Evaluating Sepsis Bundle Compliance in the Adult and Older Adult Patient

Nathan Thornton

Oregon Health and Science University

Abstract

Sepsis is one of the largest contributors of ICU and hospital admissions and hospital mortality. In particular, older patients (≥65 years) not only have a higher risk of developing sepsis than adult patients (<65 years), but also have a higher risk of mortality (Martin, Mannino, & Moss, 2006). While early recognition and prompt treatment that follows the Surviving Sepsis Campaign (SSC) guidelines for sepsis and septic shock have been proven to decrease hospital length of stay (LOS) and decrease hospital mortality, current compliance remains poor (Rhodes et al., 2015). *Methods*: This was a single-center, retrospective chart review, for quality improvement, that examined SSC guideline compliance of adult patients admitted from the ED to an inpatient unit between October 1, 2015 and September 30, 2016 with a diagnosis of severe sepsis or septic shock. *Results*: A total of 241 patients were included. There was a significant difference in overall SSC guideline compliance between adults and older adults (37.37% vs. 27.19%, p = .04486). There was no difference between age groups when compliance to the 3-hour bundle was measured (52.76% vs. 45.61%, p = .27006), nor was there any difference between age groups when compliance to the 6-hour bundle was measured (60.64% vs. 50.00%, p = .15095). *Conclusion*: Overall compliance with the entire SSC sepsis guidelines was significantly less in the older adult patient compared to the adult patient.

Keywords: Sepsis, Compliance, Surviving Sepsis Campaign, Guideline, Bundle, Older Adult

Evaluating Sepsis Bundle Compliance in the Adult and Older Adult Patient

Sepsis, an infection-induced dysregulation of the immune system which can result in life-threatening organ dysfunction, is a leading cause of hospital admissions with over 35 million sepsis cases worldwide each year (Arefian et al., 2017; Singer et al., 2016). Sepsis is now the most common diagnosis among Medicare beneficiaries hospitalized in the ICU and as of 2008 has become the most common diagnosis in ICU patients overall (Sjoding, Prescott, Wunsch, Iwashyna, & Cooke, 2016). If not promptly recognized and treated, sepsis increases the risk of mortality as sepsis-induced organ dysfunction progresses (Dellinger et al., 2013; Singer et al., 2016). In 2011, sepsis accounted for $20 billion in healthcare costs in the United States, rising to $23.6 billion in costs in 2013 (Arefian et al., 2017; Leisman et al., 2017; Torio & Moore, 2016). Globally, sepsis is the leading cause of death and healthcare spending, prompting the SSC has to issue guidelines in an effort to improve these outcomes (Arefian et al., 2017; Leisman et al., 2017; Rhodes et al., 2017).

In an attempt to improve outcomes, the SSC released its initial set of guidelines in 2004, and has periodically released updated guidelines, most recently in 2017 (Rhodes et al., 2017). These guidelines contain time-sensitive treatment elements that are grouped into two bundles: 3-hour and 6-hour (see Appendix A) (Dellinger et al., 2013). Adherence to the guidelines has been associated with improved outcomes of decreased mortality and hospital LOS (Levy et al., 2012; Levy et al., 2015; Rhodes et al., 2015; Scheer et al., 2016; L. Stoneking, Denninghoff, Deluca, Keim, & Munger, 2011).

While all patients have the potential to develop sepsis, older adults have unique pathophysiological changes that result in an increased risk of infection and risk of developing sepsis (Clifford et al., 2016; De Gaudio, Rinaldi, Chelazzi, & Borracci, 2009; Englert & Ross,

2015; Girard & Ely, 2007; Nasa, Juneja, & Singh, 2012). These include, but are not limited to, adaptive and innate immune system dysfunction (i.e. immunosenescence), increased occurrence of one or more comorbidities, and decreased functional status (Clifford et al., 2016; De Gaudio et al., 2009; Englert & Ross, 2015; Girard & Ely, 2007; Nasa, Juneja, & Singh, 2012). Compounding this, the typical presentations of sepsis, such as fever and leukocytosis, are not always present in the older adult. Leukocytosis has been found to only be present in 60% of septic older adult patients, while fever has been found to be present in only 53 to 77% of septic older adult patients (compared to 96% in adult patients) (Clifford et al., 2016; De Gaudio et al., 2009; Englert & Ross, 2015; Girard & Ely, 2007; Girard, Opal, & Ely, 2005; Nasa, Juneja, & Singh, 2012). Instead, the older adult more commonly presents with nonspecific symptoms such as altered mental status, weakness, anorexia, increased falls, urinary incontinence, and malaise (Clifford et al., 2016; De Gaudio et al., 2009; Englert & Ross, 2015; Girard & Ely, 2007; Nasa, Juneja, & Singh, 2012). Because of the predisposition to infection and atypical sepsis presentation, it has been identified that being ≥65 is an independent risk factor for sepsis (Clifford et al., 2016; Martin et al., 2006; Nasa, Juneja, & Singh, 2012).

Since 2008, sepsis has been the most common intensive care unit (ICU) admission diagnosis in older adult patients, accounting for 10.2% of all ICU admissions of older adults (Sjoding et al., 2016). In the United States, the prevalence of sepsis exceeds one million cases per year for patients ≥65 years of age (Leisman et al., 2017). Due to the often-atypical presentation of sepsis, or concern of exacerbating or exposing undiagnosed comorbidities (such as heart failure or chronic kidney disease), older adult patients often receive less compliant care to the SSC guidelines (Clifford et al., 2016; Girard & Ely, 2007; Nasa, Juneja, Singh, Dang, & Arora, 2012; Palomba, Correa, Silva, Pardini, & Assuncao, 2015; L. Stoneking et al., 2011).

To date, no studies exist that evaluate the compliance rate to the SSC guidelines in the older adult population (El Solh, Akinnusi, Alsawalha, & Pineda, 2008; Madsen et al., 2014; Palomba et al., 2015; L. R. Stoneking et al., 2015). Given the above, there is a critical need for evaluation to compare actual compliance rates among adult and older adult populations to understand where and to what extent SSC guideline compliance differs. This can ultimately address where changes in practice must be made to improve outcomes in older adults.

Literature Review

Purpose

The aim of this literature review is twofold. First, to identify the frequency of and outcomes associated with sepsis bundle compliance. Second, to identify the frequency of and outcomes associated with sepsis bundle compliance in older adults compared to adults.

Methods

A systematic literature review was conducted, searching Medline (PubMed), CINAHL, ScienceDirect, and Google Scholar databases (see Appendix B). The initial keywords used were "sepsis compliance," "sepsis compliance AND older adult," and "sepsis compliance AND geriatric." The timeframe reviewed was from 2004 to 2016. The timeframe was restricted because the first publication of the Surviving Sepsis Campaign's International Guidelines for severe sepsis and septic shock occurred in 2004. Additional inclusion criteria were that the study was available in English, looked at septic patients over the age of 17, and provided results on sepsis bundle compliance and outcomes. Articles were excluded if they included subjects less than 17 years of age, were not available in English, or if they did not include an abstract and full text. Additionally, the references from the cited studies were also evaluated to find other potential sources.

Initial searches revealed only two studies that addressed the geriatric or older adult and sepsis bundle compliance. To identify if any other studies were available on the geriatric and older adult septic population a second round of literature searches were conducted through the same databases. Keywords for these second round of searches included "older adult AND sepsis" and "geriatric AND sepsis" with further narrowing of results by including the terms "OR septic shock, OR severe sepsis, OR septicemia" and "AND outcomes." The second round of identified studies' abstracts were reviewed and two additional studies that addressed the older adult and sepsis compliance were added to the review. A total of 21 articles (4 of which specifically address the older adult and sepsis compliance) were included in this review and synthesized. Following the literature search, synthesis of the literature was conducted and common themes, variances, and study differences are addressed in the following sections.

Synthesis of the Literature

Study design comparisons. There was an equal number of retrospective vs prospective studies of the 21 identified through the literature search. The majority of the studies were single center, three of the studies were multicenter (two prospective, one retrospective), and three were global multicenter studies (involving two or more countries). Of the retrospective single center studies, all were observational cohorts or chart reviews. Of the prospective single center studies, the majority were observational or cohort, and only two involved a pre-intervention to post-intervention analysis. There were three systematic reviews and one expert review. No random controlled trial (RCT) study was identified.

The high number of single center studies and lack of multicenter studies available makes the data difficult to generalize. One single-center study by Scheer et al. (2016) argues that their data may be more generalizable compared to other single center studies due to the fact that all

adult patients in their medical and surgical ICUs were screened and included in the study if severe sepsis and septic shock was present. Unlike many studies, Scheer et al. (2016) states that "all patients were included with no exceptions" which may make their outcomes more realistic to actual ICU patient populations and therefore generalizable to other ICUs. This argument does have some merit as the majority of the studies excluded those with conditions such as terminal malignancy. By including all patients without exclusion, such as including those with terminal illness, the sample population in the study more accurately reflects actual patient populations in hospitals elsewhere (i.e. the results may be more generalizable) and therefore may closer reflect actual compliance and outcomes.

Several of the studies, both single center and multicenter, were conducted internationally, which makes it challenging to generalize findings to centers based in the United States. International study locations included Germany, Brazil, The Netherlands, South Korea and India (Kang et al., 2012; Nasa, Juneja, Singh, et al., 2012; Palomba et al., 2015; Scheer et al., 2016; van Zanten et al., 2014). Differences in cultural, socioeconomics, and hospital system design between countries (e.g. the U.S. has more direct Emergency Department to ICU admits compared to Europe) changes the populations included in each respective study and therefore the outcomes and generalizability of the data (Levy et al., 2012; Rhodes et al., 2015). Several of the international studies had a younger average age in their patient populations which correlated with less severe illness based on SOFA or APACHE II scores (Kang et al., 2012; Nasa, Juneja, Singh, et al., 2012). Three studies that compared global rates of compliance and mortality outcomes among different continents included a much higher percentage of patients from the US compared to Europe or other continents, making results potentially swayed (Levy et al., 2012; Levy et al., 2015; Rhodes et al., 2015). With a significantly smaller percentage of patients included from

Europe or other continents, there is a greater chance that practice and compliance reported by the studies are not reflective of actual practice and compliance in those regions, and instead reflect a mostly U.S.-centric approach.

Differences in sepsis guideline bundles. In restricting sources to those published from 2004 to 2016, there were differences in the sepsis bundles used for treatment of adult patients with sepsis and septic shock. An unexpected finding through the synthesis of these studies was that only one study evaluated compliance based on the 2012 SSC International guidelines—the most current sepsis and septic shock guidelines published in 2013 (Rhodes et al., 2015). All the remaining studies followed either the initial 2004 or updated 2008 guidelines. The 2004 and 2008 guidelines direct a 6-hour resuscitation and 24-hour management bundle, while the current guidelines split the resuscitation bundle into 3-hour and 6-hour bundles and remove the management bundle (Dellinger et al., 2013). Within each bundle, the amount, type, and frequency of interventions changed as well. However, the same two themes of improving sepsis recognition and decreasing time to intervention have remained through updates to the guidelines.

As new evidence was provided on how to further improve care and outcomes, these two themes have become the foundation for treatment of sepsis and septic shock. Some of the most recent studies, published in 2015 and 2016, follow pre-2012 SSC guidelines that were the current guidelines at the time of study conduction—which is due more to the delay in publishing study results in a peer-review journal than to study design (Levy et al., 2015; Madsen et al., 2014; Palomba et al., 2015; Scheer et al., 2016; L. R. Stoneking et al., 2015; van Zanten et al., 2014). Interestingly, one retrospective cohort study that was conducted between 2006 and 2012, but not published until 2015, mentions the current guidelines in the introduction of the study, but the

institutional severe sepsis and septic shock protocol used for treatment of patients in the study was based on older guidelines (Palomba et al., 2015).

Defining sepsis. All studies included in this review followed definitions of sepsis, severe sepsis, and septic shock that were current at the time the study commenced. The initial definition of sepsis was published in 1991 and then reevaluated and upheld in 2001 (Levy et al., 2003). The definition of sepsis relies on the presence of systemic inflammatory response syndrome (SIRS); the definition of severe sepsis relies on organ dysfunction plus SIRS; and the definition of septic shock relies on refractory hypotension in severe sepsis despite adequate fluid resuscitation (see Appendix C) (Levy et al., 2003).

