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School of Nursing

DOCTOR OF NURSING PRACTICE (DNP) PROGRAM

A DNP PROJECT

TITLE: EVALUATING THE IMPACT OF END-TIDAL CARBON DIOXIDE MONITORING IN EMERGENCY DEPARTMENT SEPSIS PATIENTS

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Abstract

Severe sepsis and septic shock remain significant international health burdens with high mortalities and financial implications. Rapid identification of the septic patient is imperative as compliance with guideline-recommended, time-specific bundles has been shown to decrease sepsis-related mortality. Despite this, compliance with the bundles remains low. Evidence has suggested that end-tidal carbon dioxide ($EtCO_2$) monitoring may be a viable intervention to aid in overcoming some barriers to sepsis identification and initiation of treatment.

The purpose of this project was to evaluate whether the use of end-tidal carbon dioxide ($EtCO_2$) monitoring in patients being evaluated for sepsis in the adult emergency department will result in decreased time to recognition and time to antibiotics, and increased bundle compliance, including overall, antibiotic, and intravenous fluid compliance, as compared to those who do not receive $EtCO_2$ monitoring.

Using the Ottawa Model of Research Use as a conceptual model, this project consisted of a pilot evaluation of $EtCO_2$ monitoring as part of an existing Code Sepsis response, followed by aggregate data review. Time to antibiotics and recognition, percent of patients receiving antibiotics in three hours, and total bundle compliance increased, while the percent of patients receiving appropriate intravenous fluids decreased. None of these results showed statistical significance. The results of the pilot evaluation do not support the addition or removal of $EtCO_2$ monitoring. There are several indications for future research, including a longer evaluation time and evaluating potential confounders.

End-Tidal Carbon Dioxide Monitoring in Emergency Department Sepsis Patients

Background and Significance

Severe sepsis and septic shock remain significant international health burdens with high mortalities and financial implications (Hall, Williams, DeFrances, & Golosinskinskiy, 2011; Rhodes et al., 2015). In 2002, the Surviving Sepsis Campaign was founded with the goals, amongst others, of generating a guideline for the identification and treatment of severe sepsis and septic shock and reducing overall mortality from these conditions (Surviving Sepsis Campaign [SSC], 2016). Since inception, the Surviving Sepsis Campaign has released multiple guidelines for the identification and treatment of severe sepsis and septic shock (Dellinger et al., 2013; Rhodes et al., 2017). Rapid identification of the septic patient is imperative as compliance with the guideline recommended, time-specific bundles has been shown to decrease sepsis-related mortality, particularly the rapid administration of appropriate antimicrobial therapy in septic shock patients (Kumar et al., 2006; Rhodes et al., 2015; Thompson et al., 2016; Tromp et al., 2010; Wang, Xiong, Schorr, & Dellinger, 2013).

Despite strong evidence that following bundle recommendations improves patient outcomes, compliance percentages for the initial resuscitation remain at only approximately 20% of cases (Levy et al., 2012; Rhodes et al., 2015; Wang et al., 2013). Failure to recognize, lack of knowledge, and resource barriers, such as laboratory testing, are cited as major reasons for poor bundle compliance (Carlbom & Rubenfeld, 2007; Daniels, 2011; Kissoon, 2014; Siontis et al., 2015). Evidence has suggested that end-tidal carbon dioxide ($EtCO_2$) monitoring may be a viable intervention to aid in the identification of sepsis and the acuity of septic patients by providing an indication of mortality risk and initial lactate level (Hunter, Silvestri, Dean, Falk, & Papa, 2013).

Problem Statement

Following the Surviving Sepsis Campaign's guideline-recommended bundles improves patient outcomes. However, timely identification and resource barriers, such as waiting for labs to result, can be barriers to compliance with the time-specific bundle metrics in the emergency department. As regulatory bodies look to make sepsis care a quality core measure, organizations can expect financial implications for poor sepsis care. Therefore, the purpose of this project was to evaluate whether the use of end-tidal carbon dioxide ($EtCO_2$) monitoring in adult emergency department sepsis patients would result in decreased documented time to recognition and time to antibiotics as well as increased compliance with applicable treatment bundles, intravenous fluid administration, and antibiotic administration as compared to those who didn't receive $EtCO_2$ monitoring.

Needs Assessment

Despite the establishment of the Surviving Sepsis Campaign (SSC) over a decade ago, sepsis remains a significant national and international health burden. Evidence suggests that septic shock is associated with an overall mortality rate of approximately 28%, with some regions of the world reporting rates as high as 59% (Rhodes et al., 2015). In the United States, sepsis alone serves as significant burden to the healthcare system, generating length of stays approximately 75% longer than all other diagnoses. Patients admitted to the hospital with a diagnosis of sepsis only represent 2% of hospitalizations but are associated with a 17% in-hospital mortality making patients admitted with sepsis approximately eight times more likely to die than any other diagnosis (Hall, Williams, DeFrances, & Golosinskiy, 2011). Financially, septicemia is the biggest financial burden to the healthcare system, representing approximately 6.2% of national hospital costs at a value of almost $23.7 billion (Torio & Moore, 2016).

Given this significant impact, it is unsurprising that the SSC, the Centers for Medicare and Medicaid Services (CMS), the New Jersey Department of Health, and the Joint Commission, among others, have worked to reduce the impact and consequences of the disease. Starting over a decade ago, the SSC has released guidelines for the care of the septic patient and has developed time-specific bundles of care to guide the treatment of the septic patient. After significant discussion, CMS and the Joint Commission has utilized these bundles to develop their first quality core measure. In response, hospitals nationwide are now required to evaluate the quality of care they give to sepsis patients (Centers for Medicare and Medicaid Services [CMS], 2015; The Joint Commission, 2016). The New Jersey Department of Health followed quickly, proposing and implementing a new rule that requires hospitals to "establish, implement, and periodically update, evidence-based protocols (sepsis protocols) for the early identification and treatment of patients in various levels of sepsis…" (New Jersey Office of Certificate of Need and Healthcare Facility Licensure, 2017; New Jersey Office of Certificate of Need and Healthcare Facility Licensure, 2018).

The proposed site has recognized an opportunity to improve in their sepsis care as the observed versus expected (O/E) mortality ratio for sepsis was 1.76 and 1.90 for 2013 and 2014, respectively (E. Howarth, personal communication, January 26, 2017). In early 2015, the organization undertook a significant campaign to improve sepsis care. Understanding that improving mortality has been linked to recognizing and treating sepsis early, the organization looked at how well patients were being recognized and treated. In the adult emergency department specifically, treatment bundle compliance averaged approximately 50% at the initiation of the campaign. Multidisciplinary hospital-wide and emergency department specific sepsis committees were formed and tasked with the evaluation of sepsis identification and

treatment in the hospital. Extensive educational campaigns were instituted, and screening tools were developed to aid in the identification of the septic patient. Case reviews were implemented for all bundle failures, with real time feedback in the form of coaching, performance improvement letters, and report cards were provided to nursing and provider staff by their respective leadership.

Stop gaps in patient flow, antibiotic availability, intravenous access, a knowledge deficit related to sepsis definitions and treatment, and a sense of urgency in treating the septic patient were barriers to the identification and treatment of sepsis that were identified in the site's adult emergency department, specifically. Among the interventions utilized to address these barriers was the implementation of a treatment pathway initiated by a positive electronic sepsis screen in triage and the collaboration with the pharmacy department to make commonly utilized antibiotics readily available in the emergency department.

Initially, these interventions appeared to be successful, with the O/E mortality ratio for sepsis decreasing in 2015 to 1.68. However, it increased again in 2016 to 1.77 and bundle compliance remains less than 90% for both the emergency department and the hospital as a whole, indicating there is additional work to be done (E. Howarth, personal communication, January 26, 2017).

Although not formally evaluated, both nursing and medical providers in the emergency department have anecdotally indicated that identification of the septic patient remains the biggest barrier to meeting bundle requirements, especially in patients with potential contraindications to some treatment recommendations. The most frequently cited example of this is the recommended fluid resuscitation in patients with risk factors for fluid overload. As the fluid resuscitation component of the bundle is guided by blood pressure and lactate parameters, the

need to wait for a lactate level to result in patients who present normotensive has been particularly concerning. Another example occurs when providers delay treatment in afebrile patients and opt instead to wait for the results of the complete blood count to initiate treatment.

