THE EFFECTIVENESS OF EMERGENCY HEALTH CARE SYSTEM ON CLINICAL SIGNS IN PATIENTS WITH SEPSIS

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ABSTRACT

Sepsis is associated with high morbidity and mortality. In particular hypoperfusion is a poor prognostic marker of sepsis. While the clinical signs of vital organs can improve from sepsis therapy within 72 hours, many patients with sepsis presented the worse clinical signs during this time since arrival at emergency department. The previous research was limited to explain what factors of emergency health care system related to these situations. The purpose of this prospective descriptive correlational study was to explore factors in the system and patient levels influencing the clinical signs in patients with sepsis in the context of an emergency health care system. Two-stage random sampling was conducted to recruit 11 hospitals including 5 tertiary or regional hospitals and 6 general hospitals in central region of Thailand. Purposive sampling was conducted for 202 patients with sepsis during September 2014 to February 2015. The multilevel logistic regression was analyzed.

The outcomes of clinical signs were deterioration (59.9%) and without deterioration (40.1%) between 6 – 72 hours since ED arrival. The 65.3% of patients who presented clinical signs with deterioration died. The results from multilevel logistic regression analysis demonstrated that a clustering effect influencing on clinical signs of patients with sepsis. The interaction effect models were not significant (all $p > 0.05$). The best model consisted of severity of illness (β = - 0.160, $p < 0.001$), level of hospital (β = 1.034 p = 0.007), and performance of sepsis resuscitation bundle (β = 2.235, p = 0.003). It was explained as follows; a one-unit increased in the severity of illness or MEDS score, the probability of clinical signs without deterioration between 6 – 72 hours since ED arrival decreased by 14.8%; the general hospital was more likely to promote the probability of clinical signs without deterioration between 6 – 72 hours since ED arrival by 2.813 times than tertiary or regional hospital; and patients who achieved in all components of medical treatment and non-invasive monitoring were more likely to promote the probability of clinical signs without deterioration between 6 – 72 hours since ED arrival by 9.349 times than patients who did not achieve.

The contexts of emergency health care system influenced to clinical outcomes in patients with sepsis. The severity of illness related to delay access, the older age, and the history of health care utilization. The level of hospital, which was differentiated in workload and the situation of access block in emergency department, influenced the clinical outcomes differently. The performance of sepsis resuscitation bundle depended on triage practice, EMS utilization, and process of nursing care.

KEY WORDS: EFFECTIVENESS / EMERGENCY HEALTH CARE SYSTEM / SEPSIS / MULTILEVEL LOGISTIC REGRESSION

150 pages

ประสิทธิผลของระบบการบริการสุขภาพฉุกเฉินต่ออาการทางคลินิกในผู้ป่วยที่มีภาวะพิษเหตุติดเชื้อ

THE EFFECTIVENESS OF EMERGENCY HEALTH CARE SYSTEM ON CLINICAL SIGNS IN PATIENTS WITH SEPSIS

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บทคัดย่อ

การศึกษาเชิงบรรยายแบบวิเคราะห์ไปข้างหน้าครั้งนี้ มีวัตถุประสงค์เพื่อศึกษาผลของปัจจัยระบบบริการสุขภาพฉุกเฉินและปัจจัยผู้ป่วยต่ออาการทางคลินิกในผู้ป่วยที่มีภาวะพิษเหตุติดเชื้อ โดยทำการสุ่มตัวอย่างแบบสองขั้นตอนเพื่อโรงพยาบาลที่ศึกษาในภาคกลาง ประเทศไทยประกอบด้วย 5 โรงพยาบาลตติยภูมิหรือโรงพยาบาลศูนย์ และ 6 โรงพยาบาลทั่วไป และเลือกผู้ป่วยมีภาวะพิษเหตุติดเชื้อแบบเจาะจงจำนวน 202 ราย ระหว่าง กันยายน 2557 ถึง กุมภาพันธ์ 2558 การวิเคราะห์ครั้งนี้ใช้สถิติถดถอยพหุระดับ

ผลการศึกษาพบว่าผู้ป่วยที่มีภาวะพิษเหตุติดเชื้อมีอาการทางคลินิกทรุดลงร้อยละ 59.9% และไม่มีอาการทางคลินิกทรุดลงร้อยละ 40.1% ระหว่าง 6 – 72 ชั่วโมงนับจากเวลาที่มาถึงห้องฉุกเฉิน โดยร้อยละ 65.3% ของผู้ป่วยที่มีอาการทางคลินิกทรุดลงเสียชีวิต ผลการวิเคราะห์สถิติถดถอยพหุระดับพบว่าปัจจัยระบบบริการสุขภาพฉุกเฉินมีผลต่ออาการทางคลินิกในผู้ป่วยที่มีภาวะพิษเหตุติดเชื้อ แต่ไม่พบความสัมพันธ์ระหว่างปัจจัยต่ออาการทางคลินิกในผู้ป่วยที่มีภาวะพิษเหตุติดเชื้อ (all $p > 0.05$) ปัจจัยที่มีผลทำนายอาการทางคลินิกในผู้ป่วยที่มีภาวะพิษเหตุติดเชื้ออย่างมีนัยสำคัญคือ ความรุนแรงของอาการ (β = - 0.160, $p < 0.001$) ระดับโรงพยาบาล (β = 1.034 p = 0.007) และแผนการรักษาผู้ป่วยที่มีภาวะพิษเหตุติดเชื้อ (β = 2.235, p = 0.003) โดยอธิบายได้ดังนี้ เมื่อความรุนแรงของอาการเพิ่มขึ้น 1 คะแนน โอกาสของการไม่เกิดอาการทางคลินิกทรุดลงจะลดลง 14.8% โรงพยาบาลทั่วไปมีโอกาสของการไม่เกิดอาการทางคลินิกทรุดลง 2.813 เท่าเมื่อเทียบกับโรงพยาบาลตติยภูมิหรือโรงพยาบาลศูนย์ และผู้ป่วยที่ได้รับแผนการรักษาผู้ป่วยที่มีภาวะพิษเหตุติดเชื้อตามเป้าหมายมีโอกาสของการไม่เกิดอาการทางคลินิกทรุดลง 9.349 เท่าเมื่อเทียบกับผู้ป่วยที่ไม่ได้รับ

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CHAPTER I
INTRODUCTION

1.1 Significance of problem

Sepsis is associated with high morbidity and mortality. In particular hypoperfusion is a poor prognostic marker of sepsis. If patients with sepsis did not access to definitive care, they had a high risk of organ dysfunction and mortality within 72 hours after presentation at the emergency department (ED) ($p < 0.001$) (Song et al., 2012). Regarding the cost effectiveness, the access to definitive care can reduce the hospital cost and length of hospital stay for those patients (Huang, Clermont, Dremsizov, & Angus, 2007). Unfortunately, they had a low rate of access to definitive care (Cronshaw, Daniels, Bleetman, Joynes, & Sheils, 2011; Kang et al., 2012; Mikkelsen et al., 2010). According to, sepsis was the most common cause of 30 - 50% of all preventable death cases in the ED, due to delay, inaccurate diagnosis, and/or inadequate management (Lu et al., 2006; Nafsi, Russell, Reid, & Rizvi, 2007). The access system for patients with sepsis also need to study and development, especially the triage system because it is a gatekeeper of emergency care.

The global incidence of sepsis has been estimated to be increasing continuously. Increasing incidence of sepsis in United States was estimated by 13.0% annually (Gaieski, Edwards, Kallan, & Carr, 2013). The annual incidence rates of sepsis in Taiwan increased by 1.6 fold from 1997 to 2006 (Shen, Lu, & Yang, 2010). In Thailand, one prospective study showed that the incidence of sepsis increased from 16.6% to 21.6% during 2004 – 2006 for intensive care unit (ICU) admissions (Khwannimit & Bhurayanontachai, 2009). While the case fatality rate of patients with sepsis tended to steady downward due to broad use of sepsis policy in developed country (Levy et al., 2010), especially in the United states by decreasing from 39% to 27% during 2000 – 2007 (Kumar et al., 2011), the mortality rate in developing countries was still high at 40 – 90% (Angkasekwinai, Rattanaumpawan, &

Thamlikitkul, 2009; Chuesakoolvanich, 2007; Grozdanovski, Milenkovic, Demiri, & Spasovska, 2012; Tanriover, Guven, Sen, Unal, & Uzun, 2006).

Sepsis is the systemic response when pathogenic organisms spread into the bloodstream (Angus & Poll, 2013). The systemic responses are various depending on the severity of sepsis. When sepsis is worse with hypoperfusion state, the organ function will be risky to failure (Bone, Grodzin, & Balk, 1997). Because the derangement result of cardiovascular system lead to inadequate tissue perfusion (Jones & Puskarich, 2011). If the hypoperfusion is not resolved, the clinical of sepsis are worse with the effect of global tissue hypoxia from the micro- and macro-circulatory dysfunction including decreased preload, diminished vasoregulatory control, myocardial depression, and microcirculatory obstruction (Nguyen et al., 2006; Ridley, 2005; Trzeciak & Rivers, 2005). The mortality rate was estimated to have increased following the stages of sepsis severity: sepsis, sepsis with organ dysfunction, and sepsis with shock as 10 - 20%, 20 - 50%, and 40 - 80% respectively (Martin, 2012).

The critical issue, most patients with sepsis (62.8%), who presented with the early signs of sepsis at first presentation to the ED (Wang et al., 2010), had the evidences of worse clinical signs after hospitalization as follows: more than 20% progressed to shock (Angkasekwinai et al., 2009; Glickman et al., 2010) and 38.6% were worse to respiratory compromise and alteration of conscious within 48 hours (Tsai et al., 2014). There is limited to explain what factors of emergency health care system related to these situations.

From International studies, the risk factors, which associated with mortality in patients with sepsis, depended on the patient and system factors. The patient factors were antecedent conditions which directly influenced to mortality in patients with sepsis. They consisted of severity of illness and time to perceive symptom onset. The system factors were structure and process in the emergency health care system including level of hospital, sepsis policy, EMS utilization, triage practice, performance of sepsis resuscitation bundle, care model, length of ED stay and ICU admission. They influenced to timely access and mortality in sepsis patients.

The severity of illness in sepsis depended on age, comorbidity, site of infection, physiological parameter, and organ dysfunction (Levy et al., 2003). The risks of sepsis severity are more pronounced in high-risk patient groups, such as the elderly and those with comorbidities such as chronic lung disease, chronic kidney disease, chronic liver disease, congestive heart failure, diabetes, and cancer (Martin, Mannino, Eaton, & Moss, 2003; O'Brien, Ali, Aberegg, & Abraham, 2007; Wang et al., 2012). Decreased immunocompetency and chronic inflammation increase the susceptibility to an infection and exaggerate the immune response to poor perfusion state (Ginaldi et al., 1999; Moore et al., 2010; Wang et al., 2012). Elderly patients with sepsis were at a significant risk for mortality during ICU admission ($p < 0.001$) (Guidet, Aegerter, Gauzit, Meshaka, & Dreyfuss, 2005). Especially those patients with chronic illness, who were associated with a higher mortality rate, which included metastatic cancer ($p < 0.001$), hematologic cancer ($p = 0.045$), chronic respiratory failure ($p = 0.001$), and chronic heart failure ($p = 0.004$) (Grozdanovski et al., 2012; Khwannimit & Bhurayanontachai, 2009).

Two or more of the systemic inflammatory response syndrome (SIRS) is associated with a higher risk of organ dysfunction and mortality (Sprung et al., 2006). The SIRS criteria included body temperature higher than 38°C or lower than 36°C, heart rate higher than 90 beats/min, respiratory rate higher than 20 breaths/min, and increased or decreased white blood cell count as >12,000/mm^3 or <4,000/mm^3 respectively or band >10% (Bone et al., 1997). In particular, the higher of heart rate (114 beats/min) and respiratory rate (26 breaths/min) were significant to cryptic shock ($p = 0.04$ and $p = 0.01$ respectively) (Puskarich et al., 2011). Organ dysfunction was significantly associated with mortality rate on the first day of admission (Jones, Trzeciak, & Kline, 2009). The 28-day mortality rate related to each organ failure was 4.5 times for hematologic failure (platelet < 100,000/mm^3), 3.6 times for respiratory failure (respiratory rate > 20 breaths/min, oxygen saturation < 90% with room air or < 94% with oxygen therapy), and 3.6 times for cardiovascular failure (systolic blood pressure < 90 mmHg) (Shapiro et al., 2006). The higher numbers of organ dysfunction were associated with an increased mortality rate as follows: 20% in 1 organ dysfunction, 40% in 2 organ dysfunctions, 70% in 3 organ dysfunctions, and 80% in 4 or more organ dysfunctions (Angus et al., 2001). The 40% of patients with lower respiratory infection had progressed to sepsis (Klouwenberg, Ong, Bonten, & Cremer, 2012).

Time to perceive symptom onset may relate to more severity of patients with sepsis. Many patients with sepsis (26%) had a high severity with at least one organ dysfunction at first presentation to the ED (Wang, Weaver, Shapiro, & Yealy, 2010). There is limited data describing the delay in access to emergency health care system in patients with sepsis (Herlitz et al., 2012). Research had demonstrated that a delay in diagnosis or interventions performed more than 48 hours after the onset of organ dysfunction increased the mortality rate by 8.73 ($p=0.004$) among elderly patients (Freitas et al., 2008). The delay in access may relate to the patients' recognition of sepsis and the pay for health. The international survey had resulted of 88% never heard sepsis term and 58% did not recognize the danger of sepsis. The researchers discussed that these results may affected to patients' decision to timely access treatment (Rubulotta et al., 2009). About the pay for health, self-payment was associated with the overall and early mortality in patients with sepsis ($p < 0.05$ and $p < 0.001$ respectively) (Powell, Khare, Courtney, & Feinglass, 2010). Jordan and colleagues (2009) found that patients with pneumonia who had low income also had low percentage of seeking health care. Most of them had duration of illness more than 7 days with higher severity of illness because of need hospitalization significantly ($p < 0.0001$).