In early 2016, new definitions were released that redefined sepsis terminology: "sepsis" and "septic shock" terms were maintained, but the definition of "severe sepsis" was absorbed into "sepsis" (Singer et al., 2016). It was identified that sepsis was not simply a straightforward infection with an inflammatory response—but rather it is a dysregulation, nonhomeostatic, host response due to infection, whose minute presence is associated with increased mortality (Singer et al., 2016). SIRS criteria, previously used to define sepsis, are often nonspecific, representing an appropriate, often adaptive, host response. This response does not conclusively suggest sepsis alone, but rather any condition that causes systemic inflammation—which is present in many hospitalized patients who may never develop infection or experience adverse outcomes (Singer et al., 2016). While SIRS criteria will continue to aid in the general identification of infection, sepsis identification now focuses on the recognition of life-threatening organ dysfunction using Sequential Organ Failure Assessment (SOFA) scoring ≥2 (Singer et al., 2016). Thus, the expansion of sepsis to include the presence of organ dysfunction, and the required prompt and

appropriate response to all sepsis, no longer necessitated a separate "severe sepsis" definition (Singer et al., 2016).

Due to the recent release of these definitions, no available studies have included these definitions into their study design. However, one study, Pettila et al. (2016), conducted a systematic review on control groups in recent septic shock trials and discussed the need for inclusion of the newest definitions into future research design. While the statement by Pettila et al. (2016) speaks towards RCTs, the same expectation should be held for any study that focuses on sepsis and outcomes—including future prospective observational and cohort studies.

Actual bundle compliance and outcomes. The most recent study that looked at global compliance and outcomes associated with the current SSC guidelines found that compliance with the 3-hour bundle was 19% and compliance with the 6-hour bundle was 36% (Rhodes et al., 2015). Overall hospital mortality was 28%, and compliance was independently associated with improvements in hospital mortality for both of the bundles (Rhodes et al., 2015). Specifically, in North America, bundle compliant hospital mortality was 17.8% and bundle noncompliant hospital mortality was 27.2% (Rhodes et al., 2015). Previous studies that evaluated compliance with the older guidelines have also reported poor actual compliance, with total compliance ranging from 12% to 21.6% and mortality rates similar to those found by Rhodes et al. (2015) (Coba et al., 2011; Levy et al., 2015). According to two reviews, actual compliance differs from control group compliance found in many of the recent large septic shock treatment RCTs, due to the fact that the control groups followed institutional protocol or current guidelines and did not report bundle compliance rates or reported compliance rates around 50% (Nguyen et al., 2016; Pettila et al., 2016). Hence, because these studies showed a compliance rate of less than 50% they do not seem to accurately reflect actual practice. Regardless of which sepsis guideline was

used, actual compliance remains poor thus negatively affecting mortality rates in health systems across the world.

The effect of increased compliance on outcomes. Even though the majority of the studies follow earlier versions of the SSC guidelines for severe sepsis and septic shock, all studies that evaluated outcomes based on the compliance reported improvement in hospital mortality (Castellanos-Ortega et al., 2011; Cronshaw, Daniels, Bleetman, Joynes, & Sheils, 2011; El Solh et al., 2008; Kang et al., 2012; Levy et al., 2012; Levy et al., 2015; Madsen et al., 2014; Nasa, Juneja, Singh, et al., 2012; Pestana et al., 2010; Rhodes et al., 2015; Scheer et al., 2016; L. R. Stoneking et al., 2015; van Zanten et al., 2014). This may be related to several factors. First, by following a bundle or institutional protocol based on the SSC bundle, awareness improves. Second, following a bundle or protocol ensures completion of interventions that as a whole will treat the pathophysiological cascade of sepsis.

Levy et al. (2015) showed that increased compliance decreases hospital mortality and LOS, and a longer duration of compliance with the sepsis bundles further decreased hospital mortality and LOS. Another study found that a longer duration of compliance reduced hospital mortality by 16.7% over 3.5 years (van Zanten et al., 2014). Even those patients who did not receive all the components of each bundle (but received a majority of them) saw improvement in hospital mortality (Castellanos-Ortega et al., 2011). This was also found in a study that evaluated the completion of bundle components within 18 hours, but not within the designated 6-hour timeframe (of the 2008 guidelines) (Coba et al., 2011). In regards to the current guidelines, Rhodes et al. (2015) identified that globally, sites with improved compliance to the current guideline bundles significantly decreased hospital mortality.

While the majority of the studies focused on mortality as the primary outcome measure, two studies associated decreased hospital mortality with improved compliance, but noticed there was no change in LOS between high compliance and low compliance (Castellanos-Ortega et al., 2011; Kang et al., 2012). Two other studies found that high compliance is associated with a decrease in hospital mortality and decreased LOS (Levy et al., 2015; Scheer et al., 2016). While there are conflicting findings on LOS outcomes, all studies noted that decreased mortality was most significant when compliance with all of the guideline bundles were followed (Castellanos-Ortega et al., 2011; Cronshaw et al., 2011; El Solh et al., 2008; Kang et al., 2012; Levy et al., 2012; Levy et al., 2015; Madsen et al., 2014; Nasa, Juneja, Singh, et al., 2012; Pestana et al., 2010; Rhodes et al., 2015; Scheer et al., 2016; L. R. Stoneking et al., 2015; van Zanten et al., 2014). The mortality findings were significantly reduced as the compliance percentage decreased (Castellanos-Ortega et al., 2011; Coba et al., 2011; Levy et al., 2015; Rhodes et al., 2015). One study by Scheer et al. (2016) reported that completing the individual bundle components of administering antibiotics within one hour was an independent factor in decreasing mortality rates. But a systematic review evaluating the impact of timing of antibiotics on outcomes in sepsis and septic shock for 16,1788 patients found that antibiotic administration within one hour of presentation is not associated with significant improvement in mortality (Sterling, Miller, Pryor, Puskarich, & Jones, 2015). No other single component of the SSC guidelines bundles has been found to independently reduce mortality (Sterling et al., 2015). This reinforces that the improvement in mortality is not measured by one single intervention at one point in time, but rather improvement in outcomes comes from completion of all bundle requirements over time.

Many of the studies in this review included some varying degree of quality improvement or education to improve outcomes leading up to or paralleling the study period (El Solh et al.,

2008; Kang et al., 2012; Scheer et al., 2016; van Zanten et al., 2014). While this may alter results, showing inflated improvement of outcomes, it reinforces that change is not likely to occur without increased knowledge and awareness. A systematic review found that quality improvement projects and or education of staff overall significantly improved compliance of sepsis bundles and decreased mortality—something to consider for any institution looking to improve compliance and outcomes (Damiani et al., 2015).

Defining and inclusion of age. An ongoing issue is that there is no standardized definition of what is considered "older adult" or "elderly" or "geriatric." The majority of the studies define these terms to be those over the age of 65 years, though several considered those over the age of 60 years to be in this "older adult" category. Still only one study referred to any organization's definition of what is considered an "older adult," basing their definition on the World Health Organization's definition of elderly—i.e. those adults ≥65 years of age (Palomba et al., 2015). Analysis of age also varied through the studies, where some studies evaluated those ≥65 years to those <65 years, while others evaluated a younger adult to two groups of older adults (old and very old adult) or included several age ranges of 18 to 60, 60-80, and >80 (Castellanos-Ortega et al., 2011; Coba et al., 2011; Cronshaw et al., 2011; El Solh et al., 2008; Kang et al., 2012; Martin et al., 2006; Nasa, Juneja, Singh, et al., 2012; Palomba et al., 2015; Pestana et al., 2010; Rhodes et al., 2015; Scheer et al., 2016; L. R. Stoneking et al., 2015; van Zanten et al., 2014). Still some studies did not include a definition of age, report patient ages, or include age in the data analysis (Kramer, Cooke, Liu, Miller, & Iwashyna, 2015; Levy et al., 2015; Pettila et al., 2016; Sterling et al., 2015).

When age was reported, there were varying values of the average age. One study in the U.S. examined the hospital discharge records of 10,422,301 septic adult patients over a 24-year

period and found that the mean age of those with sepsis significantly increased over time from 64.1 to 68.2 years of age, while the median age increased from 67 years to 71 years of age (Martin et al., 2006). The majority of the studies looked specifically at severe sepsis and septic shock and not sepsis (which were the current terms used at the time of the study), but had a much younger average age of their patient populations than what Martin et al. (2006) identified. The average age ranged from 52.5 to 65 to 80 depending on study (Cronshaw et al., 2011; Madsen et al., 2014; Palomba et al., 2015; Pestana et al., 2010; Scheer et al., 2016). Those studies that included a younger average age in their respective studies often found less severe illness and improved outcomes (Kang et al., 2012; Nasa, Juneja, Singh, et al., 2012). Since both older age and severity of illness on presentation are risk factors for mortality, it follows that the absence of these would ultimately improve mortality outcomes—which then explains why studies with an older average age of patients or higher severity of illness had worse outcomes.

One study by Palomba et al. (2015) that compared the outcomes between elderly (≥65 years of age) to nonelderly (<65 years of age), had a median age of 80 years in the elderly group and 51 years in the nonelderly group, but did not include any patients under the age of 50 or between the age of 60-72 in the study—meaning that a large age range of older adult patients was not included in the study evaluating outcomes of the older adult with sepsis. Given that the available literature has gaps in the age spectrum of patients (e.g. not including patients under the age of 50 years, or patients between the ages of 60 and 72), it becomes clear that there is a need to examine the outcomes of septic patients who span the entirety of ages in the older adult spectrum.

It has been well documented in the literature that older age (≥65 years) is an independent risk factor for acquiring sepsis and also mortality from sepsis (Clifford et al., 2016; De Gaudio et

al., 2009; Englert & Ross, 2015; Girard & Ely, 2007; Martin et al., 2006; Nasa, Juneja, & Singh, 2012). A prospective single center study in Germany, whose average patient age was 65, identified that their subjects had a higher mortality rate compared to other studies, even after improved compliance through a quality improvement project (Scheer et al., 2016). Scheer et al. (2016) argues that many other studies included a younger patient population in their studies—which makes data comparison challenging given that age is an independent predictor of mortality (Scheer et al., 2016). Future studies, when possible, should evaluate outcomes based on standardized age groupings to improve the utility of their findings.

Compliance and outcomes of the older adult with sepsis. The pathophysiology of the older adult predisposes the patient to infection and sepsis progression (Clifford et al., 2016; De Gaudio et al., 2009; Englert & Ross, 2015; Girard & Ely, 2007; Nasa, Juneja, & Singh, 2012). Dysfunction of the innate and adaptive immune system (i.e. immunosenescence), increased coagulopathy, increased occurrence of institutionalization, malnutrition, and comorbidities such as chronic liver failure, diabetes, and chronic obstructive lung disease all predispose the older adult to develop an infection and inability to fight an infection, leading to sepsis progression. Furthermore, nonspecific presentation in the older adult patient is more frequent and predisposes this population to having their symptoms be overlooked until the patient has progressed further into sepsis or septic shock (Clifford et al., 2016; De Gaudio et al., 2009; Englert & Ross, 2015; Girard & Ely, 2007; Nasa, Juneja, & Singh, 2012). Also, due to increased occurrences of one or more chronic comorbidities, the older adult may not receive the same sepsis bundle compliance that a younger adult would (Clifford et al., 2016; De Gaudio et al., 2009; Englert & Ross, 2015; Girard & Ely, 2007; Nasa, Juneja, & Singh, 2012). It is commonly reported that septic older adults are under-resuscitated due to concerns of exposing or worsening heart failure or chronic

renal dysfunction (Clifford et al., 2016; De Gaudio et al., 2009; Englert & Ross, 2015; Girard & Ely, 2007; Girard et al., 2005). While many reviews speculate that compliance in older adult patients is worse than with younger patients, the actual compliance percentage with sepsis bundles specific to the older adult was not reported in any study. Madsen et al. (2014) looked primarily at sepsis bundle compliance between genders, but also identified that age was not associated with bundle compliance. Several studies did discuss findings that suggested differences in what and to what degree the sepsis bundles were completed in the older adult (El Solh et al., 2008; L. R. Stoneking et al., 2015). A retrospective cohort study conducted by Stoneking et al. (2015) found that older adults were more often in the "recognized group" (determined by evaluating provider documentation) of having sepsis. It was also identified that the "recognized group" received more fluid and a shorter time duration to antibiotics compared to the "unrecognized group" (L. R. Stoneking et al., 2015).