Rapidly available, cost-effective intervention to aid providers in identifying septic patients would potentially be beneficial. One such intervention- $EtCO_2$ monitoring- has shown potential to predict mortality and the presence of hyperlactatemia but has not been evaluated in its ability to improve sepsis care in the form of improving time to recognition and completion of treatment metrics. Therefore, the purpose of this project is to evaluate whether the use of end-tidal carbon dioxide ($EtCO_2$) monitoring in patients with suspected sepsis in the adult emergency department will result in improvement in identification and treatment metrics as compared to patients with suspected sepsis who do not receive $EtCO_2$ monitoring.

Objectives and Aims

AIM: Evaluate the effectiveness of $EtCO_2$ monitoring as an adjunct therapeutic intervention in the identification of patients with suspected sepsis in the adult emergency department.

Objective 1: Evaluate whether there is a significant difference in documented time to recognition between those that receive $EtCO_2$ monitoring and those that don't.

AIM: Evaluate the effectiveness of $EtCO_2$ monitoring as an adjunct therapeutic intervention on treatment of sepsis.

Objective 1: Evaluate whether there is a significant difference in overall applicable bundle compliance in patients being evaluated for sepsis between those that receive $EtCO_2$ monitoring and those that don't.

Objective 2: Evaluate whether there is a significant difference in time to antibiotics in patients being evaluated for sepsis between those that receive $EtCO_2$ monitoring and those that don't.

Objective 3: Evaluate whether there is a significant difference in percent of patients who receive antibiotics within three hours in patients being evaluated for sepsis between those that receive $EtCO_2$ monitoring and those that don't.

Objective 4: Evaluate whether there is a significant difference in appropriate intravenous fluid administration in patients being evaluated for sepsis between those that receive $EtCO_2$ monitoring and those that don't.

Review of Literature

Search Strategy

The search strategy for the review of literature included combinations of keywords end-tidal carbon dioxide, end-tidal carbon dioxide monitoring, end-tidal CO2, end-tidal CO2 monitoring, sepsis, lactate, bundle compliance, mortality, and financial impact. Databases searched were Ovid, CINAHL, and MEDLINE as well as using the search engine Google Scholar.

Sepsis Definition

The term sepsis is a generalized term for a continuum of illnesses which starts as a systemic inflammatory response and extends to a shock state that includes sepsis-associated organ dysfunction (Levy et al., 2003). In 1992, the American College of Chest Physicians (ACCP) and the Society of Critical Care Medicine (SCCM) released several key definitions needed to define the varying states within the sepsis illness continuum. The Systemic Inflammatory Response Syndrome (SIRS) was defined as the systemic immune response to a

variety of injurious agents (i.e. trauma, infection, etc.) and clinically was defined by having two or more of the following findings: a body temperature of > 38ºC or < 36ºC, a heart rate of > 90 beats per minute, a respiratory rate of > 20 breaths per minute, a $Paco_2$ < 32, and a white blood cell count of > 12,000 cells μL or < 4,000 cells μL. Sepsis was defined as SIRS in the presence of a suspected or known infection. Severe sepsis was defined as sepsis with the presence of organ dysfunction, hypoperfusion, or hypotension. Septic shock was defined as sepsis with evidence of shock, namely arterial hypotension refractory to adequate fluid resuscitation (Levy et al., 2003).

From January 2014 to January 2015, the European Society of Intensive Care Medicine and the Society of Critical Care Medicine formed a task force to review sepsis definitions. In February 2016, this task force released new recommended definitions of sepsis and septic shock, removed severe sepsis from the sepsis spectrum, and recommended new screening tools to identify the level of critical illness present in the septic patient. The task force now recommends that sepsis be defined as "life-threatening organ dysfunction caused by a dysregulated host response to infection" (Singer et al., 2016, p. 804). Septic shock has been redefined as "a subset of sepsis in which underlying circulatory and cellular metabolism abnormalities are profound enough to substantially increase mortality" (Singer et al., 2016, p. 806). However, these definitions do not come without controversy and have not been endorsed by a variety of medical societies, including the American College of Emergency Physicians and the American College of Chest Physicians (Slesinger & Dubensky, n.d.). As such, their applicability in practice remains questionable.

The Burden of Sepsis

Hospital burden and mortality. Overall mortality sepsis mortality rates vary depending on the source of the data (Epstein, Dantes, Magill, & Fiore, 2016). In the time period since the inception of the Surviving Sepsis Campaign, hospitalizations in the United States have decreased by 11% and inpatient mortality has decreased by 8% (Hall, Levant, & DeFrances, 2013; Krumholz, Nuti, Downing, Wang, & Normand, 2015). Despite these decreases, the impact of sepsis on United States healthcare has surged. In 1999, septicemia did not rank within the top ten most common discharge diagnoses for Medicare patients in the country. By 2013, septicemia had become the second most common discharge diagnosis among the same population (Krumholz et al., 2015). An analysis of the eight most frequent causes of inpatient mortality between 2000 and 2010 showed that mortality from septicemia was the only diagnosis to increase in frequency (Hall, Levant, & DeFrances, 2013). Furthermore, between 2000 and 2010, septicemia tied with stroke for the fourth most common cause of hospitalization for patients aged 85 years old and older, representing an increase of 84.8% (Kochanek, Murphy, Xu, & Arias, 2014). However, no definitive mortality rate consensus has been reached, with estimates varying from 25% to as high as 50% of cases (Liu et al., 2014; Rhodes et al., 2017).

Furthermore, sepsis has shown high rates of recidivism and morbidity. Persistent organ dysfunction has been seen in as high as 27% of surviving sepsis patients and nearly a third of patients in one retrospective analysis were readmitted to the hospital between 28 to 90 days after the initial septic episode, half of which were readmitted for a second septic event (Guirgis et al., 2016). Mayr et al. (2017) found that among unplanned 30-day readmissions, sepsis was the leading diagnosis (12.2%) over acute myocardial infarction (1.3%), heart failure (6.7%), chronic obstructive pulmonary disease (4.6%), and pneumonia (5.0%) and had the longest estimated mean length of stay.

Financial Impact. Septicemia was the most expensive diagnosis treated in United States hospitals as of 2013, the last year for which data is available.

Total hospital costs. Aggregate hospital costs for septicemia in 2013 was $23.7 billion, which represented 6.2% of all hospital costs for all payers for 2013 and an over $3 billion increase from 2011 (Torio & Andrews, 2013; Torio & Moore, 2016). Furthermore, in 2011 septicemia represented 13.4% of all hospitalized Medicare nursing home residents, resulting in a total Medicare bill of almost $3 billion. This price tag represented nearly 21% of all Medicare hospital reimbursements associated with nursing home resident hospitalization and was approximately 3.5 times more expensive than then next nearest diagnosis (pneumonia; 5.9%) (Office of the Inspector General, 2013).

Length of stay and readmissions. The long length of stays and readmissions for sepsis make it one of the more expensive diagnoses in the country. Mayr et al. (2017) found that sepsis had the highest estimated mean cost per readmission ($10,070) as compared to acute myocardial infarction ($9,424), heart failure ($9,051), chronic obstructive pulmonary disease ($8,417), and pneumonia ($9,533).

Reimbursement and CMS Core Measure. The high readmission rate for sepsis has led some to suggest the diagnosis be added to the Centers for Medicare and Medicaid Service's Readmissions Reduction Program (HRRP) (Mayr et al., 2017). Enacted in 2012, the HRRP serve to reduce Medicare payments to participating hospitals with excess readmissions (Centers for Medicare and Medicaid Services [CMS], 2016b). Given the high cost per readmission, it would not be unreasonable for CMS to look to add sepsis to the diagnoses included in the HRRP, which would result in a significant financial impact to hospital organizations nationwide.