The different levels of hospital have different resources and patient volumes. Powell and colleagues (2010) found that teaching hospitals were associated with a higher volume of patients with sepsis in their ED ($p < 0.001$) due to the expected quality of care. Teaching hospitals and hospitals with a large number of patient bed capacity had 1.21 and 1.20 times higher risk of the mortality when compared to non-teaching hospitals ($p < 0.001$) and hospitals with a small number of patient bed capacity ($p < 0.05$) respectively. The highest volume of patients with sepsis at the ED was greater associated with a mortality rate than the lower volume of patients, such 27% for more than 371 cases/year, 17% for 146 – 248 cases/year, and 10% for 249 – 371 cases/year ($p < 0.001$).

However, if the hospitals have available of sepsis policy, a decreased mortality rate resulted. Many studies revealed that the decreased mortality rate was shown in the hospitals which provided a sepsis policy including protocol and educational program within the process of continuous quality improvement (Ferrer et al., 2008; Girardis et al., 2009; Levy et al., 2012; Tromp et al., 2010). This policy was initiated in order for quicker identification and treatment for patients with sepsis. It also supported the higher compliance rate of sepsis resuscitate bundle usage. While Mahavanakul and colleagues (2012) found that the increased mortality rate in patients with sepsis was found in the tertiary hospital with a sepsis policy in the limited resources.

The EMS utilization in patients with sepsis was associated with decreased timing in antibiotic administration and intravenous fluids in patients with sepsis when compared to non-EMS patients from 152 to 116 minutes from 68 to 34 minutes (Band et al., 2011). However, when EMS providers correctly recognized and notified the clinical instability of their patients with sepsis, including the SIRS criteria and clinical signs of organ dysfunction such as deteriorating neurological system, hypotension, oliguria, and hypoxemia, these processes had dramatically decreased the time of antibiotic administration from 122 to 70 minutes ($p = 0.003$) and the time of sepsis resuscitate bundle administration from 131 to 69 minutes ($p = 0.001$) when compared with non-EMS patients (Studnek, Artho, Garner, & Jones, 2012) and increased the survival rate in patients with sepsis ($p = 0.04$) (Guerra, Mayfield, Meyers, Clouatre, & Riccio, 2013).

Triage practice is an important to early detection of sepsis signs. Sepsis is difficult to identify with patients according to their chief complaint (Begier et al., 2003) whereas it requires more timely assessment and treatment instead. Only one-third of patients with sepsis had been accurately diagnosed at the ED (Rezende et al., 2008; Uittenbogaard et al., 2013). Moreover, sepsis was the most under-triaged group, which consequently influenced a delayed time of intensive care unit (ICU) admission (Yurkova & Wolf, 2011) and a significant number of deaths after the first few days after admission (Dent, Rofe, & Sansom, 1999). When triage nurse performed the assessment of sepsis signs in patients and alerted the medical team with these signs, more than double of the patient numbers had faster access time to therapy (Larsen, Mecham, & Greenberg, 2011) in addition to the decrease in 28-day mortality and in-hospital mortality ($p < 0.001$) (Westphal et al., 2011). The sepsis signs consisted of the SIRS and organ dysfunction. When clinical staff did not alert the team with an inaccurate triage level as urgent or lower severity level for patients with sepsis, the mortality rate increased (Yurkova & Wolf, 2011).

The performance of sepsis resuscitation bundle is a practice in order to reduce the mortality in patients with sepsis following the guideline. Nowadays, there are two approved guidelines including the Surviving Sepsis Campaign 2012 (Dellinger et al., 2013) and the protocol-based standard therapy (Yealy et al., 2014). The principle of those guidelines are stressed on early fluid challenge with vasopressor application in non – response cases and early antibiotic administration. The Surviving Sepsis Campaign 2012 recommended fluid challenge with crystalloid 30 ml/kg minimally within three hours, vasopressor application within six hours and antibiotic administration for patients with septic shock within one hour. The protocol-based standard therapy recommended early fluid challenge with crystalloid at least 2,000 ml with vasopressor application until systolic blood pressure $\geq$ 100 mmHg within one hour and antibiotic administration for patients with septic shock within three hours. They are different in the achieved goal of monitoring. The Surviving Sepsis Campaign 2012 stressed on the achievement of non – invasive and invasive monitoring within six hours including urine output $\geq$ 0.5 ml/kg/hr, mean arterial pressure (MAP) $\geq$ 65 mmHg, central venous pressure (CVP) 8-12 mmHg, and central venous oxygen saturation ($ScvO_2$) $\geq$70%. While the protocol-based standard therapy stressed on the achievement of systolic blood pressure $\geq$ 100 mmHg and/or shock index < 0.8 within one hour.

However, there were not different results between both guidelines on 60-day mortality rate (21.0% and 18.2% respectively, p = 0.83), 90-day mortality rate (31.9% and 30.8% respectively, p = 0.66), and serious adverse events during admission (5.2% and 4.9% respectively, p = 0.32) (Yealy et al., 2014). According to, some arguments question the effectiveness of existing invasive monitoring, such as the CVP monitoring which was not useful in representing hemodynamic after the fluid challenge (Marik, Baram, & Vahid, 2008); and the achieved $ScvO_2$ $\geq$70% did not correlate with the mortality rate (Peake et al., 2009; Pope et al., 2010). Many studies were also presented that a decreased mortality rate in patients with sepsis was associated with using non-invasive monitoring (Hanzelka et al., 2013; Patel, Roderman, Gehring, Saad, & Bartek, 2010)

Care model had influenced the performance and eventual survival outcome. Na and colleagues (2012) found that the survival rate after complete sepsis resuscitation bundle was not significant ($p = 0.58$) after adjusting for severity of illness and care model. There are three care models including ED-centric model, ICU-centric model, and collaborative model. They are different in people and place to have a responsibility to completely perform the sepsis resuscitation bundle. Emergency physician and nurse are prominent role to complete the sepsis resuscitation bundle at ED in ED-centric model while intensive physician and nurse do it at ICU in ICU-centric model. If both physician and nurse at ED and ICU or ward cooperate to do since ED to ICU or ward, it is called the collaborative model. The effectiveness of each model depended on policy and resources such as, ICU-centric and collaborative models depended on the availability of ICUs and a timely consultation for sepsis service ($p < 0.001$) (Mikkelsen et al., 2010), and ER-centric and collaborative models depended on the experience and competency of providers for the adherence to treatment protocol including more than three years of clinical experience for nurses, and senior residents or board of certification in emergency medicine (Kang et al., 2012). Huang and colleagues (2007) found that the ICU-centric model was the least effectiveness due to delayed implementation while Na and colleagues (2012) presented that it had a higher compliant rate of sepsis resuscitation bundle than the ED-centric model. The collaborative model resulted in timely treatments (Casserly et al., 2011). Nevertheless, there are limited resources in Thailand such as the number of 247 emergency physicians (Leethongde, 2013) and unavailable resources for invasive – monitoring (Mahavanakul et al., 2012).

The length of ED stay was associated with a mortality rate in the patients with emergency conditions (Singer, Thode, Viccellio, & Pines, 2011). It was associated with an increased mortality rate corresponding to the increased time in the ED, such as 2.5% for less than two hours, 2.7% for two to six hours, 3.9 for six to twelve hours, and 4.5% for more than twelve hours (Singer et al., 2011). Patients with sepsis, who had length of stay in the ED had with more than a three hour, had the highest mortality rate as 47.1% when compared with equal or less than three hours (Degoricija et al., 2006).

In the case of the ICU, admissions were associated with a higher compliance rate of sepsis resuscitation bundle usage when compared with the general ward at 21.6% and 18.4% respectively (Levy et al., 2012). The workload for patients with sepsis was the highest mean of nursing activities score at 57.0 due to care needed for invasive monitoring when compared with acute renal failure and acute coronary syndrome (55.3 and 43.0 respectively, $p < 0.01$) (Carmona-Monge et al., 2013). The mortality rate of patients with sepsis who were admitted to the ICU within six hours had a lower mortality rate than those patients who were admitted to the ICU in more than six hours as 8.4% and 10.7% of ICU mortality ($p < 0.01$) and 12.9% and 17.4% of hospital mortality ($p < 0.001$) respectively (Chalfin, Trzeciak, Likourezos, Baumann, & Dellinger, 2007).

From International studies stated above, all factors related to the outcomes of timely treatment and/or mortality in patients with sepsis. Unfortunately, they were studied in one level analysis. The results may be an aggregation bias. Nevertheless, triage management of EMS and ED was essential factor that led patients with sepsis to timely access to definitive care. If triage nurses perform the effective assessment in those patients, the remaining factors will be high probable continue with the effective outcomes. While the situation of access to definitive care in patients with sepsis in Thailand was an issue, because the process of care for patients with sepsis in the medical wards have shown that 11% received the sepsis resuscitation bundle therapy and 39% received antibiotics within 6 hours (Angkasekwinai et al., 2009) and the situations of emergency health care system were unknown. The study for supporting the access to definitive care for patients with sepsis is interested, especially triage management. However, the effective access to definitive care depends on the integrated factors of emergency health care system not only triage system, the researcher also study to the overall factors for predicting the outcome in patients with sepsis.

According to the clinical studies, the clinical of sepsis patients can be worse from sepsis progression within 72 hours, which included the clinical signs of cardiovascular, renal, respiratory, and neurological (Moreno et al., 1999; Vosylius, Sipylaite, & Ivaskevicius, 2004). Conversely, the clinical signs of vital organs can improve from sepsis therapy within 72 hours (Levy et al., 2005). Therefore the clinical signs are measured in patients with sepsis in this study through the integration of many factors involved in the emergency health care system in Thailand. The evaluation of the emergency health care system in those patients will lead to improving the access system with the development in nursing care and emergency health care delivery in the health system of Thailand.

1.2 Research Framework

The Donabedian model, which provides an evaluation of the health service system through the structure and process in relation to the patient outcomes, has been widely used and successful in improving patient outcomes (Hanna & Kangolle, 2010; Lawson & Yazdany, 2012). The framework encompassed building an explanation to how the variation occurred, how the composition related to each other, and what the consequences of a policy change would be in improving the organization (Donabedian, 1983a). The indication is that a health maintenance organization would grow and influence the policy makers to change or continue each policy composition in review. This objective promotes an evaluation among coordinated factors rather than scattered fragments due to their consequences (Donabedian, 1983b). Validated knowledge of three different parts already exists as an important base of a valid causal progression (Donabedian, 1988a). Before evaluation, the researcher should define how the quality is, how health and its responsibility relate to each other, what the optimal care is, and what the effective outcome of a patient is (Donabedian, 1988b). Donabedian made concerns that the result of approaching structure and process was an aggregate outcome even though structure increased the likelihood of an improved process, which then increased the likelihood of an improved outcome (Donabedian, 1988b).

For patient safety, Donabedian model was developed with adding the antecedent conditions of a patient in the model and it was considered as a part of patient which influenced the outcomes (Hickam et al., 2003). Donabedian (1988a) suggested that the research framework should depend on preexisting knowledge and the study objective. Regarding the literature review, the outcomes of patients with sepsis were mostly derived from studies that examined each factor and circumstance. All reviewed factors were grouped according to the patient and system factors. The patient factors were antecedent conditions. They consisted of the severity of illness and time to perceive symptom onset. The system factors were structure and process in emergency health care system including level of hospital, sepsis policy, EMS utilization, triage practice, performance of sepsis resuscitation bundle, care model, length of ED stay and ICU admission. The system factors influenced to timely access while both of system and patient factors affected the health status in patients with sepsis. Therefore, this research framework is designed to explain the outcomes among variability with the system and patient factors on evaluating the clinical signs in patients with sepsis as shown in Figure 1.1.