Yet more studies argue that older adults often receive poor compliance to the sepsis bundles. One study found that a younger age was more common in the group that received on-time compliance to the bundles (Castellanos-Ortega et al., 2011). Another study found that older adults received less fluids when compared to younger adults (Palomba et al., 2015). A prospective study by El Solh et al. (2008) looked at the older adult population outcomes following a sepsis protocol based on the SSC 2004 guidelines compared to older adult outcomes in a historical control group and found improvement in the amount of fluid resuscitation administered and decreased use of norepinephrine and vasopressor duration compared to the historical control group—suggesting that older adults were not receiving full compliance to the guideline bundles in the control group.

Though there is disagreement between higher or lower compliance to the sepsis guideline bundles in the older adult compared to the younger adult, the majority of the studies discuss that increased age was associated with an increased risk of mortality, even if initial analysis was found to show no differences in mortality (El Solh et al., 2008; Martin et al., 2006; Nasa, Juneja, Singh, et al., 2012; Palomba et al., 2015; Pestana et al., 2010; Scheer et al., 2016). Palomba et al. (2015) found that there was no difference in hospital mortality and mortality at day-28 between adults and older adults, but after a "multivariable logistic regression model, age was associated with increased risk of hospital mortality in older adult patients with severe sepsis or septic shock." Martin et al. (2006) identified, based on hospital discharge reports of 10,422,301 patients, that those over the age of 65 were 13.1 times more likely to develop sepsis and were 1.56 times more likely to die, when compared to those <65 years of age. With so few studies reporting outcome differences between older and younger adults and no studies reporting the compliance rates of SSC guideline bundles, there is a glaring need for future studies to evaluate differences based on the population.

Summary of Literature Review

Our knowledge of sepsis and how to treat it is constantly evolving. Studies continually re-evaluate available data and postulate on new information, and both are used to improve international guidelines. While these are important advancements, comparing compliance and outcomes between studies utilizing differing guidelines is very challenging. Across the studies evaluated in this review, a unanimous consensus emerged that showed a clear correlation between increased compliance and improved outcomes of decreased mortality and decreased hospital length of stay (Castellanos-Ortega et al., 2011; Cronshaw et al., 2011; El Solh et al., 2008; Kang et al., 2012; Levy et al., 2012; Levy et al., 2015; Madsen et al., 2014; Nasa, Juneja,

Singh, et al., 2012; Pestana et al., 2010; Rhodes et al., 2015; Scheer et al., 2016; L. R. Stoneking et al., 2015; van Zanten et al., 2014). While only one study evaluated compliance rates and outcomes with the most current guidelines (Rhodes et al., 2015), the message is consistent—improved compliance improves mortality. Even though sepsis outcomes have improved over the years, health systems are still challenged by poor actual compliance and high mortality from sepsis—regardless of the guideline version used (Levy et al., 2012; Levy et al., 2015; Martin et al., 2006; Rhodes et al., 2015).

Data shows that advanced age is a clear independent risk factor for acquiring sepsis (El Solh et al., 2008; Martin et al., 2006; Nasa, Juneja, Singh, et al., 2012; Palomba et al., 2015; Pestana et al., 2010; Scheer et al., 2016). The majority of studies that evaluate sepsis compliance found a mean age of ≥65 years, further confirming that older age is a definite risk factor for sepsis. Given the scarcity of direct studies evaluating compliance between the adult and older adult, further research is needed to study this population so that health systems can become more aware of how compliance may differ. To date, no studies exist that evaluate the overall compliance rate in the septic older adult, much less researching what types of noncompliance contribute the most to poor outcomes and mortality (El Solh et al., 2008; Madsen et al., 2014; Palomba et al., 2015; L. R. Stoneking et al., 2015). Only then can key recommendations be identified to help improve outcomes for adults and older adults with sepsis and septic shock.

Purpose of the Study

The purpose of this study is to determine Oregon Health and Science University's (OHSU) institutional compliance with the SSC guideline bundles for patients admitted through the Emergency Department with sepsis, to determine how compliance differs between adult and older adult patients for quality improvement. The primary question for this project is to identify

if there is a difference in OHSU's institutional overall SSC compliance rates between older adults and adults with sepsis.

Project Methods

This study was approved and informed consent waived by the Oregon Health and Science University Institutional Review Board.

Definitions

Sepsis definitions for this study followed those set by the 2001 International Sepsis Definition Conference which were recognized as the current definitions in the 2012 SSC International Sepsis Guidelines for Severe Sepsis and Septic Shock (Dellinger et al., 2013; Levy et al., 2003). These define severe sepsis to be "suspected or confirmed infection, with present SIRS response, and organ dysfunction," and septic shock to be "severe sepsis with a lactate >4mmol/L or refractory hypotension unresponsive to initial fluid resuscitation" (Dellinger et al., 2013; Levy et al., 2003). While it is recognized that the updated sepsis definitions by Singer et al. (2016) and updated SSC guidelines by Rhodes et al. (2017) were released before data collection commenced, both updates were released after patient encounters had occurred, and thus the older definitions and the 2012 guidelines were considered to be the current standards at the time of patient encounters. Terminology and other definitions for sepsis related care and data collection not defined by the international definitions or guidelines are outlined in Appendix D.

Setting

The project examined compliance to the SSC guidelines of all adult patients (age ≥18) who were admitted from OHSU's ED to an OHSU adult hospital unit between October 1, 2015 and September 30, 2016 with the diagnosis of severe sepsis or septic shock.

Population

Study size. The study screened 332 adult patients. Subjects included in the study were required to have been admitted to OHSU through the ED with a diagnosis of severe sepsis or septic shock (based on ICD-10 coding) between October 1, 2015 and September 30, 2016. Electronic Health Records (EHR) for the identified patients were screened to determine if inclusion criteria were met. Those patients whose records qualified for study inclusion, based on the criteria below, had their EHRs evaluated further to determine compliance to the SSC guidelines.

Inclusion and exclusion criteria. Inclusion criteria for the study included all patients ≥18 years of age who were admitted from the OHSU ED to either an ICU or acute care unit with an admission diagnosis of severe sepsis or septic shock, and who either had documentation of severe sepsis or septic shock or clinical confirmation (present SIRS criteria, organ dysfunction, and suspected or confirmed infection).

Exclusion criteria included:

1. Patients who refused sepsis related-care during the first 24 hours of their ED and hospital admission. The reasoning for this is that patients who refused sepsis related care during the first 24 hours would not meet the guidelines as a result of patient choice and therefore are not an accurate reflection of compliance to the SSC Guidelines.
2. Patients with a code status of "Comfort Measures Only" (CMO) prior to hospital arrival or within the first 3 hours of severe sepsis presentation or within the first 6 hours of septic shock presentation. The reasoning for this is that patients who have a code status of CMO, request that interventions focus on comfort for the patient and not artificially

prolonging life or cause further suffering—therefore SSC guidelines would not be initiated or continued since they do not focus on patient comfort.

3. Patients who were directly admitted from a clinic or transferred from an outside hospital. The reason for this is that it is not possible to track when sepsis presentation began or what treatment was initiated at another facility before patients arrive at OHSU, and therefore this is not an accurate representation of OHSU's compliance.
4. Patients who were determined to be pregnant during time of severe sepsis or septic shock presentation. The reason for this is that pregnant women with sepsis are physiologically unique and differ in regards to the care required from that of the non-pregnant adult, and such care is not outlined in the SSC Guidelines.
5. Patients who expired within 3 hours of severe sepsis presentation or within 6 hours of septic shock presentation. The reason for this is that those patients who expire within the first 3 hours of severe sepsis presentation or the first 6 hours of septic shock presentation have a profound physiological progression of sepsis which does not necessarily reflect the providers' compliance to the time requirements in the SSC guidelines.

Recruitment methods. All patients age ≥18 who were admitted through the ED for severe sepsis or septic shock were screened for eligibility through EHR and Vizient™ query reports. These reports identify patients who were diagnosed with severe sepsis or septic shock in the Emergency Department based on coding/billing information. Then a member of the research group screened each chart for eligibility and inclusion in the study, based on EHR chart review. There was no direct patient recruiting for this retrospective analysis.

Data and participant protection. To maintain privacy and confidentiality, all records and recorded data were kept in a locked, password file in OHSU's X drive, which resides behind

OHSU's firewall. All data was recorded using an electronic form and no paper forms were used for this study. Only members of the research team with IRB-approved permissions were allowed access to the file.

Outcome Evaluation

Primary endpoint. The primary endpoint was to identify the difference in SSC compliance rates between adults and older adults with sepsis.

Processes and procedures. All patients whose EHR contains documentation of severe sepsis or septic shock on admission to the Emergency Department, and whose admission occurred between October 1, 2015 and September 30, 2016, were screened for inclusion in the study. Vizient™ query reports identified eligible patients who had severe sepsis or septic shock coding present on admission during the determined study date range. Eligible patients had their EHRs reviewed to determine if inclusion and exclusion criteria were met. Those patients confirmed to meet the study criteria underwent further chart review to determine adherence to the sepsis bundles (see Appendix B). Data was collected by a single data collector, and stored electronically in a Microsoft Excel file (see Table 1). The spreadsheet was designed with embedded formulas that were based on the 2012 SSC sepsis guidelines for clinical determination of severe sepsis and septic shock presentation, as well as the time requirements for each bundle element. This ensured that severe sepsis or septic shock time zero was accurately calculated and if all bundle elements were completed within the correct time. The use of Excel formulas was employed to ensure that values were uniformly calculated, and to remove the potential for human calculation error. Chiefly, Excel formulas were developed to calculate whether patient care was in compliance with the 3-hour and 6-hour bundle elements, and these formulas were based on the 2012 SSC sepsis guidelines. Each patient had specific cells in the Excel spreadsheet that

calculated whether the patient received care that was in compliance with the SSC guideline bundles: the formula displayed “yes” in the cell to indicate that the patient received compliant care, the formula displayed “no” in the cell to indicate that the patient did not receive complaint care, and the formula displayed “N/A” in the cell if the patient did not qualify to receive the 6-hour bundle care. After data collection, an Excel formula was used to convert a “yes” into a value of 1, convert a “N/A” into a value of 1 (only for entire guideline compliance), and convert a “no” into a value of 0 for the purposes of further statistical analysis.

