on the SEP-1 measures or face reduction in reimbursement (CMS, 2015). Mandatory reporting of SEP-1 measures began in October 2015 in an effort to improve time to interventions, early recognition and improve outcomes and mortality rates (Schorr, 2016; Department of Health and Human Services, 2014).

Application of the “Evidence-Based Advancing Research and Clinical Practice Through Close Collaboration (ARCC) Model: A Model for System-Wide Implementation and Sustainability of Evidence-Based Practice” in combination with key components of the literature synthesis will be used as the framework for this quality improvement project. The purpose of this quality improvement project is to analyze whether implementation of the MEWS at triage improves time to specific interventions for sepsis patients entering the emergency department compared with the current triage protocol. Data will be collected three months prior to MEWS implementation and three months post-implementation. The goal is to improve door to intervention time for patients with a MEWS score of  $> 4$ . The purpose of this chapter is to outline the study design and methods utilized in analyzing the effect of the MEWS on patient outcomes for adult patients entering the emergency department with sepsis, severe sepsis and septic shock.

### **3.2 Design**

A non-experimental study design was used to collect and analyze data through a retrospective chart review of patients diagnosed with sepsis, severe sepsis and septic shock, as coded using ICD-10 codes before and after MEWS implementation. Melnyk & Fineout-Overholt (2015) state non-experimental designs are used to “describe, explain, or predict a phenomenon.” Identifying information was not collected from the charts.

Demographic information including gender, age, and race will be collected.

### **3.3 Instruments**

The Modified Early Warning Score (MEWS) was developed in 1999 by Stenhouse et al. in an attempt to improve patient outcomes for sepsis by earlier recognition and intervention of sepsis protocol treatments (See Appendix A). The MEWS assigns a numerical value to specific vital signs and assessment parameters including respiratory rate, heart rate, systolic blood pressure, temperature, urine output and level of consciousness. The MEWS was incorporated into the triage nurse assessment and charting system. The MEWS is calculated automatically based on the values recorded by the nurse for specific assessment parameters. A MEWS greater than 4 indicates a higher risk of patient deterioration and requires immediate intervention.

### **3.4 Sample.**

Two independent groups were analyzed for this quality improvement project. The first group consisted of adult patients, eighteen years and older, entering the emergency department between January 2016 and March 2016 diagnosed with sepsis, severe sepsis or septic shock. The second group consisted of adult patients, eighteen years and older, entering the emergency department between January 2017 and March 2017 after implementation of the MEWS with the same diagnostic codes. Inclusion criteria included: 18 years of age or older, diagnosed with sepsis, severe sepsis or septic shock.

### **3.5 Setting.**

This university hospital system located in the southeast is a non-profit, academic institution. The medical center is a 478-bed hospital, with 154-bed children's hospital serving more than 13 counties across two states in the southeast. In 2015, the emergency

department treated over 89,000 patients and in 2016, more than 87,000 have been treated.

### 3.6 Procedures

Following the University of South Carolina Institutional Review Board approval and Augusta University Institutional Review Board approval for the quality improvement project, data collection occurred pre- and post-intervention through a retrospective chart review in coordination with the Quality Management Department at the medical center. Patients entering the emergency department between January 2016 and March 2017 were filtered by ICD-10 codes of sepsis, severe sepsis, and septic shock.

Demographic data was obtained on all patients to include race, age, and gender. Data is obtained for presence of co-morbidities including congestive heart failure (CHF), diabetes, and hypertension as well as data on patient disposition from hospital. No personal identifiers were maintained that could be traced to the patient. Patients were assigned numbers only for data collection purposes such as Subject # 1. Data was collected onto an encrypted flash drive for transfer for analyses. Once the data was transferred to an excel spreadsheet for analyses, the flash drive was destroyed. Data was collected from the patients' charts for both the pre-implementation and post-implementation groups on the outcome measures from the sampled patient charts including data on interventions completed, time of presentation to the emergency department, time of antibiotic administration, time of lactate measurement, and time of blood culture draw. This data was then entered into *Excel* spreadsheets for data analyses. SAS 9.4 will be used to conduct the analysis.

**Table 3.1 Time Interval for Quality Improvement Project**

Time Frame	Activity
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Obtain IRB approval	Week One through four: May 22, 2017- June 22, 2017
Obtain data from sample charts	Week Five through Seven : June 26, 2017- August 8, 2017
Data Analysis:	Week Eight through Nine: August 8,-18 2017

### 3.7 Outcomes Measured.

Investigator sought to determine if the MEWS application at triage led to a decrease in door to intervention time for patients with a MEWS > 4 as measured by:

Time in minutes as well as results for:

1. Lactate measurement levels
  - a. A lactate level greater than 4mmol/L has been associated with a higher mortality rate when compared with those patients with lactate levels less than 4mmol/L (Boschert, 2007).
2. Blood culture draws
  - a. A positive blood culture for any bacterial or fungal organism provides identification of susceptibility testing and typing to optimize empirical antibiotic therapy in order to treat sepsis. Rapid and appropriate administration of antibiotics is crucial in the treatment of sepsis (Westh et al., 2009).

Time in minutes for:

1. Administration of appropriate broad-spectrum antibiotics.

All times are to be within the 3-hour timeframe outlined by the SSC guidelines.

### **3.8 Data Analysis Methods**

The SAS 9.4 program was utilized for statistical analyses and then imported for descriptive data such as frequency tables; using SAS to conduct frequency distribution tables. The data was analyzed for differences in time to intervention between the pre-implementation group and post-implementation group after introduction of the MEWS at triage. An independent T-Test and nonparametric test (Wilcoxon-Mann-Whitney) were used to examine if the average time is different between the pre-intervention group and post-intervention group. Dr. Abbas Tavakoli provided statistical support, expertise for analyses, and assistance with data management of importing data into *Excel* files.

### **3.9 Theoretical Framework.**

In evidence-based projects, it is recommended that change be guided by a theoretical framework or model (Melnyk & Fineout-Overholt, 2015). This quality improvement project is guided by “Evidence-Based Advancing Research and Clinical Practice Through Close Collaboration (ARCC) Model: A Model for System-Wide Implementation and Sustainability of Evidence-Based Practice.” The purpose of the model is to guide clinicians and institutions through system-wide implementation of an evidence-based project and promote sustainability in order to achieve quality outcomes (Melnyk & Fineout-Overholt, 2015). The steps of the ARCC model include organizational assessment of readiness, EBP mentors, and EBP beliefs scale (Melnyk & Fineout-Overholt, 2015). For this project, a quality improvement team at the medical center was established and included an emergency room nurse leader, emergency room director, the chief medical officer, a pharmacist, quality improvement coordinator,

laboratory representative and epidemiology representative. For step one of the ARCC model, the medical center assessed the organizational readiness within the emergency department prior to implementation. The quality improvement team collects data on sepsis patients and compares time to intervention in the emergency department with the times outlined in the SSC guidelines. The emergency room nurse leader and emergency room director conducted an assessment to ascertain the department and organizations' readiness to implement the MEWS at triage. They determined that it was a feasible tool to integrate into the charting system and triage process. During the second phase, the organization assigned mentors to assess the staff's current knowledge of sepsis and the MEWS tool and to educate the staff on how to use the MEWS when assessing a patient. Members of the quality improvement team educated the staff on the SSC guidelines, interventions, and the importance of time to intervention. In the third phase, the mentors assessed the staff's beliefs and ideas regarding the MEWS tool and identified strengths, weaknesses and barriers that are present regarding implementation of the project and the knowledge of the staff. Over 90% of the staff believes the MEWS could be feasibly implemented into the ED triage assessment. The project evaluated the effect of implementation of the MEWS on time to intervention for septic patients entering the emergency department.

### **3.10 Strategies to Reduce Barriers and Increase Supports**

The participants involved in the presentation for change within the emergency department included the emergency room nursing director, chief medical officer, chief attending for the emergency department, quality management officers, pharmacists, laboratory director, epidemiology, and emergency department nursing representatives. A

barrier was acceptance by nursing staff and providers of change in assessment and identification of patients with sepsis. In order to reduce this barrier, education was conducted initially and on a continuous basis for nurses, providers and EMTs. The quality improvement team developed and conducted education on the new triage process, MEWS, sepsis disease process, and sepsis treatment guidelines for emergency department staff.

Another barrier was ensuring complete and adequate charting so that the MEWS could be calculated in the electronic medical record. In order to reduce this barrier, the quality improvement team conducted in-services to the nursing staff on the MEWS components and how to chart correctly in order to calculate the MEWS. The quality management team member followed charting behavior in order to recognize whether the MEWS was being charted correctly and completely. Throughout the process, the quality improvement team continued education and in-services for the staff to improve compliance.

