The Reality of Sepsis

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Abstract

Background: Sepsis is a potentially life-threatening infection affecting millions of individuals. Nearly three million individuals are affected annually, killing one in every two to four individuals. Sepsis mortality rates are highest in those 65 and older, making it the most expensive diagnosis paid by Medicare and worldwide at $24 billion dollars. Early goal directed therapy (EGDT), created by the International Surviving sepsis campaign, is a bundled protocol created to decrease mortality rates, however, utilization and completion remains a problem in the emergency department (ED).

Purpose: This project sought to evaluate the gap that exists between best practice and current practice, for sepsis identification and EGDT implementation.

Methods: The project was completed over a four-month period with prior Institutional Review Board (IRB) approval and consisted of evaluation of sepsis knowledge and barriers to EGDT. Questionnaires included demographics, sepsis knowledge, barriers to EGDT and AHRQ quality indicators toolkit.

Results: Sample (N=16) included registered nurses (RN) and healthcare providers. Descriptive statistics were utilized for evaluation of questionnaires. Results indicate staff have sound understanding of signs and symptoms of sepsis, however application through case studies demonstrated lower performance. Overall system barriers were minimal, with greatest barriers in central line monitoring and staff shortages. High level unit teamwork exists within the ED, however collaboration is lacking between ED staff and upper management. Results demonstrate moderate disengagement between upper management and staff leading to miscommunication. Recommendations included increased, consistent sepsis education, utilization of Institution for Healthcare

Improvement (IHI) triple aim framework for evaluating systems, implementing a closed loop approach to communication, and having a staff champion for sepsis be included in meetings with upper management.

Key words: sepsis, gap analysis, emergency room, early goal directed therapy

The Reality of Sepsis

Sepsis is a potentially life-threatening condition brought about by an infection that affects millions of individuals every year with the very young and very old at greatest risk for mortality (Englert & Ross, 2015). Infections can be associated with healthcare delivery systems or community acquired, coupled with risk factors, make individuals more susceptible to infection. The annual healthcare costs in the United States (US) for those hospitalized with sepsis exceeds $24 billion, with nearly three million individuals affected. For inpatient admissions, sepsis has accounted for a mortality rate of one in every two to four individuals (Maley, Gaieski, & Mikkelsen, 2015; Sadaka, O'Brien, & Prakash, 2012) making it the leading cause of in-hospital deaths in the U.S. (Stoller, et al. 2016).

Unfortunately, identification of sepsis remains a problem for hospital staff, as it presents itself in varying ways with symptoms also being attributable to a myriad of disease states (Maley, Gaieski, & Mikkelsen, 2015). International efforts have been devised to aid in identification, management and treatment of sepsis through the Surviving Sepsis Campaign as well as other national initiatives (Vanzant & Schmelzerio, 2011). This paper will examine the problem of sepsis, discuss the rationale to prioritize this issue, as well as offer greater background and significance presented through studies and programs currently in place that attempt to address the urgency of sepsis identification and timely treatment.

Problem Statement

The Third International Consensus Definitions Task Force for Sepsis and Septic Shock defines sepsis as a “life-threatening organ dysfunction due to a dysregulated host response to infection” (Seymour et al., 2016, p. 771). Sepsis is a systemic response to infection that leads to subsequent acute organ dysfunction after documented or suspected infection, known as severe

sepsis as well as septic shock, occurring from severe sepsis combined with hypotension that is not reversed with fluid resuscitation. In severe sepsis, organ dysfunction presents itself in multiple forms, including liver and pulmonary dysfunction, hemodynamic compromise, acute kidney injury and altered mental status (Maley, Gaieski, & Mikkelsen, 2015). Severe sepsis and septic shock affect millions of individuals around the world each year. (Dellinger et al., 2012; Stoller et al., 2016).

Worldwide the number of severe sepsis cases is not well known given many areas where Intensive care unit (ICU) healthcare delivery is scarce. Utilizing data from the US, it is estimated that up to 19 million cases of sepsis occur in the world each year, killing one in every two to four individuals (Angelelli, 2016; Maley, Gaieski, & Mikkelsen, 2015). In the US, the number of cases is estimated at nearly one million to three million (Dellinger et al., 2012; Maley, Gaieski, & Mikkelsen, 2015) individuals per year, accounting for 10% of ICU admissions (Dellinger et al., 2012). It is estimated that nearly 3000 new cases of sepsis are identified and treated in hospitals in the U.S. each day (Angelelli, 2016) with an annual rate of increase of 13% (Maley, Gaieski, & Mikkelsen, 2015).

Mortality rates from septic shock, although still high at 14 %-30%, have decreased significantly over the past 30 years, when in hospital death rates were 80% (Angelelli, 2016; Maley, Gaieski, & Mikkelsen, 2015; Stoller, et al., 2016). The National Center for Health Statistics (2011) report, patients with sepsis are eight times more likely to die when compared to patients with other diagnoses (Angelelli, 2016).

Although mortality rates have dropped, the long-term effects of surviving sepsis can be debilitating. Individuals surviving sepsis are still at greater risk for death in the following months and years (Angelelli, 2016). In this longitudinal study of aging Americans, conducted by the

Health and Retirement Study, indicated an increased rate of physical and neurocognitive decline in those having survived severe sepsis. Individuals often experience mood disorders and overall decreased quality of life (Angus & Van der Poll, 2013; Maley, Gaieski, & Mikkelsen, 2015; Sadaka, O'Brien, & Prakash, 2012; Stoller, et al., 2016). Many survivors transition to a post-acute health care facility at discharge, increasing their risk of obtaining a nosocomial infection (Maley, Gaieski, & Mikkelsen, 2015; Stoller, et al., 2016). Sepsis survivors are also at greater risk for hospital readmission within 30 days with one-quarter of individuals being readmitted and half of those readmissions resulting from another life-threatening infection (Maley, Gaieski, & Mikkelsen, 2015). Other considerations for risk of readmission include the patient's need for ICU stay upon initial hospitalization, hospital length of stay, severity of illness, and patient age (Maley, Gaieski, & Mikkelsen, 2015).

The financial implications of sepsis are grave with an estimated cost, across all payers in the US, in excess of $24 billion annually, which only accounts for costs directly related to emergent and intensive hospital care necessary to treat sepsis (Angelelli, 2016; Maley, Gaieski, & Mikkelsen, 2015). Englert and Ross, (2015) report that sepsis was among the top five admitting diagnoses for older Americans. In 2011, the Agency for Healthcare Research and Quality (AHRQ) found that sepsis accounts for 5.2% of all hospitalization costs, making it the most expensive condition billed to Medicare and Medicaid. AHRQ used the Healthcare Cost and Utilization Project data to identify sepsis diagnosis costs and found that 722,000 Medicare beneficiaries were discharged from the hospital post-sepsis and accounted for 6.9% of all Medicare inpatient hospital costs. Medicaid reported 113,000 discharges accounting for 4.5% of all Medicaid costs nationally (Angelelli, 2016).

Age represents a significant risk factor for acquiring and being hospitalized for sepsis (Englert & Ross, 2015; Stoller et al., 2016). Englert and Ross, (2015) describe an unprecedented rate increase in hospitalization for sepsis among adults 45 and older, with those aged 45-64 showing 180% increase, adults 65-84 years showing 104% increase, and adults 85 years and older showing a 74% increase. Not only have hospitalization rates increased, but mortality rates have also shown an increase of 26% in those 60-64 years and 38% for those 85 years and older (Englert & Ross, 2015). Englert and Ross, (2015) found that adults 65 or older were 13 times more likely to develop sepsis with a 2-fold increased risk of death from sepsis. When considering the aging baby boomer population, estimates predict that over the next 25 years the number of Americans 65 years and older will double, by 2030 they will total 72.1 million individuals comprising 19% of the population (Englert & Ross, 2015). With an already overburdened healthcare system experiencing high costs and decreasing resources, a drastic increase in older Americans will continue to utilize precious resources, expanding the healthcare problems to even greater proportions.

Purpose and Rationale

Individuals older than 65 are at greatest risk for acquiring and dying from sepsis as well as a lower quality of life post survival (Englert & Ross, 2015; Stoller et al., 2016). With this population growing at such a rapid rate, it is likely more cases will present to hospitals and emergency departments, causing the burden of this condition to grow. Significant research has been done examining ways to identify, manage, and treat this condition, allowing any healthcare facility or hospital to pull from a vast array of information to aid in decreasing, not only the financial burden, but most importantly the burden of morbidity and mortality caused by a sepsis

diagnosis. The purpose of this work is to examine best practices, barriers and facilitators to achieving the goals of the International Surviving Sepsis Campaign.

Background/Significance

Critical to proper identification of sepsis is an understanding of risk factors that increase the likelihood of developing sepsis. Individuals with chronic organ dysfunction, pre-existing comorbid conditions, immune system dysregulation due to diseases such as cancer, Chronic Obstructive Pulmonary Disease (COPD) and Human Immunodeficiency Virus and Acquired Immune Deficiency Syndrome (HIV/AIDS) are at greater risk along with those using immunosuppressive medications (Angus & Van der Poll, 2013; Maley, Gaieski, & Mikkelsen, 2015; Stoller, et al., 2016). Advanced age, sex, race and ethnicity can also impact rates of sepsis. The very young and very old are more susceptible, males have higher rates than females and blacks have higher rates than whites for severe sepsis, with Asians showing the lowest rates overall (Angus & Van der Poll, 2013; Stoller et al., 2016). In a study conducted by Stoller et al. (2016) young and comorbidity-free patients with sepsis had a mortality rate of only 4.6%-14% compared to 35% mortality rate for those with co-existing diseases.

Risk factor stratification tools can be utilized to evaluate mortality risk, such as the use of lactic acid levels for suspected sepsis patients. Maley, Gaieski, and Mikkelsen (2015), examined the correlation between lactate levels and mortality rates; in patients with lactate levels of 3.5mmol/L or greater had an in-hospital mortality rate of 41% compared to 12 % for levels less than 3.5mmol/L (Maley, Gaieski, & Mikkelsen, 2015). Another value that is underutilized to determine risk for mortality from sepsis and septic shock is the red cell distribution width (RDW). An elevated RDW results from any disease process that causes a release of premature red cells into circulation. Sadaka, O'Brien, & Prakash, (2012) describe how elevations in RDW is

associated with elevated inflammatory markers such as those seen in sepsis and septic shock. Their study found that upon diagnosis of septic shock, having an increased RDW was strongly associated with risk of hospital and ICU mortality. If the RDW was then used in conjunction with the Acute Physiology and Chronic Health Evaluation (APACHE) II score, a severity of disease scoring system, it became a stronger predictor of mortality (Sadaka, O'Brien, & Prakash, 2012).

Recurrent hospitalizations as well as recurrent need for procedures associated with chronic conditions, increased patients' risk for sepsis (Englert & Ross, 2015). Other risk factors include the presence of invasive devices such as urinary catheters (Englert & Ross, 2015). With suspected or confirmed sepsis, source control -- finding the source of the infection and removing if possible-- is essential to the treatment of infection (Vanzant & Schmelzerio, 2011).