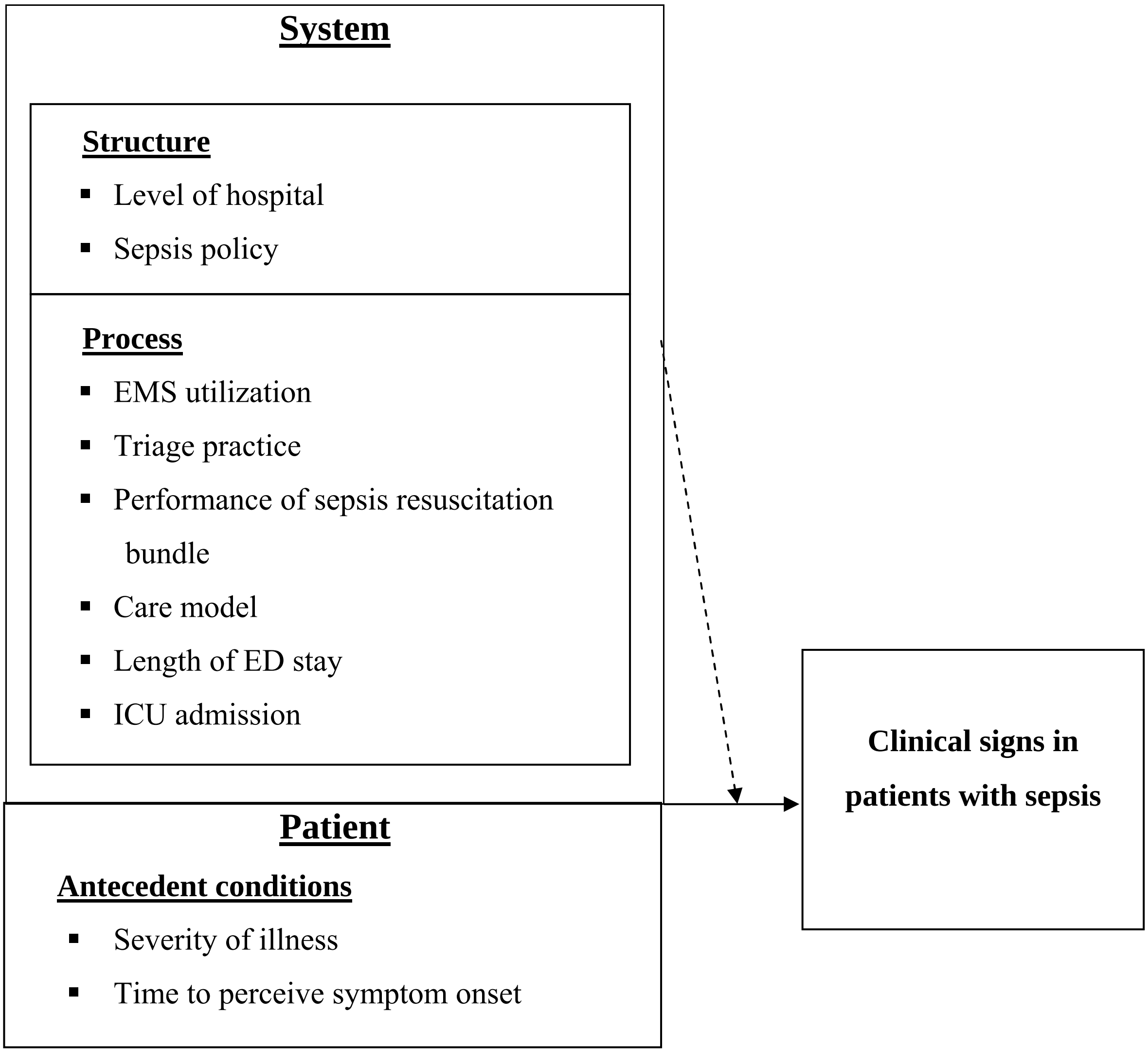

Figure 1.1 Research framework

1.3 Research Questions

What are the system and patient issues influencing clinical signs in patients with sepsis in the emergency health care system in Thailand?

1.4 Research Purposes

1.4.1 To describe the characteristics of patients with sepsis, the structure of emergency health care system, process of care, and the outcome of clinical signs in patients with sepsis.

1.4.2 To examine the clustering effect of system and patient levels influencing on clinical signs in patients with sepsis.

1.4.3 To examine the factors in system and patient levels influencing on clinical signs in patients with sepsis.

1.4.4 To examine the interaction effect between factors in system and patient levels on clinical signs in patients with sepsis.

1.5 Research Hypothesis

1.5.1 There is clustering effect of system level influencing on clinical signs in patients with sepsis.

1.5.2 Factors in the system and patient levels, including level of hospital, sepsis policy, EMS utilization, triage practice, performance of sepsis resuscitation bundle, care model, length of ED stay, ICU admission, severity of illness, and time to perceive symptom onset, influence clinical signs in patients with sepsis.

1.5.3 Factors in the system and patient levels have interaction effect on clinical signs in patients with sepsis.

1.6 Scope of the Study

This study is conducted in patients with sepsis who register at emergency departments during September 2014 to February 2015 in the tertiary or regional and general hospitals in central region of Thailand.

1.7 Expected Outcomes and Benefits

1.7.1 This study would provide the knowledge concerning the effectiveness of emergency health care system for preventing the progressive of disease and preventable death in patients with sepsis through the evaluation of fact system.

1.7.2 Triage and access systems would be developed following the effective policy for timely and optimal access to definitive care in patients with sepsis.

1.8 Definition of Terms

1.8.1 Sepsis is the systemic responses with hypoperfusion state due to an infection by presenting the sign of SIRS criteria and shock index $\geq$ 1 (Berger et al., 2013), as well as severe sepsis and septic shock.

1.8.2 Clinical signs were clinical with or without deterioration between 6 – 72 hours since ED arrival. The clinical signs with deterioration consisted of respiratory, circulatory, and neurological compromises following the society of critical care medicine (Sebat & Burg, 2010). The data of clinical signs with deterioration was collected when the clinical signs were worse than the data at six hours. The severity of clinical signs with deterioration based on the national early warning score (NEWS) (The Royal College of Physicians, 2012).

1.8.3 System factors are the structure and process of emergency health care system. They consist of eight as the following factors:

1.8.3.1 Level of hospital is the selected hospital-based services according to the facility to care for patients with sepsis following the service plan of Ministry of Public Health in Thailand. There are two levels including a general hospital and a tertiary or regional hospital.

1.8.3.2 Sepsis policy is a hospital policy for sepsis, which includes a protocol, an educational program, and a process for continuous quality improvement (Capuzzo et al., 2012; Castellanos-Ortega et al., 2010; Ferrer et al., 2008; Girardis et al., 2009; Seoane et al., 2013). It is either available or not. The protocol includes the instructions for clinical identification, sepsis team activation, and sepsis treatment or management. The educational program consists of the definition, recognition, and treatment of severe sepsis in the context of the protocol. The process of continuous quality improvement includes an audit and feedback process, such as monitoring sepsis performance and outcomes, an evaluation meeting per month or more frequently, and mortality case conference

1.8.3.3 EMS utilization is the use of EMS to arrival to the ED with the assessment of EMS provider. The EMS assessment is based on the clinical signs and the history suggestion of new infection of the modified Robson screening tool (Wallgren, Castren, Svensson, & Kurland, 2013). Clinical signs include pulse rate, respiration rate, body temperature, neurological sign, and blood glucose level. There are three different types of EMS utilization: non-EMS utilization, EMS utilization without complete assessment, and EMS utilization with complete assessment.

1.8.3.4 Triage practice is the triage performance with essential components for sepsis identification before or a first time seeing with physician at bedside. The essential components consist of three items, which are as follows (Dent et al., 1999; Larsen et al., 2011; Westphal et al., 2011): first, a complete vital signs assessment, including blood pressure, pulse rate, respiratory rate, and temperature; second, one or more organ function assessments, such as a neurological assessment with a Glasgow coma scale or AVPU scale, oxygenation with pulse oximetry saturation (SpO_2), and urine output; and third, alerting team with an accuracy of acuity level based on Emergency Severity Index (Gilboy, Tanabe, Travers, & Rosenau, 2012). The criteria of resuscitation level are systolic blood pressure < 90 mmHg, oxygen saturation $< 90\%$, and/or acute mental status deterioration to pain stimuli or unresponsive. The criteria of emergent level are potential threat to life with hypoperfusion in sepsis including ≥ 2 SIRS criteria and presenting shock index ≥ 1 (Berger et al., 2013). It is categorized as either completed triage practice or not.

1.8.3.5 The performance of the sepsis resuscitation bundle is the achievement of medical treatment and non-invasive monitoring following the Surviving Sepsis Campaign 2012 (Dellinger et al., 2013) as follows; 1) fluid challenge with crystalloids at least 2,000 ml within three hours, 2) broad spectrum antibiotic administration within one hour, 3) the achieved mean arterial pressure (MAP) ≥ 65

mmHg within six hours, and 4) the achieved urine output $\geq$ 0.5 ml/kg/hr within six hours. It is categorized as either achieved in all medical treatment and non-invasive monitoring or not. The achieved time is counted since a first time to ED arrival.

1.8.3.6 Care model is the management of feasible components of sepsis resuscitation bundle at ED that bases on the situation in Thailand. The feasible components include fluid challenge with crystalloid at least 2,000 ml within three hours, antibiotic administration within 1 hour, and MAP $\geq$ 65 mmHg before admission including within 6 hours if the length of ED stay more than 6 hours (Mahavanakul et al., 2012). There are two models including ED centric model and non - ED centric model. The ED centric model is the achievement of all feasible components at ED. The non-ED centric model is no achievement in any feasible component at ED.

1.8.3.7 Length of ED stay is the duration of time a patient with sepsis stays at the ED.

1.8.3.8 ICU admission is the status admissions at ICU or intermediate ward within six hours for patients with sepsis after receiving care in the emergency department. It is categorized as either ICU or intermediate ward admissions within six hours or not.

1.8.4 Patient factors are antecedent conditions. They consist of two of the following factors:

1.8.4.1 Severity of illness is the combination of components following the predisposition, infection, response, and organ failure (PIRO) sepsis staging system, which can measure the level of severity in sepsis patients (Levy et al., 2003). It is measured with the Mortality in Emergency Department Sepsis (MEDS) score (Shapiro et al., 2003). A high score represents a higher severity.

1.8.4.2 Time to perceive symptom onset, is the duration between the perceived time of symptom onset and the time of latest ED arrival in patients with sepsis.

CHAPTER II
LITERATURE REVIEW

This literature review conceptualizes the situations and factors of emergency health care system that related to health status outcomes and preventable deaths in patients with sepsis. This information demonstrates how sepsis can be aggravated and how emergency health care system can contribute to timely treatment and survival for those patients in the following in five issues:

2.1 The global burden of sepsis

2.2 Sepsis is a preventable death and its contributing factors

2.3 Sepsis with hypoperfusion is a high risk group

2.4 Existing gaps of knowledge in the emergency health care system

2.5 Theoretical framework for research

2.1 The global burden of sepsis

Sepsis is a global burden throughout all developed and developing countries. The evidences shows that it has been increasing continuously since 1979 in many countries, such as United States, India, and Taiwan (Chatterjee, Todi, Sahu, & Bhattacharyya, 2009; Dombrovskiy, Martin, Sunderram, & Paz, 2007; Lagu et al., 2012; Martin et al., 2003; Melamed & Sorvillo, 2009; Shen et al., 2010). Incident reports of sepsis from the eight national level studies from developed countries, including United States, Brazil, United Kingdom, Norway and Australia, varied from 22 to 240/100,000 in sepsis depending on the methodological data collection (Jawad, Luksic, & Rafnsson, 2012). However, after benchmarking, the incidence of sepsis in United States is estimated to be increasing at an annual rate of 13.0% (Gaieski et al., 2013), such that the number of sepsis cases is anticipated to increase to 1,110,000 by 2020 (Angus et al., 2001).

In emergency service settings, the prevalence of patients with sepsis is greater than any other time-sensitive illness in use of EMS, with 3.3% for sepsis, 2.3% for acute myocardial infarction, and 2.2% for stroke (Seymour et al., 2012). The sepsis acuity of EMS patients was significantly higher than non-EMS patients as 6 and 3 of MEDS score respectively ($p < 0.001$), with 26% of those patients presenting with organ dysfunction and shock (Wang et al., 2010). More than 60% of patients with sepsis had two or more organ dysfunctions when arrived to the ED. The mean number of organ dysfunctions increased from 1.6 to 1.9 during admissions in 2000 - 2007 ($p < 0.001$) (Kumar et al., 2011). Therefore, the hospitalization rate of sepsis had annually increased by 8.2% ($p < 0.001$) (Dombrovskiy et al., 2007), especially in ICU admissions, which increased progressively from 7.7% in 1997 to 14.0% in 2005 (Australasian resuscitation of sepsis evaluation, 2007). According to one prospective study in Thailand, the incidence of ICU admissions for sepsis increased from 16.6% to 21.6% during 2004 – 2006 (Khwannimit & Bhurayanontachai, 2009). The most common site and cause of sepsis were pneumonia and bacteremia. (Angkasekwinai et al., 2009; Angus et al., 2001; Lagu et al., 2012).

The mortality rate of sepsis depends on the staging and is increased when sepsis was made worse by sepsis, sepsis with organ dysfunction, and sepsis with shock as 10 - 20%, 20 - 50%, and 40 - 80% respectively (Martin, 2012). Patients with sepsis and three or more organ dysfunctions had a 3.93 times higher risk of mortality ($p = 0.002$) (Grozdanovski et al., 2012). The emergency health care delivery system is especially a concern due to the evidences that presented more than 20% of patients with sepsis had progressed to septic shock (Angkasekwinai et al., 2009; Glickman et al., 2010) and 38.6% were worse to respiratory compromise and/or alteration of conscious within 48 hours (Tsai et al., 2014) in hospital later admissions.

2.2 Sepsis is a preventable death and its contributing factors

Preventable death is death that can be prevented from timely and accurate diagnosis and management. It was significant in emergency patients ($p = 0.02$) (Hogan et al., 2012). Sepsis caused the most preventable death at 30 - 50% due to delay or inaccurate diagnosis and/or inadequate management at the ED in Taiwan and the

United Kingdom (Lu et al., 2006; Nafsi et al., 2007). Some of these problems included the process of clinical monitoring (31.3%), diagnosis (29.7%), and drugs and fluid management (21.1%) (Hogan et al., 2012).