Additionally, CMS (2015) released its first version of the sepsis core measure to begin its data collection phase. CMS has partnered with non-governmental resources through the Core Quality Measures Collaborative and other organizations to identify and develop core sets of quality measures for certain disease processes. Called core measures, their aim is to aid in consumer decision making, value-based payment and purchasing, and decreased provider collection burden and cost, among other objectives (Centers for Medicare and Medicaid Services [CMS], 2016a). Incorporated into Medicare's Hospital Value-Based Purchasing (VBP) Program, core measures compliance can influence how much reimbursement an organization receives from Medicare. Additionally, once adopted, the information is made available to the consumer, which may influence their choice of organizations to go to (Hospital Compare, n.d.).

Guideline and Treatment History

In 2004, the Surviving Sepsis Campaign released their first set of guidelines for the identification and treatment of severe sepsis and septic shock. The guidelines have since undergone two revisions, with the last revision being released in early 2013. The Campaign and guideline authors further developed time-specific bundles to guide compliance with treatment recommendations. Initially, the bundles focused on a 6-hour resuscitation and a 24-hour management grouping. With the 2012 Guideline release, these bundles separate resuscitation measures into a 3-hour and 6-hour grouping and drop the management bundle altogether. Metrics to be achieved in the 3-hour bundle include measuring an initial lactate level, obtaining blood cultures prior to antibiotic administration, administration of broad spectrum antibiotics, and administration of 30 mL/kg of crystalloid intravenous fluid when hypotension or hyperlactatemia (lactate $\geq$ 4 mmol) are present. Metrics to be achieved in the 6-hour bundle include the application of vasopressors for refractory hypotension, reassessment of volume status and tissue

perfusion with documentation of findings in the presence of refractory hypotension, and reassessment of the lactate level if the initial level was elevated. (SSC, 2015).

Compliance with a protocolized, evidence-based sepsis identification and treatment pathway has been shown to decrease sepsis-related mortality (Rhodes et al., 2015; Tromp et al., 2010; Wang et al., 2013). Levy et al. (2012) found that early identification and compliance with early resuscitation bundles are keys to sepsis survival, resulting in less severe illness and decreased mortality. Compliance with sepsis guidelines and bundles, however, remains low, with compliance percentages for the initial resuscitation typically less than 20% and compliance with later resuscitation and/or management only slightly better (Rhodes et al., 2015, Wang et al., 2013).

Barriers to Bundle Compliance

Barriers to bundle compliance are varied and sometimes dependent on the provider being questioned. Failure to recognize the septic patient is consistently cited as a major barrier to bundle compliance; with lack of knowledge and resource barriers, such as laboratory testing, cited as additional reasons for poor bundle compliance (Carlbom & Rubenfeld, 2007; Daniels, 2011; Kissoon, 2014; Siontis et al., 2015). However, while looking at patients getting early goal-directed therapy (EGDT), Mikkelsen et al. (2010) found that patients who required a lactate result before being recognized as septic ("occult shock") were less likely to receive EGDT, indicating that the wait for lab results is a barrier to the initiation of care.

End-Tidal Carbon Dioxide Monitoring

Physiology. End-tidal carbon dioxide (EtCO2) monitoring, or capnography, is a measurement of the partial pressure of carbon dioxide (CO2) exhaled during respiration (Krauss, Silvestri, & Falk, 2016). In normal physiologic conditions, CO2 is produced as a byproduct of

pyruvate oxidation during aerobic metabolism. This CO2 is then transported to the lung capillaries from the tissues and is excreted during expiration (Murias, Blanch, & Lucangelo, 2014).

Equipment. EtCO2 monitoring is accomplished via two equipment mechanisms-mainstream and sidestream measurement. In mainstream measurement, the reading is taken directly from the airway, often as an adapter at the hub of an endotracheal tube. In sidestream measurement, a sample of expired breath is collected via cannula tubing and transmitted to a sensor. In quantitative EtCO2 monitoring, the presence of a waveform indicates a patent airway and a reading of 35-45 mmHg indicates adequate perfusion (Krauss, Silvestri, & Falk, 2016).

Indications. A number of indications for EtCO2 monitoring for both intubated and spontaneously breathing patient are now considered standard of practice. Verification of endotracheal tube placement, monitoring of perfusion status during cardiac arrest, and determining the adequacy of ventilation are all standard applications of EtCO2 monitoring in intubated patients. In spontaneously breathing patients, EtCO2 monitoring can be used to rapidly assess critically ill patients and to determine the adequacy of ventilation during procedural sedation or in obtunded or unconscious patients (Krauss, Silvestri, & Falk, 2016).

Limitations. EtCO2 monitoring is most accurate when monitoring for individual alterations in ventilation, perfusion, or metabolism. Complex pathophysiologic processes can complicate the interpretation of the reading, as ventilation, perfusion, and metabolism may be affected (Krauss, Silvestri, & Falk, 2016).

End-Tidal Carbon Dioxide and Lactate

Research has indicated there may be an inverse correlation between EtCO2 reading and lactate levels across multiple disease processes (Belenkiy et al., 2011; Caputo et al., 2012;

Guirgis et al., 2014; Hunter, Silvestri, Dean, Falk, & Papa, 2013; Hunter et al., 2016; Lee et al., 2009). Furthermore, several studies have demonstrated the reliability of EtCO2 monitoring as an indicator of lactate level prior to resuscitation (Chalkias et al., 2015; Guiris et al., 2014; Hunter et al., 2013).

The biochemistry of energy production easily explains this relationship. Glycolysis results in the formation of two pyruvate molecules per glucose molecule. In the presence of oxygen, this pyruvate is then further oxidized into carbon dioxide by pyruvate dehydrogenase and the tricarboxylic acid cycle. However, when oxygen supply is limited, pyruvate is reduced by lactate dehydrogenase to lactate (Smith, Marks, & Lieberman, 2005, pp. 399-406).

In 2013, Hunter, Silvestri, Dean, Falk, & Papa showed a similar AUC for lactate and mortality (0.75, CI [0.65-0.86]) and EtCO2 and mortality (0.73, CI [0.61-0.84]). They further showed an association between EtCO2 and mortality across a range of disease severity that was similar to the association between lactate and mortality across the same range of disease severity (Appendix A**)**. Guirgis et al. (2014) gave support to the idea of EtCO2 monitoring as an adjunct identification tool in sepsis as their research indicated baseline EtCO2 levels may correlate with initial lactate levels in sepsis patients. Hunter et al. (2016) added EtCO2 monitoring to a sepsis screening tool to evaluate the ability of the combination to identify sepsis. Combining a screening tool and EtCO2 monitoring resulted in a significant increase in the ability to predict sepsis across a range of disease severity as compared to EtCO2 alone. The combination also yielded a sensitivity of 90%, a specificity of 58%, and a negative predictive value of 93% for patients with severe sepsis (Hunter et al., 2016).

Indications for Study

Sepsis is at baseline a deadly and expensive disease process and failure to treat it appropriately results in increased mortality and hospital expenditures. Given that failure to recognize the septic patient is cited as a major barrier to appropriately initiating treatment, any diagnostic tool that can improve this identification could have important clinical applicability.

As a large tertiary care center, the project site has focused on improving sepsis outcomes in its high acuity population. Despite a number of evidence-based interventions previously implemented, sepsis outcomes remain subpar. Anecdotal evidence from the site indicates that waiting for laboratory studies is one barrier to recognition that has not been addressed in previous interventions conducted at the site. $EtCO_2$ monitoring has been shown in a variety of processes to have a correlation to lactate level, which is a key metric in identifying sepsis. Additionally, it is a readily available diagnostic tool that can easily be used on arrival to the emergency department. If proven successful, this is an intervention that can be used in a variety of emergency settings as well as in the prehospital setting to identify and initiate treatment in possible sepsis patients.

Theoretical Framework

The Ottawa Model of Research Use is a knowledge translation theory that utilizes a six-step method split into three phases to implementing a new intervention. The first phase consists of an assessment of the barriers and support systems within the domains of the practice environment, potential adopters, and the innovation. The practice environment includes the physical space where the intervention is to be implemented as well as the socioeconomic factors and culture of the setting. Potential adopters refers to the individuals involved in the intervention and their attitudes, perceptions, and knowledge base surrounding the practice. The innovation

refers to the evidence-based intervention and includes its attributes and applicability (Graham & Logan, 2004).