In 2013, the Surviving Sepsis Campaign (SSC) developed guidelines on bundled sepsis care focusing on aggressive, protocol-driven resuscitation of patients experiencing severe sepsis and septic shock. Evidence at the time showed decreased mortality through Early Goal Directed Therapy (EGDT) and bundled care (Burney, et al., 2012; Burrell, McLaws, Fullick, Sullivan, & Sindhusake, 2016; Fasut & Weingart, 2017; Mikkelsen, et al., 2010). Utilization of SCC's protocol in the ED guides staff to meet three hour and six hour requirements; with lactate level measurement, blood culture obtainment and antibiotic initiation and fluid resuscitation at three hours, and a repeat of lactate level at six hours (Fasut & Weingart, 2017). More recent declines in mortality rates have coincided with advancements and improvement in early identification, as well as treatment of sepsis (Maley, Gaieski, & Mikkelsen, 2015).

Proper identification, therefore, becomes a crucial aspect of triage as well as during the ED stay. Research identifies several tools used in assessment and diagnosis of sepsis, including

APACHE II, systemic inflammatory response syndrome (SIRS) and other sepsis algorithms. Utilization of SIRS criteria, as part of a sepsis bundle, is characteristic of sepsis identification, although it is understood that utilization of these criteria is not specific for sepsis but can accurately identify a high percentage of sepsis and severe sepsis patients. Constant evaluation of vitals is imperative and SIRS criteria is a useful established tool, as are other illness severity tools such as the shock index (heart rate/systolic blood pressure), where an index >0.7 is associated with increased severity of illness (Maley, Gaieski, & Mikkelsen, 2015). Multiple SIRS based on screening algorithms exist to facilitate recognition of sepsis in triage as well as allowing detection of high risk patients when combined with certain diagnostic tests. Shetty, et al. (2016) found the Ireland and John F Kennedy (JFK) Medical Center sepsis algorithms performed the best in a study conducted comparing multiple algorithms already in use.

Mikkelsen et al., 2010, completed a study identifying factors associated with ED staff not initiating and/or compleing EGDT. Compliance with protocol ranged from 0%-100%, with four risk factors being independently associated with lower odds of initiating EGDT: Female sex of patient ($p=0.018$), female sex of clinician ($p=0.041$), serum lactate leves not completed ($p=0.018$) and lack of consultation with Severe Sepsis Service ($p<0.001$). In a separate study Burney et al., (2012), polled physican and nursing staff and found that barriers to completion of EGDT included, for physicians, inability to perform central venous pressure monitoring, limited physical space in ED, lack of sufficient nursing staff and lack of ICU beds and nursing delays; for nurses, barriers included delays in treatment due to delay in diagnosis by physicians.

Hospital length of stay (HLOS) for sepsis patients over the past five years has decreased from nine to seven days in a study conducted by Stoller et al., (2016). Before 2000, HLOS averaged 17-20 days, and by 2007 it decreased to nine to fifteen days, showing an overall

decrease, in the past 12 years, from 17.3 to 7 days (Stoller, et al., 2016). In examining sepsis survival, Nesseler et al., (2013) found that patients surviving septic shock, 180 days post discharge, had stayed in the hospital longer (41 days), compared to only 27 days for those who were not living 180 days post discharge.

The one year mortality rate of patients surviving sepsis is not only higher than healthy individuals not having experienced a sepsis diagnosis, but it also persists at this higher rate even up to five years post discharge. The long term sequelae affects the ability to return to work, as well as overall quality of life (Nesseler et al., 2013). Nesseler et al., 2013 conducted a study on long-term health related quality of life (HRQOL) up to 180 days post discharge and found that, compared to the general population, those surviving sepsis and septic shock had a significantly decreased quality of life post discharge. Areas assessed were physical functioning, role physical, bodily pain, general health, vitality, social functioning, role emotional, and mental health (Nesseler et al., 2013).

Internal Evidence

At a local community-based hospital ED department in the Southwestern U.S., key stakeholders identified a gap in care whereby the facility SSC bundle system protocol was not being completed or documented accurately, missing critical steps. Identification of the root cause was not fully understood at this site; however, lack of adherence to EGDT in the emergency department setting is not an isolated problem for this facility. This has led to the clinically relevant PICOT question:

In patients at high risk for sepsis, how does a focused sepsis identification tool and initiation of sepsis bundles, compared to current care delivery, affect hospital length of stay, morbidity and mortality and health related quality of life?

Search Strategy

Databases used to search for the literature review included PubMed, Cumulative Index of Nursing and Allied Health Literature (CINAHL), and Web of Science. Keywords included; *length of stay, sickness impact profile, quality of life, sequelae, long term adverse effects, morbidity, hospital mortality, mortality, outcome assessment (health care), sepsis, shock, septic, sepsis ID, sepsis identification, risk factors, emergency department, emergency room.* Initially search terms were grouped and searched such as *sepsis* or *shock, sepsis* or *septic* or *sepsis ID* or *sepsis identification;* yielding 104,842 in Pub Med. The search clustered terms from the PICOT question together and in the end combined them all (Appendix A). The ending grouping was utilized for CINHAL and Web of Science with a few further refinements. The final search for pub med was *length of stay* or *sickness impact profile* or *quality of life* or *sequelae* or *long term adverse effects* or *morbidity* or *hospital mortality* or *mortality* or *outcome assessment (health care)* and *sepsis* or *shock, septic* or *sepsis ID* or *sepsis identification* and *risk factors;* yielding 278 articles, with further limits placed for English language, age of adult 19+ years.

CINAL (Appendix B) searching started with similar grouping searches as completed for PubMed and then final grouping being almost exactly as in PubMed with *length of stay* or *sickness impact profile* or *quality of life* or *sequelae* or *long term adverse effects* or *morbidity* or *hospital mortality* or *mortality* or *outcome assessment (health care)* and *sepsis* or *shock, septic* or *sepsis ID* or *sepsis identification* and *risk factors* addition of terms *emergency room* and *emergency department* were added to refine search; yielding 481 articles with further refinement added for English language, aged, 60 & over, and adult 19-44 years.

Web of science (Appendix C) started with the grouping from the previous two searches, with further refinement added given the large number of articles obtained initially. The final

large grouping was *length of stay* or *sickness impact profile* or *quality of life* or *sequelae* or *long term adverse effects* or *morbidity* or *hospital mortality* or *mortality* or *outcome assessment (health care)* and *sepsis* or *shock, septic* or *sepsis ID* or *sepsis identification* and *risk factors;* yielding 1,057,080 articles. The following limits were applied: Document type-articles, publication year-2006-2016, languages-English, Specialty- Emergency Medicine, Critical Care, Nursing, Topic-*sepsis;* yielding 504 articles. Although *sepsis* had already been added to the original search phrase, a lack of specific *sepsis* articles was noted. Upon refinement, many more articles specific to all the search terms were found.

Exclusion criteria included articles earlier than 2006, non-English studies, unpublished work, and articles involving children. Studies included involved adults in the Emergency Department (ED) or Critical Care Unit/ICU. All studies were reviewed for relevance and separated into partial-final selection of 60 articles and using critical appraisal, 10 articles were retained for further review. Articles included evaluated varying aspects of sepsis EGDT in hospital ED's, risk factors and mortality rates of sepsis, as well as tools utilized for identification of sepsis in the ED (Appendix D).

Critical Appraisal & Synthesis

In defining the level of evidence Melnyk & Fineout-Overholt (2016) guidelines were utilized. All but one of the studies were level IV evidence, with one of level III evidence (Appendix D) Most studies used quantitative designs and were well conducted case control or cohort studies that utilized chart review, prospectively or retrospectively, to assess differing criteria associated with sepsis (Appendix D). The average study ran over three years with a four month average for the lowest studies and ten years as the longest study (Appendix D). Studies found majority of sepsis patients were in mid to late 60's, with one study finding a slightly lower

age between 55 and 60 years; with majority studies also unanimously finding increased likelihood for males over females to develop sepsis (Appendix D). All but one study by Stoller et al. (2016) identify EGDT as a dependent variable with all studies addressing varying dependent variables including biomarkers, APACHE II score, SOFA score, comorbidities, etc. (Appendix D). Three studies addressed staff roles and perception to barriers to implementation of EGDT. The settings of the studies were slightly greater in the ED with the others in the ICU and one study by Stoller et al. (2016) labeled as both ICU and ED, given that it looked at any discharge diagnosis of sepsis regardless of hospital location (Appendix D). Three studies addressed tools used to identify sepsis with the study by Stoller et al. (2016) focusing soley on comparing six different tools by their sensitivity, specificity and positive predictive value.

Independent variables studied identified outcomes of initiation of EGDT, adherence to protocols and mortality in 50% of cases; while 60% of studies identified HLOS. Three studies identified barriers to EGDT as an independent variable with the study by Burney et al. (2012) addressing specific staff barriers showing differences expereinced by nurses (RN) and physicians (MD) (Appendix D). Bias across the studies was not mentioned nor was any bias observed through reading of the articles and evaluation of who conducted the studies and where they took place (Appedix D).

From the synthesis table (Appendix E), the heterogeneity of the studies is evident as many variables are not overlapping. To look at all aspects of the PICOT questions, this type of sampling was necessary. Evidence showed that biomarkers are a key aspect of identifying sepsis and EGDT is an important element in both successful identification and treatment of sepsis. Evidence also shows that although protocols exist in many instances they are not being followed and reasons for barriers to adherence to protocols are, in some cases, similar between nursing

and healthcare provider, while in others, it is evident that both disciplines rank one another's professional role as a barrier (Appendix E). The independent variables are important in showing how sepsis affects patients as well as staff. Two studies show that patients in long and short term studies show greater mortality rates after sepsis diagnosis compared to general population as well as how patient's overall HRQOL is significantly decreased in the year's post sepsis diagnosis (Appendix E). Understanding the clinical presentation of sepsis patients as well as mortality characteristics can be beneficial to ED and hospital staff that have to identify sepsis patients. This ability to idenitfy sepsis patients earlier, coupled with implementation of EGDT, shows improved adherence to sepsis bundles that have shown better outcomes for patients with sepsis.

Theoretical/Conceptual Framework

The theoretical framework chosen is the Knowledge to Action Framework (Appendix F). The WHO (2017) describes this framework as a cyclical process integrating knowledge generation and implementation of existing and new solutions to solve a particular problem. Utilizing this approach in the healthcare setting allows for barriers and complexities inherent in the implementation of evidence-based research to be overcome by tailoring the specific outcomes to local barriers. The data collected for this PICOT questions looks at various aspects of sepsis identification, treatment initiation and mortality as well as EGDT and its outcomes. When looking to disseminate these findings and utilize them in the chosen setting, a framework such as the Knowledge-to-Action framework can help guide the process of change.

Evidence-Based Practice Model

The Evidence-Based Practice (EBP) model chosen is the ACE Start Model (Appendix G). This model is composed of various forms of knowledge that allow for a systematic process of putting EBP into practice. There are five major stages of knowledge transformation: 1)

Discovery Research; 2) Evidence Summary; 3) Translation to Guidelines; 4) Practice Integration; 5) Process, Outcome Evaluation. Stage one utilized existing research and compiles relevant information about the clinical action. Stage two is for evidence synthesis and summary. It is the knowledge generating stage where relevant findings from literature are brought together to produce concise findings. Stage three is the first part of a two-stage process for transformation of evidence into actual practice. The translation is meant to package the information gathered into relevant and useful summary of evidence to present to clinicians and stakeholders, usually termed *clinical practice guidelines*. Stage four is the process of changing individual and organizational practices through formal and informal channels; addressing factors that affect individuals and organizational rate of integration and adoption of innovation. Stage five is where outcomes are evaluated, including the impact of EBP on patient health outcomes, provider and patient satisfaction, efficacy, and efficiency, etc. (UTHSCSA, 2016).