When the sepsis acuity was higher, the mortality rate increased (Howell et al., 2011; Shapiro et al., 2003; Vincent et al., 1996), especially when patients with higher sepsis acuity did not receive the optimal care, such as the delay of appropriate antibiotic administration ($p < 0.0001$) (Kumar et al., 2006) and the unable access to ICU care ($p = 0.002$) (Groot, Deckere, Flameling, Sandel, & Vis, 2012). However the mortality rate of patients with higher sepsis acuity had a significant decrease when they received optimal care with timely treatment and monitoring ($p < 0.01$) (Gao, Melody, Daniels, Giles, & Fox, 2005). Policy and resources were associated with the performance of optimal care and the decreased mortality rate (MacRedmond et al., 2010; Nguyen et al., 2010; Nguyen, Schiavoni, Scott, & Tanios, 2012).

Therefore risk factors associated with preventable death depend on the patient conditions and the unavailable strategic policy and resource in emergency health care system. All factors can be concluded to involve patient and system factors. The system factors had influenced the consequence of sepsis through patient factors as timely and accurately diagnosis and management while all factors had contributed the health outcome as mortality.

2.2.1 Patient factors are antecedent conditions.

2.2.1.1 Severity of illness: Severity of illness is as a basic component that influences the clinical outcomes in patients with sepsis. The predisposition, infection, response and organ dysfunction (PIRO) system have influenced the severity of illness following sepsis staging (Levy et al., 2003). When all components of PIRO system were analyzed to represent the severity of sepsis by scoring, the higher scores always equated to a high mortality rate (Howell et al., 2011; Shapiro et al., 2003). The high scores indicated high risk in each component.

Predisposition is premorbid factors, which include increased age and comorbidity. The elderly, with more than 65 years of age, had a 13.1 times higher risk of developing sepsis (O'Brien et al., 2007). Comorbidity or specific chronic inflammation was associated with sepsis, such as chronic lung disease, chronic kidney disease, chronic liver disease, congestive heart failure, diabetes, HIV infection, and cancer (Martin et al., 2003; O'Brien et al., 2007; Wang et al., 2012). These diseases have a multitude of risk factors to developing sepsis. Patients with hematologic cancer had a 15.7 times higher risk of developing sepsis than patients without cancer; a 2.8 times higher risk for patients with any cancer compared to patients without cancer; 2.6 times higher risk for patients with cirrhosis compared to patients without cirrhosis; and a 5.1 times higher risk for patients with HIV infection compared to patients with no HIV infection (O'Brien et al., 2007). The patients with the higher numbers of chronic medical conditions were associated with a higher risk of sepsis. Patients with one chronic medical condition had a 1.91 times higher risk, two chronic medical conditions a 2.65 times higher risk, and so on: 3.11, 3.81, 4.99, 5.40, 10.54 and 14.49 times higher risk respectively (Wang et al., 2012). Studies have shown that more than 50% of patients with sepsis were 65 years and older and/or presented with one or more comorbidities (Powell et al., 2010; Wang et al., 2012).

Decreased immunocompetence and the state of chronic inflammation increased the susceptibility and exaggerated the response to infection, as a result of the hypoperfusion state (Ginaldi et al., 1999; Moore et al., 2010; Wang et al., 2012). The elderly were associated with a higher mortality and had two or more organ dysfunctions during ICU admissions ($p < 0.001$) (Guidet et al., 2005). The 40 – 70% of the patients with sepsis presented with one or more comorbidities which are a higher risk of death, such as metastatic cancer ($p < 0.001$), hematologic cancer ($p = 0.045$) (Khwannimit & Bhurayanontachai, 2009), chronic respiratory failure ($p = 0.001$), and chronic heart failure ($p = 0.004$) (Grozdanovski et al., 2012). Lung cancer had a 2.3 times higher risk of progression to septic shock within 72 hours ($p = 0.005$) (Glickman et al., 2010) whereas liver failure and cancer had the highest risk, with 1.78 and 1.74 times higher risk to early mortality within two days respectively (Powell et al., 2010).

Infection and response are impacted by the prognosis. Respiratory was the most common site of infection. The 40% of patients with respiratory infection estimated to sepsis progression (Klouwenberg et al., 2012). Sepsis manifests in systemic responses when the uncontrolled infection occurs in the systemic circulation. The system responds to an infection process by stimulating the signs of systemic inflammatory response syndrome (SIRS), which include an increase in body temperature greater than 38°C or lower than 36°C, heart rate higher than 90 beats/min, respiratory rate higher than 20 breaths/min and white blood cell count higher than 12,000 cells/mm^3 or lower than 4,000/mm^3 or the presence of more than 10 percent bands or immature neutrophils (Bone et al., 1992). The increased number of SIRS is associated with a higher risk of organ dysfunction and mortality (Sprung et al., 2006). In particular, the higher heart rate (114 beats /min) and respiratory rate (26 breaths/min) were significant to cryptic shock or the state of normotension with blood lactate level > 4 mmol/L ($p = 0.04$ and $p = 0.01$ respectively) (Puskarich et al., 2011).

Organ dysfunction was significantly associated with mortality rate on the first day of admission (Jones, Trzeciak, & Kline, 2009). The 28-day mortality rate related to each organ failure was 4.5 times for hematologic failure (platelet < 100,000/mm^3), 3.6 times for respiratory failure (respiratory rate > 20 breath/min, oxygen saturation < 90% with room air or < 94% with oxygen therapy), and 3.6 times for cardiovascular failure (systolic blood pressure < 90 mmHg) (Shapiro et al., 2006). The higher numbers of organ dysfunction were associated with an increased mortality rate as follows: 20% in 1 organ dysfunction, 40% in 2 organ dysfunctions, 70% in 3 organ dysfunctions, and 80% in 4 or more organ dysfunctions (Angus et al., 2001).

2.2.1.2 Time to perceive symptom onset: Research had demonstrated that a delay in diagnosis or interventions performed more than 48 hours after the onset of organ dysfunction increased the mortality rate by 8.73 ($p=0.004$) among elderly patients with sepsis (Freitas et al., 2008). There is limited data describing the delay in access to emergency health care system in patients with sepsis (Herlitz et al., 2012). Jordan and colleagues (2009) found that the patients with pneumonia who had low income also had low percentage of seeking health care. Most of them had duration of illness more than 7 days with higher severity of illness because of need hospitalization significantly ($p < 0.0001$).

2.2.2 System factors are the structure and process in the emergency health care system.

2.2.2.1 Level of hospital: Different hospital levels have varying resources and patient volumes. Powell and colleagues (2010) found that the teaching hospitals were associated with a high volume of patients with sepsis at emergency department ($p < 0.001$) due to the high expected quality of care. The teaching hospital and large number of beds at the hospital had 1.21 and 1.20 times high risk of the mortality case when compared to nonteaching hospitals ($p < 0.001$) and small number of beds ($p < 0.05$). The highest volume of patients with sepsis at the emergency department as more than 371 cases/year, had 27% of the mortality when compared to the lower volume, such 17% for 146 – 248 cases/year and 10% for 249 – 371 ($p < 0.001$).

All of those hospital levels however, can contribute to a decreased mortality rate in patients with sepsis when resources are appropriately managed for sepsis care (Nguyen et al., 2010). Many studies have revealed that a decreased mortality rate presented in hospitals with more resources. The more available resources at the tertiary hospitals resulted in a decreased mortality rate in patients with sepsis (Champunot, Kamsawang, Tuandoung, & Tansuphaswasdikul, 2012; Gao et al., 2005; Levy et al., 2010; Permpikul et al., 2010). However, the mortality rate in patients with sepsis increased when the tertiary hospitals restricted resources (Mahavanakul et al., 2012). While the community hospitals had difficultly adhering to invasive-monitoring because of the limited resources (Gerber, 2010; O'Neill, Morales, & Jule, 2012), some researchers demonstrated that a decreased mortality rate in patients with sepsis was found in the community hospitals with utilizing the non-invasive monitoring (Nguyen et al., 2012; Patel et al., 2010).

2.2.2.2 Sepsis policy: Sepsis policy is a policy for facilitating earlier diagnosis and treatment of sepsis regarding management at the emergency department level. During 1993 - 2003, the mortality rate in patients with sepsis increased from 30.3 $\pm$ 0.11 to 49.7 $\pm$ 0.13 per 100,000 persons ($p < 0.001$), whereas case fatality rate decreased from 45.8% $\pm$ 0.17% to 37.8% $\pm$ 0.10% ($p < 0.001$) after the use a sepsis management policy (Dombrovskiy et al., 2007).

The strategies of sepsis policy include a protocol, an educational program, and a quality improvement program, which influenced the improvement of sepsis treatment and decreased the mortality in both academic and community hospitals (Nguyen et al., 2010). Those intervention contributed to an increase in the complete compliance rate of the sepsis resuscitation bundle from 8% before intervention to 35% after the intervention ($P < 0.01$) and a decrease in the mortality rate from 79% before intervention to 32% after intervention ($P < 0.01$) (Girardis et al., 2009). The sepsis protocol and quality improvement program both helped to speed up the time for antibiotic administration and from 140 minutes to 72 minutes ($p \leq 0.001$) and decrease the length of hospital stay from 8 days to 7 days ($p = 0.036$) (Seoane et al., 2013). The education program contributed to the success of implementing the protocol (Nguyen et al., 2010) by increasing the compliance rate of the sepsis resuscitation bundle with the achieved goal of monitoring ($p < 0.001$) (Jeon et al., 2012).

2.2.2.3 EMS utilization: EMS patients had significantly higher sepsis acuity than non-EMS patients with MEDS score at 6 and 3 respectively ($p < 0.001$) (Wang et al., 2010). EMS patients with sepsis also presented with a higher organ failure and mortality rate than non EMS patients ($p < 0.001$) (Studnek et al., 2012; Wang et al., 2010). The mode of arrival with EMS resulted in decreased timing in antibiotic administration from 152 to 116 minutes, as well as decreased timing in intravenous fluids from 68 to 34 minutes in EMS patients with sepsis when compared to non-EMS patients. Despite the shorter access time to treatment, the mortality rate was not significantly different in patients with sepsis (Band et al., 2011). Nevertheless, when the EMS provider recognized sepsis and notified at ED, the survival rate in patients with sepsis increased ($p = 0.04$) (Guerra et al., 2013). When the EMS providers correctly recognized the hemodynamic state and clinical instability of patients with sepsis, using the SIRS criteria and clinical signs of organ dysfunction, these processes had dramatically decreased the time of antibiotic administration from 122 to 70 minutes ($p = 0.003$) and the time of the sepsis resuscitation bundle administration from 131 to 69 minutes ($p = 0.001$) when compared with non EMS patients (Studnek et al., 2012).

The benefits of pre-hospital treatment for patients with sepsis were unclear. From a retrospective study, a 10% increase in oxygen saturation was associated with a 13.9% decrease in blood lactate levels ($p < 0.001$). In addition, an increase in systolic blood pressure of 10 mmHg was associated with a 3.9% decrease in blood lactate levels ($p = 0.03$). However, pre-hospital treatment, which includes supplemental oxygen, intravenous fluid replacement, and ECG monitoring, was not associated with organ dysfunction at a maximum score and was not associated with the outcome of organ dysfunction after adjustments from other factors (Seymour et al., 2010a). From another study, the 1.1 L of intravenous fluid replacement was not associated with the achievement of MAP $\geq$ 65 mmHg ($p = 0.09$), CVP 8 – 12 mmHg ($p = 0.6$) and $ScvO_2 > 70\%$ ($p = 0.25$) within six hours (Seymour et al., 2010b).

2.2.2.4 Triage practice: Triage is vital for initiating quick sepsis treatment. The role of a triage nurse is early detection and rapid recognition for time-sensitive illnesses, such as sepsis. However, sepsis is difficult to identify with only a chief complaint (Begier et al., 2003). Because of the difficult identification process, only one-third of patients with sepsis had been accurately identified at the ED (Rezende et al., 2008; Uittenbogaard et al., 2013). Furthermore, sepsis was the most under-triaged illness, which delayed timing of ICU admissions and impacted a significant number of deaths after the first few days of admission (Dent et al., 1999; Yurkova & Wolf, 2011). The lack of sepsis recognition in the triage area was the cause of sepsis treatment delay according to the perception of nurses (15.8%) and physician (18.2%) at the ED (Burney et al., 2012).

The strategies of triaging sepsis includes a complete vital sign assessment using SIRS criteria, assessment of one or more organ dysfunctions, followed with notification to the team with an emergent or a resuscitation triage level when sepsis is suspected. Early recognition with the assessment of SIRS criteria and organ dysfunction, including deteriorating neurological system, hypotension, oliguria, and hypoxemia, was related to a lower 28-day mortality (47% and 24.3%, $p < 0.001$) and in-hospital mortality (61.7% and 36.5%, $p < 0.001$) than only SIRS assessment (Westphal et al., 2011). When alerted teams were notified of sepsis, more than double the number of patients had a faster access time to treatment (Larsen et al., 2011).

When a triage level of urgency or lower severity level was indicated for patients with sepsis, the mortality rate increased (Yurkova & Wolf, 2011).