The second phase of the model consists of monitoring the intervention and its degree of use and includes implementation strategies and adoption of the practice. Implementation strategies refer to the tactics utilized to assist in the understanding and utilization of the intervention while adoption refers to the physical use of the intervention as well as the intention to use it. The final phase of the model is the outcomes phase and consists of evaluating the impact of the intervention on determined outcomes (Appendix B) (Graham & Logan, 2004; Hogan & Logan, 2004).

Methodology

This project consisted of a pilot study implementing $EtCO_2$ monitoring in patients who were being evaluated for sepsis in the adult emergency department. After the proposed study time, an analysis of the impact that the proposed intervention had on recognition and treatment of sepsis was conducted.

Setting

The project took place at a 965-bed academic medical center that serves as the primary teaching hospital for a local medical school and is the flagship hospital of a local cancer center. The center has two campuses and has been recognized as a national leader in a variety of specialties, including trauma care as a Level I trauma center and stroke care as a Comprehensive Stroke Center (RWJUH, n.d.). Emergency services at the implementation site offers specialized pediatric and adult services. The adult emergency department serves patients 21 years old and above, with an annual census of 71,000 patients and admits 31% of patients to the hospital annually (L. Schmidt, personal communication, April 10, 2017).

Study Population

The target population of this project was patients that fall into the "Code Sepsis" arm of the department's current sepsis identification and treatment protocol (Appendix C). These patients are identified using the National Early Warning Score (NEWS), which has previously been implemented in triage at the proposed site. The NEWS score is an early warning mortality score that takes into account vital signs, level of consciousness, and oxygen use, and assigns a score based on these parameters. Higher scores reflect higher acuity patients, and patients that score a five or greater are prioritized as "Code Sepsis." This triggers staff to respond to the patient immediately and evaluate the patient for sepsis. This evaluation currently includes cardiac monitoring, frequent vital sign monitoring, laboratory collection, and medication administration.

Inclusion criteria. The intervention was utilized as part of the department's Code Sepsis protocol. Therefore, inclusion criteria included patients who fell into this response and the staff responsible for treating them.

Exclusion criteria. Pediatric providers were excluded from this study as the current department protocol does not include patients treated in the pediatric emergency department. Any adult emergency patient that does not fall into the Code Sepsis response will not be included.

Sample size. This pilot study aimed to evaluate the intervention for a one-month period and looked at aggregate data comparing the month in which the intervention was used to a month in which it was not. Therefore, there is not a goal sample "size."

Study Interventions

This study was a pilot evaluation of $EtCO_2$ monitoring in patients that are evaluated on the "Code Sepsis" arm of the current sepsis identification and treatment protocol at the proposed site (Appendix C).

Licensed staff were asked to utilize $EtCO_2$ monitoring in addition to current monitoring adjuncts. Hemodynamic monitors in the resuscitation bay where these patients are initially evaluated all have $EtCO_2$ monitoring capability and $EtCO_2$ cannulas are considered floor stock in the department. Prior to the intervention month clinical staff were made aware of the addition of the intervention to the Code Sepsis protocol through daily staff meetings (called huddles at the organization) for a period of two weeks.

Outcome Measures

Deidentified aggregate data was evaluated and analyzed for any significant differences. The metrics, including demographics, to be evaluated are:

- Number of patients
- Time to recognition
- Bundle Compliance
    - Overall compliance
    - Time to antibiotics (overall)
    - Percent of patients who receive antibiotic therapy within three hours
    - Intravenous fluid administered

Risks or Harms

The risks to patients were minimal during this pilot evaluation. $EtCO_2$ monitoring is accomplished using tubing that settles at the end of the nose and wraps around the ears, similar to an oxygen cannula. Risks related to the $EtCO_2$ cannula use included skin breakdown from the

tubing, particularly behind the ears. This risk was minimized as staff receive annual competencies in the prevention of pressure wounds, including the risk of breakdown from devices such as cannulas. Additionally, this intervention was only evaluating $EtCO_2$ monitoring in the resuscitative phase. Therefore, individuals who did not require continuous oxygenation were not exposed to the device outside of the immediate resuscitative period, which is generally too short a time for skin breakdown to occur (< 60 minutes). Outcomes were measured retrospectively and had no impact on the patient's real-time treatment.

Finally, providers are in the resuscitation bay for the entirety of the resuscitative period. Any significant EtCO2 reading were immediately available to the provider. As providers were free to respond as they saw fit there was no foreseeable risk to staff involved in the treatment of the patients during this pilot evaluation.

Subject Recruitment

There was no active recruitment for this pilot evaluation of the intervention. It as utilized as part of the Code Sepsis response. Therefore, any individual who met the site's previously established Code Sepsis criteria and the staff that was involved in their treatment were included.

Consent Procedures

A waiver of consent was requested and approved for this pilot evaluation. $EtCO_2$ monitoring is standard of care in the emergency department. This pilot evaluation looked to see whether there was a benefit to adding the $EtCO_2$ to the department's Code Sepsis protocol, which is also standard of care at the site.

As the research is not FDA-regulated, did not involve non-viable neonates or newborn dried blood spots, and did not involve more than minimal risk to the subjects as their care was not altered, the waiver was deemed to not adversely affect the rights and welfare of the subjects.

Subject Costs and Compensation

There were no costs to the subjects as $EtCO_2$ monitoring is currently a standard of care for many emergency department situations and cannulas are therefore already included in the department's equipment budget. There was no compensation to the subjects.

Project Timeline

This project consisted of a two-week introduction period, where staff was informed of the addition of the intervention to the current protocol. This started on December 17, 2018. This was followed by a one-month intervention from January 1, 2019 to January 31, 2019.

Resources Needed/Economic Considerations

Resources needed included office supplies, including computer programs such as Microsoft Word and Excel.

Evaluation Plan

Data Maintenance/Security

Aggregate data was provided to the primary investigator through the established performance improvement process.

Data Analysis

Statistical analysis of the deidentified, aggregate data was completed to determine significance in outcomes. Statistical analysis was completed using Microsoft Excel functions.

Findings

This pilot evaluation sought to determine if the use of end-tidal carbon dioxide ($EtCO_2$) monitoring would help providers identify and treat adult emergency department sepsis patients. The use of $EtCO_2$ monitoring was implemented for a one-month time period in January 2019 as part of the Code Sepsis response at an academic medical center. This intervention month was

compared to the immediately preceding month to avoid significant changes in patient volume and acuity as well as changes in staffing. The intervention month saw an increased time to recognition, total time to antibiotics, percentage of patients that received antibiotics within three hours of recognition, and applicable bundle compliance as well as a decrease in the percentage of patients that received appropriate intravenous fluid resuscitation (Appendix D).

Time to Recognition and Time to Antibiotics

The average time to recognition and the average time to antibiotic administration both increased in the intervention month. The average time to recognition increased from 44.3 minutes in December 2018 to an average of 49 minutes in January 2019. The average time to antibiotics increased from 69.5 minutes in December 2018 to an average of 75.5 minutes in January 2019. Evaluation of the sample distribution for the time to recognition and time to antibiotics was performed using the Microsoft Excel Data Analysis feature. This evaluation illustrated that the data was not normally distributed, as both the comparison and intervention samples had skewness and kurtosis values outside of the acceptable range of -2 to 2 for normal distribution (Appendix E). Since these samples did not follow normal distribution, the nonparametric Mann-Whitney U test was used to eval if the samples were statistically significantly different.

Using the calculated U statistic for the time to recognition, an obtained z-score of $z = -0.24$ was determined for the average time to recognition. With relatively larger sample sizes, the absolute value of the obtained z-score is compared to a critical value of 1.96 (Billiet, 2003). Given that 0.24 is less than the critical 1.96, the difference in in average time to recognition for the two samples cannot be considered statistically significantly different.

Considering the same method for the average time to antibiotics, the calculated U statistic resulted in an obtained z-score of z = -0.534. Again, the absolute value of the obtained z-score is less than the critical value of 1.96. Therefore, the intervention was deemed to not have any statistically significant impact on these outcome metrics.