This model provides the framework necessary to assess the needs of the site utilizing information already gathered and find a way to create a practice guideline and implement it in a way that is acceptable to the organization to achieve a positive and significant outcome.

Method

The gap analysis was performed with ED staff at an urban hospital in the Southwestern United States. Concentration was placed on knowledge of sepsis presentation, perceived barriers to implementation of sepsis protocol, as well as an analysis of the management support through utilization of AHRQ gap analysis questions. Questionnaires, including a demographics data, were utilized to assess the areas of concentration. IRB approval was obtained September 6, 2017.

Sample and Participant Selection

The gap analysis was performed in the ED where questionnaires were given to participants for individual completion. Q&A sessions were held during pre-shift huddles. The analysis was performed over a 4-month time frame. Participation was limited to adults 18 years and older, English speaking and current staff in the ED. This includes nursing, practitioners (MD, DO, NP, PA), and medical residents. There is no exclusion to gender or race, so long as the participant is employed by the facility and affects or is affected by sepsis identification, treatment, and/or outcomes. Exclusion criteria were anyone that was not currently staff in the ED.

Variables

The variables examined were separated into a sepsis knowledge questionnaire, a barriers to early goal directed therapy (EGDT) questionnaire and AHRQ quality indicators toolkit (QI) questions. Both the sepsis and EGDT questionnaires were utilized, with permission from authors, in previously published studies with reliability and validity established from use in these published studies. Demographic, sepsis knowledge and barriers to EGDT questionnaires were combined into one survey. The sepsis knowledge questionnaire was authored by Robson, Beavis, and Spittle, (2007), the orginianl questionnaire was modified to contain 32-items which assessed knowledge of signs and symptoms of sepsis/severe sepsis. The barriers to EGDT questionnaire came from Carlbom, (2007), and was modified to fit this analysis. The 17-item questionnaire assessed perceived barriers to EGDT protocol initiation. Each variable utilized assessed whether staff feel a particular barrier applied to their facility or not. The AHRQ QI toolkit questions were part of a larger toolkit designed for hospital systems to evaluate various components including identifying and documenting gaps (Agency for Healthcare Research and Quality (AHRQ), 2017). Eleven questions were selected based on the focused nature of this EBP analysis,

encompassing various areas such as collaboration, teamwork, training, management processes, data systems, and results focused.

Data Analysis

Descriptive statistics were utilized to describe sample and outcome variables. The sample consisted of sixteen participants (N=16) completing questionnaires, with three Q&A sessions consisting of varying numbers of staff. The majority of participants were female, 62.5% (n=10), and nurses, 87.5%(n=14) with 6.3% (n=1) NP/PA, and 6.3% MD/DO (n=1). Participants years in current role ranged from 1 year to 27 years with an average of 11.8 (SD=8). Participant ages ranged from 26 years to 55 years with an average age of 40.7 (SD 9.3). The majority completed a bachelor's degree, 68.8% (n=11), with 18% (n=3) having associates degrees and 12.5% (n=2) having graduate degrees. Participants assigned shifts were majority days, 43.8% (n=7), with nights accounting for 25% (n=4) and the remaining working varied shifts, 31.3% (n=5).

For both the sepsis knowledge questionnaire and the barriers to EGDT questionnaire, total scores were calculated. Possible responses were *yes, no* and *don't know*. *Yes*, was the correct response for all variable but one, giving it a 1 and making the highest score a 32. *No* and *Don't Know* were both incorrect responses except for one question, therefore, scored as 0. Correct and incorrect were utilized to calculate overall score, taking into account the one question with opposite scoring. Total scores for participants were tabulated and crosstabulation analysese conducted to examine results. The barriers to EGDT questionnaire had 17 questions assessing barriers and a total score was given for each participant. When assessing barriers, possible responses were *yes, no, and I don't know*, with a the highest score being a 17. Scoring was assigned based on *No* being the desired result, equating to 1, and *Yes*, and *Don't Know* the

undersirable resulst, being 0. Therefore, the higher the result the fewer the perceived barriers. The AHRQ Q&A session was conducted in groups without measuring the number of individuals in the group but the overall response to the questions. Responses were complied as an agreement or disagreement with the question and descriptive statistics utilized to quanitfy the frequency of agreement or disagreement with the questions posed.

Results

Total scores for both the sepsis knowledge questionnaire and the barriers to EGDT questionnaire were tabulated and utilized to evaluate descriptive statistics. The Sepsis knowledge questionnaire had a mean of 26.31 (SD 3.28), with a median of 27.00, minimum of 21.00 and maximum of 32.00. The mean and median were in close proximity indiating an even distribution of values surrounding the mean. Total scores were compared to variables such as education, role, years in role utilizing the the mean to separate participant. Education compared to total score showed participants with associates degrees were 2(66%) above the mean, bachelors degrees had 6(55%) above the mean, and participants with graduate degrees were 1(100%) above the mean. Comparing roles to total scores we see that for nurses 8(57%) scored above the mean, with NP/PA's scoring 1(100%) above the mean, and MD/DO's scoring 1(100%) above the mean as well. For comparing years in role to total score a grouping of ≤ 5 years, 5-10 years, and >10 years was utilized. For participants with ≤ 5 years scores showed 3 (75%) above the mean, 6-10 years scored 3 (60%) above the mean, and those with > 10 years scoring 5 (71%) above the mean. Lastly, the shift worked was compared to the total score, for day shift participants total scores showed 5(71%) above the mean, nights scores showed 2(50%) above the mean, and those working varied shift had scores of 3(60%) above the mean.

The barriers to EGDT questionnaire was tabulated as a total score with 17 being the highest number, indicating the least number of perceived barriers. The mean for this data set was 10.9 (SD 5.25), with a minimum of 3.00, maximum of 17.00, and median of 13.5. The median value of this data set is to the right of the mean indicating the data is skewed to the left. In comparing roles to total score all roles (Nurse, NP/PA, MD/DO) data were examined together showing 9 (56%) to be above the mean. For years in role, participants with ≤ 5 years in role 3(75%) were above the mean, 6-10 years in role 5 (100%) were below the mean, and those >10 years scored 6 (86%) above the mean. Comparing shift to total score, day shift had 4(57%) above the mean, night shift had 3(75%) above the mean, and those working varied shifts showed 3 (60%) below the mean.

The AHRQ Q&A session consisted of 11 questions asked to three groups of staff members. Corresponding results were completed using descriptive statistics. Question categories included, management processes, training, accountability, data systems, results focused, collaboration between staff, management and administration and collaboration within the department. Collaboration within the department had 100% (n=3) of *Yes* responses, indicating teamwork within the department and support among immediate staff to be very high. Results focused, which looked at ways to improve the system, was 100% (n=3) *No,* indicating staff did not feel improvements were results focused. The remaining areas have *Yes* responses for 33.3% (n=1), and *No* responses *66*.7% (n=2).

Discussion

To identify initial signs of sepsis, the Surviving sepsis campaign utilizes systemic inflammatory response syndrome (SIRS) criteria. Two or more criteria being positive, which can

include altered mental status, can indicate possible sepsis and warrant further sepsis workup and protocol initiation. The SIRS criteria are as follows (Robson, Beavis, & Spittle, 2007):

• Temperature >38_C

• Temperature <36_C

• White cell count <4 _ 109/L

• White cell count >12 _ 109/L

• Respiratory rate >20 breaths per minute

• Heart rate >90 bpm

The goal of the sepsis knowledge questionnaire was to establish baseline understanding of staff regarding identification of patients presenting with the above signs and symptoms, as well as signs and symptoms for severe sepsis. Participants overall did well with identifying signs and symptoms of sepsis criteria, however were challenged with knowledge application in case studies regarding clinical presentation of sepsis. Evaluation of the case studies showed staff scored 75% or greater where signs and symptoms of sepsis were more obvious. The subtleties in presentation in two of the case study scenarios allow some staff to not classify individuals as having possible sepsis. Education geared at some of the subtler and minimally elevated SIRS results could help increase overall knowledge and increase clinical application scores.

The barriers to initiation of EGDT questionnaire showed the majority of staff perceived fewer barriers, with over 50% being greater than the mean, indicating less barriers. The most common barriers were central catheter insertion 8(50%), monitoring of central venous pressure (CVP) 11(68.8%), monitoring of central venous oxygen saturation ($ScVO_2$) 11(68.8%), access to protocol medications 9(56%), physical space in the ED 11(68.8%), and insufficient nursing staff 12(75.0%). Since an answer of *No* was the desired result responses of *Yes* and *Don't Know* were

grouped to facilitate data calculations. Therefore, some of these higher values could be skewed since some responses were *don't know* and not necessarily *yes.*

The AHRQ QI toolkit questions helped to understand staff's perceptions of support from management and administration, as well as assessment of staff understanding regarding hospitals quality initiatives, who ran those initiatives and how it related to their role, job performance, and system quality metrics. Understanding the larger picture can be valuable insight into staff realizing why they have to do certain things and what sepsis monitoring numbers really indicate, as well as why they are important. The results of the questions indicate that there is a hierarchical leadership style between upper management, department of quality and ED staff. This leadership style results in a lack of strong, meaningful connections within the system, as well as reduced relationships within the organization due to communication barriers. The prior solutions to the problem at hand were prescribed through a linear thinking model that led to system inefficiencies.

The sepsis quality measures showed difficulty in system aims above 50% consistently. Analysis of the gap for sepsis identification and protocol initiation allow for identification of areas where interventions could be created that might help staff improve on their identification of sepsis as well as initiation of protocol measures already in place. Although there were not areas requiring major improvements, the data showed areas where education and changes in staff and upper management involvement could be useful, with the goal of increasing sepsis quality measures overall.

Recommendations

Moving forward recommendations for the facility focus on the system and efforts are made to close communication loops among staff and upper management in addition to increased

education and practical application. Utilizing the Institute for Healthcare Improvement (IHI) Triple Aim guide to create a systematic approach at all levels of the system will be of benefit. Integration of all departments, by sharing key indicators will allow for planning, strategizing, innovation and performance measures to be understood by all staff. Additionally, creation of an environment where mistakes are discussed openly, and pitfalls learned from to help foster innovation and solutions instead of creating an environment that inhibits change and stifles innovation will foster transparency and performance improvement. Supporting staff through continuous learning, by sending staff to conferences, workshops, and presentations regularly will promote enhanced skill in sepsis identification. And lastly, capitalizing on the staff inherent value of teams, utilize the strong teamwork and trust within the department to create a sepsis superuser/point person, that can act, not only as a resource for the staff, but also as a means of closing the information loop between staff, management, QI director and executives by attending meetings and reporting back to the department.