### **3.11 Summary**

Early recognition and early management of symptoms related to sepsis can be complicated and requires an active approach by all individuals involved in the delivery of care to this susceptible population. Implementing evidence-based treatment goals and interventions into the care of septic patients improves outcomes. Incorporating the MEWS into the triage assessment is used to detect clinical decline early in the disease process so that nurses can intervene and notify providers, preventing treatment delays. Early recognition and prompt treatment are the keys to improving outcomes in patients

with sepsis and septic shock. This active approach to delivering quality care for septic patients can potentially improve quality measures and outcomes.

## **Chapter 4 Results**

### **4.1 Description of the Sample**

Between January 2016 and March 2016, a total of 290 adult patients were diagnosed with sepsis, severe sepsis or septic shock in the Emergency Department. During the same time frame in 2017, 312 patients were diagnosed with sepsis, severe sepsis or septic shock. Using a level of significance  $\alpha=0.05$  and a power of 80%, it was determined each group needed a minimum sample size of  $n=64$ . Using a random selection process of approximately every 5 charts, for a total of 64 charts were reviewed for the pre-intervention group and a total of 67 charts were reviewed for the post-intervention group for a final sample size of ( $n=130$ ). This sample was comprised of adults that presented to the emergency room and diagnosed with sepsis, severe sepsis and septic shock.

### **4.2 Analysis of the Research Question**

Table 4.1 depicts the results of the frequency distributions for sex, race, presence of congestive heart failure, diabetes and hypertension, disposition status, lactate measurement and blood culture draws for the two groups. They summarize the distribution of values from the sample population. The results indicate that the two groups were similar in race and gender characteristics. There were demographic differences seen between the pre-implementation group and post-implementation group in regards to patients with CHF, diabetes and hypertension with fewer patients having CHF, diabetes and hypertension. In the pre-implementation group 14.06% of patients had

CHF where as only 1.52% were seen in post-implementation group. In the pre-implementation group 73.44% had hypertension compared with 62.12% in the post-implementation group. There was a decrease in those with diabetes as well with 43.75% in the pre-implementation group compared with 30.30% in the post-implementation group. There were also differences between the two groups in regards to disposition status. The pre-implementation group had more deaths (19.35%) compared with the post-implementation group (12.5%) and more patients were discharged home in the post-implementation group (41.94% vs. 64.06%). There was an increase in lactate measurements from pre-implementation (81.25%) to post-implementation (87.88%) however it was not statistically significant. Blood culture draws decreased from pre-implementation (81.25%) to post-implementation (71.21%).

Chi-square analysis and Fisher Exact Test determined if any significant differences existed between the two groups for these variables. There was not a statistically significant difference between the pre-implementation and post-implementation groups for sex ( $p=0.2253$ ) or race ( $p=0.8451$ ). There was a statistically significant difference between the two groups with regards to patients with CHF ( $p=0.0082$ ). There was not a statistically significant difference with regards to diabetes ( $p=0.146$ ) and hypertension ( $p=0.192$ ). A statistically significant difference was seen in disposition status between the two groups ( $p=0.0501$ ). There was no statistically significant difference seen between the two groups with regards to lactate measurements ( $p=0.3376$ ). The results indicated there was not a statistically significant difference in blood cultures before and after implementation of the MEWS at triage ( $p=0.218$ ).

**Table 4.1 Frequency Distributions**

Variables	Pre		Post	
	N	%	N	%
<b>Sex</b>				
Female	37	57.81	31	46.97
Male	27	42.19	35	53.03
<b>Race</b>				
Black	29	45.31	34	51.52
White	33	51.56	30	45.45
Other	2	3.13	2	3.03
<b>CHF</b>				
Yes	9	14.06	1	1.52
No	55	85.94	65	98.48
<b>Diabetes</b>				
Yes	28	43.75	20	30.30
No	36	56.35	46	69.70
<b>Hypertension</b>				
Yes	47	73.44	41	62.12
No	17	26.56	25	37.88
<b>Disposition</b>				
Home	26	41.94	41	64.06
Death	12	19.35	8	12.50
Skilled Nursing Facility/Rehab	24	38.71	15	23.44
<b>Lactate Measurement</b>				
Yes	52	81.25	58	87.88
No	12	18.75	8	12.12
<b>Blood Cultures</b>				
Yes	52	81.25	47	71.21
No	12	18.75	19	28.79

Table 4.2 depicts the results of the t-test for age and minutes to antibiotic administration from presentation time. The mean age for the pre-implementation group was 61.68 with standard deviation of 17.11 (95% CI: 57.41, 65.96) and for post-



implementation the mean age was 55.93 with standard deviation of 15.25 (95% CI 52.19, 59.68).

**Table 4.2 Means and Standard Deviations for Age and Minutes.**

Variables	Pre-Implementation			Post-Implementation			
	N	Mean	SD	N	Mean	SD	T-test
<b>AGE<sup>a</sup></b>	64	61.87	17.11	66	55.93	15.25	(p=0.0451)
<b>MINUTES</b>	64	353.10	475.9	66	362.20	532.50	(p=0.9184)

The t-test revealed a statistically significant difference for the average for age (p=0.0451). However the results did not indicate a statistically significant difference in the average for minutes for pre-implementation and post-implementation groups (p=0.9184).

### **4.3 Conclusion**

Frequency distributions were calculated for outcome measures of lactate measurement, blood culture draws and minutes to antibiotic administration as well as sex, race, age, co-morbidities (CHF, diabetes, and hypertension) and disposition status. Chi-square and Fisher exact test were calculated for the categorical variables. There were differences seen between the pre-and post-implementation groups, however statistically significant differences were only identified between pre-and post-implementation groups for presence of CHF and disposition status. The frequency distributions showed a decrease in deaths between the pre-implementation group (19.35%) and post-implementation group (12.5%). There was an increase in lactate measurements from pre-implementation (81.25%) to post-implementation (87.88%) however it was not

statistically significant. Blood culture draws actually decreased from pre-implementation (81.25%) to post-implementation (71.21%).

There was a statistically significant difference seen between the two groups with regards to age. The average age in the pre-implementation group was 61.68 compared with 55.93 in the post-implementation group. However, there was not a statistically significant difference in time in minutes of antibiotic administration between the two groups. The average time in minutes to antibiotic administration was 353.10 in the pre-implementation group compared with 362.2 in the post-implementation group.

Although statistically significant changes were not identified for time in minutes for antibiotic administration, there was clinical significance seen between the two groups. Antibiotic administration time improved in the post-implementation group for the 3-hour, 6-hour, and greater than 8-hour time frames. The pre-implementation group had 28% of patients who received antibiotics greater than 8 hours after presentation with the post-implementation group having 20% of patients who received antibiotics greater than 8 hours. There was also a 6-percentage point improvement for those receiving antibiotics within the 3-hour time frame as recommended by the SSC guidelines. The pre-implementation group had 50% of patients receive antibiotics within 3-hours and the post-implementation group saw 56% of patients receive antibiotics within 3 hours. When looking at 6 hours after presentation, the pre-implementation group had 37% of patients receive antibiotics within 6 hours and the post-implementation group had 47% of patients receive antibiotics within 6 hours.

#### **4.4 Summary**

After the MEWS score was implemented, frequency data and statistical analyses indicated there were no statistically significant changes in lactate measurements, blood culture draws or time in minutes to antibiotic administration. Statistically significant differences were seen in disposition status for patients that were diagnosed with sepsis, severe sepsis or septic shock, however this project did not analyze mortality or overall outcomes for patients. Clinical significance was identified for antibiotic administration with time in minutes to administration improving at the 3-hour, 6-hour and greater than 8-hour marks. Although not statistically significant for this sample, these improvements do support the findings in the literature. Evidence-based literature demonstrates improvement in recognition and time to interventions with implementation of early warning systems, however this was not demonstrated in this quality improvement project.

## **Chapter 5 Discussion**

### **5.1 Recommendations for Practice**

Although, this quality improvement project did not demonstrate statistically significant changes between the two groups on some variables, implementing the MEWS scale did demonstrate statistically significant differences for patients with CHF and for disposition. This project did identify clinically significant differences in time in minutes to antibiotic administration, with improvement seen at the 3-hour, 6-hour and greater than 8-hour marks. This improvement in time to antibiotic administration in coordination with the MEWS is supported by the findings in the literature.

The literature supports utilization of the MEWS during triage can improve recognition of sepsis and improves times to interventions. The MEWS can easily be incorporated into the triage assessment and allows clinicians the ability to effectively and accurately utilize an early-warning score with sepsis patients (Corfield et al., 2014). Using the MEWS, allows nurses to initiate bundle interventions, which the literature illustrates improve outcomes, decreases costs and improves clinical efficacy. The literature demonstrated early-warning scores, in combination with nursing judgment, detects deterioration earlier and are shown to improve outcomes and assist clinicians in seeking higher level care (Corfield et al., 2014). The literature supports that nurse assessment with frequent recording of vital signs improves recognition of deterioration. Incorporating the MEWS into the EHR, aided nurses in recognizing abnormal vital signs and prompted them to alert a provider for immediate assessment and intervention.