Antibiotics, intravenous fluid, and total bundle compliance

The percentage of patients that received antibiotics within three hours of recognition increased in the intervention month, from 97.1% in December 2018 to 100% in January 2019. The percentage of patients that received the total applicable bundle (bundle compliant) also increased in the intervention month, from 82.8% in December 2018 to 88.6% in January 2019. The percentage of patients that received appropriate intravenous fluid resuscitation, however, decreased in the intervention month, from 93.8% in December 2018 to 87.5% in January 2109. The differences in these metrics were analyzed using the "N-1" Chi-squared test as the sample, again, does not follow normal distribution (Campbell, 2007). The relation between the comparison and intervention month for the percent of patients who received antibiotics within three hours of recognition was not significantly different, χ^2 (1, N = 70) = 1.015, p > 0.05. The difference between the comparison and intervention month for the percent of patients who received appropriate intravenous fluid resuscitation was also not significantly different, χ^2 (1, N = 32) = 0.363, p > 0.05. Finally, the change in bundle compliance between the comparison and intervention months was also not significantly different, χ^2 (1, N = 70) = 0.459, p > 0.05.

Recommendations and Discussion

Although the majority of the evaluated outcomes did not show significant improvement, they also did not offer any evidence that the use of $EtCO_2$ monitoring will hinder the identification and treatment of sepsis. The average times to recognition and antibiotic

administration increased and the percent of patients receiving appropriate intravenous fluid resuscitation decreased, which is contrary to the hypothesized impact of this intervention. Similarly, the percentage of patients receiving antibiotics within three hours of recognition and the total bundle compliance both increased. This was consistent with the hypothesized impact of the intervention. However, these changes were not determined statistically to be a result of the intervention. Therefore, the intervention did not appear to either help or hinder sepsis identification and treatment.

Translation

Organizations that already have $EtCO_2$ monitoring capabilities and routinely utilize it could add it to sepsis protocols and potentially see some improvement. However, these results alone do not support the financial expenditure of obtaining and training on EtCO2 monitoring if an organization does not already have the capabilities. As such, the results of this study alone do not offer significant influence on current practice.

However, there is evidence to promote future research. This pilot evaluation was limited by its short duration and small sample size. Evaluation for a longer timeframe and larger sample size may yield more definitive and broadly applicable results. Additionally, this pilot evaluation did not collect nor control for any potential confounding variables, such as acuity or overall department volume. Although the consecutive months of December 2018 and January 2019 were chosen to attempt to minimize variations in potential confounders, without collecting this information, it was impossible to determine if any were present that may have impacted the results. Further research controlling for variables that may impact patient care in the emergency department, such as department volume or boarding in the emergency department, would be beneficial.

Dissemination

In 2015, the project site founded a hospital-wide sepsis committee as well as an emergency department-specific steering committee. Both of these committees meet monthly to evaluate sepsis outcomes, challenges in sepsis care, and interventions to overcomes challenges. The results of this pilot evaluation will be shared with these committees to determine if further research into the use of the intervention is desired by the department. Additionally, the healthcare system associated with the project site hosts a Nursing Research Day annually in November, where nurses of the project site can present posters regarding research they have conducted. The results of this evaluation will be shared at the 2019 Nursing Research Day. Finally, the healthcare system hosts an annual emergency department symposium. The results of this research can be disseminated at this symposium.

Professional Reporting

The results of this pilot evaluation can be applicable at the state and national level. In addition to local dissemination strategies, the Emergency Nurses Association offers state and national tailored to emergency department nurses, educators, and leadership. The New Jersey Emergency Nurses Association State Council hosts an annual emergency care conference in March and the national Emergency Nurses Association hosts an annual conference in early fall. Dissemination strategies at either of these conferences include poster presentations or lectures. Publication strategies for these results include the Emergency Nurses' Association's Journal of Emergency Nursing.

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Appendix A

Comparison of lactate and end-tidal carbon dioxide monitoring in identifying mortality, sepsis, severe sepsis, and septic shock

	Lactate	*End-Tidal Carbon Dioxide*
Mortality	0.75 (CI, 0.65-0.86)	0.73 (CI, 0.61-0.84)
Sepsis	0.61 (CI, 0.36-0.87)	0.60 (CI, 0.37-083)
Severe Sepsis	0.69 (CI, 0.48-0.89)	0.67 (CI, 0.46-0.88)
Septic Shock	0.74 (CI, 0.55-0.93)	0.78 (CI, 0.59-0.96)

Figure A1: Receiver operating characteristic curve comparing the ability of lactate and end-tidal carbon dioxide monitoring to predict mortality, sepsis, severe sepsis, and septic shock (Hunter, Silvestri, Dean, Falk, & Papa, 2013).

Appendix B

Current Emergency Department Sepsis Identification and Treatment Policy

I. All patients are triaged in the electronic medical record except as documented in the triage policy.

II. A National Early Warning Score (NEWS) is generated based on input vital signs, level of consciousness, and oxygen use.

III. Patients are stratified into one of three pathways dependent on their NEWS score.

   a. NEWS 0-2: usual care pathway based on established policy

   b. NEWS 3-4: Sepsis Alert

      i. Orange sepsis sticker placed on triage sheet & triage prioritized in the "To Be Seen" rack.

      ii. Primary RN and prescribing provider prioritize the evaluation of the patient.

      iii. 3-hour sepsis bundle initiated if appropriate.

   c. NEWS 5+: Code Sepsis

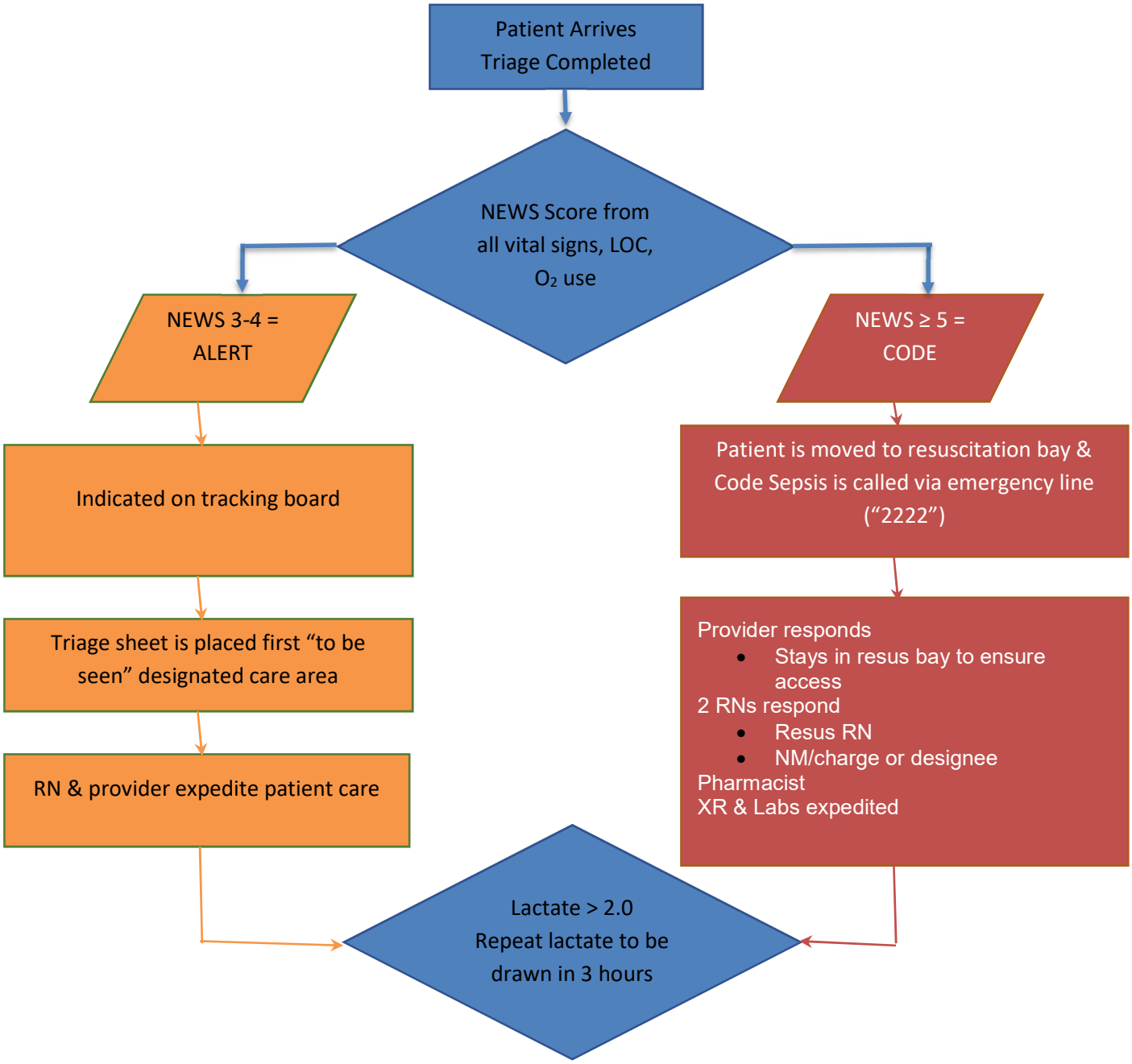
      i. Departmental overhead "Code Sepsis" is initiated.

      ii. Patient is placed in the resuscitation bay.

      iii. Prescribing provider and primary RN immediately respond for emergent resuscitation.

      iv. 3-hour sepsis bundle initiated if appropriate.