2.2.2.5 Performance of sepsis resuscitation bundle: Emergency health care delivery has a prominent role in the first six hours for sepsis resuscitation through the recognition of sepsis, maintenance of tissue perfusion and oxygenation, and rapid treatment of infection for patients with sepsis. The sepsis resuscitation bundle is defined as the combination of evidence-based practices of medical treatment and monitoring. For the Surviving Sepsis Campaign 2012 (Dellinger et al., 2013), the achieved goals are medical treatment and non – invasive and invasive monitoring as follows; 1) fluid challenge of crystalloid 30 ml/kg minimally within three hours and with vasopressor application in those with non-response within six hours, 2) broad spectrum antibiotic administration within three hours and especially one hour in septic shock, and 3) the achieved monitoring within six hours including urine output $\geq$ 0.5 ml/kg/hr, MAP $\geq$ 65 mmHg, CVP 8-12 mmHg, and $ScvO_2 \geq 70\%$. For the protocol-based standard therapy (Yealy et al., 2014), the achieved goals are medical treatment and non – invasive monitoring as follows; 1) initial fluid challenge with crystalloid 2,000 ml minimally in case without replete volume and vasopressor application in non-response cases within one hour 2) broad spectrum antibiotic administration within three hours, and 3) the achieved monitoring with systolic blood pressure $\geq$ 100 mmHg and/or shock index < 0.8 within one hour.

Each component of the sepsis resuscitation bundle was associated with a significantly increase in the survival rate in patients with sepsis. Firstly, the fluid challenge of crystalloid 30 ml/kg minimally such as fluid loading more than 800 ml at first hour significantly influenced the survival rate ($p < 0.001$) (Permpikul, Tongyoo, Ratanarat, Wilachone, & Poompichet, 2010) and the application of vasopressor, especially norepinephrine, was also associated with an increased survival rate in non-responsive cases (Vasu et al., 2012). Secondly, broad spectrum antibiotic administration within three hours had a lower mortality rate than administration in more than three hours in 28-day mortality rate ($p = 0.006$) and overall mortality rate ($p = 0.009$) (Lueangarun & Leelarasamee, 2012), especially when the duration time from triage to antibiotic administration less than or equal one hour ($p < 0.02$) (Gaieski et.al., 2010). If sepsis patients with hypotension or shock were delayed to receive antibiotic, the survival rate decreased by 7.6% in each hour of delay (Kumar et.al., 2006). Thirdly, the achieved urine output $\geq$ 0.5 ml/kg/hr within six hours influenced the survival rate by 4.1 times ($p = 0.016$) (Angkasekwinai, et al., 2009). Fourthly, achieved mean arterial pressure (MAP) $\geq$ 65 mmHg within six hours increased the survival rate ($P = 0.019$) (Chung et al., 2012). Fifthly, achieved central venous pressure (CVP) 8-12 mmHg within six hours increased the survival rate ($P = 0.001$) (Chung et al., 2012). Lastly, achieved central venous oxygen saturation ($ScvO_2$) $\geq$70% was associated in surviving patients ($p = 0.008$) (Ferrer et al., 2009).

Completing the sepsis resuscitation bundle following the Surviving Sepsis Campaign resulted in a reduced mortality (30.5% and 46.5% respectively, $P = 0.009$) and a decrease by two folds in the incidence of sudden cardiopulmonary complications ($P = 0.02$) when compared with standard care (Rivers et al., 2001). If patients with sepsis did not receive the entire care, the mortality rate increased significantly (Nguyen et al., 2011; Varpula et al., 2007). However some arguments exist related to the effectiveness of the invasive monitoring as follows: the CVP monitoring was unreliable to predict the hemodynamic response after fluid challenge (Marik et al., 2008); and the achieved $ScvO_2$ $\geq$70% was not associated with mortality rate (Peake et al., 2009; Pope et al., 2010). According to, the evidence showed that the appropriate non-invasive monitoring was associated with a decreased mortality rate in patients with sepsis (Chuesakoolvanich, 2007; Hanzelka et al., 2013; Nguyen et al., 2012; Patel et al., 2010). In addition, the performance of the protocol-based standard therapy did not different results in 60-day mortality rate (18.2%, 21.0% and 18.9% respectively, $p = 0.83$), 90-day mortality rate (30.8%, 31.9% and 33.7% respectively, $p = 0.66$), and serious adverse events during admission (4.9%, 5.2% and 8.1% respectively, $p = 0.32$) when compared with the protocol-based early goal directed therapy and usual care (Yealy et al., 2014).

2.2.2.6 Care model: The three care models for the performance of sepsis therapy are as follows: ED-centric model, ICU-centric model, and collaborative model. The ED-centric model is when emergency providers have full responsibility to completely perform the sepsis resuscitation bundle in the ED, whereas the ICU-centric model gives full responsibility to the intensive care providers to perform the resuscitation bundle in the ICU. The collaborative model shares responsibility between emergency and intensive providers to initiate the identification of sepsis with starting of sepsis treatment at ED and continue to complete the resuscitation bundle at intensive care unit (Cowan & Trzeciak, 2005).

Na and colleagues (2012) found that the ICU-centric model was a mediator for the effective administration of the sepsis resuscitation bundle and was associated with a higher compliance rate of the sepsis resuscitation bundle, as well as an increased survival rate in patients with sepsis. On the contrary, Huang and colleagues (Huang et al., 2007) presented that the ICU-centric model was the least effective by delaying early intervention. Nguyen and colleagues (2011) found that the collaborative model was significantly associated with a higher survival rate due to the recovery from hypoperfusion state and an increased lactate clearance compared to the ED-centric model. In addition, according to the study of Casserly and colleagues (2011), the collaborative model was significantly associated with timely fluid administration ($p = 0.02$) and vascular access ($p = 0.01$) when compared with the ED-centric model. Meanwhile Peake and colleagues (2009) found that the mortality rate was no different in the ICU and general ward admissions when sepsis treatment was performed at ED in the ED-centric model.

In Thailand, the sepsis resuscitation bundle had a low compliance rate, especially in invasive monitoring (Angkasekwinai et al., 2009; Chuesakoolvanich, 2007). The feasible components of sepsis resuscitation bundle, which included in care model, consisted of fluid management, broad spectrum antibiotic administration, and non-invasive monitoring (Mahavanakul et al., 2012).

2.2.2.7 Length of ED stay: The length of stay in the ED was associated with an increased mortality rate corresponding to the increased time in the ED, such as 2.5% for less than two hours, 2.7% for two to six hours, 3.9 for six to twelve hours, and 4.5% for more than twelve hours (Singer et al., 2011). The mean length of time for sepsis patients in the ED was 4.7 hours with 20% of them staying for more than 6 hours (Wang, Shapiro, Angus, & Yealy, 2007). The patients with sepsis, who had length of stay at the ED with more than three hours, had a higher mortality rate than patients who only stayed for three hours or less. The mortality rate was associated with length of stay at the ED as follows: 47.1% for more than three hours, 10.9% for between two and three hours, 15.2% for between one and two hours, and 26.8% for less than one hour (Degoricija et al., 2006). While the study of Haji and colleagues (2010) found that the median length of ED stay was 8.3 hours, it was not associated to mortality rate.

2.2.2.8 ICU admission: The workload of nurses caring for patients with sepsis was higher than any other illness, including acute renal failure and acute coronary syndrome due to the intense invasive monitoring needed. The mean nursing activities scores for sepsis, acute renal failure, and acute coronary syndrome were 57.0, 55.3 and 43.0 respectively ($p < 0.01$) (Carmona-Monge et al., 2013). In addition, the location of where patients were admitted affected the monitoring and treatment for patients with sepsis, such that patients who were admitted to the general ward had a prolonged duration of organ dysfunction without treatment than ICU admissions (2.2 $\pm$ 2.0 days and 1.2 $\pm$ 1.3 days respectively) (Freitas et al., 2008). The complete compliance rate of the sepsis resuscitation bundle was higher in patients who first had admission to the ICU versus the general ward (21.6% and 18.4% respectively) (Levy et al., 2012). ICU admissions were also associated with a decreased mortality rate in patients with sepsis, particularly when the duration of ICU admission was within six hours. The ICU morality rate was 8.4% for ICU admissions within six hours and 10.7% for ICU admission with more than six hours ($p < 0.01$) and hospital mortality was 12.9% for ICU admissions within six hours and 17.4% for ICU admissions with more than six hours ($p < 0.001$) (Chalfin et al., 2007). Overall, the median time of delay for ICU admissions was 24 hours (Rezende et al., 2008).

Sepsis was the most common cause for unplanned transfers to the ICU with a transfer 2.5 times more likely to occur (Delgado et al., 2013), which consequently increased the risk of death (Liu, Kipnis, Rizk, & Escobar, 2012) due to deteriorating physiological ($P < 0.001$) (Makris, Dulhunty, Paratz, Bandeshe, & Gowardman, 2010) and organ dysfunction on the general ward ($P < 0.015$) (Freitas et al., 2008). Unplanned transfers to the ICU had a 1.44 times higher risk of death than direct ICU admissions ($p < 0.01$) (Liu et al., 2012). As a result, sepsis had the highest rate of admission refusal to the ICU due to the decision criteria in the ICUs (Joynt et al., 2001). Tsai and colleagues (2014) found that patients with infection, who were admitted to the general ward, were worse in the clinical signs within 48 hours more than patients without an infection (38.6% and 25.5% respectively, $p < 0.001$).

Although the sepsis patients were quickly deteriorating, the transfer process to the ICU was more than 4 hours in most cases (Young, Gooder, McBride, James, & Fisher, 2003). Escobar and colleagues (2011) found that patients who were transferred to a higher level of care had higher mortality rate (19.2%, 2.3%, and 3.2% respectively) and length of hospital stay (14.4 $\pm$ 21.3, 4.0 $\pm$ 5.7, and 4.4 $\pm$ 6.9 days respectively) than patients who were admitted on a general or intermediate ward and were not transferred.

2.3 Sepsis with hypoperfusion is high risk group

Sepsis is a systemic response when pathogenic organisms spread into the bloodstream (Angus & Poll, 2013). The early clinical responses of sepsis present with the systemic inflammatory response syndrome (SIRS), which include fever, tachycardia, tachypnea, and abnormal white blood cell count (Bone et al., 1997). When sepsis affects the cardiovascular system, the derangement results in inadequate oxygen, inadequate tissue perfusion and anaerobic metabolism. It leads to accumulated serum lactate level, otherwise known as sepsis with hypoperfusion (Jones & Puskarich, 2011).

Sepsis with hypoperfusion is a high risk of poor prognosis, lack of identification, and inaccessible standard of care. Hyperlactatemia is having a serum lactate $\geq$ 4mmol/l and indicates hypoperfusion in patients with sepsis, which relates to deteriorating organ function ($p < 0.00001$) (Jansen, Bommel, Woodward, Mulder, & Bakker, 2009), 9.5 times higher risk of early death within 3 days than any other laboratory measurement (Shapiro et al., 2005), 7.1 times higher risk of 28-day in hospital death than lower serum lactate levels (Howell, Donnino, Clardy, Talmor, & Shapiro, 2007), and 4.87 times higher risk of mortality in both of shock and non-shock group than lower serum lactate levels ($p < 0.001$) (Mikkelsen et al., 2009).

Unfortunately, the measurement of serum lactate is rare in Asia. Only 60% have available resources for measuring serum lactate and only 20% use serum lactate levels for detection sepsis with hypoperfusion in ED (Phua et al., 2011). However, nearly 50% of medical professionals did not use of serum lactate measurement and they perceived that it caused the delay of treatment in patients with organ dysfunction and shock (Burney et al., 2012). This may be due to the fact that hyperlactatemia in patients with sepsis and hypoperfusion has a low sensitivity to predict mortality (Shapiro et al., 2005; Trzeciak et al., 2007). As a result, patients with sepsis and hypoperfusion had no initiation of the sepsis resuscitation bundle (Mikkelsen et al., 2010) and/or a low compliance rate of sepsis treatment, which included failing to provide fluid resuscitation (Cronshaw et al., 2011; Kang et al., 2012). In spite of, the decreased mortality rate due to sepsis resuscitation bundle was not different between sepsis with hypoperfusion and sepsis with shock (Puskarich et al., 2011).

2.4 Existing gaps of knowledge in the emergency health care system

2.4.1 Limited studies the relationship between the clinical signs in patients with sepsis and emergency health care system

The evidences of clinical getting worse in patients with sepsis after hospitalization were demonstrated as follows; more than 20% progressed to shock (Angkasekwinai et al., 2009; Glickman et al., 2010) and 38.6% were worse in clinical signs of respiratory and neurological within 48 hours (Tsai et al., 2014). According to when sepsis developed to hypoperfusion state, the clinical signs of vital organs were high risk to deterioration (Jansen et al., 2009), especially within 72 hours including cardiovascular, renal, respiratory, and neurological function (Moreno et al., 1999; Vosylius et al., 2004) while the clinical of vital organs could improve from sepsis therapy within 72 hours (Levy et al., 2005). However, the current knowledge was limited what factors of emergency health care system were related to clinical signs in patients with sepsis especially in the hypoperfusion state.

2.4.2 Limited studies in the variation of emergency service setting

Most studies have been performed in a unique setting. The decreased mortality rate also resulted from unique policies and resources. The studies in tertiary hospital usually demonstrated an effective outcome from a treatment protocol followed a surviving sepsis campaign (Champunot, 2012; Gao et al., 2005; Levy et al., 2010; Permpikul et al., 2010) while the studies in general hospital demonstrated an effective outcome with non-invasive monitoring under limited resources (Nguyen et al., 2012; Patel et al., 2010). Therefore the current knowledge was limited to the actual outcome coming from studies comparing a variation of settings.