This project further outlined the need for multi-disciplinary involvement in order to successfully recognize, monitor and treat sepsis. ED staff and ICU staff must work closely together to monitor for physiological deterioration and facilitate prompt transfer to the ICU, if patient necessitates close monitoring of hemodynamic status. The literature further illustrated the need of allied health departments, such as pharmacy, to work with ED staff and clinicians to prepare and deliver antibiotic therapy quickly to meet the three-hour requirement of antibiotics set out in the SSC guidelines. The literature identified prompt administration of antibiotics as a key factor in improving patient outcomes in septic patients.

## **5.2 Recommendation for Policy**

CMS requirement for reporting on core measures is continuously expanding. In 2015, sepsis was added as a core measure, requiring hospitals to begin reporting on performance measures. In 2017, these performance measures were associated with reimbursement to organizations. It is imperative that hospitals treating sepsis patients are able to recognize sepsis and initiate evidence-based interventions outlined in the SEP-1 measures. Hospitals need to strategically plan to avoid any decrease in Medicare reimbursement through continuous monitoring of compliance with SEP-1 measures. In order to ensure compliance, hospitals must educate and train health care providers how to assess and recognize signs and symptoms of sepsis. Using the MEWS can assist nurses and caregivers in quickly identifying early deterioration.

Current policies in the healthcare system hold hospitals more accountable for their delivery of care utilizing performance measures like those in the SEP-1 measure. These performance results impact organizations both financially and through marketing

potential. CMS displays hospital rankings based on hospitals' performance on core measures. These rankings are accessible to the public and hold organizations accountable to potential patients.

Improving compliance with these measures and increasing performance measurements affords hospitals the ability to avoid decreases in Medicare reimbursement. Improving recognition and prompt treatment of sepsis could alleviate poor scores and improved compliance on measures, thereby improving reimbursement and overall professional reputation.

### **5.3 Recommendations for Education**

In order to improve healthcare providers' ability to recognize signs and symptoms of sepsis and identify deterioration early, research indicates it is imperative organizations continuously educate caregivers on sepsis and evidence-based interventions. Clinicians must receive education and training on current protocols and performance measures and understand the full scope of interventions shown to improve outcomes. Evidence suggests performance tracking and regular feedback are necessary to improve compliance. Regular feedback can be accomplished through educational handouts, verbal education during patient encounters as well as review of performance measure scores with clinicians.

The evidence suggests education on sepsis and identification must be a significant portion of education. A major barrier identified in the literature was the difficulty in diagnosing and recognizing sepsis. Additional training and education on recognition of signs and symptoms of sepsis should be an integral part of clinician education.

Clinicians must also recognize the importance of multi-disciplinary teams in treating septic patients. Collaborating and educating all members of the multi-disciplinary

team on sepsis physiology and treatment will improve compliance with bundle targets. It is critical that all members are educated on current sepsis protocols and performance measures outlined by CMS. Evidence indicates that involving all disciplines improves compliance with evidence-based treatments.

#### **5.4 Recommendations for Research**

Further research is needed in determining the best criteria in which to diagnose sepsis. Prior to 2016, SIRS has been the clinical criteria for suspicion of sepsis. Although SIRS is shown to recognize signs of sepsis, its validity in identifying organ dysfunction, a major component of sepsis, is lower than other criteria measures. In 2016, the Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3) found the predictive value of the Sequential (Sepsis-related) Organ Failure Assessment (SOFA) was higher than SIRS for in-hospital mortality and recommended the use of SOFA as clinical criteria for sepsis (Seymour et al., 2016). Further research will assist clinicians in identifying valid and reliable clinical and diagnostic criteria to improve early recognition of sepsis. Improving sepsis definitions and criteria for diagnosis will improve recognition, prompt intervention and decrease mortality.

Further research is necessary in identifying which components of treatment bundles are most effective and how to incorporate these key elements into the ED setting. It is important to recognize that although all bundle components are important in decreasing mortality, it is critical for clinicians to recognize which interventions are priority based on patient presentation. Rapid fluid resuscitation, administration of antibiotics, and hemodynamic monitoring, including blood pressure, lactate and urine output, are the key elements to be considered and should be at the forefront of any sepsis

bundle. It is important that clinicians are able to provide these interventions in the ED setting in a prompt manner. Further research is necessary to identify best processes in ensuring these elements are integrated into ED sepsis bundles. A significant area of further research should focus on the ability to consult a critical care team earlier in patient presentation through pathways such as sepsis rapid response teams. Collaboration with critical care, pharmacy and ED staff is crucial to initiate care earlier in patient presentation.

Increasing nurse involvement in initiation of interventions, starting in the ER setting has been shown to improve outcomes and further research is needed in identifying ways to integrate nurse-driven bundles into sepsis treatment. Calculation of the MEWS at triage by the nurse can improve time to treatment however research is needed in identifying ways to educate nurses in recognizing signs and symptoms of sepsis, components of sepsis treatment, as well as the importance of timely implementation of treatment for sepsis patients. Research indicates that nurse-driven bundles improve patient outcomes however research has identified knowledge gaps of sepsis recognition and process components, which creates barriers to successful implementation of sepsis bundles. Recognition of sepsis is paramount and should continue to be the focus to improve patient outcomes. Multi-disciplinary team education can assist in closing these knowledge gaps and assist nurses and clinicians in obtaining full compliance of sepsis bundle components.

## **5.5 Limitations**

In terms of limitations, the sample size was small and may have limited ability to identify statistical significance between the groups. The sample was from a single-center



facility in a specific region, limiting the generalizability of the results. The length of time was also a limitation, with only three months studied before and after implementation. Finally, this was a non-experimental design of a random sampling of patients that entered the ER during the time periods studied. The application of the MEWs by nurses was not controlled, creating possible differences in timing of treatment and assessment of the MEWS at triage. It is possible that nurse behavior was influenced by information and “word of mouth” prior to implementation of the MEWS, which could affect the pre-implementation group.

## **5.6 Conclusion**

Early recognition of sepsis is key to improving patient outcomes and decreasing mortality. With the ability to recognize sepsis early in presentation, clinicians can implement treatment promptly, within the 3-hour time frame outlined in the SSC bundle, which has proven to improve outcomes among sepsis patients. Use of the MEWS, as a triage tool used to identify patient deterioration, improved time to treatment and improved clinician monitoring of certain hemodynamic components such as lactate. With reducing times to interventions, the MEWS has shown to be an effective tool in assisting clinicians in identifying sepsis early in presentation in the ER setting.

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## APPENDIX A

### Johns Hopkins Evidence Model and Guidelines

Evidence Levels	Quality Guides
<p><b>Level I</b> Experimental study, randomized controlled trial (RCT), systematic review of RCTs, with or without meta-analysis</p> <p><b>Level II</b> Quasi-experimental study; systematic review of a combination of RCTs and quasi-experimental, or quasi-experimental studies only, with or without meta-analysis</p> <p><b>Level III</b> Non-experimental study, systematic review of a combination of RCTs, quasi-experimental and non-experimental studies, or non-experimental studies only with or without meta-analysis;</p>	<p><b>A <u>High Quality</u>:</b> Consistent, generalizable results, sufficient sample size for the study design, adequate control; definitive conclusions; consistent recommendations based on comprehensive literature review that includes thorough reference to scientific research</p> <p><b>B <u>Good Quality</u>:</b> Reasonably consistent results; sufficient sample size for the study design; some control, fairly definitive conclusions; reasonably consistent recommendations based on fairly comprehensive literature review that includes some reference to scientific evidence</p> <p><b>C <u>Low Quality or major flaws</u>:</b> Little evidence with inconsistent results; insufficient sample size for the study design; conclusions cannot be drawn.</p>

<p>Qualitative study or systematic review with or without a meta-analysis</p>	
<p><b>Level IV</b> Opinion of respected authorities and/or nationally recognized expert committees/consensus panels based on scientific evidence</p> <p>Includes:</p> <ul style="list-style-type: none"> <li>• Clinical Practice Guidelines</li> <li>• Consensus Panels</li> </ul>	<p><b>A <u>High Quality</u>:</b> Material officially sponsored by a professional, public, private organization or government agency; documentation of a systematic literature search strategy; consistent results with sufficient numbers of well-designed studies; criteria-based evaluation of overall scientific strength and quality of included studies and definitive conclusions; national expertise is clearly evident; developed or revised within the last 5 years.</p> <p><b>B <u>Good Quality</u>:</b> Material officially sponsored by a professional, public, private, organization or government agency, reasonably thorough and appropriate systematic literature search strategy; reasonably consistent results, sufficient numbers of well-designed studies; evaluation of strengths and limitations of included studies with fairly definitive conclusions; national expertise is clearly evident; developed or revised within the last 5 years</p> <p><b>C <u>Low Quality or major flaws</u>:</b> material not sponsored by an official organization or agency; undefined, poorly defined, or limited literature search strategy; no evaluate of strengths and limitations of included studies; insufficient evidence with inconsistent results, conclusions cannot be drawn, not revised within the last 5 years.</p>