Table 1:

Data Collection Form Outline

Patient/ Subject
MRN
Date/ Time of Encounter
Age (years)
Gender
Height (cm)
Weight (kg)
BMI
Infection Documentation
Provider Documentation of Severe Sepsis (Yes/ No)
Date/Time of Provider Documentation of Severe Sepsis
Documentation of Suspected or Confirmed Source of Infection (Yes/ No)
Date/ Time of Suspected or Confirmed Source of Infection
SIRS Criteria
Temperature Value (<36 or >38c)
Temperature Date/Time (MM/DD/YY HH:MM)
Heart Rate Value (>90bpm)
Heart Rate Date/Time
Respirations Value (>20 per min)
Respiration Date/Time
WBC Value (<4,000 or >12,000)
WBC Date/Time

Table 1 Continued

SIRS Criteria Met (2 or more of the above) Yes/ No
SIRS Criteria Met Date/ Time
Organ Dysfunction
Systolic Blood Pressure Value (SBP <90)
Systolic BP Date/ Time
Mean Arterial Pressure Value (MAP <65)
MAP Date/ Time
Creatinine Value (SCr >2)
Creatinine Date/ Time
Bilirubin Value (Tbili >2mg/dL)
Bilirubin Date/ Time
Platelet Count Value (Plt <100,000)
Platelet Count Date/ Time
INR Value (INR >1.5)
INR Date/ Time
aPTT Value (aPTT >60sec)
aPTT Date/ Time
Lactate Value (Lact >2mmol/L)
Lactate Date/ Time
Organ Dysfunction Present (Yes/ No)
Date/ Time of Organ Dysfunction Presentation
Severe Sepsis Present? (Yes/ No)
Date/ Time of Severe Sepsis Presentation
Have the below been completed within three hours of:
Initial lactate level measured (Yes/ No)
Date/ Time of Initial Lactate Level
Blood Cultures obtained before abx administration (Yes/ No)
Date/ Time of blood Cultures
IV broad spectrum abx ordered by provider (Yes/ No)
Date/ Time of ABX order
IV ABX given (Yes/ No)
Date/ Time of ABX given
IV Crystalloid Administered Completely in 3 hours (Yes/ No)
IV Crystalloid administered amount value (mL)
Date/ Time of IV Crystalloid completion
Within 6 hours of Time Zero

Table 1 Continued

Was repeat Lactate Level Check (If initial lactate level >2) (YES/ No)
Repeat Lactate Level Value
Repeat Lactate Date/ Time
Was Complete 3-hour Bundle Met (Yes/ No)
Reason Why Bundle Was Not Met (Drop down List, or write below in "Other")
Other Reason not listed above
Septic Shock
Septic Shock Documented by Provider (Yes/ No)
Date/ Time of septic shock documentation
Persistent tissue hypoperfusion
Systolic BP Value <90 1 hour after fluid resuscitation completion (Yes/ No)
Date/ Time of SBP <90 1 hour after fluid resuscitation completed
MAP Value <65 1 hour after fluid resuscitation completion (Yes/ No)
Date/ Time of MAP <65 1 hour after fluid resuscitation completed
SBP decreased >40 points 1 hour after fluid resuscitation completion (Yes/ No)
Date/ Time of SBP decrease >40 points 1 hour after fluid resuscitation complete
Is persistent tissue hypoperfusion present (Yes/No)
Date/ Time of Persistent tissue hypoperfusion
Lactate
Lactate Level >4 (Yes/ No)
Date/ Time of Lactate Level >4
Septic Shock Present (Yes/ No)
Date/ Time of Septic Shock Presentation (earliest date/ time of Septic Shock criteria)
Within 6 hours of Time Zero for Septic Shock
Vasopressor Ordered for persistent hypotension by provider (Yes/ No)
Vasopressor Ordered for persistent hypotension by provider (Date/ Time)
Date/ Time Vasopressor started
Was Vasopressor Started within 6 hours of Time Zero if Persistent Hypotension Present (Yes/ No)
Was a Focused exam documented by provider with T, HR, RR, BP, Cardio-pulm exam, and skin exam (Yes/ No)
Date/ Time a Focused exam was performed
Were two assessments performed (CVP, SCVO2, Bedside Cardio US, Dynamic assessment of Passive leg raise or fluid challenge) (Yes/ No)
Type of assessment performed #1 (Drop down list)

Table 1 Continued

Type of assessment performed #2 (Drop down list)
Date/ Time of Assessment
Was repeat Lactate Level Checked (If initial lactate level >2) (YES/ No)
Repeat Lactate Level Value
Repeat Lactate Date/ Time
Was 6-hour Bundle Met (Yes/ No)
Reason Why Bundle Was Not Met (Drop down with common reasons and other for free form)
Other Reason Not Specified
Additional Info
Admission Unit Location from ED
Date/ Time of Arrival to Unit
Direct ICU admission (Yes/ No)
Discharge Info
Hospital LOS (Days)
ICU LOS (Days; if applicable)
Discharge Disposition (drop down list)
Hospital Mortality (Yes/ No)
Concurrent Heart Failure Diagnosis (Yes/ No)
Concurrent Renal Failure Diagnosis (Yes/ No)

Note. Grey content in table signifies calculated response based on embedded Microsoft Excel formulas.

Data analysis. The primary analysis evaluated the difference in overall bundle compliance between the adult and older adult. A two-tailed t-test with unequal variance was used to compare the difference between the two groups with a probability level of <0.05 to determine significance. Descriptive statistics were used to summarize the findings on patient characteristics, which included mean, Median (Mdn), and Standard Deviations (SD) of the characteristics.

Cost. The cost of this project included the time spent by Quality Department staff providing Vizient™ query reports on eligible patients for study screening and time spent by study members on this project.

Implementation of Project

Results

A total of 332 patients were initially screened for inclusion in the study. Seventy-two were found to not have clinical findings or provider documentation of severe sepsis or septic shock present, and hence did not meet study inclusion criteria. An additional 19 patients were excluded for other reasons: 10 received initial sepsis related care, such as antibiotics, at an outside hospital or clinic; six refused sepsis related care that effected the ability to adhere to the guidelines; two had a code status of "comfort care measures only" that effected the ability to adhere to the guidelines; and one had missing vital signs and laboratory data (see Figure 1). In the end, this analysis included 241 patients who had provider documentation or clinical findings of severe sepsis or septic shock on admission from the ED to the hospital.

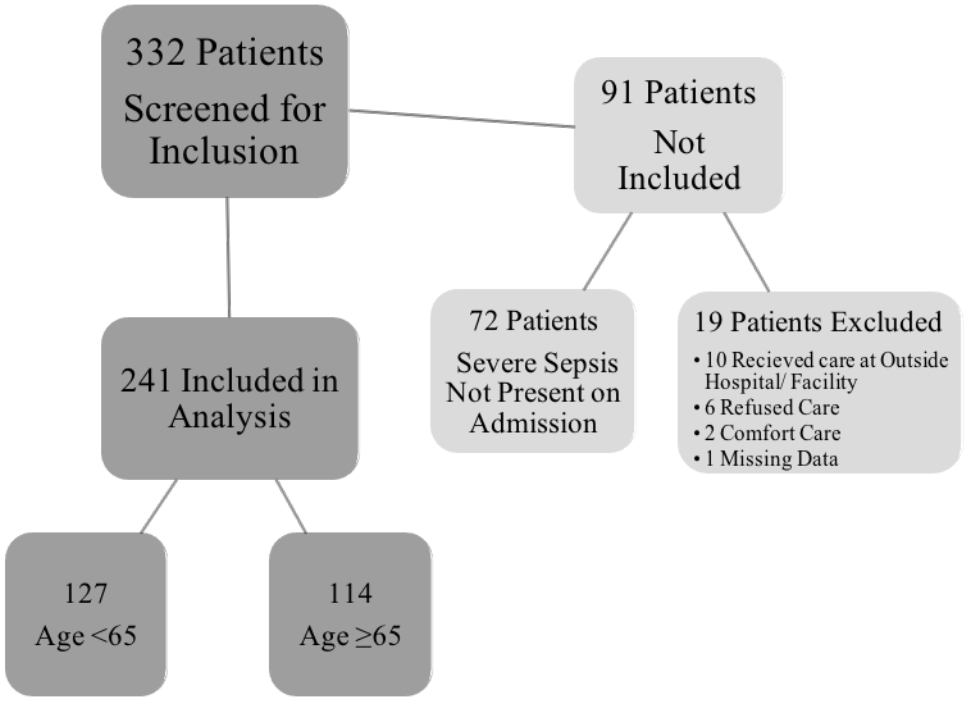


Figure 1. Process of patient selection.

Patients. Of the 241 patients included in the analysis, adult patients (<65 years) accounted for 52.7% (127/241) and older adult patients (≥65 years) accounted for 47.3% (114/241; see Table 2). The mean age for adult patients was 48.6 (SD = 12.59, Mdn = 51) and older adult patients was 75.1 (SD = 8.42, Mdn = 73; see Table 2). Male patients accounted for 55.19% (133/241) and female patients accounted for 44.81% (108/241). For adult patients, 22.41% (54/241) were female and 30.29% (73/241) were male (see Figure 2). For older adult patients, 22.41% (54/241) were female, 24.90% (60/241) were male (see Figure 2).

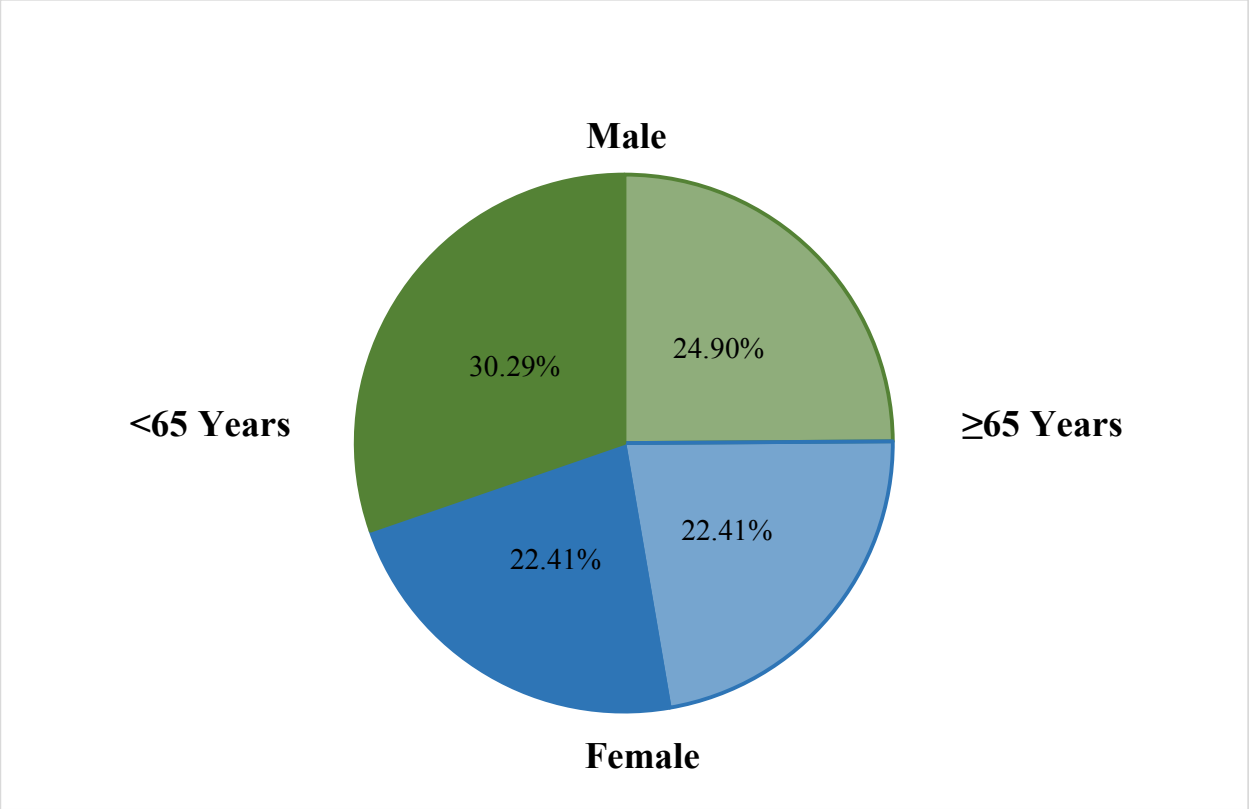


Figure 2. Distribution of age among gender

Compliance to the SSC guidelines. Adult patients were more likely to receive overall compliant care (combined 3-hour and, if applicable, 6-hour care) to the SSC sepsis guidelines compared to older adult patients (39.37% versus 27.19%, p = .04486; see Figure 3). There was no difference in compliance between adult and older adult patients when measured solely against

Table 2:

Study Demographics

Characteristics	<65 Years 127 (52.70%) n (%)	≥65 Years 114 (47.30%) n (%)	Total 241
Male n (%)	73 (30.29%)	60 (24.90%)	133 (55.19%)
Female n (%)	54 (22.41%)	54 (22.41%)	108 (44.81%)
Age Mean (Mdn, SD)	48.64 (51.00, 21.59)	75.14 (73.00, 8.42)	61.17 (64.00, 17.10)
BMI Mean (Mdn, SD)	29.37 (26.29, 11.38)	27.89 (26.60, 10.11)	28.67 (26.60, 9.79)

the 3-hour bundle (52.76% versus 45.61%, p = .27006; see Figure 3). There was also no difference in compliance between adult and older adult patients when measured solely against the 6-hour bundle (60.64% versus 50.00%, p = .15095; see Figure 3). Across the entire study population (adults and older adults combined), overall compliance to the SSC guidelines was 33.61% (81/241; see Figure 4). Similarly, compliance across the entire study population to the 3-hour bundle was 49.38% (119/241), and compliance to the 6-hour bundle was 55.49% (101/182; see Figure 4).