2.4.3 May be biased due to one level of analysis

From the literature review, the outcomes of patients with sepsis were derived from the studies with one level analysis. Medical treatment using the sepsis resuscitation bundle was significantly associated with a decreased mortality rate in patients with sepsis in the meta-analysis study (Chamberlain, Willis, & Bersten, 2011). While Na and colleagues (2012) found that the survival after complete sepsis resuscitation bundle was not significant ($p = 0.58$) after adjusting factors of severity of illness and care model. Although the structure and process factors affected the outcome of mortality through the antecedent conditions of patient factors, these factors were not studied across factors on the mortality rate, as studied only within one level analysis. This result was explained in term of combination factors that may be inflated the level of relationships.

2.5 Theoretical framework for research

According to the study that explores what the patient and system factors can influence the outcome of clinical signs in patients with sepsis, the theoretical models of access and Donabedian are interested. Access means the available services when patients need it and where the system is the potential and actual entry (Aday & Andersen, 1974). The behavioral models of health service use of Andersen phase 3 (Andersen, 1995) recognize that the health outcomes influence subsequent health behaviors through the personal health practices and utilization of health services. It was used to understand why people seek health services and how personal practices maintain and improved health status, as a goal of health service delivery. It explains the disparities in access to health service, especially when people need it within the context of predisposing and enabling components. This access model also stressed to depict the health behavior in people depending on their function, social structures, economic, and community resources than the evaluation of health service (Cox, 1982).

Donabedian model encompassed the structure and process that explained how the variation occurred, how the composition related to each other, and what the consequence of policy change would be for organizational improvement (Donabedian, 1983a). This result would be to grow and shape the policy makers to develop the construction. The objective of the model promoted the evaluation among coordinated factors rather than scattered fragments for their consequences (Donabedian, 1983b). Donabedian (1988b) concerned that the outcome of approach on structure and process was only result possible, even though structure increased the likelihood of improved process and that the process would increase the likelihood of an improved outcome. He suggested that the research framework should depend on preexisting knowledge and the study objective, especially an already validated knowledge of three different parts exist as an important base of a valid causal progression (Donabedian, 1988a). For patient safety, Donabedian model was developed with adding the antecedent conditions of a patient in the model and it was considered as a part of patient which influenced the outcomes (Hickam et al., 2003).

From literature review, the system factors had influenced to the consequence of sepsis through patient factors as timely and accurately diagnosis and management while both of system and patient factors had contributed the health outcome as mortality. Therefore, Donabedian model is suitable to explore the association between the integrated factors and the evaluated health status as clinical signs in patients with sepsis among variability of emergency health service delivery.

CHAPTER III
METHODOLOGY

This study was to explore factors in the system and patient levels influencing the clinical signs in patients with sepsis in the context of emergency health care system. The multilevel logistic regression analysis was statistical used. The research methodology presented in this chapter including research design, characteristics of population, sample size estimation, sampling procedure, instruments, data collection, ethical considerations, and statistical analysis.

3.1 Research design

A prospective descriptive correlational design was conducted to examine the effect of factors in the system and patient levels on clinical signs in patients with sepsis. Factors in patient level were severity of illness and time to perceive symptom onset. Factors in system level were level of hospital, sepsis policy, EMS utilization, triage practice, performance of sepsis resuscitation bundle, care model, length of ED stay and ICU admission.

3.2 Population and sample

3.2.1 Population

The two levels of population were the patient within patient level and the hospital within system level.

3.2.1.1 The patient level: They consisted of patients who access through the ED, were diagnosed with infectious disease, and presenting in both signs of sepsis and hypoperfusion at first time presentation as follows: 1) Sepsis was two or more of SIRS criteria. The SIRS criteria consisted of 4 items including body temperature >38°C or <36°C, pulse rate > 90 beats/min, respiratory rate > 20 breaths/min or $PaC0_2$ <32 mm Hg, and white blood cell count as >12,000/mm^3 or <4,000/mm^3 or band >10% (Bone et al., 1997); 2) Hypoperfusion was shock index $\geq$ 1, as the ratio of heart rate per a minute to systolic blood pressure at more than or equal one, that predicted the state of hyperlactatemia with positive predictive value at 0.24, negative predictive value at 0.92, sensitivity at 0.48, and specificity at 0.81 (Berger et al., 2013).

3.2.1.2 The system level: It consisted of the hospitals in central region which had the facility to perform the sepsis therapy following the service plan of Ministry of Public Health in Thailand, which were the tertiary or regional and general hospitals.

3.2.2 Sample size estimation

Sample size estimation for hospital setting in multilevel analysis requires the maximize statistical power that depends on desired power, the level of significance, effect size, the intra-class correlation (ICC) coefficient, and possible sample size of patient (Scherbaum & Ferreter, 2009b). The desired power and level of significance were considered at 0.90 and 0.05 respectively. The effect size (d) of 0.61 was calculated on the data of quasi-experimental research in patients with sepsis (Onswadipong, Sungkard, Kusuma, Ayuthya, & Rongrungruan, 2011) with the different means (X_1-X_2) divide by the pooled standard deviation (σ_{pooled}) (Cohen, 1977) as the formula below:

$$d = \frac{[X_1 - X_2]}{\sigma_{pooled}} \quad , \quad \sigma^2_{pooled} = = \frac{(n_1-1)\sigma_1^2 + (n_2-1)\,\sigma_2^2}{n_1 + n_2 - 2}$$

X_1 = mean score of SOFA score at 48 hours of control group (= 5)

X_2 = mean score of SOFA score at 48 hours of treatment group (= 3)

σ_1 = standard deviation of SOFA score at 48 hours of control group (= 3.86)

σ_2 = standard deviation of SOFA score at 48 hours of treatment group (= 2.63)

n_1 = n of control group (= 35)

n_2 = n of treatment group (= 35)

Therefore; $\sigma^2_{pooled} = \frac{(35-1)(3.86)^2+(35-1)(2.63)^2}{35+35-2} = \frac{506.59+235.17}{68} = 10.91$

$\sigma_{pooled} = 3.30$

$d = \frac{[5-3]}{3.30} = 0.61$

The sample size of hospital (n_j) depends on the intraclass correlation (ICC, ρ), the variance and the sample size of patient (n_i) as the formula below (Scherbaum & Ferreter, 2009b). The variance of 0.04 was calculated with the effect size (d) of 0.61 of previous study (Onswadipong et al., 2011) dividing by the Z score of significance level and desired power at 0.05 (1.96) and 0.90 (1.29) respectively. The sample size of patient was determined 30 samples in each hospital for a closed normal approximation of distribution. Because there was limited data of the between-group variance for the ICC calculation in sepsis patients, the desired ICC for this study also based on the typically range between 0.05 and 0.30 in previous multilevel research (Snijders & Bosker, 2012). Therefore, the estimated sample sizes of hospital (n_j) following the ICC of 0.05, 0.10, 0.15, 0.20, and 0.30 were 8, 13, 18, 24 and 34 respectively (Table 3.1). For this study, the sample size of 18 hospitals, based on the ICC of 0.15, was selected because the cost of sampling depends on the number of unit (Scherbaum & Ferreter, 2009a) while the budget of this study is limited. However, the number of more than 10 units is adequate to analyze in the multilevel modeling (Snijders & Bosker, 2012). For anticipated the dropouts rate, the sample size of patient should be added at least 10% (Kadam & Bhalerao, 2010). Conclusion, the sample sizes consisted of 18 hospitals and 594 patients or 33 patients in each hospital.

$$\text{Variance} = \frac{4\,[\rho + \{(1-\rho)/n_i\}]}{n_j} \; ; \quad \text{Standard error} = \sqrt{\text{Variance}}$$

$$\text{Standard error} \leq \frac{d}{Z_{1-\alpha/2} + Z_{1-\beta}} \;, \quad \leq \frac{0.61}{1.96 + 1.29} \;, \quad \leq 0.19$$

$$\text{Variance} = 0.04$$

$$0.04 = \frac{4\,[0.15 + \{(1 - 0.15)/30\}]}{n_j}$$

$$n_j = 17.8 \sim 18 \text{ hospitals}$$

Table 3.1 The estimated sample size of hospital based on the desired intraclass correlation (ICC) between 0.05 and 0.30 and the sample size of 30 patients/hospital

The estimated ICC	The sample size of patient	The sample size of hospital
0.05	30	8
0.10	30	13
0.15	30	18
0.20	30	24
0.30	30	34

After conduct the study, there were 17 hospitals for enrollment in the study by permission of each director. For six months of collecting data, the sample size was 202 patients from 11 hospitals (Appendix A). Because the research assistants of 6 hospitals reported that did not found the patients with sepsis and inclusion criteria. However, the sample size of 202 patients from 11 hospitals was acceptable for multilevel logistic regression analysis following the ICC value at 0.08 of this study. According to the study of Jansomboon (2010) that revealed the average biases were stable at 0.200 when the sample sizes of level one or patient level was at least 5 cases in each setting under the sample size of level two or hospital level was at 10, 30, 50, and 100 hospitals.

3.2.3 Sampling procedure

3.2.3.1 System level: The hospitals were enrolled with two - stage random sampling for the selected provinces and then the selected hospital from the central region of Thailand (Figure 3.1). There were total 22 provinces following the Royal Institute. They consisted of 22 tertiary or regional hospitals in 11 provinces and 26 general hospitals in 18 provinces. There are two processes for two – stage random sampling. Firstly, it was started with random sampling for 8 provinces with presenting the tertiary or regional hospitals and 10 provinces with presenting the general hospitals. Because the study was determined to select a hospital from a province in each level, the selected numbers of provinces in each level were also calculated by the ratio of total numbers of hospital with each level and total numbers of hospital in both levels and then multiply with the sample size of 18 hospitals. This process was not calculated with the proportional number of sepsis patients because the number of patients with sepsis was unavailable in many ED setting from informal survey. Secondly, if a province had more than one hospital in a level, a selected hospital was enrolled with simple random sampling.

The inclusion criteria for hospital setting were as follows;

1. Public hospitals, except specialist hospitals
2. Permission of director of each hospital to participate in this study

Conclusion, there were 11 hospitals in the study including 5 tertiary or regional hospitals and 6 general hospitals (Appendix A).

Total 22 provinces in the central region of Thailand

11 provinces presenting with 22 tertiary or regional hospitals

18 provinces presenting with 26 general hospitals

First stage 8 provinces | 10 provinces

Second stage 8 tertiary or regional hospitals | 10 general hospitals

Figure 3.1 Two-stage random sampling of hospital setting

3.2.3.2 Patient level: The patients were enrolled with the purposive sampling by using the inclusion criteria as follows;

1. A patient $\geq$ 18 years of age and no pregnancy
2. Diagnosis and admission at medical ward with infectious disease at least 72 hours after ED arrival or presenting with the worse clinical between 6 and 72 hours after ED arrival
3. No need for immediate surgery
4. A patient or family member was willing to participate in the study

Exclusion criteria were as follows;

1. Diagnosed with Dengue and Malaria infection
2. Diagnosed tachyarrhythmia from conduction disorder
3. Transfer cases from another hospital with receiving fluid challenge and/or antibiotic already

3.3 Research instruments

The six instruments were used to collect the information or data of patients, emergency health care system including structure and process components, and the outcome of clinical signs.

3.3.1 Clinical and sociodemographic questionnaires

The instrument was developed by the researcher for collecting the patient information (Appendix D). It consisted of two parts.

3.3.1.1 Part one was personal information. There were six questions including age, gender, marital status, education level, monthly income, and health service payment.

3.3.1.2 Part two was health history and utilization. There were six questions including underlying disease, health service utilization for the current illness before the latest ED arrival, time of perceived symptoms onset, a first time to health service utilization, time to the latest ED arrival and the symptoms urge to decide to utilize the latest ED. The time to perceive symptom onset was counted since time to perceive symptoms onset to time to the latest ED arrival.

3.3.2 Organizational data- level of hospital

The instrument was developed by the researcher that based on literature review and the questionnaire of "standardization of severe sepsis management" (Nguyen, et al., 2010) (Appendix D). It consisted of two parts.

3.3.2.1 Part one was the hospital information and characteristics. There were four questions including the number of beds in hospital, level of hospital, the annual volume of ED, and the number of patients with sepsis present to ED in monthly. The score of hospital levels was categorized with a scale of 0 to 1 as sequenced from lower to higher resources as following: score at 0 was a general hospital and score at 1 was a regional or tertiary hospital.

3.3.2.2 Part two was contained information about the available of sepsis policy that consisted of protocol, educational program, and process of continuous quality improvement in a hospital (Capuzzo et al., 2012; Castellanos-Ortega et al., 2010; Ferrer et al., 2008; Girardis et al., 2009; Seoane et al., 2013). The protocol included the instructions for clinical identification, sepsis team activation, and sepsis treatment. The educational program consisted of the definition, recognition, and treatment as the content in protocol. Process of continuous quality improvement included an audit and feedback process such as monitoring sepsis performance and outcomes, evaluation meeting per monthly or more, and mortality case conference. There were nine questions about the sepsis policy including the available of sepsis policy, the components of sepsis policy, the place to initiate sepsis policy, the available of the identification guideline for sepsis conditions at triage, team main in each part of sepsis protocol at ED including sepsis protocol, education, and process of continuous quality improvement, the duration of initiated sepsis policy, and the components of sepsis resuscitation bundle consisted in the sepsis protocol of hospital.

The scores of sepsis policy were categorized from 0 to 1 as following; score at 0 was the unavailable all or some items of sepsis policy and score at 1 was the available of sepsis policy including protocol, educational program, and process of continuous quality improvement.