<p><b>Level V</b></p> <p>Based on experiential and non-research evidence</p> <p>Includes</p> <ul style="list-style-type: none"> <li>• Literature reviews</li> <li>• Quality improvement, program or financial evaluation</li> <li>• Case Reports</li> <li>• Opinion of nationally recognized experts based on experiential evidence</li> </ul>	<p><b>A <u>High Quality</u>:</b> Clear aims and objectives, consistent results across multiple settings, formal quality improvement, financial or program evaluation methods used; definitive conclusions, consistent recommendations with thorough reference to scientific evidence</p> <p><b>B <u>Good Quality</u>:</b> Clear aims and objectives, consistent results in a single setting; formal quality improvement, financial or program evaluation methods used; reasonably consistent recommendations with some reference to scientific evidence</p> <p><b>C <u>Low Quality or major flaws</u>:</b> Unclear or missing aims and objectives, inconsistent results; poorly defined quality improvement, financial, or program evaluation methods, recommendations cannot be made.</p> <p>Literature Review, Expert Opinion, Case Report, Community Standard, Clinician Experience, Consumer Preference:</p> <p><b>A <u>High Quality</u>:</b> Expertise is clearly evident; draws definitive conclusions; provides scientific rationale; thought leader(s) in the field</p> <p><b>B <u>Good Quality</u>:</b> Expertise appears to be credible; draws fairly definitive conclusions; provides logical argument for opinions</p> <p><b>C <u>Low quality or major flaws</u>:</b> Expertise is not discernable or is dubious; conclusions cannot be drawn.</p>
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## Appendix B

### MEWS Scale

# ED MEWS Criteria

SCORE	3	2	1	0	1	2	3
PULSE		Less than 40	41-50	51-100	101-120	121-130	Greater than 130
RR	8 or less		9-11	12-20	21-25	26-29	30 or higher
TEMP		35.1 or less	35.1-35.8	35.9-38	38.1-38.6	38.7 or higher	
SBP	Less than 70	71-80	81-89	90-160	161-180	181-199	200 or higher
SPO2	Less than 86	86-88	89-91	92 or greater			

\*Score of  $\geq 4$  requires nursing intervention

## **Appendix C**

### **Michigan Quality Improvement Consortium (2008)**

Definitions: Levels of Evidence for the Most Significant Recommendations

A. Randomized Controlled Trials

B. Controlled Trials, Non-Randomized (Case Study and Cohort Study)

C. Observational Studies (Descriptive Studies)

D. Expert Panel

(Michigan Quality Improvement Consortium, 2008)

## Appendix D

### Evidence Table

Brief Reference, Type of study, Quality rating	Methods	Threats to validity/ reliability	Findings	Conclusions
<p>Alam, Hobbelenk, van Tienhoven, van de Ven, &amp; Nanayakkara. (2014). The impact of the use of the Early Warning Score (EMS) on patient outcomes: a systematic review. <i>Resuscitation</i>, 85, 587-594.</p> <p><b>-Systematic review - Study Quality-Level B</b></p>	<p>Systematic review of studies identified through PUBMED, EMBASE, and Cochrane Library; studies included those measuring in-hospital mortality, length of stay, cardiac arrests and serious adverse events in hospitals utilizing EWS; seven studies included in review</p>	<p>Mixed results in studies reviewed, small sample sizes and differences in methodologies among studies.</p>	<p>Studies found reduction in mortality among 6 of the 7 studies. Mixed results regarding length of stay; serious adverse events showed mixed results in 2 studies, higher admission rates in one study using EWS;</p>	<p>Although mixed results found amongst the studies, positive outcomes noted when using EWS in hospitals including decreased mortality and improved recognition of patient deterioration.</p>
<p>Arnold, R.C., Shapiro, N.I., Jones, A.E., Schorr, C., Pope, J., Casner, E... Trzeciak.S.(2009). Multicenter study of early lactate clearance as a determinant of survival in patients with presumed sepsis. <i>Shock Society</i>, 32(1), 35-39.</p> <p><b>Prospective observational study</b></p>	<p>ED patients diagnosed with severe sepsis at three urban hospitals between 2004 and 2007 were studied. Each ED utilized an ED-based protocol for sepsis. 166 patients were included in study. Authors analyzed difference in proportion of death between lactate clearance group and non-clearance group</p>	<p>Non-experimental design can only detect an association; serial lactate measurements were at the discretion of physician so some bias could have been introduced; all centers had aggressive resuscitation protocols which could lead to higher lactate clearance than other institutions without protocols. Deviations in protocol may</p>	<p>Overall mortality rate of 23% was noted with no location effect on in-hospital mortality; clearance of lactate occurred in 91% of subjects. Mortality rate was 60% among the non-clearance group and 19% in clearance group. No significant difference in vasopressor use among patients; no significant difference among ScvO2 goal and no relationship found between lactate clearance and</p>	<p>Early lactate clearance is an important determinant of survival in severe sepsis. Lactate non-clearance was shown to be a strong independent predictor of death. Further clinical trials needed to determine lactate clearance as an end point of sepsis resuscitation.</p>



Brief Reference, Type of study, Quality rating	Methods	Threats to validity/ reliability	Findings	Conclusions
<b>Study Quality: Level B.</b>		have occurred leading to confounding variables.	ScvO <sub>2</sub> goals. Four factors were significantly different between survivors and non-survivors: initial cardiovascular organ failure; persistent hypotension despite fluids; maximum ScvO <sub>2</sub> 70%; and lactate non-clearance	
Armstrong-Briley, D. Hozhabri, N.S., Armstrong, K., Puthottile, J., Benavides, R. and Beal, S. (2015). Comparison of length of stay and outcomes of patients with positive versus negative blood culture results  <b>-retrospective study</b> <b>Study quality-Level B</b>	Search of electronic health system for two patient populations in December 2013 who had blood cultures drawn if sepsis suspected and all patients with blood cultures drawn in ED prior to admission. Demographic information obtained along with type of pathogen, length of stay, in-hospital mortality, ICU admission and hospital admission or readmission.	Single center study leads to limits on generalizing to other settings. Patients with infections may not have been cultured resulting in selection bias	189 patients included. 54 coded for sepsis and 135 patients presented to ED. In the sepsis cohort, 34 patients had positive blood culture and 20 had negative culture. There were no statistically significant differences in outcomes between the patients with positive culture vs negative culture. Of those with negative cultures, 73.5% were admitted to ICU and 90% of positive cultures were admitted. 32% of those with negative cultures died in hospital compared with 30% with positive cultures. In the ED cohort, 93% had negative cultures, 7% positive. 25% of negative culture patients were admitted compared with 75% admitted to general floor. No significant difference in ICU admission between negative and positive culture patients.	The study did not show a statistically significant increase in mortality or ICU admission for those with positive cultures however there were increases in length of stay. Utility of blood cultures has not been determined and liberal use of cultures is not cost-effective or shows any positive outcome. More studies are needed to identify utility of blood cultures and effects on outcomes and antibiotic use.
Bruce, H.R., Maiden, J.,	Retrospective chart review of	Internal validity- cannot	Compliance with serum lactate	Rapid identification and timely