Sepsis Treatment Pathway



Appendix C

Ottawa Model of Research Use and Adapted Framework

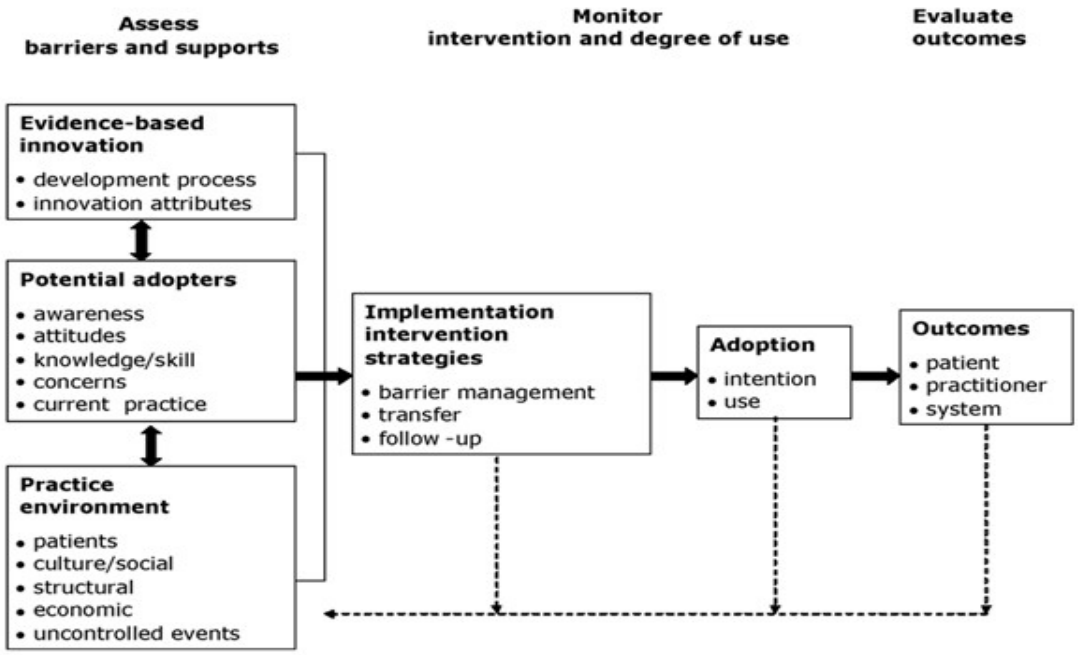


Figure C1: Ottawa Model of Research Use diagram (Graham & Logan, 2004; Hogan & Logan, 2004)

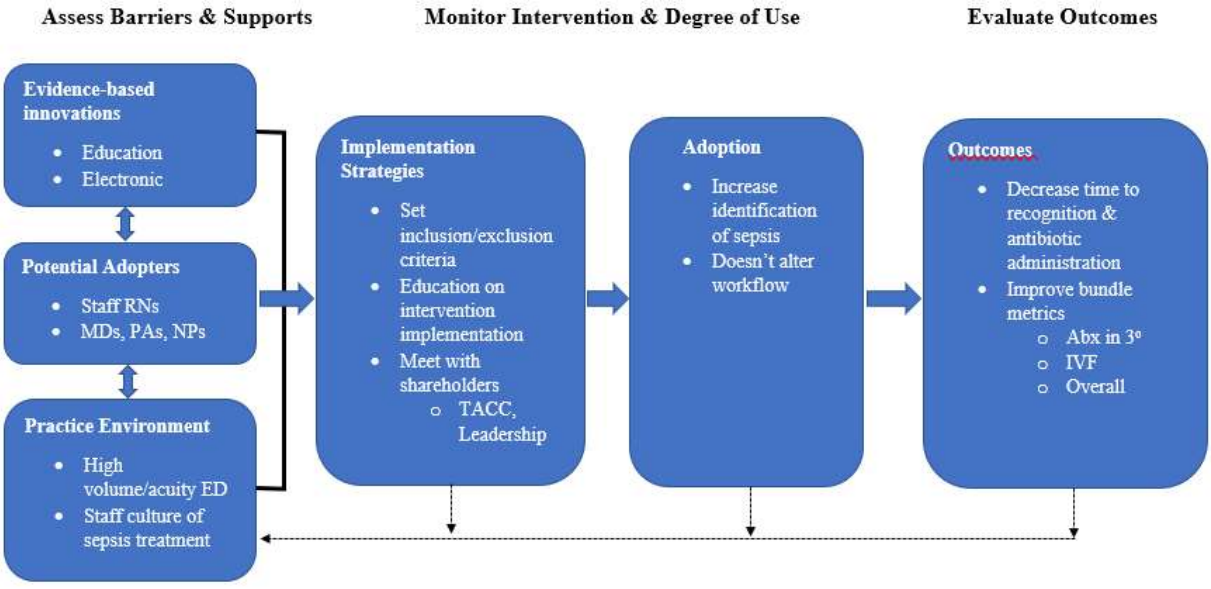


Figure C2: Adapted implementation strategy

Appendix D

Pilot Evaluation Results

Table D1

Time to recognition and antibiotics

Month	Time to Recognition	Time to Antibiotics
Comparison	44.3 minutes	69.5 minutes
Intervention	49 minutes	75.7 minutes

Table D2

Percentages of patients receiving antibiotics, intravenous fluids, and all applicable bundle metrics

Month	% Abx Compliant	% IVF Compliant	% Total Bundle Compliant
Comparison	97.1%	93.8%	82.8%
Intervention	100%	87.5%	88.6%

Note: Abx = antibiotics; IVF = intravenous fluid

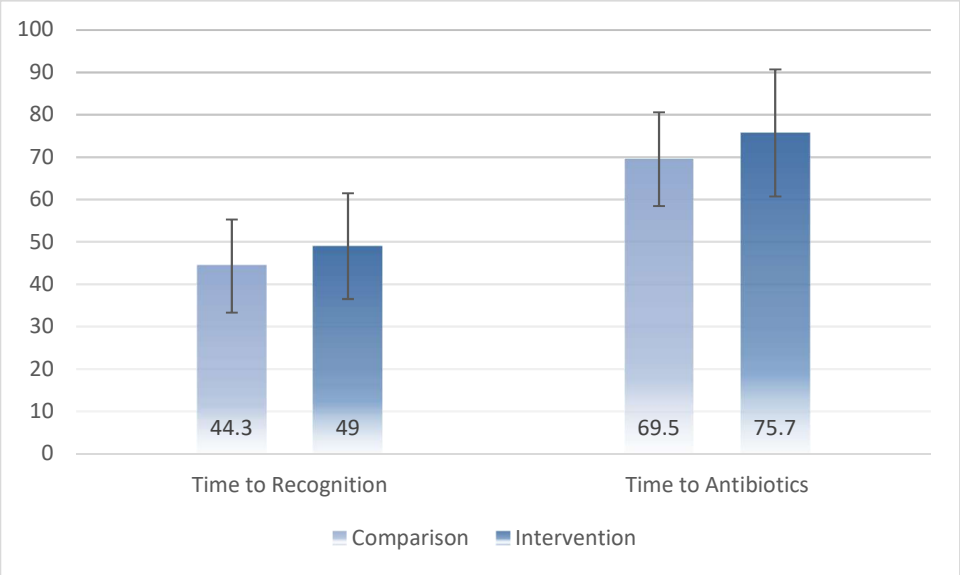


Figure D1: Average time in minutes to recognition and antibiotic administration in comparison month and intervention month