Limitations

There were a few limitations to the project, principally small sample size. Although initial recruitment was 20 participants, due to missing data, four participants were removed from final data analysis. Variability of participants was also an area for improvement given that then majority, 14 of 16 participants were nurses, having more NP/PA and physicians would allow for a broader perspective, especially when addressing barriers to EGDT protocol initiation. At the time of the project, new electronic medical records (EHR) system had been implemented leading to a decrease in number of participants filling out questionnaires for the timeframe initially after EHR implementation. Therefore, any future projects of this nature could find it beneficial to

forecast large, stressful events are not being implemented soon to ensure greater participation among staff members.

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Appendix A

Search Strategy 1

Pubmed

Search	Add to builder	Query	Items found	Time
#10	Add	Search **((((((((Length of Stay[MeSH Terms]) OR Sickness Impact Profile[MeSH Terms]) OR Quality of Life[MeSH Terms]) OR sequelae[Title/Abstract]) OR Long Term Adverse Effects[MeSH Terms]) OR (((Morbidity[MeSH Terms]) OR Hospital Mortality[MeSH Terms]) OR Mortality[MeSH Terms])) OR Outcome Assessment (Health Care))) AND ((((((Sepsis[MeSH Terms]) OR Shock, Septic[MeSH Terms]) OR "Sepsis ID"[Title/Abstract]) OR "sepsis identification"[Title/Abstract])) AND Risk Factors[MeSH Terms])** Filters: **English; Adult: 19+ years**	278	14:05:38
#9	Add	Search **((((((((Length of Stay[MeSH Terms]) OR Sickness Impact Profile[MeSH Terms]) OR Quality of Life[MeSH Terms]) OR sequelae[Title/Abstract]) OR Long Term Adverse Effects[MeSH Terms]) OR (((Morbidity[MeSH Terms]) OR Hospital Mortality[MeSH Terms]) OR Mortality[MeSH Terms])) OR Outcome Assessment (Health Care))) AND ((((((Sepsis[MeSH Terms]) OR Shock, Septic[MeSH Terms]) OR "Sepsis ID"[Title/Abstract]) OR "sepsis identification"[Title/Abstract])) AND Risk Factors[MeSH Terms])** Filters: **Adult: 19+ years**	293	14:02:39
#8	Add	Search **((((((((Length of Stay[MeSH Terms]) OR Sickness Impact Profile[MeSH Terms]) OR Quality of Life[MeSH Terms]) OR sequelae[Title/Abstract]) OR Long Term Adverse Effects[MeSH Terms]) OR (((Morbidity[MeSH Terms]) OR Hospital Mortality[MeSH Terms])) OR Outcome Assessment (Health Care))) AND ((((((Sepsis[MeSH Terms]) OR Shock, Septic[MeSH Terms]) OR "Sepsis ID"[Title/Abstract]) OR "sepsis identification"[Title/Abstract])) AND Risk Factors[MeSH Terms])**	473	14:02:05
#7	Add	Search **((((((Length of Stay[MeSH Terms]) OR Sickness Impact Profile[MeSH Terms]) OR Quality of Life[MeSH Terms]) OR sequelae[Title/Abstract]) OR Long Term Adverse Effects[MeSH Terms]) OR (((Morbidity[MeSH Terms]) OR Hospital Mortality[MeSH Terms]) OR Mortality[MeSH Terms])) OR Outcome Assessment (Health Care)**	299274	14:01:50
#6	Add	Search **"sepsis bundle"[Title/Abstract]**	53	13:54:38
#5	Add	Search **((((Morbidity[MeSH Terms]) OR Hospital Mortality[MeSH Terms]) OR Mortality[MeSH Terms])) AND ((((((Sepsis[MeSH Terms]) OR Shock, Septic[MeSH Terms]) OR "Sepsis ID"[Title/Abstract]) OR "sepsis identification"[Title/Abstract])) AND Risk Factors[MeSH Terms])**	2231	13:53:13
#4	Add	Search **((Morbidity[MeSH Terms]) OR Hospital Mortality[MeSH Terms]) OR Mortality[MeSH Terms]**	732616	13:52:37
#3	Add	Search **(((((Sepsis[MeSH Terms]) OR Shock, Septic[MeSH Terms]) OR "Sepsis ID"[Title/Abstract]) OR "sepsis identification"[Title/Abstract])) AND Risk Factors[MeSH Terms]**	6714	13:45:18
#2	Add	Search **Risk Factors[MeSH Terms]**	660987	13:44:49
#1	Add	Search **(((Sepsis[MeSH Terms]) OR Shock, Septic[MeSH Terms]) OR "Sepsis ID"[Title/Abstract]) OR "sepsis identification"[Title/Abstract]**	104842	13:43:15
#0	Add	**pubmed** clipboard	278	14:12:11

Appendix B

Search Strategy 2

CINHAL

Search History/Alerts

Print Search History | Retrieve Searches | Retrieve Alerts | Save Searches / Alerts

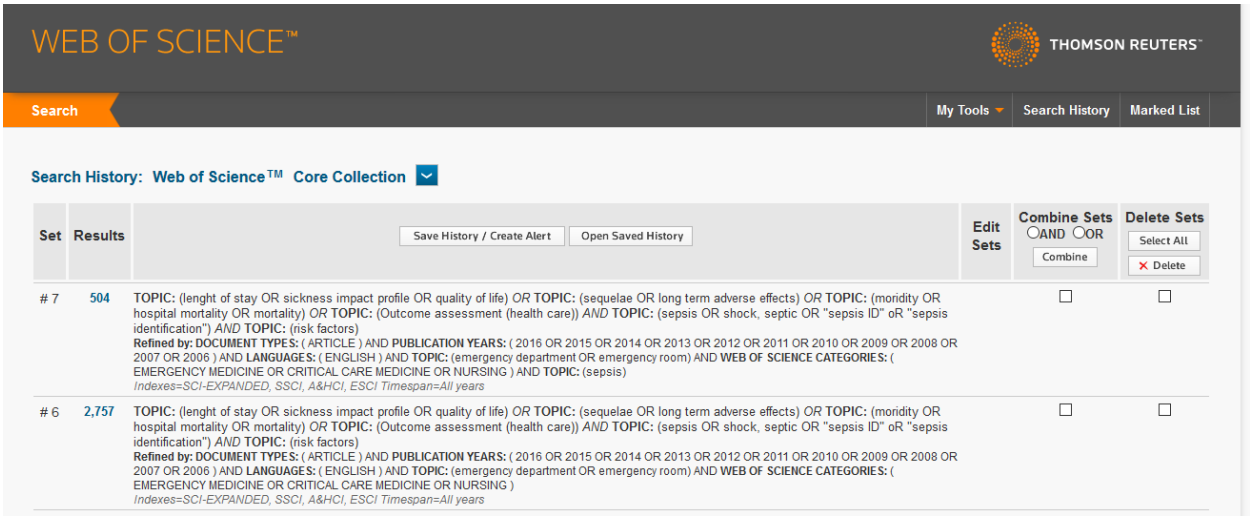
Select / deselect all | Search with AND | Search with OR | Delete Searches | Refresh Search Results

	Search ID#	Search Terms	Search Options	Actions
☐	S19	S14 AND S15	**Narrow by SubjectAge:** - adult: 19-44 years **Narrow by SubjectAge:** - aged, 80 & over **Narrow by Language:** - english **Search modes** - Boolean/Phrase	View Results (481) | View Details | Edit
☐	S18	S14 AND S15	**Narrow by SubjectAge:** - aged, 80 & over **Narrow by Language:** - english **Search modes** - Boolean/Phrase	View Results (933) | View Details | Edit
☐	S17	S14 AND S15	**Narrow by Language:** - english **Search modes** - Boolean/Phrase	View Results (2,990) | View Details | Edit
☐	S16	S14 AND S15	**Search modes** - Boolean/Phrase	View Results (2,990) | View Details | Edit
☐	S15	emergency department OR emergency Room	**Search modes** - Boolean/Phrase	View Results (35,694) | View Details | Edit
☐	S14	Length of stay OR sickness impact profile OR quality of life OR sequelae OR long term adverse effects OR (morbidity OR hospital Mortality OR Mortality) OR Outcome assessment AND (Sepsis OR Shock, septic OR "sepsis ID"	**Narrow by Language:** - english **Narrow by SubjectAge:** - all adult	View Results (154,697) | View Details | Edit
☐	S13	Length of stay OR sickness impact profile OR quality of life OR sequelae OR long term adverse effects OR (morbidity OR hospital Mortality OR Mortality) OR Outcome assessment AND (Sepsis OR Shock, septic OR "sepsis ID" OR "sepsis identification") AND risk factors	**Narrow by SubjectAge:** - all adult **Search modes** - Boolean/Phrase	View Results (157,521) | View Details | Edit
☐	S12	Length of stay OR sickness impact profile OR quality of life OR sequelae OR long term adverse effects OR (morbidity OR hospital Mortality OR Mortality) OR Outcome assessment AND (Sepsis OR Shock, septic OR "sepsis ID" OR "sepsis identification") AND risk factors	**Search modes** - Boolean/Phrase	View Results (341,733) | View Details | Edit
☐	S11	S1 OR S2 OR S5 OR S7 OR S9	**Narrow by SubjectAge:** - all adult **Search modes** - Boolean/Phrase	View Results (236,256) | View Details | Edit
☐	S10	S1 OR S2 OR S5 OR S7 OR S9	**Search modes** - Boolean/Phrase	View Results (531,511) | View Details | Edit
☐	S9	Length of stay OR sickness impact profile AND quality of life AND sequelae	**Search modes** - Boolean/Phrase	View Results (36,484) | View Details | Edit
☐	S8	S5 OR S7	**Search modes** - Boolean/Phrase	View Results (264,288) | View Details | Edit
☐	S7	length of stay OR Long Term Adverse Effects OR outcome assessment	**Search modes** - Boolean/Phrase	View Results (70,984) | View Details | Edit
☐	S6	sepsis bundle	**Search modes** - Boolean/Phrase	View Results (131) | View Details | Edit
☐	S5	morbidity OR hospital mortality OR mortality	**Search modes** - Boolean/Phrase	View Results (207,496) | View Details | Edit
☐	S4	(TI sepsis identification AND risk factors) AND (S1)	**Search modes** - Boolean/Phrase	View Results (4) | View Details | Edit
☐	S3	S1	**Search modes** - Boolean/Phrase	View Results (20,679) | View Details | Edit
☐	S2	risk factors	**Search modes** - Boolean/Phrase	View Results (302,729) | View Details | Edit
☐	S1	sepsis OR shock, septic OR sepsis ID OR sepsis identification	**Search modes** - Boolean/Phrase	View Results (20,679) | View Details | Edit