Brief Reference, Type of study, Quality rating	Methods	Threats to validity/ reliability	Findings	Conclusions
<p>Fedullo, P.F., &amp; Kim, S.C. (2015). Impact of nurse-initiated ED sepsis protocol on compliance with sepsis bundles, time to initial antibiotic administration, and in-hospital mortality. <i>Journal of Emergency Nursing, 41(2)</i>, 130-137.</p> <p><b>-Retrospective chart review</b> <b>-Study quality-Level A-B</b></p>	<p>all adult patients admitted through 2 ERs with diagnosis of severe sepsis or septic shock, n=195. Looked at pre and post protocol implementation data examined both compliance with 3 hour bundle targets and outcomes</p>	<p>look at mortality predictors as cause and effect due to retrospective design, power analysis for sample size not done. Training module not evaluated for understanding prior to nurse education. Due to retrospective design, those patients in which protocol was triggered without diagnosis of sepsis were not reviewed and conversely how many septic patients did not trigger protocol External validity- small sample size and only at 2 ERs so generalizability is limited.</p>	<p>measurement, blood cultures prior to antibiotic administration showed almost perfect compliance after protocol; post-protocol implementation showed significant reduction in time to initial antibiotic administration; time frame for admission to antibiotic interval was shortened between pre and post protocol phase. Change in fluid administration within 3 hours and lactate level did not show statistically significant changes. In-hospital mortality and LOS were not statistically significant either.</p>	<p>treatment in ED of patients with sepsis and septic shock can reduce in-hospital mortality and reduce time to initial antibiotic administration; improvement with serum lactate measurement with bundle initiation</p>
<p>Burney, M., Underwood, J., McEvoy, S., Nelson, G., Dzierba, A., Kauari, V, and Chong, D. (2012). Early detection and treatment of severe sepsis in the emergency department: identifying barriers to implementation of a protocol-based approach. <i>Journal of Emergency Nursing, 38(6)</i>, 512-517.</p> <p><b>- Cross-sectional survey</b></p>	<p>Cross-sectional survey design of full-time staff nurses and physicians in ED of major urban area between Nov 1- Dec 31, 2010. Survey consisted of 14 items for nurses and 13 for physicians- survey questions dealt with baseline knowledge and confidence in identification of SIRS, current practices/treatments, difficulties encountered in treatment of sepsis, perceived</p>	<p>Internal validity: Participation was voluntary meaning those with greater interest and knowledge may have participated;  External validity: results not reproducible as survey based on single ER needs and assessment of sepsis protocol.</p>	<p>Response rate was 43% for nurses and 57% for physicians. Barriers identified were delay in diagnosis by physicians, delay in completion of orders by nurses. Availability of ICU beds were barriers for physicians (41%), lack of access to CVP/ScvO2 monitoring (79.5%), lack of space in ER (64.9%), lack of staff; familiarity with sepsis identification and signs and symptoms, lactate measurement and normal and abnormal ranges</p>	<p>A multidisciplinary education program is necessary to focus on individual roles in treatment and identification; interdisciplinary approach to treatment in protocol implementation</p>

Brief Reference, Type of study, Quality rating	Methods	Threats to validity/ reliability	Findings	Conclusions
<b>design</b> <b>-Study quality-Level A-B</b>	barriers to implementation of protocol, and suggestions for improvement.		were unknown by both nurses and physicians (63.6% vs. 62.5%); fluid resuscitation and management of status; both nurses and physicians identified education in service for staff as well as rapid response team ; greater collaboration. 89.5% of nurses and 86% of physicians believed a protocol similar to STEMI and stroke protocols would be beneficial. Only 50% of physicians were confident in ordering appropriate abx.	
Burrell, McLaws, Fullick, Sullivan, & Sindhusake. (2016). Sepsis KILLS: early intervention saves lives. <i>MJA</i> , 204, <b>- quality improvement program</b> <b>- study quality-Level B</b>	SEPSIS KILLS implemented in 97 ER in New South Wales that promoted intervention within 60 minutes of recognition and outcome measures including time to antibiotics, fluid resuscitation, mortality rates and length of stay	Prolonged period added bias to study. Data was voluntarily collected resulting inconsistent submission, lack of strict criteria. Resources were limited in some areas causing no data submission	Time to antibiotics increased from 29.3% to 52.2%; 2 <sup>nd</sup> liter of fluid within 60 minutes increased from 10.6% to 27.5%; proportion of patients classed using triage scale increased across all levels, significant decline in ICU stay and total length of stay; mortality rates did change significantly but survival benefit was greater in those with hemodynamic instability	Sepsis KILLS program improves care for patients and improves recognition of sepsis and improves sepsis management in New South Wales in ER and general wards.
Corfield, A.R., Lees, F., Zealley, I., Houston, G., Dickie, S., Ward, K. McGuffie, C. (2014). Utility of single early warning score in patients with sepsis in the	Data collected over 3 months of all adult septic patients admitted for at least 2 days or those who died within 2 days. Patients with 2 SIRS criteria were included. Early warning score calculated in the ED	Sample size was limited due to missing observations in records; study excluded those discharge within 2 days and no information on co-morbidity was obtained to minimize confounding	Study found those admitted to ICU had higher NEWS than non-ICU patients and those that died within 30 days had higher NEWS. A one-point rise in NEWS an increased mortality risk; those with a NEWS > 7 had	Use of EWS in the emergency department can improve outcomes in sepsis patients and can determine need for higher level care while in ED.

Brief Reference, Type of study, Quality rating	Methods	Threats to validity/ reliability	Findings	Conclusions
<p>emergency department. <i>Emergency Medicine Journal</i>, 31(6), 482-487.</p> <p><b>Prospective observational study</b> <b>Study quality: Level B</b></p>	<p>using NEWS</p>	<p>variables</p>	<p>a positive predictive value of 27% for ICU admission and increased mortality within 30 days. The PPV rose to 35% if NEWS &gt; 9. No demographic differences were found.</p>	
<p>Delgado-Hurtado, J.J., Berger, A., Bansal, A.B. (2016). Emergency department modified early warning score association with admission, admission disposition, mortality, and length of stay. <i>Journal of Community Hospital Internal Medicine Perspectives</i>, 6.</p> <p><b>Retrospective study</b> <b>Study quality: Level B</b></p>	<p>Chart review of a random sample of 3000 patients entering the ED between Jan 1 2014 and May 31, 2015. Variables of interest included demographics, mean of arrival to ED, date and time of clinical events, ED MEWS, admission to hospital, mortality and date of discharge.</p>	<p>Physicians not blinded to MEWS and scores may have determined decision on admission; selection bias present due to retrospective nature of study.</p>	<p>80.7% of patients were not admitted while 19.3% were admitted to general medicine or critical care unit. 2.147 had MEWS automatically calculated in EHR. Those admitted were older, arrived by ambulance and had higher MEWS. Those admitted to ICU had higher MEWS and there was a significant relationship between length of stay and mean, maximum and median MEWS</p>	<p>MEWS can be integrated into an EHR and score helps predict deterioration. MEWS can be used at triage to determine admission criteria.</p>
<p>Ferrer, R., Martin-Loeches, I., Phillips, G., Osborne, T.M., Townsend, S., Dellinger, R.P...Levy, M.M. (2014). Empiric antibiotic treatment reduces mortality of severe sepsis and septic shock from the first</p>	<p>28,150 patients across 165 ICU between 2005 and 2010 were studied. Data extrapolated from patient charts included demographic data, time of presentation of severe sepsis; time to antibiotic treatment, name of antibiotic given. Study included patients that</p>	<p>Design creates potential for confounding variables to affect results; authors did not determine appropriateness of antibiotics; no analysis or ability to determine delay in treatment; not randomized so may not be able to generalize findings.</p>	<p>Higher mortality rate (46.6%) found in patients who were diagnosed in ICU; higher respiratory failure (30.8%), nosocomial infections (21.9%), and septic shock (69.9%). Those who were identified in ICU also had longer hospital stays and longer ICU stays. When identified in ER, mortality rate</p>	<p>Authors concluded delay in antibiotic administration was associated with increased in-hospital mortality and there was a linear increase in mortality risk with each hour antibiotic was delayed</p>

Brief Reference, Type of study, Quality rating	Methods	Threats to validity/ reliability	Findings	Conclusions
<p>hour: from a guideline-based performance improvement program. <i>Society of Critical Care Medicine</i>, 42(8), 1749-1755.</p> <p><b>Retrospective design</b> <b>Study quality: Level B</b></p>	<p>presented to ED, direct admit to ICU or from general wards.</p>		<p>was 26.3% and decreased to 25.2% when antibiotic received within 1<sup>st</sup> hour; mortality rate increased to 31.2% if antibiotic delayed over 6 hours. Significant relationship found between mortality rate and time to first antibiotic administration</p>	
<p>Gaieski, D., Mikkelsen, M., Band, R., Pines, J., Massone, R., Furia, F...Goyal, M. (2010). Impact of time to antibiotics on survival in patients with severe sepsis or septic shock in whom early goal-directed therapy was initiated in the emergency department. <i>Journal of Critical Care Medicine</i>, 38(4), 1045-1053.</p> <p><b>-retrospective analysis</b> <b>- Level III good quality</b></p>	<p>Study in single center ER January 5, 2005 to December 31, 2006. Inclusion criteria: inclusion in severe sepsis/septic shock database, initiation of EGDT during ED stay. Data recorded using standard software. Data entry completed by four personnel trained before start of the study. Comparison of hospital mortality in patients receiving antibiotics at different time cutoffs: elapsed time from triage to antibiotic administration, qualification of EGDT to administration, from triage to appropriate antibiotic admin. N=261</p>	<p><b>External Validity:</b> Performed at a single center using uniform, algorithmic resuscitation strategy so cannot guarantee generalizability in institutions with differing resources.</p> <p><b>Internal Validity:</b> Cannot rule out sicker patients received abx quicker and that could be confounding variable. Possible other confounders existed including differences in times to EGDT end points. Also bias from one author meeting with data abstractor weekly to address questions could have occurred. Sample size was relatively small.</p>	<p>47% qualified for EGDT at triage, 53% later qualified during ED stay. 48% diagnosed with cryptic shock and 52% septic shock. All patients received antibiotics during ER stay. Median length of time to antibiotic (abx); from triage 119 mins, from EGDT qualification 42 mins, from triage to appropriate abx 127 mins and from qualification to appropriate abx 47 mins. In hospital mortality was 31%, 35.1% for culture positive patients vs. 25.7% for culture negative. Mortality for culture positive receiving appropriate abx in ED 32.5% vs. 50% of those that did not receive appropriate abx in ED. No relationship between time from triage to administration and mortality outcome after adjusting for</p>	<p>Three factors identified: 1. Time the patient qualified for EGDT 2. The length of time from qualification of EGDT to administration of appropriate abx 3. Length of time from triage to appropriate abx administration. Study recommends practitioners administer appropriate antibiotics as quickly as possible once reasonable suspicion of sever sepsis</p>