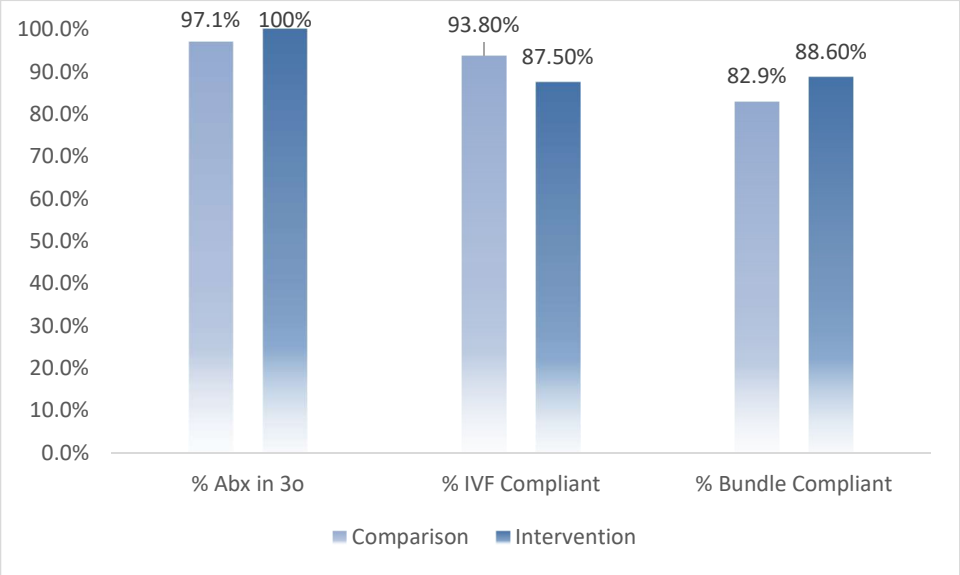


Figure D2: Percentage of patients compliant with antibiotic administration, intravenous fluid administration, and overall bundle metrics in the comparison and intervention months.

Appendix E

Sample Distribution Statistics

Table E1

Time to Recognition				Time to Antibiotics			
Comparison		*Intervention*		*Comparison*		*Intervention*	
Mean	44.31	Mean	48.97	Mean	69.55	Mean	75.54
Standard Error	11.00	Standard Error	12.47	Standard Error	11.07	Standard Error	14.98
Median	11.00	Median	25.00	Median	41.00	Median	37.00
Mode	1.00	Mode	1.00	Mode	16.00	Mode	32.00
Standard Deviation	65.08	Standard Deviation	73.79	Standard Deviation	63.58	Standard Deviation	88.65
Sample Variance	4235.9	Sample Variance	5444.73	Sample Variance	4042.4	Sample Variance	7859.2
Kurtosis	9	Kurtosis	10.37	Kurtosis	4	Kurtosis	6
Skewness	5.39	Skewness	2.91	Skewness	2.08	Skewness	3.98
Range	2.22	Range	370.00	Range	1.70	Range	2.14
Minimum	288.00	Minimum	1.00	Minimum	243.00	Minimum	358.00
Maximum	0.00	Maximum	371.00	Maximum	16.00	Maximum	14.00
Sum	288.00	Sum	1714.00	Sum	259.00	Sum	372.00
Count	1551.0	Count	35.00	Count	2295.0	Count	2644.0
	35.00				0		0
					33.00		35.00

Appendix F

Evidence Table

Article #	Author & Date*	Evidence Type	Sample, Sample Size, Setting	Study findings that help answer the EBP Question	Limitations	Evidence Level/Quality
1	Hunter Silvestri Dean Falk Papa 2013	Retrospective Observational	Setting - Adult tertiary hospital - Annual census ~ 70k Sample Inclusions - Adult (≥ 18 y.o.) - + suspect/known infection w/ 2+ SIRS criteria *excluding* WBC ct. Sample Exclusions - Refused standard therapy - Cranial facial abnormalities that would prevent EtCO2 measurement - Known COPD, asthma - Hyperthermic from environmental causes (not r/t febrile) - Intubated PTA	No significant difference between venous & arterial lactate Inverse corr. Between EtCO2 & lactate in all categories - Sepsis: -0.421 ($p < .001$) - Severe: -.597 ($p < .001$) - Shock: -0.482 ($p < .001$) Predictive qual of lactate & EtCO2 for mortality - Lactate: 0.75 (CI, 065-0.86) - EtCO2: 0.75 (CI, 0.61-0.84 Lactate AUC-ROC - Sepsis: 0.64 (CI, 0.36-0.87)	Convenience sampling - MD discretion - Selection bias may be present Only single-point EtCO2 & lactate assesement Single location RSI may physiologically alter EtCO2	Level III

			Sample Notes - Pts intubated *after* inclusion were included & analyzed separately - N = 201 Method Notes - Initial EtCO2 obtained after several verification breaths, before mech vent - Stable pts: via NC when capnographic wave peaks were constant end-tidal for 3-5 resp - Unstable: immediately after intub with 3-5 manual resp - Used RSI, min. bag-valve vent before intubation - Used "old" definitions Data Collected - Baseline VSS, demographics - EtCO2 & serum lactate obtained at approx.	- Severe: 0.69 (0.48-0.89) - Shock: 0.74 (CI, 0.55-0.93) EtCO2 AUC-ROC - Sepsis: 0.60 (CI, 0.37-0.83) - Severe: 0.67 (CI, 0.46-0.88) - Shock: 0.78 (CI, 0.59-0.96)		

			simultaneous *before* resus - LOS, ICU adm, mech vent during stay, vasopressor use, ED bld cx results, infectious dx, pt med hx.			
Article #	Author & Date*	Evidence Type	Sample, Sample Size, Setting	Study findings that help answer the EBP Question	Limitations	Evidence Level/Quality
2	Jacquet-Lagreze Baudin David Fellahi Hu Lilot Piriou (2016)	Prospective Observational	Setting - Secondary care university hospital in France. Sample Notes - N = 40 Inclusion Criteria - Pt undergoing general anesthesia w/ mech vent & esophageal Doppler monitoring - Fluid bolus for volume expansion admin Exclusion Criteria - Patient refusal - Pregnancy - Fluid overload prior to anesthesia	No significant correlation between CI & EtCO2 - r = 0.178, $p = 0.272$ Significant correlation btw ΔCI & ΔEtCO2 after 500 mL - r = 0.566, $p < 0.001$. Weak correlation btw ΔCI & ΔEtCO2 after 100 mL - r = 0.39, $p = 0.013$ ΔEtCO2 > 5.8% → all patients were fluid responders How will answer PICO - Bundle complian	Variation of EtCO2 could be dependent on depth of anesthesia Mech vent settings made SVV or PPV unable to predict fluid responsiveness. AUC-ROC after 500 mL bolus = 0.75. - May influence applicability of ΔEtCO2	Level III

			- Laparoscopic surgery - No avail Doppler signals - Contraindications to Doppler technique Method Notes - EtCO2 measured at 0, 1, and 13 min - Corresponded to before, during & after bolus admin - Pts w/ > 15% increase in CI after bolus defined as fluid responders Data Collected - EKG, SpO2, SBP, DBP, MAP q5min - Pulse pressure - Airway, peak, plateau pressures - RR, tidal volume - Partial inspiratory pressures of O2 & CO2	ce incl fluid resus. - Provider confidence in admin fluid is low, especially in dx predisposed to fluid overload - If EtCO2 can be used to inc. provider confidence, bundle compliance will increase		