Discussion

This single-center retrospective chart review demonstrated that overall compliance (i.e. compliance with the 3-hour and, if applicable, the 6-hour bundle) to the SSC sepsis guidelines was greater in adult patients (at 39.37%) than in older adult patients (at 27.19%; see Figure 3). However, there was no difference in guideline compliance to each individual time-bundle between adults and older adults (see Figure 3). These findings reflect the current literature consensus that lower guideline compliance occurs more often in the older adult (Castellanos-Ortega et al., 2011; Clifford et al., 2016; De Gaudio et al., 2009; El Solh et al., 2008; Nasa, Juneja, & Singh, 2012; Palomba et al., 2015). While no previously-identified study reported overall compliance rates to the entire 2012 SSC guidelines nor overall compliance rates based on age, studies using earlier versions of the SSC guidelines did report commonly missed bundle elements—indicating that the rate of overall compliance in the older adult is less than in the adult patient (Castellanos-Ortega et al., 2011; Clifford et al., 2016; De Gaudio et al., 2009; El Solh et al., 2008; Palomba et al., 2015). Earlier studies that evaluated compliance (with older versions of the SSC guidelines) identified that poor compliance was often a result of delayed recognition by providers or under-resuscitation of

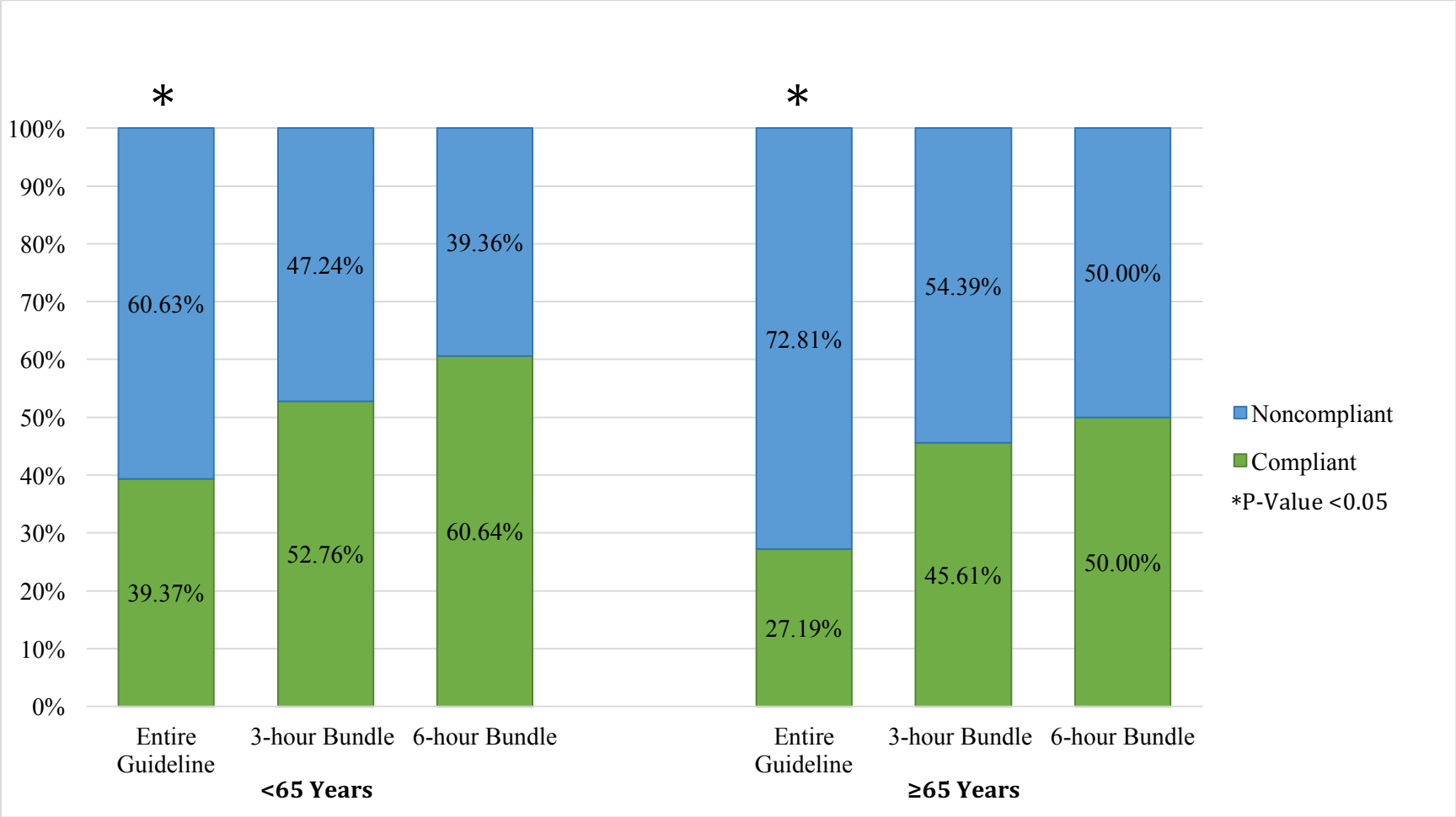


Figure 3. Age difference with compliance.

crystalloid due to concerns of exacerbating or exposing heart failure and chronic kidney disease (Clifford et al., 2016; De Gaudio et al., 2009; Englert & Ross, 2015; Girard & Ely, 2007; Palomba et al., 2015).

Previous studies that included an older adult population had varying average ages for their analyzed populations. Some studies had an average patient age in the 80s, while other studies reported the average age in the 60s, yet still other studies were missing those aged 60 to 72 completely (Palomba et al., 2015; Pestana et al., 2010; Scheer et al., 2016). This study had a balanced representation of all adults (based on the means and standard deviations) that evaluated a more complete age range in both groups.

While recent studies have reported on care compliance for patients who developed sepsis during any point of their hospital stay, this study only analyzed patients who were admitted with sepsis through the ED. It does not evaluate patients who developed sepsis following admission

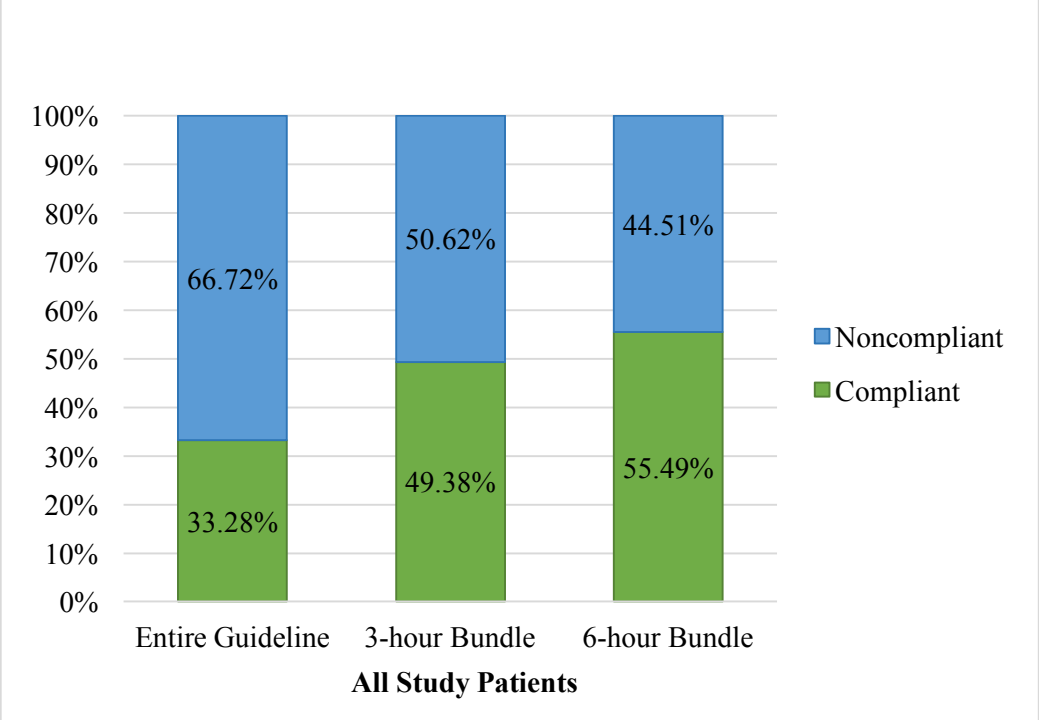


Figure 4. Compliance of all study patients (combined <65 and ≥65 age groups)

during their hospital stay (Rhodes et al., 2015). Regardless, the findings of this study may provide an idea of the potential rate of actual hospital compliance with the entire guidelines since several studies have found that the most common location for adult and older adult sepsis diagnosis was in the ED (Palomba et al., 2015; Rhodes et al., 2015).

The findings of this study can also provide insight into how OHSU may compare globally as an institution with regard to compliance to the 3-hour bundle and the 6-hour bundle. Rhodes et al. (2015) identified that global compliance was 19% for the 3-hour bundle, and 36% for the 6-hour bundle. Our findings suggest that OHSU's compliance to the 2012 SSC guidelines was above the global average: independent 3-hour bundle compliance was 49.38% (compared to the global rate of 19%), and independent 6-hour bundle compliance was 55.49% (compared to the global rate of 36%). There is no study identified that reports overall compliance of the entire 2012 SSC guidelines, and so we cannot compare OHSU's compliance to a global rate.

Compliance with the 2012 guidelines 3-hour bundle has been associated with a 40% reduction in the odds of in-hospital mortality, and compliance with the 6-hour bundle has been associated with a 36% reduction in the odds of in-hospital mortality (Rhodes et al., 2015). Further studies have shown that increasing compliance by 10% can decrease mortality by 3 to 5%; similarly, maintaining higher compliance over 3.5 years can decrease mortality by 16.7% (Levy et al., 2015; van Zanten et al., 2014). While recent studies have shown that improving compliance is associated with decreased hospital LOS and decreased mortality, it has also been shown that improving compliance to the guidelines can also improve the cost savings of each patient diagnosed with sepsis by $1,571 (Leisman et al., 2017; Levy et al., 2012; Levy et al., 2015; Rhodes et al., 2015; L. Stoneking et al., 2011; van Zanten et al., 2014). Leisman et al. (2017) provided a conservative estimate that $1.5 billion could be saved each year in the United

States by providing compliant sepsis care. The positive outcomes that arise from compliance to the SSC guidelines is trifold—decreasing short-term and long-term mortality, decreasing hospital LOS, and improving cost savings.

While there is no consensus on what specific mechanisms result in positive outcomes, recent studies suggest that improved outcomes of hospital LOS and decreased mortality may be due to specific individual bundle elements (e.g. antibiotics within one hour as the driver of improved outcomes). Yet another large meta-analysis did not find a significant difference in mortality when antibiotic administration was within one hour (Ferrer et al., 2014; Kalil, Johnson, Lisco, & Sun, 2017; Sterling et al., 2015). Other recent studies suggest that certain individual bundles may be a driver of negative outcomes and actually increase the risk of mortality, e.g. fluid resuscitation leading to volume overload (Kalil et al., 2017; Sakr et al., 2017). These studies did not associate initial resuscitation with increased mortality risks, and instead suggest that the increased risk results from worsening volume overload several days after initial sepsis intervention. Also, these studies are based on previous versions of SSC sepsis guidelines utilizing 6-hour and 24-hour bundles with different fluid, colloid, and blood product requirements—often resulting in larger volume administration which may not accurately reflect fluid resuscitation recommended by the 2012 guidelines (Dellinger et al., 2013; Kalil et al., 2017). The conflicting evidence of whether a bundle element is beneficial or detrimental to patient outcomes reinforces the notion that improvement in mortality comes from the completion of all bundle requirements that manage and treat the cascade of effects from sepsis. One study saw a decrease in the risk of mortality by 40% when compliance to the 2012 guidelines was maintained, and another study saw a decrease in mortality by 3-5% after improving compliance by 10% (Levy et al., 2015; Rhodes et al., 2015). More research is needed to further clarify the

benefits of partial versus complete bundle element compliance, which should include those admitted to acute care units as well as ICU patients.