Appendix C

Search Strategy 3

Web of Science



WEB OF SCIENCE™ THOMSON REUTERS

Search | My Tools | Search History | Marked List

Search History: Web of Science™ Core Collection

Set	Results	Save History / Create Alert / Open Saved History	Edit Sets	Combine Sets (AND OR) Combine	Delete Sets Select All / Delete
# 7	504	**TOPIC:** (lenght of stay OR sickness impact profile OR quality of life) *OR* **TOPIC:** (sequelae OR long term adverse effects) *OR* **TOPIC:** (moridity OR hospital mortality OR mortality) *OR* **TOPIC:** (Outcome assessment (health care)) *AND* **TOPIC:** (sepsis OR shock, septic OR "sepsis ID" oR "sepsis identification") *AND* **TOPIC:** (risk factors) **Refined by: DOCUMENT TYPES:** (ARTICLE) AND **PUBLICATION YEARS:** (2016 OR 2015 OR 2014 OR 2013 OR 2012 OR 2011 OR 2010 OR 2009 OR 2008 OR 2007 OR 2006) AND **LANGUAGES:** (ENGLISH) AND **TOPIC:** (emergency department OR emergency room) AND **WEB OF SCIENCE CATEGORIES:** (EMERGENCY MEDICINE OR CRITICAL CARE MEDICINE OR NURSING) AND **TOPIC:** (sepsis) *Indexes=SCI-EXPANDED, SSCI, A&HCI, ESCI Timespan=All years*		☐	☐
# 6	2,757	**TOPIC:** (lenght of stay OR sickness impact profile OR quality of life) *OR* **TOPIC:** (sequelae OR long term adverse effects) *OR* **TOPIC:** (moridity OR hospital mortality OR mortality) *OR* **TOPIC:** (Outcome assessment (health care)) *AND* **TOPIC:** (sepsis OR shock, septic OR "sepsis ID" oR "sepsis identification") *AND* **TOPIC:** (risk factors) **Refined by: DOCUMENT TYPES:** (ARTICLE) AND **PUBLICATION YEARS:** (2016 OR 2015 OR 2014 OR 2013 OR 2012 OR 2011 OR 2010 OR 2009 OR 2008 OR 2007 OR 2006) AND **LANGUAGES:** (ENGLISH) AND **TOPIC:** (emergency department OR emergency room) AND **WEB OF SCIENCE CATEGORIES:** (EMERGENCY MEDICINE OR CRITICAL CARE MEDICINE OR NURSING) *Indexes=SCI-EXPANDED, SSCI, A&HCI, ESCI Timespan=All years*		☐	☐
# 5	8,853	**TOPIC:** (lenght of stay OR sickness impact profile OR quality of life) *OR* **TOPIC:** (sequelae OR long term adverse effects) *OR* **TOPIC:** (moridity OR hospital mortality OR mortality) *OR* **TOPIC:** (Outcome assessment (health care)) *AND* **TOPIC:** (sepsis OR shock, septic OR "sepsis ID" oR "sepsis identification") *AND* **TOPIC:** (risk factors) **Refined by: DOCUMENT TYPES:** (ARTICLE) AND **PUBLICATION YEARS:** (2016 OR 2015 OR 2014 OR 2013 OR 2012 OR 2011 OR 2010 OR 2009 OR 2008 OR 2007 OR 2006) AND **LANGUAGES:** (ENGLISH) AND **TOPIC:** (emergency department OR emergency room) *Indexes=SCI-EXPANDED, SSCI, A&HCI, ESCI Timespan=All years*		☐	☐
# 4	533,908	**TOPIC:** (lenght of stay OR sickness impact profile OR quality of life) *OR* **TOPIC:** (sequelae OR long term adverse effects) *OR* **TOPIC:** (moridity OR hospital mortality OR mortality) *OR* **TOPIC:** (Outcome assessment (health care)) *AND* **TOPIC:** (sepsis OR shock, septic OR "sepsis ID" oR "sepsis identification") *AND* **TOPIC:** (risk factors) **Refined by: DOCUMENT TYPES:** (ARTICLE) AND **PUBLICATION YEARS:** (2016 OR 2015 OR 2014 OR 2013 OR 2012 OR 2011 OR 2010 OR 2009 OR 2008 OR 2007 OR 2006) AND **LANGUAGES:** (ENGLISH) *Indexes=SCI-EXPANDED, SSCI, A&HCI, ESCI Timespan=All years*		☐	☐
# 3	561,046	**TOPIC:** (lenght of stay OR sickness impact profile OR quality of life) *OR* **TOPIC:** (sequelae OR long term adverse effects) *OR* **TOPIC:** (moridity OR hospital mortality OR mortality) *OR* **TOPIC:** (Outcome assessment (health care)) *AND* **TOPIC:** (sepsis OR shock, septic OR "sepsis ID" oR "sepsis identification") *AND* **TOPIC:** (risk factors) **Refined by: DOCUMENT TYPES:** (ARTICLE) AND **PUBLICATION YEARS:** (2016 OR 2015 OR 2014 OR 2013 OR 2012 OR 2011 OR 2010 OR 2009 OR 2008 OR 2007 OR 2006) *Indexes=SCI-EXPANDED, SSCI, A&HCI, ESCI Timespan=All years*		☐	☐
# 2	843,591	**TOPIC:** (lenght of stay OR sickness impact profile OR quality of life) *OR* **TOPIC:** (sequelae OR long term adverse effects) *OR* **TOPIC:** (moridity OR hospital mortality OR mortality) *OR* **TOPIC:** (Outcome assessment (health care)) *AND* **TOPIC:** (sepsis OR shock, septic OR "sepsis ID" oR "sepsis identification") *AND* **TOPIC:** (risk factors) **Refined by: DOCUMENT TYPES:** (ARTICLE) *Indexes=SCI-EXPANDED, SSCI, A&HCI, ESCI Timespan=All years*		☐	☐
# 1	1,057,080	**TOPIC:** (lenght of stay OR sickness impact profile OR quality of life) *OR* **TOPIC:** (sequelae OR long term adverse effects) *OR* **TOPIC:** (moridity OR hospital mortality OR mortality) *OR* **TOPIC:** (Outcome assessment (health care)) *AND* **TOPIC:** (sepsis OR shock, septic OR "sepsis ID" oR "sepsis identification") *AND* **TOPIC:** (risk factors) *Indexes=SCI-EXPANDED, SSCI, A&HCI, ESCI Timespan=All years*	Edit	☐	☐

Appendix D Sample Quantitative/Qualitative Studies

Table 1

Evaluation Table

Citation/ Country/ Funding/ Bias	Theory/ Conceptual Framework	Design/ Method	Sample/ Setting (describe) Demo, setting, exclusion, attrition	Major Variables studied & their Definitions	Measurement/ Instrumentation (focus group, 1:1, researcher(s)	Data Analysis (stats used)	Findings/ Results/ Themes	Level/Quality of Evidence; Decision for practice/ application to practice/Generalization (Melnyk & Fineout-Overholt, 2016)
Artero et al., (2010) Prognostic factors of mortality in patients with community-acquired bloodstream infection with severe sepsis and septic shock Country: Spain Bias: None noted Funding: None	Comparative Quantification of Health Risks	Design/Method: Quantitative, Single-site prosp cohort study Purpose: Determine indp risk factors on mort in pts w/ com-acq severe sepsis & septic shock	N= 112 Sample/Setting: Pts with com-acq severe sepsis and septic shock in med-surg ICU Demo: Mean age 63.5, 60%male, 40%female Exclusion: None Attrition: 0	DV1: Pts w/ severe sepsis & septic shock-Hosp survivor DV2: Pts w/ severe sepsis & septic shock-Hosp death IV1: APACHE II IV2: Albumin IV3: ≥3 Organ Disf IV4: Mean Age Yrs.	Not stated. Inferred to be through EMR data collection/chart review.	Univariate analysis: Independent risk factors for mortality. Chi-squared test or Fisher exact test: Comparing categorical variables. Mean ±SD and Student *t* test: Comparing means Multivariate analysis, nonconditional: Variables with P≤0.05 &	Mean Apache II Score (SD): Total- 22.0 (8.0), Hosp surv- 18.7 (7.1), Hosp nsurv- 26.5(7.0); OR(95%CI): 1.16 (1.08-1.23); P= <0.001 Albumin <g/L: Total-27 (31.3%), Hosp surv- 10(21.2%), Hosp nsurv-17(43.5%); OR (95%CI)-2.85 (1.11-7.33); P= 0.026. ≥3 Organ dysfunctions: Total- 56(50%),	Level of Evidence: IV Strengths: Although the population was defined as Community acquired sepsis patients they were otherwise a random selection of individuals within the population. The study also looked at all variables independently to see independent significance. The total number of 112 is a large cohort. Weaknesses: Study was completed at a single site. Study did not account for health care-associated blood stream infections

1º-prmary; **2º**-secondary; **3º**-tertiary; **Abs**-Absence, **Add**-addition; **AMC**-academic medical center; **Antbs**- antibiotics; **Antimi**-antimicrobial; **APACHEII**- acute physiologic and chronic health evaluation II; **App**-appropriate; **ASS**-Associated, **BC**-British Columbia sepsis guidelines algorithm; **BP**-blood pressure; **CEC**-clinical excellence commission; **CI**- Confidence Intervals, **Com-acq**-community-acquired; **Comor**-comorbidities; **CVC**-central venous catheter; **CVP**-Central venous pressure; **D**-days; **Demo**-demographics; **Dev**-development; **Diff**-differing; **Dis**-disease; **Disf**-disfunction; **Dx**-diagnosis; **DV**-dependent variable; **ED**-Emergency department; **EGDT**-early goal directed therapy; **Eval**-evaluate; **Fb**-feedback; **Fld**- fluid; **GCS**-Glascow coma scale; **GP**-General population; **Hemo**-hematological; **Hosp**-hospial; **HRQOL**-health related quality of life; **HTN**-Hypertension; **ICU**-intensive care unit; **ID**-identification; **Immsup**-immunosuppressive; **Impl**-implementation; **Inad**-inadequate; **Indp**-independent; **ING**-Ireland international guideline; **Intv**-intervention; **Intrav**-intravenous; **IV**- independent variable; **JFK**-JFK medical center; **LO-Reg**-Logistical regression, **LI-Reg**-Linear regression, **LOS**-length of stay; **Malig**-malignancy; **MAP**-mean arterial pressure; **Med-Surg**-medical-surgical; **Micro**-microbiological; **Min**-minimum; **Mins**-minutes; **mmHg**-millimeters of mercury; **Mo**-months; **Mort**-mortality; **N**-number of studies; **n**- number of participants; **NNM**-Number needed to misdiagnose; **N/A**-not applicable**; Nsurv**-Nonsurvivors, **NUH**-Nottingham university hospitals; **NSW**- New South Wales; **OR**-Odds ratio; **Osf**- Organ system failures; **Perf**-performance; **PH**-public hospitals; **Pred**-prediction; **Pres**-Presence, **Presp**-presentation; **Prog**-program; **Prosp**-prospective; **PS**-Post sepsis; **Pts**-patients; **RBC**-red blood cell; **RDW**-red cell distribution width; **RE-AIM**-reach, effectiveness, adoption, implementation, and maintenance; **Req**-requiring; **Res**-resuscitation; **RN**-nurse; **SF**-Short form, **SH**-specialty hospital; **Sig**-Significance; **SIRS**-systemic inflammatory response system; **SOFA**-sequential organ failure assessment; **Stats**-statistics; **Surv**- Survivors, **Susp**-suspected; **ScvO2**-Central venous oxygen saturation; **Transf**-transfusion; **UKST**-UK sepsis trust; **UP**-university of Pennsylvania; **USA**-United States of America; Comparative Quantification of Health Risks **VP**-vasopressor; **W/**-with; **Wk**-weak; **Yrs**-years

						plausible biological relationship to dependent outcome variable to determine indp factors as w/pres or abs of hosp mort	Hosp surv-19(29.2%), Hosp nsurv-37(78.7%); OR(95%CI)-3.70 (2.04-6.68) Mean Age yrs (SD): Total-63.5 (15.8), Hops surv- 61.0 (16.6), Hosp nsurv- 67.1 (14.0); OR(95%CI)-1.02 (1.00-1.05); P= 0.047	Conclusions: APACHEII and serum Albumin are independently associated with mortality. Feasibility: Measuring both APACHE II and Serum albumin are very easy and feasible and can lead to better prediction of mortality among sepsis and septic shock patients.
Citation/ Country/ Funding/ Bias	Theory/ Conceptual Framework	Design/ Method	Sample/ Setting (describe) Demo, setting, exclusion, attrition	Major Variables studied & their Definitions	Measurement/ Instrumentation (focus group, 1:1, researcher(s)	Data Analysis (stats used)	Findings/ Results/Themes	Level/Quality of Evidence; Decision for practice/ application to practice/Generalization