Article #	Author & Date*	Evidence Type	Sample, Sample Size, Setting	Study findings that help answer the EBP Question	Limitations	Evidence Level/Quality
3	Chalkias Spyropoulos Koutsovasilis Papalois Kouskouni Xanthos (2015)	Experimental	10 healthy female pigs Septicemia intentionally induced. Hemodynamic monitoring during induction, arrest, & resuscitation: - HR, SBP, DBP, MAP, EtCO2, shock index, SpO2, pH, PaO2, PaCO2, PaO2/FiO2, HCO3, BE, lactate	EtCO2 did not correlate with ROSC During sepsis progression, EtCO2 fell while lactate rose. - Study did not address the correlation or if it was significant Monitoring after ROSC - Both lactate and EtCO2 fell How answers PICO? - Prior to arrest, EtCO2 may correlate with lactate. - Not of use post-arrest	Study conducted in healthy pigs - No underlying respiratory disease Model based on endotoxins & not live infections. Correlation between hemodynamic parameters not measured.	Level II

4	Belenkiy Berry Batchinsky Kendrick Necsoiu Jordan Salinas Cancio (2014)	Experimental	Ten pigs were hemorrhaged Noninvasive CO2 monitoring technologies compared with each other and with lactate.	Correlation between EtCO2 and lactate low - R2 = 0.26 (p < 0.001) EtCO2 < 20 mmHg detected lactate > 4 mmol/L - Sens 100% - Spec 56% - Accuracy 60% NICO2 (diff. btw tPCO2 & EtCO2) best predictive ability	Small sample size Animals were hypercapnic & hyperlactatemic at baseline	Level II
Article #	Author & Date*	Evidence Type	Sample, Sample Size, Setting	Study findings that help answer the EBP Question	Limitations	Evidence Level/Quality
5	Lee Hong Han Kim Moon Shin Baek (2009)	Prospective observational	Setting - University teaching hospital - Annual census ~40k Inclusion Criteria - Adult patient w/ brain injury after trauma - > 20 y.o. - GCS < 9 - Mechanical ventilation support w/ETT	Inhospital mortality & P(a-et)CO2 - 80% in pts w/ < 30 mmHg P(a-et)CO2 High P(a-et)CO2 showed significantly lower EtCO2 than normal P(a-et)CO2 group. - These pts had low BP,	Respiratory support not controlled - SIMV v. CMV - May affect readings	Level III

			- Brain lesion dx w/ head CT or MRI Exclusion Criteria - Nontraumatic brain injury - Cardiac arrest PTA or at arrival - Medical hx of COPD Data collected - Demographics - Initial GCS - SBP, DBP, RR, HR, ABGs, EtCO2, PaCO2, serum lactate obtained w/in 30 min of start of mech vent - ISS, AIS Sample Size - 66 patients, 55 men/11 women	high serum lactate levels & metabolic acidosis (p = 0.039)		

6	Hunter Silvestri Ralls Stone Walker Papa (2016)	Prospective cohort study	Setting - Orange County, FL; prehospital EMS Inclusion Criteria - Any pt that EMS activated a "sepsis alert" Exclusion Criteria - Pediatric patients - Patients without available hospital records Method Notes - Sepsis alert incl. pts with 2+ SIRS criteria (excl. WBC), suspected infection, & EtCO2 ≤ 25 mmHg. - Comparison made between "protocol compliant" vs. "protocol noncompliant" groups Data Collected - Age, gender, race, EtCO2, RR, SBP, DBP, HR,	EtCO2 able to predict sepsis, severe sepsis, mortality>other metrics. - AUC-ROC for sepsis = 0.99 (95% CI 0.99-1.00; $p <$ 0.001) - AUC-ROC for severe = 0.80 (95% CI 0.73-0.86; $p <$ .001) - AUC-ROC for mortality = 0.70 (95% CI 0.57-0.83; $p =$ .005) Negative correlation btw EtCO2 & lactate - Corr. Coeff. -0.394 ($p <$ .001) Alert predict ability sepsis - Sens 69%	Does not include pts who were septic but did not receive a "sepsis alert" activation. Did not control for differences in demographics across cohorts Doesn't address if prehospital activation	Level II

			SpO2 from prehospital - Mortality, ICU vs. non-ICU adm, initial ED VSS, PMH, principle & adm dx (ICD-9) - Serum bicarb, lactate, anion gap Sample Size - 330 (183 compliant vs. 147 noncompliant)	- Spec 67% - PPV 78% - NPV 99% Alert predictive ability for sever sepsis - Sens 90% - Spec 58% - PPV 47% - NPV 93% Alert predictive ability for mortality - Sens 76% - Spec 46% - PPV 11% - NPV 95%		
Article #	Author & Date*	Evidence Type	Sample, Sample Size, Setting	Study findings that help answer the EBP Question	Limitations	Evidence Level/Quality
7	Guirgis Williams Kalynych Hardy Jones Dodani Wears (2014)	Prospective, observational, cohort	Setting - Urban, academic hosp - ~90k annual visits Inclusion Criteria - PI, research asst. present - ≥ 18 y.o.	Correlation between initial EtCO2 & lactate - (β) = -.051, $t(69) = -1.90$, $R^2 = 3.6$, $p = .06$	Sample size - Small - Only pts receiving invasive tx included Pulmonary dx - Did not address	Level III

			- Doc. Severe sepsis or septic shock - Being tx w/ quantitative resus & CVC to neck or chest Exclusion Criteria - Incarcerated, pregnant - Req. emergency surgery prohibiting EtCO2 - Rec. noninvasive ventilation tx - Had another severe metabolic acidosis of nonsepsis etiology Method Notes - Enrolled within 3 hrs of recognition - EtCO2 taken during 1-min intervals at 0, 3, & 6 hrs. Data Collected - VSS, vent setting, FiO2, MAP, CVP, UO Sample Size- 69 pts	- + correlation - Not sig but close Correlation between 6 hr EtCO2 & lactate - No correlation	pts with potential poor alveolar gas exchange. - Skewed results?	

Article #	Author & Date*	Evidence Type	Sample, Sample Size, Setting	Study findings that help answer the EBP Question	Limitations	Evidence Level/Quality
8	Caputo Fraser Paliga Matarlo Kanter Hosford Madlinger (2012)	Prospective, cohort study	Setting - Level I Trauma center in NYC Inclusion Criteria - Penetrating trauma w/ trauma team activation Exclusion Criteria - Intubated PTA - Absence of VSS PTA - Need for surgical airway support Data Collected - EtCO2, VSS, POC lactate on arrival Sample Size- 105 pts	Lactate, EtCO2 correlation - Strong inverse - R = -0.86 ($[rho]$ = 0.74; 95% CI, 0.63-0.81; p = 0.0001 No cases of normal EtCO2 & increased serum lactate. No correlation btw SBP & lactate or EtCO2 - May indicate that SBP fxn independently of perfusion	Single center study Used NC w/ side stream detectors - Readings vary w/ resp	Level III
9	Burney Underwood McEvoy Nelson Dzierba Kauari Chong (2012)	Cross-sectional, qualitative	Setting: - Urban, academic hospital - ~ 72k annual census Sample size - 101 (57 RNs, 28 MDs, 16 residents)	Perceived reasons for tx delays - Dx delay by MDs, in triage Lab delays cited 7% time by RNs - 2.3% by MDs MDs “hardly ever” order lactate 43.2%	Voluntary evaluation - Selection bias Single center - Results may not be applicable in other institutions	Level III, non-experimental

				CVP/ScvO2 access & nursing staff cited as biggest perceived barriers - Trend now toward lactate clearance		

Article #	Author & Date*	Evidence Type	Sample, Sample Size, Setting	Study findings that help answer the EBP Question	Limitations	Evidence Level/Quality
10	Mikkelsen Gaieski Goyal Miltiades Munson Pines Fuchs Shah Bellamy Christie (2010)	Retrospective, observational, cohort study	Setting - UPenn ED Inclusion Criteria - Serum lactate measured - MD doc of sepsis, severe sepsis, cryptic septic shock, septic shock, EGDT Exclusion Criteria - Severe sepsis criteria not met - Serum lactate not measured	EGDT less likely to be initiated in occult shock pts - 50% vs. 65%, p = .006 - Occult shock accounted for 46% eligible pts, EGDT not initiated in 50% How relates to PICO? - Evidence that "waiting" for lactate may delay/impede initiation of care	Cause & effect not evaluated Subject to type 1 error. Potential misclassification bias on definition of EGDT - If ScvO2/CVC not used, not included.	Level III

			- CVC refused - DNR Sample Size- 340 pts			

Evidence Table References

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