Future Implications

Further evaluation of the data collected in this study is needed to evaluate where noncompliance occurs in each age group and what consequences may subsequently arise (e.g. hospital length of stay and mortality). This will help determine where compliance fallout occurs in each respected age group, which can then help determine where quality improvement may be most beneficial. Large prospective studies are also needed to prove how certain bundle elements, compliance, age, and other factors may increase or decrease the risk of mortality in patients with sepsis.

Limitations

The study had several limitations. The patients screened were identified based on having a diagnosis of severe sepsis or septic shock being present on admission, as identified through the Vizient™ application. While the included study population represents patients with sepsis admitted through the ED at this institution, this study does not capture those who may have been under-diagnosed with sepsis instead of severe sepsis. A number of patients identified by Vizient™ query reports were not included in the study because a clinical presentation or documentation of severe sepsis was not met. This does not mean these patients were necessarily wrongfully coded, but present or suspected infection may have not progressed to severe sepsis until later in their hospital stay.

Also, during the study, new definitions and guidelines were released (Rhodes et al., 2017; Singer et al., 2016). While best-practice care should be provided using the most up-to-date evidence, this study utilized the 2012 SSC guidelines and definitions as a rubric since they were

the current standards at the time of patient care. Hence, this study identified severe sepsis through the combination of suspected or confirmed infection, present SIRS criteria, and organ dysfunction. While not formally analyzed, the release of updated sepsis definitions in the middle of the study's date range, could have potentially reduced the number of patients that were included in the study based on the removal of severe sepsis terminology, though severe sepsis has remained a recognized ICD-10 code. However, the selection of the date range of this study was based on available sepsis diagnosis tracking, which was not readily available until implementation of the CMS SEP-1 core measure required reporting. This may have impacted awareness through written and verbal education offered to providers, and thus improved compliance over time of the study, but such colloquial information was not formally evaluated.

Lastly, data collection for this study was based heavily on analysis of provider documentation, and so absent, delayed, and disorganized notes made interpretation and data collection challenging. Nevertheless, the use of one data collector ensured that consistency was maintained in the interpretation of data, including challenging provider documentation.

Conclusion

Sepsis is a leading diagnosis and cause of in-hospital mortality among patients admitted to the hospital (Martin et al., 2006; Singer et al., 2016; Sjoding et al., 2016). Older adults often do not present with sepsis the same way adults do. In addition, the risk of mortality is higher among those ≥65 years because of unique pathophysiological changes (Clifford et al., 2016; De Gaudio et al., 2009; Girard & Ely, 2007; Nasa, Juneja, & Singh, 2012). Compliance with the 2012 SSC guidelines has been shown to decrease the risk of mortality by 40% and is also associated with a decrease in hospital LOS and an increase in cost savings (Leisman et al., 2017; Levy et al., 2015; Rhodes et al., 2015). This single-center, retrospective chart review further

confirms previous evidence that older adults receive less compliant care to the SSC Guidelines when compared to adults. Further analysis is needed to determine which specific bundle elements are most often missed in each age group, which can then be used to determine where quality improvement projects may prove the most beneficial to improve outcomes.

References

Arefian, H., Heublein, S., Scherag, A., Brunkhorst, F. M., Younis, M. Z., Moerer, O., . . . Hartmann, M. (2017). Hospital-related cost of sepsis: A systematic review. *J Infect, 74*(2), 107-117. doi:10.1016/j.jinf.2016.11.006

Castellanos-Ortega, A., Suberviola, B., Garcia-Astudillo, L. A., Ortiz, F., Llorca, J., & Delgado-Rodriguez, M. (2011). Late compliance with the sepsis resuscitation bundle: impact on mortality. *Shock, 36*(6), 542-547. doi:10.1097/SHK.0b013e3182360f7c

Clifford, K. M., Dy-Boarman, E. A., Haase, K. K., Maxvill, K., Pass, S. E., & Alvarez, C. A. (2016). Challenges with Diagnosing and Managing Sepsis in Older Adults. *Expert Rev Anti Infect Ther, 14*(2), 231-241. doi:10.1586/14787210.2016.1135052

Coba, V., Whitmill, M., Mooney, R., Horst, H. M., Brandt, M. M., Digiovine, B., . . . Jordan, J. (2011). Resuscitation bundle compliance in severe sepsis and septic shock: improves survival, is better late than never. *J Intensive Care Med, 26*(5), 304-313. doi:10.1177/0885066610392499

Cronshaw, H. L., Daniels, R., Bleetman, A., Joynes, E., & Sheils, M. (2011). Impact of the Surviving Sepsis Campaign on the recognition and management of severe sepsis in the emergency department: are we failing? *Emerg Med J, 28*(8), 670-675. doi:10.1136/emj.2009.089581

Damiani, E., Donati, A., Serafini, G., Rinaldi, L., Adrario, E., Pelaia, P., . . . Girardis, M. (2015). Effect of performance improvement programs on compliance with sepsis bundles and mortality: a systematic review and meta-analysis of observational studies. *PLoS One, 10*(5), e0125827. doi:10.1371/journal.pone.0125827

De Gaudio, A. R., Rinaldi, S., Chelazzi, C., & Borracci, T. (2009). Pathophysiology of sepsis in the elderly: clinical impact and therapeutic considerations. *Curr Drug Targets, 10*(1), 60-70.

Dellinger, R. P., Levy, M. M., Rhodes, A., Annane, D., Gerlach, H., Opal, S. M., . . . Surviving Sepsis Campaign Guidelines Committee including the Pediatric, S. (2013). Surviving sepsis campaign: international guidelines for management of severe sepsis and septic shock: 2012. *Crit Care Med, 41*(2), 580-637. doi:10.1097/CCM.0b013e31827e83af

El Solh, A. A., Akinnusi, M. E., Alsawalha, L. N., & Pineda, L. A. (2008). Outcome of septic shock in older adults after implementation of the sepsis "bundle". *J Am Geriatr Soc, 56*(2), 272-278. doi:10.1111/j.1532-5415.2007.01529.x

Englert, N. C., & Ross, C. (2015). The older adult experiencing sepsis. *Crit Care Nurs Q, 38*(2), 175-181. doi:10.1097/cnq.0000000000000059

Ferrer, R., Martin-Loeches, I., Phillips, G., Osborn, T. M., Townsend, S., Dellinger, R. P., . . . Levy, M. M. (2014). Empiric antibiotic treatment reduces mortality in severe sepsis and septic shock from the first hour: results from a guideline-based performance improvement program. *Crit Care Med, 42*(8), 1749-1755. doi:10.1097/ccm.0000000000000330

Girard, T. D., & Ely, E. W. (2007). Bacteremia and sepsis in older adults. *Clin Geriatr Med, 23*(3), 633-647, viii. doi:10.1016/j.cger.2007.05.003

Girard, T. D., Opal, S. M., & Ely, E. W. (2005). Insights into severe sepsis in older patients: from epidemiology to evidence-based management. *Clin Infect Dis, 40*(5), 719-727. doi:10.1086/427876

Kalil, A. C., Johnson, D. W., Lisco, S. J., & Sun, J. (2017). Early Goal-Directed Therapy for Sepsis: A Novel Solution for Discordant Survival Outcomes in Clinical Trials. *Crit Care Med, 45*(4), 607-614. doi:10.1097/ccm.0000000000002235

Kang, M. J., Shin, T. G., Jo, I. J., Jeon, K., Suh, G. Y., Sim, M. S., . . . Jeong, Y. K. (2012). Factors influencing compliance with early resuscitation bundle in the management of severe sepsis and septic shock. *Shock, 38*(5), 474-479. doi:10.1097/SHK.0b013e31826eea2b

Kramer, R. D., Cooke, C. R., Liu, V., Miller, R. R., 3rd, & Iwashyna, T. J. (2015). Variation in the Contents of Sepsis Bundles and Quality Measures. A Systematic Review. *Ann Am Thorac Soc, 12*(11), 1676-1684. doi:10.1513/AnnalsATS.201503-163BC

Leisman, D. E., Doerfler, M. E., Ward, M. F., Masick, K. D., Wie, B. J., Gribben, J. L., . . . D'Amore, J. A. (2017). Survival Benefit and Cost Savings From Compliance With a Simplified 3-Hour Sepsis Bundle in a Series of Prospective, Multisite, Observational Cohorts. *Crit Care Med, 45*(3), 395-406. doi:10.1097/ccm.0000000000002184

Levy, M. M., Artigas, A., Phillips, G. S., Rhodes, A., Beale, R., Osborn, T., . . . Dellinger, R. P. (2012). Outcomes of the Surviving Sepsis Campaign in intensive care units in the USA and Europe: a prospective cohort study. *Lancet Infect Dis, 12*(12), 919-924. doi:10.1016/s1473-3099(12)70239-6

Levy, M. M., Fink, M. P., Marshall, J. C., Abraham, E., Angus, D., Cook, D., . . . Sccm/Esicm/Accp/Ats/Sis. (2003). 2001 SCCM/ESICM/ACCP/ATS/SIS International Sepsis Definitions Conference. *Crit Care Med, 31*(4), 1250-1256. doi:10.1097/01.CCM.0000050454.01978.3B

Levy, M. M., Rhodes, A., Phillips, G. S., Townsend, S. R., Schorr, C. A., Beale, R., . . . Dellinger, R. P. (2015). Surviving Sepsis Campaign: association between performance metrics and outcomes in a 7.5-year study. *Crit Care Med, 43*(1), 3-12. doi:10.1097/ccm.0000000000000723

Madsen, T. E., Simmons, J., Choo, E. K., Portelli, D., McGregor, A. J., & Napoli, A. M. (2014). The DISPARITY Study: do gender differences exist in Surviving Sepsis Campaign resuscitation bundle completion, completion of individual bundle elements, or sepsis mortality? *J Crit Care, 29*(3), 473.e477-411. doi:10.1016/j.jcrc.2014.01.002

Martin, G. S., Mannino, D. M., & Moss, M. (2006). The effect of age on the development and outcome of adult sepsis*. *Critical Care Medicine, 34*(1), 15-21. doi:10.1097/01.ccm.0000194535.82812.ba

Nasa, P., Juneja, D., & Singh, O. (2012). Severe sepsis and septic shock in the elderly: An overview. *World J Crit Care Med, 1*(1), 23-30. doi:10.5492/wjccm.v1.i1.23

Nasa, P., Juneja, D., Singh, O., Dang, R., & Arora, V. (2012). Severe sepsis and its impact on outcome in elderly and very elderly patients admitted in intensive care unit. *J Intensive Care Med, 27*(3), 179-183. doi:10.1177/0885066610397116

Nguyen, H. B., Jaehne, A. K., Jayaprakash, N., Semler, M. W., Hegab, S., Yataco, A. C., . . . Rivers, E. P. (2016). Early goal-directed therapy in severe sepsis and septic shock: insights and comparisons to ProCESS, ProMISe, and ARISE. *Crit Care, 20*(1), 160. doi:10.1186/s13054-016-1288-3

Palomba, H., Correa, T. D., Silva, E., Pardini, A., & Assuncao, M. S. (2015). Comparative analysis of survival between elderly and non-elderly severe sepsis and septic shock

resuscitated patients. *Einstein (Sao Paulo), 13*(3), 357-363. doi:10.1590/S1679-45082015AO3313

Pestana, D., Espinosa, E., Sanguesa-Molina, J. R., Ramos, R., Perez-Fernandez, E., Duque, M., & Martinez-Casanova, E. (2010). Compliance with a sepsis bundle and its effect on intensive care unit mortality in surgical septic shock patients. *J Trauma, 69*(5), 1282-1287. doi:10.1097/TA.0b013e3181c4539f

Pettila, V., Hjortrup, P. B., Jakob, S. M., Wilkman, E., Perner, A., & Takala, J. (2016). Control groups in recent septic shock trials: a systematic review. *Intensive Care Med*. doi:10.1007/s00134-016-4444-y