Brief Reference, Type of study, Quality rating	Methods	Threats to validity/ reliability	Findings	Conclusions
			<p>confounders. Also no relationship between time from qualification for EGDT and antibiotics and mortality. However with time from triage to appropriate abx administration, mortality was decreased when given &lt; 1hr vs. &gt;1 hr. (26.1% vs. 32.1%. Same was true with EGDT qualification and appropriate abx &lt; 1hr vs. &gt; 1 hr. (26.6% vs. 37.4%).</p>	
<p>Kyracios, U., Jelsma, J., and Jordan, S. (2011). Monitoring vital signs using early warning scoring systems: a review of the literature. <i>Journal of Nursing Management</i>, 19, 311-330. <b>Systematic literature review</b> <b>Study Quality: Level B</b></p>	<p>Published literature reviewed for development and clinical significance of MEWS/EWS systems .Research focused on adult inpatients outside of ICU and ED. Search included literature 1998 to present. A total of 18 sources were included out of 534 papers located in search.</p>	<p>There was lack of randomized controlled trials included in search; there was considerable variation in vital sign parameters and entry among studies; only one study met all criteria and only observational studies were found.</p>	<p>There is little evidence of validity and effectiveness of MEWS due to difficulty in conducting randomized control trials; literature found lack of monitoring and suboptimal care on general wards is associated with poorer outcomes and infrequent monitoring of vital signs prevents early identification, leading to poorer outcome; lack of teamwork and misrepresentation of data causes delays in treatment; patient survival is dependent on nurses' decisions to alert providers. 11.3% of patients' treatments were delayed up to one hour and 8.9% of treatment was delayed greater than 3 hours; only 2.8%</p>	<p>Authors found better monitoring and more frequent vital signs leads to better care however there is lack of evidence regarding validity, implementation, evaluation and clinical testing of EWS on general wards. Found nursing judgment is critical in preventing delays in treatment and early recognition of deterioration.</p>

Brief Reference, Type of study, Quality rating	Methods	Threats to validity/ reliability	Findings	Conclusions
			of nurses would call emergency team for change in vital signs; nurses lack confidence in knowledge of certain medical conditions, causing delays in treatment	
<p>Jones, Focht, Horton, &amp; Kline (2007). Prospective external validation of the clinical effectiveness of an emergency department-based early goal directed therapy protocol for severe sepsis and septic shock.</p> <p><b>-prospective interventional study</b> <b>-Level III, good quality</b></p>	<p>Single center ED enrolled 156 adults with SIRS criteria and either systolic BP &lt;90mmHg after fluid bolus or lactate concentration &gt; 4mmol/L. Authors recorded pre-intervention clinical and mortality data on consecutive eligible patients for 1 year when treatment was at the physician's discretion. An EGDT protocol was then implemented and clinical data and mortality rates were recorded for 1 year after implementation. A 33% relative reduction in mortality to indicate clinical effectiveness</p>		<p>79 patients in pre-intervention and 77 patients in post-intervention. Patients in post-intervention received more crystalloid fluid than pre-intervention (2.54L vs 4.66L) and increased vasopressor administration (34% vs 69%) during initial resuscitation. In-hospital mortality was 27% pre-intervention and 18% post-intervention with an absolute difference of 9% (33% relative mortality reduction). Patients in post group had an increase in ICU LOS of 1.8 days and mean hospital LOS of 1.2 days</p>	<p>Implementing an EGDT protocol in the ED is shown to reduce mortality of patients with sepsis. These patients are also shown to receive more fluid and more vasopressors in the ED than the non-EGDT group.</p>
<p>Kumar et al. (2006). Duration of hypotension before initiation of effective antimicrobial therapy is the critical determinant of survival in human septic shock. <i>Society of Critical Care</i></p>	<p>Retrospective cohort study between July 1989 and June 2004 at 14 ICUs at 10 hospitals. A total of 2,731 patients were included. Main outcome measure was survival to hospital discharge. Three cohorts created: 1-all</p>	<p>This was not a randomized controlled trial and patients were not randomly selected which could lead to selection bias. The length of the study could lead to changes in care that could also affect the outcomes or</p>	<p>All cohorts were similar in terms of average APACHE II scores, distribution of clinical infections, time to effective antibiotic therapy following onset of hypotension and outcome. All data combined for analysis. Documented infections</p>	<p>Initiation of effective antibiotic therapy following onset of hypotension is a critical variable associated with mortality in septic shock. Initiation of therapy within the first hour was associated with 79.9% survival. This study supports</p>

Brief Reference, Type of study, Quality rating	Methods	Threats to validity/ reliability	Findings	Conclusions
<p><i>Medicine</i>, 34(6), 1589-1596.</p> <p><b>Retrospective cohort study</b></p> <p><b>Study Quality-Level B</b></p>	<p>septic shock cases admitted to adult ICUs of all hospitals from May 1999-June 2004; 2- all septic shock cases from June 1989 and April 1999 at a single adult tertiary care center in Canada and 3- consecutive adult septic shock patients from July 1999 to June 2004 at three academic institutions in US. Data obtained included choice of antimicrobial used and time of administration</p>	<p>changes in therapeutic measures.</p>	<p>present in 77.9% of cases. A microbial pathogen was identified in 70% of cases and isolated from blood in 34.2% of cases. Overall mortality was 56.2% and survival similar whether pathogen was documented or suspected. 19 patients did not receive effective antimicrobial treatment before death and 558 were on effective antibiotic treatment before the onset of hypotension. Mortality rate was 58% in those that received effective antimicrobial treatment after onset of hypotension. During the first 6 hours after onset of hypotension, each hour delay of administration of effective antibiotic therapy was associated in a 7.6% decrease in survival. Survival was 82.7% if treatment administered within 30 mins of hypotension, 77.2% in second half hour and 42% in the 6<sup>th</sup> hour. Median time to administration of antibiotic therapy was 6 hours, Average times were 13.51±0.45 hrs. Delay in initial recurrent or persistent hypotension to administration of antibiotics was</p>	<p>empirical, broad-spectrum antibiotic administration be completed within the first hour of onset of hypotension and be considered an intrinsic component of initial resuscitation of septic shock.</p>



Brief Reference, Type of study, Quality rating	Methods	Threats to validity/ reliability	Findings	Conclusions
			<p>a critical determinant of survival to ICU and hospital discharge (P&lt;0.0001) The odds ratio of death climbed with progressive delays in treatment to a maximum value of 92.54 with delays &gt; 36hrs after onset of hypotension. When delay assessed as continuous variable, odds ratio was 1.119 or a 12% decrease in probability of survival with each hour delay. In multivariate analysis with other variables including effectiveness of antibiotic, choice and amount of IV fluid resuscitation, single vs multiple drug class therapy, choice and rapidity of vasopressors, time to antibiotic therapy was most strongly associated with outcome and remained even when considering other variables such as APACHE II scores, number of organ failures and clinical infection site.</p>	
<p>Nguyen, H.B., Rivers, E.P., Knoblich, B.P., Jacobsen, G., Muzzin, A., Ressler, J.A., Tomlanovich, M.C. (2004). Early lactate clearance is associated</p>	<p>Studied patients in ER with severe sepsis and septic shock between February 1, 1999 and February 1, 2000. Data collected from charts including vital signs, lab values, APACHE II scores,</p>	<p>Limited to single center which can limit ability to generalize findings. Acuity of patients in hospital is higher than national average which can limit generalizability.</p>	<p>111 patients were enrolled. 52.3% presented with septic shock and overall hospital mortality was 42.3%, baseline APACHE II score was 20.2 ± 6.8 and baseline lactate level was 6.9 ± 4.9 mmol/L. Survivors</p>	<p>Lactate clearance early in sepsis course is associated with improved morbidity and mortality rates . Lactate level and clearance is an excellent marker of tissue hypoxia, independent of other variables.</p>