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Burney et al., (2012) Early detection and treatment of severe sepsis in the emergency department: Identifying barriers to implementation of a protocol-based approach Country: USA Bias: Selection bias Funding: None discussed	The Knowledge to Action Framework	Design/method: Quantitative, Cross-sectional design with self-completed surveys Purpose: Identify and address barriers to implementation of planned sepsis treatment initiatives.	N=101 n= 57 (43%) all ED staff nurses n= 28 (57%) all ED staff physicians n=16 (38%) all ED residents Sample/Setting: Staff nurses and physicians of a major urban academic medical center ED Exclusions: None Attrition: 0	DV: RN, MD IV: Questionnaire items	Online survey completed anonymously and independently	Descriptive stats for baseline knowledge, attitudes, and behaviors of each group. Pearson's Chi-squared for differences between groups,	Identified barriers: Lack of available nursing staff- RN 45.6%, MD 75.1% Access to CVP/ScvO2 monitoring- RN 40.4%, MD 79.5% Central catheter insertion- RN33.3%, MD 52.3% Handoff between ED and ICU- RN 24.6%, MD 15.9% Access to protocol medications- RN 10.6, MD 4.5% Other- RN 5.3%, MD 9.1% Lack of agreement with protocol- RN 0, MD 27.3%	Level of Evidence: VI Strengths: Demonstrated barriers to implementation of EGDT experienced by ED staff. Weaknesses: Limited to one site. Selection bias due to voluntary nature of participation for practitioners. Survey developed only for this study and not a validated case study Conclusions: Revelation of knowledge deficits and other barriers to clinical pathway implementation that need to be addressed through education and increased interdisciplinary and interprofessional collaboration. Feasibility: This information, although limited to a specific site, could be a guiding factor to understanding barriers at the local ED where my project will be conducted.

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Citation/ Country/ Funding/ Bias	Theory/ Conceptual Framework	Design/ Method	Sample/ Setting (describe) Demo, setting, exclusion, attrition	Major Variables studied & their Definitions	Measurement/ Instrumentation (focus group, 1:1, researcher(s)	Data Analysis (stats used)	Findings/ Results/Themes	Level/Quality of Evidence; Decision for practice/ application to practice/Generalization
Burrell et al., (2016) Sepsis kills: early intervention saves lives. Country: Australia Bias: None noted Funding: None	The Knowledge to Action Framework	Design/Method: Quantitative, Prospective and retrospective study Purpose: Qualitative improvement program promoting early intv. measuring time to antbs, fld res, mort rates, LOS	N= 13,567 Sample/Setting: 97 ED's in NSW hospitals Demo: Adult and pediatric pts (only adult stats completed) Exclusion: None noted Attrition: 0	DV: Patients with sepsis or severe sepsis IV1: Intrav fld res w/in 60 mins IV2: Fld res IV3:Triage ID IV4: Mort IV5: Time to antbs	Chart review Data reviewed and taken from SEPSIS KILLS database as well as the Admitted patient, Emergency Department attendance and Deaths Register. Data entered prospectively, by ED staff, to the online sepsis database.	Descriptive and inferential analyses: Odds ratios and 95% CI, and Chi-squared tests for trends. Regression models for trends over time and process and outcome measures. LO-Reg for in-hosp deaths. LI-Reg for time in ICU and LOS Statistical Sig P=<0.05	Implementation of a quality improvement program resulted in increased compliance with EGDT initiation. Reduced mortality over time, improved ID of sepsis pts in triage increase in IV antibiotics and fluid res within 60 mins, and decrease in LOS.	Level of Evidence: III Strengths: Completed over 3 years utilizing 97 ED's Patients chosen based on sepsis suspected or confirmed dx but otherwise a randomized selection. Weaknesses: Not all 97 sites submitted data consistently. Patient data might have included individuals lacking final dx of sepsis. Lack of a standardized risk stratification tool for sepsis patients in ED Conclusions: Implementation of a quality improvement process across multiple ED's improved care for patients.

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								Feasibility: Implementation of a EGDT program similar to the study is a large undertaking but feasible with proper intervention and staff education.
Citation/ Country/ Funding/ Bias	Theory/ Conceptual Framework	Design/ Method	Sample/ Setting (describe) Demo, setting, exclusion, attrition	Major Variables studied & their Definitions	Measurement/ Instrumentation (focus group, 1:1, researcher(s)	Data Analysis (stats used)	Findings/ Results/Themes	Level/Quality of Evidence; Decision for practice/ application to practice/Generalization
Castegren et al., (2015) Initial levels of organ failure, microbial findings, and mortality in intensive-care treated primary, secondary and tertiary sepsis Country: Sweden Bias: None noted	Comparative Quantification of Health Risks	Design/Method: Retrospective, observational study Purpose: Analyze if pts w primary, secondary & tertiary dis, show diff clinical prest, micro test, treat received & outcome	N= 213 n(1º)=121 n(2º)=65 n(3º)=27 Sample/Setting: Patients with varying sepsis designations in hospital ICU from 1/1/2006-12/31/2011 Demo: ≥18yrs Exclusion: Pts w/hemo malig or immsup dis, or being treat	DV: Patients with severe sepsis and septic shock IV1: SOFA IV2: ≥3 SIRS criteria IV3: APACHE II score IV4: Mortality rate at day 28 IV5: Hospital LOS	Chart review	Kruskall-Wallis, Chi-squared or Fisher exact tests used to analyze differences between groups. Survival analysis and log-rank tests for survival differences. Significance P<0.05	IV1: D1 SOFA score: Total-7 (4-9) 1°- 7 (4-10) 2°- 6 (4-9) 3°- 5 (3-8) P=0.04 IV2: ≥3 SIRS criteria- 1°- 73 (60%) 2°- 28 (43%) 3°- 14 (52%) P=0.08 IV3: APACHE II score (median)- Total- 18 (14-23) 1°- 18 (14-24) 2°- 16 (14-21)	Level of Evidence: IV Strengths: Evaluation of multiple independent parameters in sepsis patients Weaknesses: Single-center study with limited number of patients. First type of study evaluating inflammatory response, no other studies available for comparison. Conclusions: Inflammatory insults before the onset of

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Funding: None			w/immsup drugs (n=60) Attrition: 0				3°- 17 (12-24) P=0.24 IV4: Mortality rate at day 28 Total- 62(29%) 1°- 33 (28%) 2°- 21 (32%) 3°- 8 (30%) P=0.77 IV5: Hospital LOS Total- 17 (6-24) 1°- 13 (4-34) 2°- 17 (8-42) 3°- 51 (19-89) P<0.001	sepsis affect the clinical picture, blood microbial findings, and in non-survivors, the time of death. The results of this study could form the basis for a new strategy stratifying patients in clinical studies for immunomodulation therapies in sepsis. Feasibility: This study may be more difficult to implement given the nature of how it separates out the groups of sepsis patients. However, it is a retrospective study and could be duplicated.
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Mikkelsen et al., (2010) Factors associated with nonadherence to early goal-directed therapy in the ED. Country: USA Bias: None noted Funding: None discussed	The Knowledge to Action Framework	Design/Method: Retrospective cohort study; collection of Empirical Data Purpose: Identify why EGDT was not initiated by physicians in the ED where formalized protocols exist.	N=340 Demo: Sepsis positive patients Sample/Setting: ED physicians at UP Hospital ED Exclusion: Criteria for severe sepsis not met (lactate not measured, CVC placement refused). Attrition: n=15	DV: EGDT protocol implementation DV2: EGDT protocol non-implementation IV: EGDT protocol	Review of EMR by 3 trained investigators using a pre-drafted case report form.	Comparison of EGDT initiation vs. non- initiation used Student *t* test or Wilcoxon rank-sum test for continuous variables and chi squared for categorical variables. Mantel-Haenszel stats for stratified analyses, Non-parametric for trends across groups. P=≤0.05	EGDT not initiated in 142 pts (42%). EGDT pts received more IV fld (P<0.001), vasoactive active agents (P<0.001), Central venous catheterizations (P<0.001). EGDT not completed in 86 of 198 (43%) patients in whom EGDT was initiated. EGDT less likely in pts w/ lower lactate levels (P<0.014), lower APACHEII score (<0.001).	Level of Evidence: IV Strengths: Demonstration of challenges and barriers that exist for EGDT Weaknesses: Completed at single location. Other factors affecting mortality outcomes, such as antibiotics use, not included in study. Conclusions: Study revealed underutilization of EGDT with identification to potential barriers for effective implementation. Feasibility: Implementation of a study like this one is feasible at any institution noting this study reviewed a 2 year period.
Citation/ Country/ Funding/ Bias	Theory/ Conceptual Framework	Design/ Method	Sample/ Setting (describe) Demo, setting,	Major Variables studied & their Definitions	Measurement/ Instrumentation (focus group, 1:1, researcher(s)	Data Analysis (stats used)	Findings/ Results/Themes	Level/Quality of Evidence; Decision for practice/ application to

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			exclusion, attrition					practice/Generalization
Nesseler, (2013) Long-term mortality and quality of life after septic shock: A follow-up observational study Country: France Bias: None noted Funding: None	Health-related quality of life conceptual framework Comparative Risk Assessment Framework	Design/Method: Prospective observational study; Mixed method with questionnaires completed by patient or proxy Purpose: Evaluation of mortality and HRQOL at 6 months' post sepsis dx	N= 96 Exclusion: Patients experiencing mixed or uncertain shock Attrition: 3 (3.1%) Demo: Male and female adult patients experiencing sepsis. Sample/setting: Hospital ICU patients experiencing their first episode of sepsis	DV1: Mortality 6 months' post sepsis dx DV2: HRQOL 6 mo post sepsis dx (10 components) compared to general population	SF-36 questionnaire-filled out by patient or family (if patient incapacitated) within 48 hours after diagnosis as well as 6 months post discharge by patient.	Univariate analysis using Wilcoxon Rank Sum test for quantitative variables Chi-square or Fisher's exact test for categorical variables Odds ratio and 95% CI for variables independently ass w/mort at 180 days. Paired sample *t*-test (2 tailed), P<0.05 for changes in baseline mort to 180 d mort	DV1: Mortality 6 mo post sepsis dx: 42(45%) DV2: HRQOL 6 mo post sepsis dx versus Gp: Physical functioning: GP-84±21; PS-58±29; P<0.001 Role physical: GP-81±32; PS-37±42; P<0.001 Bodily pain: GP-73±24; PS-55±29; P<0.001 General health: GP-69±19; PS-56±10; P<0.001 Vitality: GP-60±18; PS-43±21; P<0.001 Social functioning: GP-82±21; PS-62±32; P<0.001 Role emotional: GP-82±32; PS-47±42; P<0.001 Mental health: GP-69±18; PS-59±21, P<0.01	Level of Evidence: IV Strengths: Unique study assessing long term consequences of sepsis. Assesses multiple dimensions of health quality. Weaknesses: Small number studied. Focus on surgical ICU patients. Conclusions: Despite advances in care, 6 mo mort remains high and HRQOL remained lower than GP at 6 months. Feasibility: Implementation of a study like this is outside of the scope of my project however, understanding the long-term health effects is an important aspect of understanding sepsis and its effects on our patient population.