Validity: The instrument of organizational data- level of hospital was evaluated for the content validity index (CVI) by a panel of five experts (Appendix C). The CVI based on relevance on the four-point scale. The CVI values of this instrument were 1.00 for 12 items and 0.80 for 2 items. The average of item-content validity index was 0.97 that is excellent content validity (Polit & Beck, 2006).

Reliability: The value of interrater reliability was 1.0 for 10 hospitals between the researcher and research assistance.

3.3.3 Emergency medical service (EMS) utilization

The instrument was to assess the emergency medical service utilization (Appendix D). There were four questions including the use of EMS for arriving to the ED, EMS assessment and treatment during EMS utilization. The EMS assessment consisted of three parts. Firstly, part I, the clinical signs of the modified Robson screening tool included pulse rate, respiration rate, body temperature, neurological sign, and blood glucose level (Wallgren et al., 2013). Secondly, part II, the other clinical signs of the Robson screening tool included blood pressure, pulse oximetry saturation, and oliguria condition (Robson, Nutbeam, & Daniels, 2009). Lastly, part III, the history suggestion of new infection with clinical signs followed the data at http://links.lww.com/EJEM/A57 of the modified Robson screening tool (Wallgren et al., 2013) including the general and specific signs related to infection. The general signs were fever, chills, new-onset weakness, malaise, nausea, vomiting, alteration of conscious, and hypotension. The specific signs were categorized to the etiology of infection as following; central nervous system, respiratory tract, intra-abdominal and gastrointestinal, urinary tract, skin/soft tissue and bone, indwelling device, and bacteremia.

The score of EMS utilization was categorized with a scale of 0 to 2 following the use of EMS and the assessment in EMS record as; score at 0 was non-EMS utilization (the answer “no” in the question number 1); score at 1 was EMS utilization without complete assessment (the answer “no” in the question number 3); and score at 2 was EMS utilization with complete assessment (the answer “yes” in the question number 3).

Validity: The CVI values of this instrument were 1.00 for 1 item and 0.80 for 2 items of the question number 1 and 2. The average of item-content validity index was 0.87. After the researcher explained the aims of 2 items that need an assessment issue not EMS level to validators, the average of item-content validity index increased to 1.00.

Reliability: The responsiveness to change or sensitivity of the modified Robson screening tool (part I and part III) was 75% for sepsis patients and 92.9% for sepsis patients with organ dysfunction (Wallgren, et al., 2013). The value of interrater reliability was 1.0 for 10 cases between the researcher and research assistance in each hospital.

3.3.4 The mortality in emergency department sepsis (MEDS) score

The MEDS score was developed by Shapiro and colleagues (Shapiro et al., 2003) (Appendix D). It was the combination of components following the sepsis staging of the predisposition, infection, response and organ failure (PIRO) system, which used to measure the level of severity in sepsis patients (Levy et al., 2003). There were nine independent predictors for 28-day mortality in infection patients. The score of each predictor based on the odd ratio values from multivariate analysis as following; score at 6 for terminal illness or metastatic cancer; score at 3 for age > 65 years, band > 5%, platelet count < 150,000 cell/mm^3, tachypnea (respiratory rate > 20 breaths/min) or hypoxemia (pulse oximetry saturation < 90%), and septic shock (systolic blood pressure < 90 mmHg after an initial fluid challenge 20 – 30 ml/kg); and score at 2 for lower respiratory infection (bronchitis or pneumonia), alteration of conscious, and nursing home resident.

High score represented a higher severity of sepsis and the range of total scores at 0 – 27 can be divided following the level risk of 28-day mortality as following; score at 0 – 4 for very low risk, score at 5 – 7 for low risk, score at 8 – 12 for moderate risk, score at 13 – 15 for high risk, and score > 15 for very high risk.

Validity: The overall accuracy of instrument was at fair to good levels with the area under receiver operating characteristic (ROC) as following; 76% and 82% in the validation and derivation sets respectively for prediction the 28-day mortality in infection patients (Shapiro et al., 2003), 88% for prediction the 28-day mortality in patients with SIRS conditions (Sankoff et al., 2008), 89% and 78% for prediction the early (5-day) and late (6 – 30 days) mortality in patients with sepsis (Lee et al., 2008), and 74% for prediction the hospital mortality patients with sepsis and organ dysfunction including shock (Crowe, Kulstad, Mistry, & Kulstad, 2010).

Reliability: The value of interrater reliability was 1.0 for 10 cases between the researcher and research assistance in each hospital.

3.3.5 The profile of emergency health care system

The instrument was developed by the researcher that based on literature review (Appendix D). It consisted of six parts.

3.3.5.1 Part one was triage practice. It contained information about chief complaint and the triage assessment as following; 1) vital signs including blood pressure or mean arterial pressure, pulse rate, respiratory rate, and body temperature, 2) signs of organ function including level of conscious, oxygenation with pulse oximetry saturation, and urine output, 3) sepsis alert with triage level. There were two questions of triage practice. The question of performance of the essential triage components was for measure the triage practice variable. The essential components consisted of 3 items, which were as follows (Dent et al., 1999; Westphal et al., 2011); 1) complete vital signs assessment, 2) one or more organ function assessments, and 3) alerting team with an accuracy of acuity level based on Emergency Severity Index (Gilboy, Tanabe, Travers, & Rosenau, 2012). The criteria of resuscitation level were systolic blood pressure < 90 mmHg, oxygen saturation $<$ 90%, and/or acute mental status deterioration to pain stimuli or unresponsive. The criteria of emergent level were potential threat to life with hypoperfusion in sepsis including ≥ 2 SIRS criteria and presenting shock index ≥ 1 (Berger et al., 2013).

The scores of triage practice were categorized with a scale of 0 to 1 as following; score at 0 was the incomplete essential triage practice; and score 1 was the complete essential triage practice.

3.3.5.2. Part two was sepsis identification. It contained the diagnosis of infectious disease and the criteria identification of sepsis. There was one question of correct criteria for sepsis with hypoperfusion.

3.3.5.3. Part three was the monitoring and treatment in ED within six hours. The monitoring contained about physiological parameters of the scoring system including systolic blood pressure, pulse rate, respiratory rate, oxygen saturation, body temperature and level of consciousness.

3.3.5.4. Part four was sepsis resuscitation bundle. It contained information about the components of sepsis resuscitation bundle including medical treatment and invasive and non-invasive monitoring. However, the performance of sepsis resuscitation bundle was the achievement of medical treatment and non-invasive monitoring following the Surviving Sepsis Campaign 2012 (Dellinger et al., 2013) as follows; 1) fluid challenge with crystalloids at least 2,000 ml within three hours that estimated from 30 ml/kg minimally with the mean body weight of 56.6 and 68.9 kg in women and men people in Thailand respectively (Wells, Treleaven, & Charoensiriwath, 2012), 2) broad spectrum antibiotic administration within one hour, 3) the achieved mean arterial pressure (MAP) $\geq$ 65 mmHg within six hours, and 4) the achieved urine output $\geq$ 0.5 ml/kg/hr within six hours. The achieved time was counted since a first time to ED arrival.

The score was categorized with a scale of 0 to 1 as either achieved in all medical treatment and non-invasive monitoring or not as following; score at 0 was not achieved in any components at 1–4; score at 1 was achieved in all components at 1–4.

3.3.5.5. Part five was care model. it is the achievement of feasible components of sepsis resuscitation bundle at ED including fluid challenge with crystalloid at least 2,000 ml within three 3 hours, antibiotic administration within 1 hour, and MAP $\geq$ 65 mmHg before admission including within 6 hours if the length of ED stay more than 6 hours (Mahavanakul et al., 2012). The scores of care model were categorized with a scale of 0 to 1 as following; score at 0 was the non-ED centric model which was no achievement in any feasible component at ED; and score at 1 was the ED centric model which was the achievement of all feasible components at ED.

3.3.5.6. Part six was admission data. It contained information about time of admission, length of ED stay, characteristics of ward admission, discharge status, time of discharge and length of hospital stay. The score of ICU admission was categorized with a scale of 0 to 1 as following; score at 0 was not admitted at ICU or intermediate ward within six hours; and score at 1 was admitted at ICU or intermediate ward within six hours.

Validity: The CVI values of this instrument were 1.00 for all items.

Reliability: The value of interrater reliability was 0.89 for 10 cases /hospital between the researcher and research assistance in all setting. It was acceptable because the value of 0.75 or higher was at very good level (Polit & Beck, 2012).

3.3.6 The detection of clinical deterioration

The instrument was evaluated between 6 hours and 72 hours after presentation at ED because the evidences had shown that the achieved goal of monitoring have to finish within 6 hours following the surviving sepsis campaign (Dellinger et al., 2013) and the clinical signs of vital organs including cardiovascular, renal, respiratory, and neurological function, could worse from sepsis progression (Moreno et al., 1999; Vosylius et al., 2004) or improve from sepsis treatment (Levy et al., 2005) within 72 hours. It consisted of three parts (Appendix D).

3.3.6.1 Part I was time table for recording the physical examination at least every four hours between 6 - 72 hours after presentation at ED including clinical signs of blood pressure, pulse rate, respiratory rate, oxygen saturation, body temperature, level of conscious, and urine output.

3.3.6.2 Part II was the detection of clinical signs with deterioration of respiratory, circulatory, and/or neurological compromises following the society of critical care medicine (Sebat & Burg, 2010) between 6 – 72 hours after presentation at ED. The data of clinical signs with deterioration was collected when the clinical signs were worse than the data at 6 hours. The signs of respiratory compromise included respiratory rate $\leq$ 8 or $\geq$ 30 breaths/min and/or oxygen saturation $\leq$ 90% even though the oxygen supplement was given. The signs of cardiovascular compromise included systolic blood pressure $\leq$ 90 mmHg or decrease > 40 mmHg, pulse rate $\leq$ 40 or $\geq$ 130 beats/min, or urine output $\leq$ 100 ml/4 hours. The sign of neurological compromise included sudden alteration of conscious.

3.3.6.3 Part III was the national early warning score (NEWS). The NEWS was developed by the royal college of physicians at United Kingdom for assessment the acute illness and evaluation the recovery status with detection of clinical deterioration (The Royal College of Physicians, 2012). If patients with sepsis presented the clinical deterioration with the signs of respiratory, circulatory, and/or neurological compromises between 6 – 72 hours in part II, the NEWS was measured at first time of getting deterioration. If they did not, the NEWS was measured at 72 hours.

There were six physiological parameters of the scoring system including respiratory rate, oxygen saturation, body temperature, systolic blood pressure, pulse rate, and level of consciousness. The score ranged from 0 – 3 point and the increased score indicated more unstable physiological parameters. If the use of any oxygen devices or supplements were presented, the score was added at 2 point. Score at zero point consisted of respiratory rate at 12 – 20 breaths/min, oxygen saturation at $\geq$ 96%, body temperature at 36.1– 38.0 $^{\circ}$C, systolic blood pressure at 111 – 219 mmHg, pulse rate at 51 – 90 beats/min, and level of consciousness at alert or fully awake and able to responsive and communicate. Score at 1 point consisted of respiratory rate at 9 – 11 breaths/min, oxygen saturation at 94 – 95%, body temperature at 35.1 – 36.0 $^{\circ}$C or 38.1 – 39.0 $^{\circ}$C, systolic blood pressure at 101 – 110 mmHg, and pulse rate at 41 – 50 or 91 – 110 beats/min. Score at 2 points consisted of respiratory rate at 21 - 24 breaths/min, oxygen saturation at 92 – 93%, body temperature at $\geq$ 39.1°C, systolic blood pressure at 91 – 100 mmHg, and pulse rate at 111 – 130 beats/min. Score at 3 points consisted of respiratory rate at $\leq$ 8 or $\geq$ 25 breaths/min, oxygen saturation at $\leq$ 91%, body temperature at $\leq$ 35.0 $^{\circ}$C, systolic blood pressure at $\leq$ 90 or $\geq$ 220 mmHg, pulse rate at $\leq$ 40 or $\geq$ 131 beats/min, and level of consciousness at verbal response or pain response or unresponsive.

The NEWS was considered to the evaluation of patients with special conditions. The respiratory rate was identified the score at 3 points when patients used mechanical ventilator following the criteria of respiratory compromise. The oxygen saturation was identified the value of > 91% as the score at zero point and still the value of $\leq$ 91% the score at 3 points when evaluated patients with chronic obstructive pulmonary disease following the recommendations of British Thoracic

Society. The systolic blood pressure was identified the score at 3 points when patients received the treatment with vasopressor. The level of consciousness was identified the score at zero points for patients who limited consciousness from underlying disease such as cerebrovascular disease and the intubated patients who were alert or fully awake, oriented and able to converse reasonably (Bastos, Sun, Wagner, Wu, & Knaus, 1993). However the score at 3 points was still when the level of conscious deteriorated from the baseline of neurological score. If patients received the sedative drug and they were not consciousness, the score of level of consciousness based on clinical of conscious before sedative use. If patients received antipyretic drug within 4 hours, the score of body temperature based on the latest body temperature before antipyretic drug used.

High score represented to higher worse clinical signs and the range of score group can be divided following the higher risk of mortality in patients with sepsis as following; 1.95 times in score at 5 – 6, 2.26 times in score at 7 – 8, and 5.64 times in score at 9 – 20 when compared with score at 0 – 4 (Corfield et al., 2013).

Validity: The overall accuracy of NEWS was at fair to good levels to predict the clinical deterioration or unplanned ICU admission and mortality with the area under receiver operating characteristic (ROC) as following; 85.7% for unplanned ICU admission and 89.4% for mortality in all medical emergency patients when compared with others early warning signs (Smith, Prytherch, Meredith, Schmidt, & Featherstone, 2013), and 67.0% for ICU admission within 2 days and 70% for mortality in sepsis patients when compared with age – adjusted in NEWS (Corfield et al., 2013).