Rhodes, A., Evans, L. E., Alhazzani, W., Levy, M. M., Antonelli, M., Ferrer, R., . . . Dellinger, R. P. (2017). Surviving Sepsis Campaign: International Guidelines for Management of Sepsis and Septic Shock: 2016. *Crit Care Med, 45*(3), 486-552. doi:10.1097/ccm.0000000000002255

Rhodes, A., Phillips, G., Beale, R., Cecconi, M., Chiche, J. D., De Backer, D., . . . Levy, M. (2015). The Surviving Sepsis Campaign bundles and outcome: results from the International Multicentre Prevalence Study on Sepsis (the IMPreSS study). *Intensive Care Med, 41*(9), 1620-1628. doi:10.1007/s00134-015-3906-y

Sakr, Y., Rubatto Birri, P. N., Kotfis, K., Nanchal, R., Shah, B., Kluge, S., . . . Vincent, J. L. (2017). Higher Fluid Balance Increases the Risk of Death From Sepsis: Results From a Large International Audit. *Crit Care Med, 45*(3), 386-394. doi:10.1097/ccm.0000000000002189

Scheer, C. S., Fuchs, C., Kuhn, S. O., Vollmer, M., Rehberg, S., Friesecke, S., . . . Grundling, M. (2016). Quality Improvement Initiative for Severe Sepsis and Septic Shock Reduces 90-

Day Mortality: A 7.5-Year Observational Study. *Crit Care Med*. doi:10.1097/ccm.0000000000002069

Singer, M., Deutschman, C. S., Seymour, C. W., Shankar-Hari, M., Annane, D., Bauer, M., . . . Angus, D. C. (2016). The Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3). *Jama, 315*(8), 801-810. doi:10.1001/jama.2016.0287

Sjoding, M. W., Prescott, H. C., Wunsch, H., Iwashyna, T. J., & Cooke, C. R. (2016). Longitudinal Changes in ICU Admissions Among Elderly Patients in the United States. *Crit Care Med, 44*(7), 1353-1360. doi:10.1097/CCM.0000000000001664

Sterling, S. A., Miller, W. R., Pryor, J., Puskarich, M. A., & Jones, A. E. (2015). The Impact of Timing of Antibiotics on Outcomes in Severe Sepsis and Septic Shock: A Systematic Review and Meta-Analysis. *Crit Care Med, 43*(9), 1907-1915. doi:10.1097/ccm.0000000000001142

Stoneking, L., Denninghoff, K., Deluca, L., Keim, S. M., & Munger, B. (2011). Sepsis bundles and compliance with clinical guidelines. *J Intensive Care Med, 26*(3), 172-182. doi:10.1177/0885066610387988

Stoneking, L. R., Winkler, J. P., DeLuca, L. A., Stolz, U., Stutz, A., Luman, J. C., . . . Denninghoff, K. R. (2015). Physician documentation of sepsis syndrome is associated with more aggressive treatment. *West J Emerg Med, 16*(3), 401-407. doi:10.5811/westjem.2015.3.25529

Torio, C. M., & Moore, B. J. (2016). *National inpatient hospital costs: The most expensive conditions by payer, 2013. HCUP Statistical brief 204* Agency for Healthcare and Research Quality Retrieved from http://www.hcup-us.ahrq.gov/reports/statbriefs/sb204-Most-Expensive-Hospital-Conditions.pdf.

van Zanten, A. R., Brinkman, S., Arbous, M. S., Abu-Hanna, A., Levy, M. M., & de Keizer, N. F. (2014). Guideline bundles adherence and mortality in severe sepsis and septic shock. *Crit Care Med, 42*(8), 1890-1898. doi:10.1097/ccm.0000000000000297

Appendix A: Surviving Sepsis Campaign Sepsis Bundles

Adapted from Dellinger et al. (2013).

Severe Sepsis and Septic Shock Guideline Bundles

To be completed within three hours*:

1. Broad spectrum IV antibiotic administration
2. Aggressive intravenous fluid therapy of 30ml/kg
3. Measurement of initial lactate level within the first three hours of recognition
4. Collection of blood cultures prior to antibiotic administration

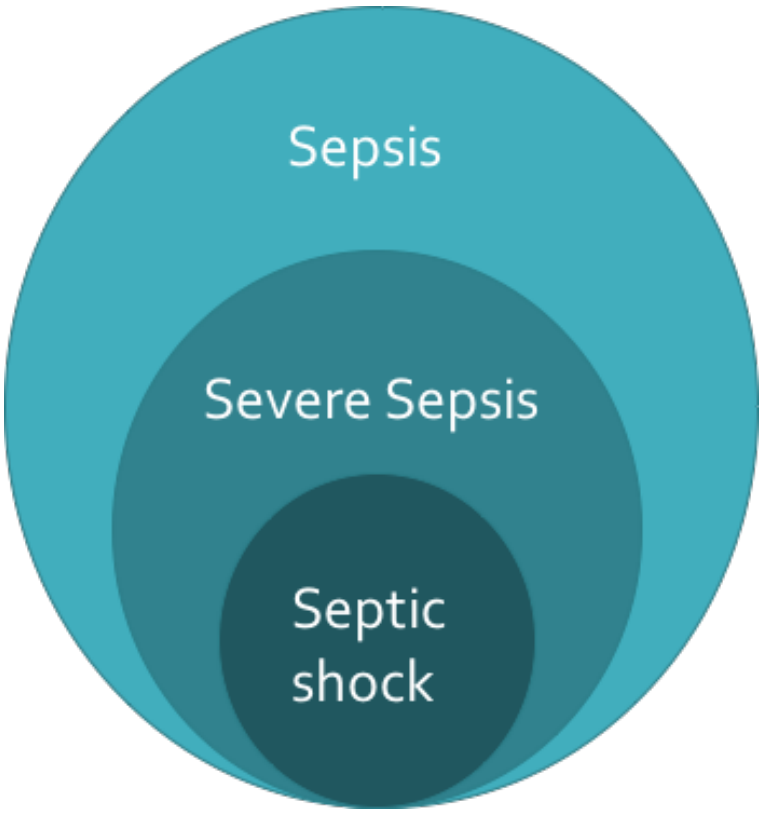
To be completed within six hours*:

1. Measurement of repeat lactate lab level (if initially elevated >2mmol/L)**
2. Administration of vasopressors for refractory hypotension (hypotension unresponsive to fluid bolus)
3. Documentation of the reassessment of volume status through physical exam, CVP measurement, SCVO2 measurement, bedside ultrasound, fluid challenge, or passive leg raise.

*when criteria are met for severe sepsis or septic shock
**within 6 hours of severe sepsis recognition

Appendix B: Diagram of Literature Search

Appendix C: Diagram of Sepsis, Severe Sepsis, and Septic Shock



Appendix D: Terms and Definitions

Terms, definitions and description of the data collection process for each variable (not described by Levy (2003) or Dellinger (2013). Terms and definitions ordered by appearance in Data Collection Form (see Table 1).

Date and Time- Reported in a MM/DD/YY and 24-hour clock format

Age- Based on the age when the patient presented to the hospital NOT the current age. Documented in years

Gender- Reported gender at time of hospital encounter documented as Male or Female

Height- The height at the time of hospital encounter. Documented in centimeters to the tenth position

Weight- First reported weight at time of hospital encounter, if no weight reported, look for the next closest recorded weight. Documented in kilograms to the tenth position based on ED admission weight, not current weight.

BMI- Calculated by using recorded height and weight. Documented to the tenth position.

Provider Documentation of Severe Sepsis- Date and Time is based on Note start time that a provider documented Severe Sepsis. If Septic Shock is documented instead-of or before severe sepsis documentation it will be recorded as documentation for severe sepsis.

Documentation of Suspected or Confirmed Source of Infection- Date and Time is based on Note start time. Acceptable notes include radiology provider impressions, nursing notes stating antibiotic administration or cultures obtained, nursing notes stating a concern for infection, or Provider Notes stating possible or confirmed infection. Whichever note is the earliest will be the documented date and time of suspected or confirmed source of infection.

Date and Time of Initial Laboratory Levels and Vital Signs- The date and time used for initial lab levels and vital signs are the earliest abnormal results after ED arrival and prior to hospital admission.

Temperature (Temp)- documented in Celsius to the tenth position

Heart Rate (HR)- documented as whole beats per min. Recorded pulse rate is an acceptable alternate

Respiratory Rate (RR)- documented in whole breaths per min

White Blood Cell Count (WBC)- lab level documented in thousands not as a decimal.

Systolic Blood Pressure (SBP)- result documented as a whole number.

Diastolic Blood Pressure (DBP)- result documented as a whole number

Mean Arterial Pressure (MAP)- Calculated using SBP and DBP. Documented as a whole number may be calculated from SBP and DBP or if available in charting

Serum Creatinine Level (SCr)- result documented to the hundredth position. Do not record if patient receives hemodialysis or peritoneal dialysis. Also, do not record if patient's baseline SCr is >2.

Total Bilirubin (Tbili)- result documented to the hundredth position. Do not record if baseline level is elevated >2.

Platelet Count (Plt)- result documented in thousands not decimal

INR- result documented to the hundredth position. Leave blank if patient is on chronic anticoagulation

aPTT- result documented to the hundredth position. Leave blank if patient is on chronic anticoagulation

Lactate- result documented to the hundredth position. POC and arterial lactate results are acceptable

SIRS Criteria Present- When 2 of the 4 following are met (Temp <36 or >38, HR >90, RR >20, WBC <4,000 or >12,000).

Organ Dysfunction Present- When 1 of the following are met (SBP <90, MAP <65, SCr >2, T Bili >2, Plt Count <100,000, INR >1.5 not on anticoagulation, aPTT >60 sec, Lactate ≥2)

Time Zero- Either (1) Date and Time when Provider documents suspected Severe Sepsis or Septic Shock OR (2) Date and Time when the last of the three following criteria are met: 1. documentation of suspected/ confirmed infection, 2. SIRS criteria met, and 3. Organ Dysfunction criteria met. Earliest Date and Time of (1) or (2) is the documented Time Zero of Severe Sepsis Presentation

Blood Cultures Before Antibiotics (abx) Administered- at least one set must be collected before abx administered to meet compliance.

IV Broad Spectrum ABX- See Acceptable Broad Spectrum Antibiotic (see Appendix E) form for acceptable ABX mono therapy and combined therapy. Form based on UHC classification of approved broad spectrum monotherapy and dual therapy abx.

IV ABX Given- Documented date and time that the antibiotic was started in the MAR. If two antibiotics for combined therapy were given, use documented date and time that the second antibiotic was started in the Medication Administration Record (MAR).

IV Crystalloid- Any isotonic fluid that is not a blood product (albumin will be considered a blood product) is acceptable. LR and NS are the most commonly used. Compliance to this element is based on administering 30ml/Kg (calculated on recorded admission weight) of IV crystalloid within 3 hours of Time Zero. Date and Time of Crystalloid administration is

based on the start time when the last administration of crystalloid in the 3-hour time of presentation window occurred (due to poor documentation of stop times in the MAR). Crystalloid that is a component of IV medication given during the 3-hour time window, i.e. crystalloid included in IV antibiotics, can be included. If fluid was not administered in 3-hours, but given within 2-hours after time zero, document amount given and document reason for failure as "Fluid given late, outside 3-hour time window". Crystalloid administered during the 6-hours leading up to Time Zero, i.e. EMS administration, may be counted towards total Crystalloid given.

Reasons Why Bundle Not Met- drop down list in the cell will have options to choose from. If option is not available, select "Other", and write in reason in the cell below.

Persistent Tissue Hypoperfusion- Examine SBP/ DBP and MAP following completion of IV fluid bolus, if SBP <90 or MAP <65 document "YES" and write date time of document blood pressure that met criteria

IV Vasopressor- If persistent tissue hypoperfusion is present by lactate level >4 or by low SBP (<90) or MAP (<65) despite initial crystalloid resuscitation, document order time/ date, type of vasopressor, and time vasopressor started infusing (based on MAR documentation). Acceptable vasopressors are any drug that constricts the blood vessels or with the goal of increasing blood pressure

Focused Exam Documentation- Provider Note must include documentation of Temperature, Heart Rate, Respiratory Rate, Blood pressure, Cardiopulmonary Exam, and Skin examination

Other Provider Assessments- 2 of 4 of the assessments must be documented to meet these criteria. They include CVP measurement, SCVO2, Bedside cardiovascular US, Passive Leg

Raise or Fluid Challenge. Document Date/ Time when the last of the two assessments were documented by the provider.