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<p>with improved outcome in severe sepsis and septic shock. <i>Society of Critical Care Medicine</i>, 32(6), 1637-1642.</p> <p><b>Prospective observational design.</b> <b>Study quality: Level B</b></p>	<p>therapies given in ER and in ICU, lactate levels.</p>		<p>had lactate clearance of 38.1%±34.6% compared with 12% ±51.6% in non survivors. Only lactate clearance was associated with decreased mortality. There was a 44.7% sensitivity; 84.4% specificity and 67.6% predictive value for in-hospital mortality for patients with lactate clearance &lt; 10% after 6 hours of intervention. Demographics were similar in both groups; Apache II scores were similar in both groups. High lactate clearance group required less fluid replacement and less vasopressor therapy in the first 6 hours and had higher platelet and lower prothrombin levels. High lactate clearance group had more severe sepsis but improved mortality rates</p>	
<p>Puskarich, M.A., Trzeciak, S., Shapiro, N.I., Arnold, R.C., Horton, J.M., Studnek, J.R...Jones, A.E. (2011). Association between timing of antibiotic administration and mortality from septic shock in patients treated with a quantitative</p>	<p>Analysis of adult patients in 3 Urban US emergency departments who received an initial dose of antibiotics after presentation to ED. Cohorts categorized based on both time from triage and time from shock recognition to initiation of antibiotics; primary outcome was in-hospital mortality.</p>	<p>The three institutions studied have long standing resuscitation protocols and results may not be generalized to those that do not. Majority of patients received antibiotics within 3 hours of triage and makes associations with mortality difficult at longer time points in the remaining</p>	<p>Of the 291 patients included, mortality did not change with hourly delays in antibiotic administration up to 6 hours after triage. 59% of patients received antibiotics after shock recognition. Overall mortality was 18.9%. Positive blood cultures obtained in 34.4%. Mortality rate for blood culture positive patients was 26% vs</p>	<p>This study did not find an association between timing of antibiotic administration from ED triage and hospital mortality however a delay in antibiotics until after shock recognition was associated with increased mortality</p>

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<p>resuscitation protocol. <i>Society of Critical Care Medicine</i>, 39(9), 2066-2067.</p> <p><b>Analysis of Multicenter, randomized trial</b></p> <p><b>Study Quality –Level B</b></p>		<p>small numbers. Due to the small sample size, a larger study may detect differences; mortality rate at baseline is lower than other studies and exact time of onset of shock was difficult to ascertain which is inherent limitation in sepsis research. No causation could be made due to design of study.</p>	<p>15.2% for blood culture negative patients. 91% blood culture positive patients received antibiotics in ED that were susceptible to organism; 7 of the 9 patients that received broad spectrum antibiotics the organism was resistant and 2 patients had untreated fungemia. The mortality rate as 25.3% for those treated appropriately and 33.3% for those receiving inappropriate antibiotics. Median time from triage to initial therapy was 115 mins. No association seen between time from ED triage to administration of antibiotics within the first 6 hours. Median time to shock recognition was 89 minutes and 59% of patients received antibiotics after shock recognition. Those receiving antibiotics after shock recognition had an increase in odds of death (OR 2.4, CI 1.1 to 4.5). No increase in mortality found with delay to administration during first 3 hours of after shock recognition . With multivariate logistic regression model which controlled for confounding</p>	

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			variables, no significant changes from unadjusted OR found.	
<p>Rivers, E., Nguyen, B., Havstad, S., Ressler, J., Muzzlin, A., Knoblich, B., Peterson, E. and Tomlanovich, M. (2001). Early goal-directed therapy in the treatment of severe sepsis and septic shock. <i>New England Journal of Medicine</i>, 345(19), 1368-1377</p> <p><b>-Randomized control trial</b> <b>-Level I- good to high quality</b></p>	<p>Randomly assigned patients in urban ER with severe sepsis and septic shock to receive 6 hours of EGDT or standard therapy prior to ICU admission. N=263</p>	<p>Internal Validity: Because of the partially blind nature of study, interaction in the initial period may have caused standard therapy patients may have received some form of goal-directed therapy.</p> <p>External Validity: Also this was a single site study which may limit generalizability</p>	<p>130 randomly assigned to EGDT and 133 to standard therapy. EGDT group mortality -30.5%; standard therapy – 46.5% (P=0.0009). EGDT group- high mean central venous O<sub>2</sub> (70.4% ±10.7 vs. 65.3±11.4) lower lactate level (3.0±4.4 vs. 3.9±4.4), lower base deficit (2.0±6.6 vs. 5.1±6.7), higher Ph (7.40±0.12 vs. 7.36±0.12). P&lt;0.02. APACHE II scores were significantly lower in EGDT group indicating less organ dysfunction (13.0±6.3 vs. 15.9±6.4, p&lt; 0.0001</p>	<p>Early goal directed therapy shows improved outcomes in patients with severe sepsis and septic shock.</p>
<p>Rusconi, A., Bossi, D., Lampard, J., Szava-Kovats, M., Bellone, A., and Lang, E. (2015). Early goal-directed therapy vs. usual care in the treatment of severe sepsis and septic shock: a systematic review and meta-analysis. <i>Internal and Emergency Medicine Journal</i>, 10, 731-743.</p> <p><b>- Systematic review of</b></p>	<p>Primary studies identified through MEDLINE and EMBASE databases and Cochrane Register to identify RCT studies assessing effectiveness of EGDT, five studies (n=4033) included.</p>	<p>Internal Validity: Blinding not possible in studies but mortality appeared not be affected,</p> <p>Reliability: Reviewed small number of articles</p>	<p>Rivers study showed significantly lower mortality in EGDT group, Wang et al., study reported reduction in primary outcome of 14-day mortality in EGDT vs. non-EGDT (25 vs. 41.2%)The other three studies mortality was not significantly affected. Overall EGDT did not reduce in-hospital mortality. Review could not draw any definitive conclusions regarding EGDT effectiveness</p>	<p>Cannot have definitive conclusion of efficacy of EGDT in severe sepsis and septic shock, partially because part of EGDT has been incorporated into usual care over last 10 years. Strict adherence to EGDT may not be necessary but review found EGDT does improve outcomes and early recognition, early intervention, prompt antibiotic administration are key elements to be considered in treatment</p>

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<b>RCTs</b> <b>- Level I- good to high quality</b>				
<p>Singer, A.J., Taylor, M., LeBlanc, D., Williams, J., Thode, Jr., H.C. (2014). ED bedside point-of-care lactate in patients with suspected sepsis is associated with reduced time to iv fluids and mortality. <i>American Journal of Emergency Medicine</i>, 32, 1120-1124</p> <p><b>Before and After study</b> <b>Study Quality: Level B</b></p>	<p>Patients identified using a institutional sepsis screening tool in the ED. Patients chose between January and September 2013. Data on time from ED triage to IV fluid; antibiotic administration; ordering of antibiotics, total volume of fluid within 6 hours or in ED; ED length of stay, use of vasoactive agents, and in-hospital mortality were obtained. A total of 160 patients were included</p>	<p>Study design can only identify association, not causality. Confounding variables may have been introduced and caused differences in mortality; the staff and physicians were aware of POC testing and could have introduced a Hawthorne effect. A convenience sample was used which could have caused selection bias. The setting was a single center, which limits generalizability to other institutions.</p>	<p>Demographics were similar in both groups along with baseline lactate measurements, antibiotic orders and administration times (62 mins vs. 69 mins). POC measurement reduced time to lactate level results by 88 minutes. There was a significant reduction in time to IV fluid administration (55 mins in after group vs. 71 mins in before). Significant reduction in in-hospital mortality (6% vs 19%) and ICU admission between after and before groups was 33% vs 51%. No differences seen in ED LOS, hospital LOS and ICU LOS. Correlation between POC lactate level and central lab lactate level was 0.94. All patients had lactate levels over 2mmol/L with serial lactate measurements conducted in 85% of patients. Mortality rate in those with serial measures was 2% compared with 12% those without serial measures.</p>	<p>Beside POC lactate measurement in adult ED patients with sepsis reduces time to test results and time to IV fluids. A significant reduction in mortality and ICU admission was also seen.</p>
Tromp, M., Hulscher,	A prospective before-and-	External Validity:	Compliance with	Using a nurse driven protocol