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Citation/ Country/ Funding/ Bias	Theory/ Conceptual Framework	Design/ Method	Sample/ Setting (describe) Demo, setting, exclusion, attrition	Major Variables studied & their Definitions	Measurement/ Instrumentation (focus group, 1:1, researcher(s)	Data Analysis (stats used)	Findings/ Results/Themes	Level/Quality of Evidence; Decision for practice/ application to practice/Generalization
Sadaka, (2012) Red cell distribution width and outcome in patients with septic shock Country: USA Bias: None noted Funding: Funds from Critical Care Medicine Department	Comparative Quantification of Health Risks	Design/Method: Quantitative analysis of a retrospective cohort study Purpose: Determining relationship between RDW & hospital mortality; eval. if APACHE II outcome pred. is increased with add. of RDW	N= 482 Exclusion: Pts. req. RBC transf. 1 wk prior or 7d after sepsis dx. Attrition: 203 (42%) Demo: Pts. ≥ 18 yrs., male and female Sample/Setting: Pts. w/ principle dx of sepsis, admission to ICU, dev. of BP < 90mmHg, no response to fluid res., vp use to maintain MAP≥ 65mmHg	DV1: Patient w/ principal dx of sepsis DV2: RDW & hospital mortality IV1: APACHE II score IV2: APACHE II+ RDW score IV3: SOFA	Review of data from Project Impact Dataset; a critical care patient dataset. APACHE II-first 24 hours of ICU admission, SOFA-day of development of septic shock. Complete blood count for RDW value.	Logistical regression, Likelihood ratio and Wald chi-squared, *F* ratios, multiple R-square, student *t* tests, Receiver operating curves (ROC).	DV2: OR (95%CI)-1.27(1.11-1.46) P<0.0005 IV1: RDW<13.5-1(reference) RDW13.5-15.5-4.6(1.0-23.4) P<0.6 RDW15.6-17.5-8.0(1.5-41.6) P<0.01 RDW17.6-19.4-25.3(4.3-149.2) P<0.001 RDW>19.4-12.3(2.1-73.3) P<0.006 IV2: 1.09(1.02-1.15) P<0.006 IV3: 1.16(1.01-1.33) P<0.04	Level of Evidence: IV Strengths: Weaknesses: Data from one site with limited number of pts. Morality rate only accounted for in hospital and ICU not any shortly after discharge. Conclusions: RDW is a better predictor of mortality than APACHE II and SOFA but mortality rate prediction was better when adding RDW to either measurement tool. Feasibility: RDW is taken from the CBC, an inexpensive, readily utilized test. The APACHE II and SOFA scores are also easily completed, therefore,

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								all aspects are easy to implement for use in a study.
Citation/ Country/ Funding/ Bias	Theory/ Conceptual Framework	Design/ Method	Sample/ Setting (describe) Demo, setting, exclusion, attrition	Major Variables studied & their Definitions	Measurement/ Instrumentation (focus group, 1:1, researcher(s)	Data Analysis (stats used)	Findings/ Results/Themes	Level/Quality of Evidence; Decision for practice/ application to practice/Generalization
Shetty et al., (2016). Systemic inflammatory response syndrome-based severe sepsis screening algorithms in emergency department patient with suspected sepsis. Country: Australia Funding: None noted Bias: None	RE-AIM framework	Design/Method: Quantitative, retrospective analysis	N= 747 Sample/Setting: Chart review performed 3 mo. after Patients presented to ED with suspected sepsis or SIRS positive sepsis. Data taken from Sydney multicenter ED sepsis archive from 1/1/2013 to 5/1/2014 Demo: N/A Exclusion: None Attrition: 0	DV: Patients w/ sepsis or suspected sepsis presenting to ED IV1: Screening algorithms-CEC IV2: Screening algorithms-ING IV3: Screening algorithms-NUH IV4: Screening algorithms-UKST	Medical record review.	Fisher's exact test for significance for dichotomous outcomes. Mann-Whitney U tests check for significance in median differences of numerical predictors. Performance of each algorithm on the cohort: Sensitivity, specificity, positive and negative predictive values and their 95% CI, NNM.	IV1 CEC: TP 181, TN 273, FN 220, FP 73, Sen% 45.1(40.2-50.2), Spef%78.9(74.2-83.1), PPV 71.3(65.3-76.7), NPV 55.4(50.9-59.8), ACC 0.61, NNM 2.55 IV2-ING: TP 290, TN 316, FN 111, FP 30, Sen% 72(67.7-76.6), Spef% 91.3(87.9-94.1), PPV 90.6(86.9-93.4), NPV 74(69.6-78.1), ACC 0.81, NNM 5.3 IV3 NUH:	Level of Evidence: IV Strengths: Detailed review of performance of multiple sepsis screening algorithms using a large population of patients. Weaknesses: SIRS characterization results from study may not be sufficiently powered even when statistically significant. Not all sepsis patients were captured over the studied timeframe. Conclusions: SIRS-based severe sepsis screening algorithms that utilize lactate levels of 2mmol/L or more

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				IV5: Screening algorithms- JFK IV6: Screening algorithms- BC			TP 287, TN 284, FN 114, FP 62, Sen% 71.5(66.9-75.9), Spef% 82.1(77.6-86), PPV 82.2(77.8-86.1), NPV 71.4(66.6-75.8), ACC 0.76, NNM 4.24 IV4-UKST: TP 312, TN 200, FN 89, FP 146, Sen% 77.8(73.4-81.8), Spef% 57.8(52.4-63.1), PPV 68.1(63.6-72.4), NPV 69.2(63.5-74.5), ACC 0.69, NNM 3.23 IV5 JFK: TP 330, TN 281, FN 71, FP 65, Sen% 82.3(78.2-85.9), Spef% 81.2(76.7-85.2), PPV 83.5(79.5-87.1), NPV 79.8(75.3-83.9), ACC 0.82, NNM 5.49 IV6 BC: TP 81, TN 328, FN 320, FP 18,	performed better than those that did not. Feasibility: Utilizing a screening algorithm in the ED would be very easy and feasible to implement as a screening tool.

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							Sen% 20.2(16.4-24.5), Spef% 94.8(91.9-96.9), PPV 81.8(72.8-88.9), NPV 50.6(46.7-54.5), ACC 0.55, NNM 2.21	
Citation/ Country/ Funding/ Bias	Theory/ Conceptual Framework	Design/ Method	Sample/ Setting (describe) Demo, setting, exclusion, attrition	Major Variables studied & their Definitions	Measurement/ Instrumentation (focus group, 1:1, researcher(s)	Data Analysis (stats used)	Findings/ Results/Themes	Level/Quality of Evidence; Decision for practice/ application to practice/Generalization
Stoller et al., (2016) Epidemiology of severe sepsis: 2008-2012 Country: USA Bias: None noted Funding: None	RE-AIM framework	Design/Method: Quantitative, retrospective database analysis. Purpose: Evaluation of epidemiologic sepsis trends from 2008-2012 in order to devise app. resource allocation decisions in new treatment paradigms'.	N= 6,067,789 Demo: Male and female patients, ≥ 18 yrs. Sample/Setting: Patients discharged for severe sepsis from SH, PH, AMC's. Exclusion: None Attrition: 0	DV1: Incidence and demographics DV2: Comorbidities DV3: Organ system failure DV4: Mortality DV5: Hospital course and charge	Review of national database health records	Nonparametric testing, Chi squared or Fisher exact test, multivariate analysis.	Incidence (Per 100,000)- 2008-346, 2012-436 Age:2008-69, 2012-68 Sex: Male 2008-50.3%, 2012-51.1% Comorbidities: Fluid and electrolyte disorder: 2008-52.3%, 2012-62.4% HTN: 2008-42.4%, 2012-57.4%	Level of Evidence: IV Strengths: Very large N, multiple variables were assessed for their significance. Weaknesses: Assessing only to discharge may not be long enough to identify long term consequences of sepsis, including readmission rates, quality of life and mortality. Conclusions: Severe sepsis continues to be a significant disease. Patients afflicted are usually in seventh decade of life, have

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							Renal Failure: 2008-23.9%, 2012-29.3% Organ Failure % w/ ≥3 Osf: 2008-31.6%, 2012-35.5% Mortality: Overall: 2008-22.2%, 2012-17.3% ≥3 Osf: 2008-32.9%-63.0%, 2012-24%-59.1% % total deaths w/ ≥3 Osf : 2008-57.2%, 2012-66.7% LOS(D), median: 2008-9, 2012-7 Charge (US dollars), median: 2008-55,544, 2012-55,749	multiple comorbidities and with 3 or more organ failures account for 2/3 total mortality. LOS continues to decrease. Feasibility: This data can be used by hospitals to ascertain who is at greatest risk for sepsis and severe sepsis so that staff is more aware of those that are most susceptible.
Citation/ Country/ Funding/ Bias	Theory/ Conceptual Framework	Design/ Method	Sample/ Setting (describe) Demo, setting, exclusion, attrition	Major Variables studied & their Definitions	Measurement/ Instrumentation (focus group, 1:1, researcher(s)	Data Analysis (stats used)	Findings/ Results/Themes	Level/Quality of Evidence; Decision for practice/ application to practice/Generalization