Appendix E: Broad Spectrum or Other Antibiotic Administration Selection

Obtained from the University HealthSystem Consortium (UHC) "Specifications Manual for National Hospital Inpatient Quality Measures—Discharges 10-01-15 (4Q15) through 06-30-16 (2Q16)"

Combination Antibiotic Therapy Table

Column A		Column B
Aminoglycosides OR Aztreonam OR Ciprofloxacin	+	Cephalosporins (1st and 2nd Generation) OR Clindamycin IV OR Daptomycin OR Glycopeptides OR Linezolid OR Macrolides OR Penicillins

NOTE: Metronidazole (Flagyl) is not represented on any table because it is not approved for monotherapy and if given, must be given with 2 other combination antibiotic therapy drugs. Since giving those 2 antibiotic therapy drugs will allow Value "1" to be chosen, the metronidazole is not required to be administered or abstracted.

Suggested Data Sources:

- Anesthesia record
- Entire Emergency Department record
- ICU flow sheet
- IV flow sheet
- Medication administration record
- Nurses notes
- Operating room record
- PACU/recovery room record
- Perfusion record
- Physician/APN/PA documentation

Inclusion Guidelines for Abstraction:

Intravenous:

- Intravenous
- IV bolus
- IV infusion

Exclusion Guidelines for Abstraction:

None

Table Number	Table Name	Medication	Generic Name and Crossw
Table 5.0	Antibiotic Monotherapy, Sepsis	Doribax	Doripenem
Table 5.0	Antibiotic Monotherapy, Sepsis	Doripenem	Doripenem
Table 5.0	Antibiotic Monotherapy, Sepsis	Eratepenem	Eratepenem
Table 5.0	Antibiotic Monotherapy, Sepsis	Invanz	Eratepenem
Table 5.0	Antibiotic Monotherapy, Sepsis	Imipenem/Cilastatin	Imipenem/Cilastatin
Table 5.0	Antibiotic Monotherapy, Sepsis	Meropenem	Meropenem
Table 5.0	Antibiotic Monotherapy, Sepsis	Merrem	Meropenem
Table 5.0	Antibiotic Monotherapy, Sepsis	Primaxin	Imipenem/Cilastatin
Table 5.0	Antibiotic Monotherapy, Sepsis	Cefotaxime	Cefotaxime
Table 5.0	Antibiotic Monotherapy, Sepsis	Claforan	Cefotaxime
Table 5.0	Antibiotic Monotherapy, Sepsis	Ceftazidime	Ceftazidime
Table 5.0	Antibiotic Monotherapy, Sepsis	Ceftriaxone	Ceftriaxone
Table 5.0	Antibiotic Monotherapy, Sepsis	Fortaz	Ceftazidime
Table 5.0	Antibiotic Monotherapy, Sepsis	Rocephin	Ceftriaxone
Table 5.0	Antibiotic Monotherapy, Sepsis	Cefepime	Cefepime
Table 5.0	Antibiotic Monotherapy, Sepsis	Maxipime	Cefepime
Table 5.0	Antibiotic Monotherapy, Sepsis	Ceftaroline fosamil	Ceftaroline fosamil
Table 5.0	Antibiotic Monotherapy, Sepsis	Teflaro	Ceftaroline fosamil
Table 5.0	Antibiotic Monotherapy, Sepsis	Avelox	Moxifloxacin
Table 5.0	Antibiotic Monotherapy, Sepsis	Gatifloxacin	Gatifloxacin
Table 5.0	Antibiotic Monotherapy, Sepsis	Levaquin	Levofloxacin
Table 5.0	Antibiotic Monotherapy, Sepsis	Levofloxacin	Levofloxacin
Table 5.0	Antibiotic Monotherapy, Sepsis	Moxifloxacin	Moxifloxacin
Table 5.0	Antibiotic Monotherapy, Sepsis	Tequin	Gatifloxacin
Table 5.0	Antibiotic Monotherapy, Sepsis	Amoxicillin/clavulanate	Amoxicillin/clavulanate
Table 5.0	Antibiotic Monotherapy, Sepsis	Ampicillin/sulbactam	Ampicillin/sulbactam
Table 5.0	Antibiotic Monotherapy, Sepsis	Augmentin	Amoxicillin/clavulanate
Table 5.0	Antibiotic Monotherapy, Sepsis	Piperacillin/tazobactam	Piperacillin/tazobactam
Table 5.0	Antibiotic Monotherapy, Sepsis	Ticarcillin/clavulanate	Ticarcillin/clavulanate
Table 5.0	Antibiotic Monotherapy, Sepsis	Timentin	Ticarcillin/clavulanate
Table 5.0	Antibiotic Monotherapy, Sepsis	Unasyn	Ampicillin/sulbactam
Table 5.0	Antibiotic Monotherapy, Sepsis	Zosyn	Piperacillin/tazobactam
Table 5.1	Antibiotic Generic/Trade Name Crosswalk, Sepsis	**Aminoglycosides**	
Table 5.1	Antibiotic Generic/Trade Name Crosswalk, Sepsis	Amikacin	Amikacin
Table 5.1	Antibiotic Generic/Trade Name Crosswalk, Sepsis	Garamycin	Gentamicin
Table 5.1	Antibiotic Generic/Trade Name Crosswalk, Sepsis	Gentamicin	Gentamicin
Table 5.1	Antibiotic Generic/Trade Name Crosswalk, Sepsis	Kanamycin	Kanamycin
Table 5.1	Antibiotic Generic/Trade Name Crosswalk, Sepsis	Kantrex	Kanamycin
Table 5.1	Antibiotic Generic/Trade Name Crosswalk, Sepsis	Nebcin	Tobramycin
Table 5.1	Antibiotic Generic/Trade Name Crosswalk, Sepsis	Tobramycin	Tobramycin
Table 5.1	Antibiotic Generic/Trade Name Crosswalk, Sepsis	**Aztreonam**	
Table 5.1	Antibiotic Generic/Trade Name Crosswalk, Sepsis	Azactam	Aztreonam
Table 5.1	Antibiotic Generic/Trade Name Crosswalk, Sepsis	Aztreonam	Aztreonam
Table 5.1	Antibiotic Generic/Trade Name Crosswalk, Sepsis	**Cephalosporins (1st and 2nd Generation)**	
Table 5.1	Antibiotic Generic/Trade Name Crosswalk, Sepsis	Ancef	Cefazolin
Table 5.1	Antibiotic Generic/Trade Name Crosswalk, Sepsis	Cefazolin	Cefazolin
Table 5.1	Antibiotic Generic/Trade Name Crosswalk, Sepsis	Cefoxitin	Cefoxitin
Table 5.1	Antibiotic Generic/Trade Name Crosswalk, Sepsis	Ceftin	Cefuroxime
Table 5.1	Antibiotic Generic/Trade Name Crosswalk, Sepsis	Cefuroxime	Cefuroxime
Table 5.1	Antibiotic Generic/Trade Name Crosswalk, Sepsis	Mefoxin	Cefoxitin
Table 5.1	Antibiotic Generic/Trade Name Crosswalk, Sepsis	**Ciprofloxacin**	
Table 5.1	Antibiotic Generic/Trade Name Crosswalk, Sepsis	Cipro	Ciprofloxacin
Table 5.1	Antibiotic Generic/Trade Name Crosswalk, Sepsis	Ciprobay	Ciprofloxacin
Table 5.1	Antibiotic Generic/Trade Name Crosswalk, Sepsis	Ciprofloxacin	Ciprofloxacin

Table Number	Table Name	Medication	Generic Name and Crossw
Table 5.1	Antibiotic Generic/Trade Name Crosswalk, Sepsis	Ciproxin	Ciprofloxacin
Table 5.1	Antibiotic Generic/Trade Name Crosswalk, Sepsis	**Clindamycin IV**	
Table 5.1	Antibiotic Generic/Trade Name Crosswalk, Sepsis	Cleocin	Clindamycin
Table 5.1	Antibiotic Generic/Trade Name Crosswalk, Sepsis	Clindamycin	Clindamycin
Table 5.1	Antibiotic Generic/Trade Name Crosswalk, Sepsis	**Daptomycin**	
Table 5.1	Antibiotic Generic/Trade Name Crosswalk, Sepsis	Cubicin	Daptomycin
Table 5.1	Antibiotic Generic/Trade Name Crosswalk, Sepsis	Daptomycin	Daptomycin
Table 5.1	Antibiotic Generic/Trade Name Crosswalk, Sepsis	**Glycopeptides**	
Table 5.1	Antibiotic Generic/Trade Name Crosswalk, Sepsis	Targocid	Teicoplanin
Table 5.1	Antibiotic Generic/Trade Name Crosswalk, Sepsis	Teicoplanin	Teicoplanin
Table 5.1	Antibiotic Generic/Trade Name Crosswalk, Sepsis	Telavancin	Telavancin
Table 5.1	Antibiotic Generic/Trade Name Crosswalk, Sepsis	Vancocin	Vancomycin
Table 5.1	Antibiotic Generic/Trade Name Crosswalk, Sepsis	Vancomycin	Vancomycin
Table 5.1	Antibiotic Generic/Trade Name Crosswalk, Sepsis	Vibativ	Telavancin
Table 5.1	Antibiotic Generic/Trade Name Crosswalk, Sepsis	**Linezolid**	
Table 5.1	Antibiotic Generic/Trade Name Crosswalk, Sepsis	Linezolid	Linezolid
Table 5.1	Antibiotic Generic/Trade Name Crosswalk, Sepsis	Zyvox	Linezolid
Table 5.1	Antibiotic Generic/Trade Name Crosswalk, Sepsis	**Macrolides**	
Table 5.1	Antibiotic Generic/Trade Name Crosswalk, Sepsis	Azithromycin	Azithromycin
Table 5.1	Antibiotic Generic/Trade Name Crosswalk, Sepsis	Erythocin	Erythromycin
Table 5.1	Antibiotic Generic/Trade Name Crosswalk, Sepsis	Erythromycin	Erythromycin
Table 5.1	Antibiotic Generic/Trade Name Crosswalk, Sepsis	Erythroped	Erythromycin
Table 5.1	Antibiotic Generic/Trade Name Crosswalk, Sepsis	Ketek	Telithromycin
Table 5.1	Antibiotic Generic/Trade Name Crosswalk, Sepsis	Sumamed	Azithromycin
Table 5.1	Antibiotic Generic/Trade Name Crosswalk, Sepsis	Telithromycin	Telithromycin
Table 5.1	Antibiotic Generic/Trade Name Crosswalk, Sepsis	Xithrone	Azithromycin
Table 5.1	Antibiotic Generic/Trade Name Crosswalk, Sepsis	Zithromax	Azithromycin
Table 5.1	Antibiotic Generic/Trade Name Crosswalk, Sepsis	**Penicillins**	
Table 5.1	Antibiotic Generic/Trade Name Crosswalk, Sepsis	Ampicillin	Ampicillin
Table 5.1	Antibiotic Generic/Trade Name Crosswalk, Sepsis	Nafcillin	Nafcillin
Table 5.1	Antibiotic Generic/Trade Name Crosswalk, Sepsis	Oxacillin	Oxacillin
Table 5.1	Antibiotic Generic/Trade Name Crosswalk, Sepsis	Penicillin G	Penicillin G
Table 5.2	Vasopressors for Septic Shock	Norepinephrine	Levophed
Table 5.2	Vasopressors for Septic Shock	Epinephrine	Adrenalin
Table 5.2	Vasopressors for Septic Shock	Phenylephrine	Neosynephrine
Table 5.2	Vasopressors for Septic Shock		Vazculep
Table 5.2	Vasopressors for Septic Shock	Dopamine	Inotropin
Table 5.2	Vasopressors for Septic Shock	Vasopressin	Pitressin