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<p>M., Bleeker-Rovers, C., Peters, L., van den Berg, D., Borm, G...Achterberg. (2010). The role of nurses in the recognition and treatment of patients with sepsis in the emergency department: a prospective before-and-after intervention study. <i>International Journal of Nursing Studies</i>, 47, 1464-1473.</p> <p><b>- Prospective before-and-after intervention study</b></p> <p><b>- Level III-good quality</b></p>	<p>after intervention study of adult patients in the ED due to known or suspected infection with 2 or more SIRS criteria to look at compliance with 6 bundle SSC recommendations during 3 different periods with specific interventions applied in each period. Period 1 before using bundle July 1, 2006-Nov 6, 2006; Period 2: after protocol but before training Nov 6, 2006-June 25, 2007; Period 3: after training and performance feedback June 25, 2007-Oct 1, 2007. N=825</p>	<p>Uncontrolled study in a single center and implementation program was for this specific hospital so cannot extrapolate results to other institutions;</p> <p>Internal Validity: possible therapeutic or diagnostic changes could have occurred during study time creating a time effect; clinical signs in sepsis screening were sensitive but not specific leading to over-diagnosis or overtreatment possibly.</p>	<p>recommendations increased in all three periods from 3.5% prior to care bundle implementation to 10.4% after implementation but prior to training and feedback to 12.4% after implementation, education and feedback; serum lactate measurements improved 23%-80%, chest x-ray (67% to 83%), urine/urinalysis and culture (49%-67%) and initiation of antibiotics (38%-56%) in each of the three periods; performed bundle elements improved over period 2 versus period 1 from 3.0-3.9 (95% CI 0.7-1.2) and increased in period 3 from 3.9 to 4.2 (95% CI 0.03-0.5) recognition of sepsis improved from 71% in period 2 to 82% in period 3.</p>	<p>in the ED combined with training and feedback can improve recognition and compliance with bundle recommendations in sepsis patients.</p>
<p>Turi, S. and Von Ah, D. (2013). Implementation of early goal directed therapy for septic patients in the emergency department: a review of the literature. <i>Journal of Emergency Nursing</i>, 39(1), 13-19.</p> <p><b>- systematic review</b></p> <p><b>- Level II- good quality</b></p>	<p>Literature review using MEDLINE, CINAHL and Cochrane, studies reviewed from 2006-2010, limited to empirical manuscripts in English examining implementation of adult sepsis guidelines in emergency department. Excluded those focused on drug administration; 7 studies included</p>	<p>Reliability: Studies limited by design, setting/sample length and follow up, no RCT or meta-analysis identified in search;</p> <p>External Validity: all studies were in single EDs and most were in large academic medical centers. Also there was lack of discussion on maintaining momentum of</p>	<p>Major barrier identified to EGDT was sepsis is often difficult to diagnose. Training and education needed to remove barrier. Studies using discussion, preplanning, and education were able to implement CVP monitoring, MAP and SVO<sub>2</sub> monitoring. Nursing interventions like urine output and obtaining blood cultures were less often considered.</p>	<p>Review outlined specific ways to successfully implement bundle. Focusing on operational and system issues significantly influenced success; more research needed to overcome barriers and to identify which aspects of guidelines are most important in achieving improved outcomes. More work and research is</p>

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		using the sepsis guidelines after initial implementation	Operational and system barriers exist with regards to training and staffing required to accomplish recommendations. Consensus on guidelines remains a barrier to ED physicians especially regarding CVP monitoring with central catheter. Another issues not reviewed in studies is LOS in ED and delay in admission to ICU	needed to understand barriers to implementation of protocols. Further research needed in rural hospitals
Vanzant, A., and Schemlzer, M. (2011). Detecting and treating sepsis in the emergency department. <i>Journal of Emergency Nursing</i> , 37(1), 47-54. <b>-Systematic literature review</b> <b>-Level V, high quality</b>	Article outlining definition of sepsis and progression to septic shock along with 4 ways to detect sepsis. Current treatments and implications for ED nurses. Uses current research and evidence in the field to make recommendations	Not a study, recommendations based on research and current evidence.  Reliability: Reviewed large number of articles and summarized current research recommendations.	Sepsis is defined as 2 or more SIRS criteria and suspected or known infection. Septic shock occurs when sepsis progresses to point where hypotension does not respond to fluid resuscitation. Elderly more at risks, more common in men and African Americans; nosocomial infections have higher mortality than community acquired; 4 major infection sites-lungs, GI tract, urinary tract and blood stream; gram positive more likely to lead to sepsis. Medical treatment focuses on respiratory support, maintain circulatory volume, remove infectious source. ED goals- recognizes sepsis, treat rapidly, and maintain tissue perfusion. Use of a bundle focusing on these goals	Review outlined 3 approaches to sepsis detection 1. Serum lactate measurement 2. SIRS/infection screening tool and 3 CAM to detect delirium. Further research needed for level of lactate that is significant. Further research needed on validity, specificity and sensitivity of screening tools. ED nurses must be educated on sepsis presentation, early signs and symptoms, vigilance in high risks patients. ED personnel should implement protocols to aid in early detection along with serum lactate measurements and monitoring mental status. Use of EHR alerts may be beneficial but further research is indicated. Studies do indicate

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			has shown improved results.	early recognition and treatment improves outcomes
<p>Wawrzoniak, I., Loss, S., Moraes, M., Vega, F. and Victorino, J. (2015). Could a protocol based on early goal-directed therapy improve outcomes in patients with severe sepsis and septic shock in the intensive care unit setting. <i>Indian Journal of Critical Care Medicine</i>, 19, (3), 159-165.</p> <p><b>-non-randomized, experimental study</b> <b>-Level II- good to high quality</b></p>	<p>ICU patients screened for severe sepsis or septic shock and included in registry and followed- split into early goal-directed therapy group and standard therapy</p>	<p>Internal Validity: Non-EGDT group was older with more respiratory infections and longer hospitalization prior to ICU admission-may biased decision</p>	<p>268 patients included with 97 using EGDT. Mortality rate was higher in standard care group 49.7% vs. 37.1% p=0.04 in hospital and 40.4% VS 29.9% P=0.08 in ICU. LOS non-EGDT vs. EGDT 45.0±59.8 vs. 29.1±30.1 p=0.0002 in hospital and 17.4±19.4 vs. 9.1±9.8 days p&lt;0.0001 in ICU</p>	<p>Study showed reduced mortality and LOS in patients receiving EGDT.</p>
<p>Westphal et al., (2011). Reduced mortality after the implementation of a protocol for the early detection of severe sepsis. <i>Journal of Critical Care</i>, 26, 76-81.</p> <p><b>-prospective cohort study</b> <b>-level II, rate B</b></p>	<p>Study conducted in 2 phases at 2 hospitals in Brazil. Phase 1 patients with severe sepsis and septic shock were identified and treated based on SSC guidelines. Phase II, patients with severe sepsis and septic shock were identified using active surveillance for signs of sepsis. Cohorts were compared for compliance with sepsis bundles and mortality rates</p>	<p>Bias was present which reduces the degree of certainty; study not randomized and providers may have utilized SSC guidelines in control group causing Hawthorne Effect. Sample size was small decreasing generalizability as well</p>	<p>217 patients total with severe sepsis and septic shock. Significant differences between the two groups were identified regarding 28-d mortality (48% vs 21.3%) and in-hospital mortality (61.7% vs 36.5%); compliance was higher in phase I than phase II (32.3% vs 28.7%); length of stay was longer in phase I patients vs phase II patients</p>	<p>Early diagnosis of sepsis is integral to improved outcomes but close observation and monitoring is essential along with careful interpretation of vital signs</p>



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<p>Wira, C., Dodge, K., Sather, J., and Dziura, J. (2014). Meta-analysis of protocolized goal-directed hemodynamic optimization for the management of severe sepsis and septic shock in the emergency department. <i>Western Journal of Emergency Medicine</i>, 15(1), 51-59.</p> <p><b>- Meta-analysis of RCT studies</b> <b>- Level I-good to high quality</b></p>	<p>Analysis structured after QUOROM and MOOSE recommendations; computer search identified articles from 1980 to December 4, 2011 using research databases. Studies included were adult controlled trials using protocols in ED patients with severe sepsis and septic shock.</p>	<p>Reliability: Limited by publication bias with no mechanism to include studies or abstracts not at national conferences or available in search results; also some studies include patients from ICU or med/surg floors- noted as “hybrid” studies; only one study was RCT with others being before-after design with retrospective control group and cross-sectional design which subjected them to selection bias, length bias, variability of practice patterns.</p>	<p>Identified 1323 articles with 65 used for review. 25 studies remained after applying inclusion and exclusion criteria (n=9597). Mortality rate receiving protocolized hemodynamic optimization was 25.8% contrasted to 41.6% in control groups (p&lt; 0.0001)</p>	<p>Protocolized hemodynamic optimization in ED patients with severe sepsis and septic shock appeared to reduce mortality</p>