1°-prmary; **2°**-secondary; **3°**-tertiary; **Abs**-Absence, **Add**-addition; **AMC**-academic medical center; **Antbs**- antibiotics; **Antimi**-antimicrobial; **APACHEII**- acute physiologic and chronic health evaluation II; **App**-appropriate; **ASS**-Associated, **BC**-British Columbia sepsis guidelines algorithm; **BP**-blood pressure; **CEC**-clinical excellence commission; **CI**- Confidence Intervals, **Com-acq**-community-acquired; **Comor**-comorbidities; **CVC**-central venous catheter; **CVP**-Central venous pressure; **D**-days; **Demo**-demographics; **Dev**-development; **Diff**-differing; **Dis**-disease; **Disf**-disfunction; **Dx**-diagnosis; **DV**-dependent variable; **ED**-Emergency department; **EGDT**-early goal directed therapy; **Eval**-evaluate; **Fb**-feedback; **Fld**- fluid; **GCS**-Glascow coma scale; **GP**-General population; **Hemo**-hematological; **Hosp**-hospial; **HRQOL**-health related quality of life; **HTN**-Hypertension; **ICU**-intensive care unit; **ID**-identification; **Immsup**-immunosuppressive; **Impl**-implementation; **Inad**-inadequate; **Indp**-independent; **ING**-Ireland international guideline; **Intv**-intervention; **Intrav**-intravenous; **IV**- independent variable; **JFK**-JFK medical center; **LO-Reg**-Logistical regression, **LI-Reg**-Linear regression, **LOS**-length of stay; **Malig**-malignancy; **MAP**-mean arterial pressure; **Med-Surg**-medical-surgical; **Micro**-microbiological; **Min**-minimum; **Mins**-minutes; **mmHg**-millimeters of mercury; **Mo**-months; **Mort**-mortality; **N**-number of studies; **n**- number of participants; **NNM**-Number needed to misdiagnose; **N/A**-not applicable**; Nsurv**-Nonsurvivors, **NUH**-Nottingham university hospitals; **NSW**- New South Wales; **OR**-Odds ratio; **Osf**- Organ system failures; **Perf**-performance; **PH**-public hospitals; **Pred**-prediction; **Pres**-Presence, **Presp**-presentation; **Prog**-program; **Prosp**-prospective; **PS**-Post sepsis; **Pts**-patients; **RBC**-red blood cell; **RDW**-red cell distribution width; **RE-AIM**-reach, effectiveness, adoption, implementation, and maintenance; **Req**-requiring; **Res**-resuscitation; **RN**-nurse; **SF**-Short form, **SH**-specialty hospital; **Sig**-Significance; **SIRS**-systemic inflammatory response system; **SOFA**-sequential organ failure assessment; **Stats**-statistics; **Surv**- Survivors, **Susp**-suspected; **ScvO2**-Central venous oxygen saturation; **Transf**-transfusion; **UKST**-UK sepsis trust; **UP**-university of Pennsylvania; **USA**-United States of America; Comparative Quantification of Health Risks **VP**-vasopressor; **W/**-with; **Wk**-weak; **Yrs**-years

Tromp et al., (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 Country: Netherlands Bias: None noted Funding: None	The Knowledge to Action Framework	Design/Method: Prospective, mixed methods; before-and-after intervention study with two interventions Purpose: Determining the effects of multifaceted impl. prog. of nurses use of protocols for identifying sepsis.	N= 825 Sample/Setting: The ED of a 953-bed university hospital in the Netherlands Demo: Adults (≥16 yrs.) with known or susp. Infection w/ min. of 2 specific dx criteria Exclusion: None Attrition: 0	DV: Patients with infection of suspected infection IV1: RN completion of sepsis bundle prior to impl. of sepsis bundle protocol IV2: RN completion of sepsis bundle post impl. of sepsis bundle protocol but before training and perf. fb. IV3: RN implementation of sepsis bundle post training and perf. fb	Evaluation of nursing staff in 3 different phases of process improvement. Evaluation of EHR completed to assess compliance.	Descriptive statistics, Generalized linear model with logarithmic link and Bernoulli distribution function, analysis of variance.	IV1: 3.5% IV2: 10.8% IV3: 12.4% Relative incidence (95% CI) of period 2 versus period 1-3.1(1.2-7.6). Relative incidence (95%CI) of period 3 versus period 1-3.6(1.4-9.0).	Level of Evidence: IV Strengths: Step wise approach to evaluation of RN use of sepsis bundle without and with a focused educational session. Weaknesses: Completed at a single facility. Tailor made program for the specific site. Sepsis screening tool is sensitive but not specific, which may have led to over diagnosis and treatment. Conclusions: Predominantly nurse-driven, care bundle based, sepsis protocol combined with training and performance feedback can significantly improve recognition of patients with sepsis in the ED. Feasibility: This study helps understand the importance of having formalized training along with bundle protocols to increase identification of sepsis. Implementation of a

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								nurse driven identification along with a teamwork approach with physicians for dx is very feasible.

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Appendix E

Synthesis Table

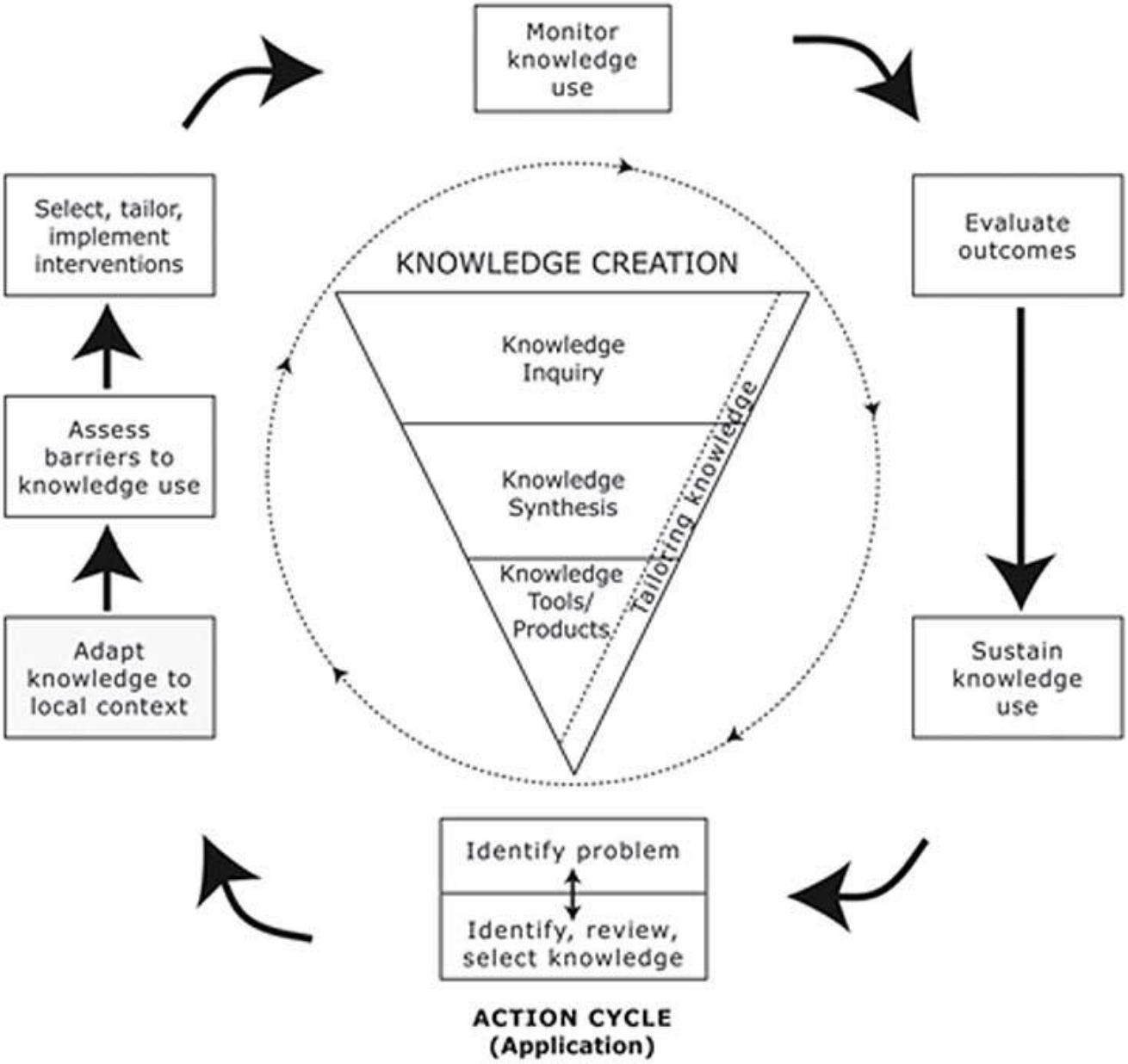
Studies		Artero	Burney	Burrell	Castegren	Mikkelsen	Nesseler	Sadaka	Shetty	Stoller	Tromp
	Year	2010	2012	2016	2015	2010	2013	2012	2016	2016	2010
Basics	LOE	IV	VI	III	IV	IV	IV	IV	IV	IV	IV
	Design	QTPCS	QTXSURV	QTPRS	ROBSS	RCS/ED	POBSS	QTRCS	QTRS	QTRS	PMMS
	Length	10 yrs	2 mo	3 yrs	5 yrs	2 yrs	6 mo	4.5 yrs	1.5 yrs	4 yrs	1.5 yrs
Demo	Age (yrs)	63.5		66	69		69	67	68	68.5	55-60
	Sex	M > F			M > F	M > F	M > F	M > F		M > F	
	Prevalence/Incidence	X	X	X			X	X		X	X
EGDT		X	X	X	X	X	X	X	X		X
	Biomarkers	X	X	X	X	X	X	X	X	X	X
	APACHE II Score	X			X	X		X			
	SOFA Score				X		X	X			
	Staff Role/Setting/Preception of barriers		X			X					X
	Time to Antibiotics/Fld		↓	↓		X					X
	Comorbidities	X			X	X	X	X		X	X
	SIRS								X		
	OSF	X						X		X	
	ICU vs. ED Setting	ICU	ED	ED	ICU	ED	ICU	ICU	ED	BOTH	ED
	Time to ID in Triage			↓							X
	Infection Source	X		X	X		X	X			X
	Identification Tools			X					X		X
Initiation EGDT			X	X		X	X				X
	Adherence to protocol		X	X		X	X				X
	HLOS			↓	X		X	X		X	X
	Staff Satisfaction		X								X
	Mortality			↓	X		X	X		X	
	Barriers to EGDT		X			X					X
	Lack of recog in triage		RN 15.8% MD 18.2%								X
	Delay in dx of sepsis by MD		RN 28.1% MD 6.8%								
	Lack of RN staff		RN 45.6% MD 75.1%								
	RN delays		RN 7.0% MD 20.5%								
	Access to CVP/ScvO2 montitoring		RN 40.4% MD 79.5%								
	CVC insertion		RN 33.3% MD 52.3%								
	Delay in aval of icu beds		RN 19.3% MD 20.5%								
	ED to ICU handoff		RN 24.6% MD 15.9%								
	Knowledge deficit		RN 14.0% MD 2.3%			X					X
	Access to protocol medication		RN 10.6% MD 4.5%								
	Lack of agreement with protocol		RN 0 MD 27.3%								
	HRQOL						X	X			

KEY	
CVC	Central Venous Catheterization
CVP	Central Venous Pressure
ED	Emergency Department
EGDT	Early Goal Directed Therapy
F	Female
Fld	Fluid
HLOS	Hospital Length of Stay
HRQOL	Health Related Quality of Life
ICU	Intensive Care Unit
M	Male
Osf	Organ system failure
PMMS	Prospective Mixed Methods Study
POBsS	Prospective Observational Study
QTPCS	Quantitative Prospective Cohort Study
QTPR	Quantitative Prospective and Retrospective Study
QTRCS	Quantitative Retrospective Cohort Study
QTRS	Quantitative Retrospective Study
QTXSurv	Quantitative Cross-sectional design w/surveys
RCS/Ed	Retrospective Cohort Study/Empirical Data
Recog	Recognition
ROBsS	Retrospective Observational Study
SIRS	Systemic inflammatory response system
SOFA	Sequential organ failure assessment
↓	Decreased

Appendix F

Theoretical/ Conceptual Framework

Knowledge to Action Framework



Appendix G

Evidence Base Practice Model

ACE Star Model