Reliability: The value of interrater reliability was 1.0 for 10 cases between the researcher and research assistance in each hospital.

3.4 Data collection

3.4.1 Ethical considerations

3.4.1.1 For human right protection, the study was approved the ethical clearance and the risk free for participants through the process of Mahidol

University Institutional Review Board (MU-IRB). All processes of data collection were implemented with the right protection in all participants since preparation to data collection procedure. They were introduced to the study including research purposes, the expected benefits, the characteristics of samples, the processes of data collection and time requirement.

3.4.1.2 Before data collection, the researcher provided the study information to participants including director of hospital and patient for understanding before ask for permission and willing to sign the consent respectively.

3.4.1.3 During data collection, all participants had a right to refuse the study at any time. All patients were observed the unstable signs and symptoms since the start to finish data collection. If anyone presents the unstable signs and symptoms from baseline, the researcher will care the patients and notify nursing or/and medical team immediately.

3.4.1.4 After the data collection, the researcher assured all participants that the data has been kept strictly confidential and only the researcher can saccess. The identification code w used instead of name, address, and workplace for all participants. The results were demonstrated as group views for the medical privacy of participants and not mentioned to the confidential responses of each participant in both of patient and hospital levels.

3.4.2 Data collection process

3.4.2.1 After the study was permitted to conduct by MU-IRB, the researcher coordinated with the director, head nurse, and staff nurses of hospital enrollments following the sampling procedure for providing the information of the purposes and procedures of study in order to gain their cooperation.

3.4.2.2 After permission of each hospital, the researcher interviewed with checklist for the organizational data including level of hospital and sepsis policy from head nurse of ED. Then the researcher asked for a research assistant at each hospital for collecting data with five instruments including the emergency medical service utilization, the mortality in emergency department sepsis (MEDS) score, the profile of emergency health care delivery, the detection of clinical deterioration, and the clinical and sociodemographic questionnaires. Therefore, the research assistants were trained clearly for collecting data with checklist until the interrater reliability is more than 0.8 in each instrument.

3.4.2.3 The researcher or research assistant collected the data of the emergency medical service utilization, the mortality in emergency department sepsis (MEDS) score, and the profile of emergency health care delivery by observation and chart review.

3.4.2.4 The research assistant coordinated with the researcher after the patients receive treatment. The researcher or research assistant approached the patients and/or family after six hours of presentation at the ED. When the clinical signs of patient were stable and both patient and family were already to participate in the study, the researcher or research assistant introduced herself and the study including the research purposes and data collection. The researcher or research assistant asked for agreement to be participant in the study after they understood the study.

3.4.2.5 After the patient and/or family signed the consent to participate in the study and had a willingness to start the data collection, the researcher or research assistant collected the data with two instruments including the clinical and sociodemographic questionnaires by interview and the detection of clinical deterioration by physical assessment and chart review.

3.4.2.6 For the detection of clinical deterioration, the data was collected between 6 – 72 hours since presentation at ED and controlled for the accuracy by followed steps:

1. Provide the patient with lying position and rest for 10 minutes before assessment.

2. Measure blood pressure on either arm.

3. Measure pulse rate for a full minute.

4. Measure respiratory rate for a full minute.

5. Measure oxygen saturation for a full minute with good wave form.

6. Measure axillary temperature with controlling the closed space for three minutes, after that add 0.5 $^{\circ}$C to the measured value for represent body temperature.

3.4.2.7 During data collection, the patients were observed the unstable signs and symptoms continuously. If the clinical signs and symptoms were not stable, the researcher or research assistant stopped the process of collecting data and notify to physician and/or nurse immediately.

3.5 Data analysis

The statistical package for the social sciences for windows program (SPSS/FW) version 18.0 and STATA version 13.1 were used to analysis in the study. The data were analyzed with descriptive statistics and multilevel logistic regression analysis under the statistically significance for the prediction of clinical signs in patients with sepsis at interval 95%.

3.5.1 Descriptive statistics with frequency and percentage were used to describe the characteristics of patients with sepsis, the structure of emergency health care system, process of care, and the outcome of clinical signs in patients with sepsis.

3.5.2 Descriptive statistic with cross tabulation was used to describe the proportion of clinical signs with deterioration in each characteristic of structure, process, and patients with sepsis, and the proportion of dead in each characteristic of the outcome of clinical signs in patient with sepsis.

3.5.3 Testing the clustering effect of system and patient levels influencing on clinical signs in patients with sepsis by performing the random intercept model with no covariate.

3.5.4 Univariate test was used to selecting the significant variables from all factors in the system and patient levels on the clinical signs in patients with sepsis for entering in the base model of multilevel logistic regression.

3.5.5 Multilevel logistic regression analysis was used to determine the predictability with regression and interaction effect models among the factors in system and patient levels on the clinical signs in patients with sepsis.

CHAPTER IV
RESULTS

A prospective descriptive correlational design was conducted to examine the effect of factors in the system and patient levels on clinical signs in patients with sepsis. There were 202 patients for 11 hospitals in data analysis. The results were presented in five parts including patient characteristics, structure characteristics, process characteristics, the outcome of clinical signs, and multilevel logistic regression analysis

4.1 The patient characteristics

From table 4.1, most patients were 65 years of age and older (55.9%), male (52.0%), and presented marital status in couple (72.3%), education level at elementary school (50.5%), no monthly income (60.4%), and health service payment with universal coverage (72.8%). The proportions of clinical signs with deterioration were highest in patients who were 55 – 64 years (65.8%), male (63.8%), and single (72.2%), and had non-education level (61.9%), monthly income at 30,001 baht or more, and used social security insurance for health service payment (80.0%).

Table 4.1 Number and percentage of patient characteristics (n = 202)

Patient characteristics	Number and Percentage	Number and proportion of clinical signs with deterioration
Age (years)		
$\leq$ 44	25 (12.4%)	15 (60.0%)
45 – 54	26 (12.9%)	15 (57.7%)
55 – 64	38 (18.8%)	25 (65.8%)
$\geq$ 65	113 (55.9%)	66 (58.4%)
Gender		
Female	97 (48.0%)	54 (55.7%)
Male	105 (52.0%)	67 (63.8%)
Marital status		
Single	18 (8.9%)	13 (72.2%)
Couple	146 (72.3%)	85 (58.2%)
Separate / window	38 (18.8%)	23 (60.5%)
Education level		
None	42 (20.8%)	26 (61.9%)
Elementary school	102 (50.5%)	62 (60.8%)
High school	24 (11.9%)	14 (58.3%)
Diploma	8 (4.0%)	4 (50.0%)
Bachelor’s degree or higher	26 (12.9%)	15 (57.7%)
Monthly income (Baht)		
None	122 (60.4%)	73 (59.8%)
$\leq$ 10,000	30 (14.9%)	16 (53.3%)
10,001 – 20,000	27 (13.4%)	16 (59.3%)
20,001 – 30,000	19 (9.4%)	13 (68.4%)
$\geq$ 30,001	4 (2.0%)	3 (75.0%)
Health service payment		
Self-payment	1 (0.5%)	0 (0%)
Universal coverage	147 (72.8%)	91 (61.9%)
Civil servants medical benefits scheme	49 (24.3%)	26 (53.1%)
Social security insurance	5 (2.5%)	4 (80.0%)

4.1.1 Health and illness

From table 4.2, most patients had one underlying disease (37.1%) especially hypertension (35.1%) and time of perceive symptom onset within 24 hours (41.1%) by perceive fever / chill as a most symptom in present illness (43.6%). Alteration of conscious was most of chief complaint (45.5%). Most site of infection was respiratory system (44.1%). About 17.4% of patients had ever utilized other health services before the latest ED arrival for the current illness.

The proportions of clinical signs with deterioration between 6 – 72 hours since ED arrival were highest in patients who had four or more underlying diseases (75.0%), chronic liver disease (84.6%), time of perceive symptom onset between 8 – 14 days (91.6%), perceived dyspnea / tachypnea in present illness (67.6%) and chief complaint (67.7%), presented the site of infection at respiratory system (73.0%), and utilized ED before the latest ED arrival for the current illness (88.9%).

Table 4.2 Number and percentage of health and illness and proportion of clinical signs with deterioration in each group (n = 202)

Health and illness	Total number of patients (n = 202)	Number and proportion of clinical signs with deterioration
Underlying disease		
Number of underlying disease		
No/Unknown	44 (21.8%)	30 (68.2%)
1	75 (37.1%)	52 (69.3%)
2	47 (23.3%)	19 (40.4%)
3	24 (11.9%)	11 (45.8%)
4 or more	12 (5.9%)	9 (75.0%)
Identify disease		
Cancer	30 (14.9%)	20 (66.7%)
Cardiovascular disease	22 (10.9%)	13 (59.1%)
Cerebrovascular disease	40 (19.8%)	24 (60.0%)
Chronic lung disease	17 (8.4%)	12 (70.6%)
Chronic kidney disease	18 (8.9%)	12 (66.7%)
Chronic liver disease	13 (6.4%)	11 (84.6%)
Diabetes	56 (27.7%)	25 (44.6%)
Dyslipidemia	24 (11.9%)	10 (5.0%)
Hypertension	71 (35.1%)	35 (41.7%)
Human immunodeficiency virus infection	3 (1.5%)	2 (66.7%)
Time of perceived symptoms onset		
≤ 24 hours	83 (41.1%)	45 (54.2%)
25 hours - 3 days	73 (36.1%)	42 (57.5%)
4 - 7 days	33 (16.3%)	23 (69.7%)
8 - 14 days	12 (5.9%)	11 (91.6%)
15 - 30 days	1 (0.5%)	0 (0%)
Present illness (answer more than one)		
Same as chief complaint	45 (22.3%)	25 (55.6%)
fever/ chill	88 (43.6%)	58 (65.9%)
loss of appetite	45 (22.3%)	25 (55.6%)
dyspnea / tachypnea	34 (16.8%)	23 (67.6%)
vomit / diarrhea	28 (13.9%)	15 (53.6%)
fatigue	18 (8.9%)	9 (50.0%)

Table 4.2 Number and percentage of health and illness and proportion of clinical signs with deterioration in each group (n = 202) (cont.)

Health and illness	**Total number of patients (n = 202)**	**Number and proportion of clinical signs with deterioration**
A chief complaint		
Alteration of conscious	92 (45.5%)	57 (62.0%)
Dyspnea / tachypnea	62 (30.7%)	42 (67.7%)
Fever / chill	16 (7.9%)	4 (25.0%)
Fainting / syncope	15 (7.4%)	8 (53.3%)
Fatigue	9 (4.5%)	6 (66.7%)
Abdominal pain	8 (4.0%)	4 (50.0%)
Site of infection		
Respiratory	89 (44.1%)	65 (73.0%)
Urinary	45 (22.3%)	20 (44.4%)
Gastrointestinal – Abdominal	35 (17.3%)	21 (60.0%)
Septicemia	25 (12.4%)	14 (56.0%)
Skin and soft tissue	6 (3.0%)	1 (16.7%)
Central nervous system	2 (1.0%)	0 (0%)
Health service utilization before the latest ED arrival		
Number of health service utilization		
None	167 (82.75%)	101 (60.5%)
1 time	29 (14.4%)	17 (58.6%)
2 times	6 (3.0%)	3 (50.0%)
Characteristic of health service utilization		
Pharmacy service	9 (4.5%)	4 (44.4%)
Primary care/private clinic	5 (2.5%)	2 (40.0%)
Out-patient department	14 (6.9%)	8 (57.1%)
Emergency department	9 (4.5%)	8 (88.9%)

4.1.2 Characteristics of clinical signs

From table 4.3, most patients presented signs at least one organ compromise (86.1%) especially in two organs (34.7%) and shock index between 1.00 – 1.25 (61.9%) at triage. There were 132 patients (65.3%) who presented SBP ≥ 90 mmHg at triage and then 54 patients (40.9%) deteriorated with SBP < 90 mmHg by a half (27 patients) progressed to septic shock. There were totally 124 patients (61.4%) who presented SBP < 90 mmHg within six hours since ED arrival. Most of them presented a period of SBP < 90 mmHg in one time (62 patients) and duration time less than or equal one hour (42 patients). Most patients presented a severity of illness at medium level with the score of the mortality in emergency department sepsis (MEDS) at 8 – 12 (48.0%) and the stage of sepsis with organ dysfunction (45.0%) including SBP < 90 mmHg, oxygen saturation < 90%, and/or acute alteration of conscious within six hours since ED arrival.

For clinical signs at triage, the proportions of clinical signs with deterioration between 6 – 72 hours since ED arrival were highest in patients who presented with three organ compromises (73.0%) including respiratory, circulatory, and neurological systems, shock index > 2.00 (100%), and a severity of illness at very high level as MEDS score > 15 (86.7%).

For clinical signs during six hours since ED arrival, the proportions of clinical signs with deterioration between 6 – 72 hours since ED arrival were highest in patients who presented the stage of sepsis shock (65.3%) especially when deteriorated in septic shock later (66.7%), and a period of SBP < 90 mmHg with more than five times (100.0%) and duration time more than four hours (86.67%).

Table 4.3 Number and percentage of characteristics of clinical signs and proportion of clinical signs with deterioration in each group (n = 202)

Characteristics of clinical signs	Total number of patients (n = 202)	Number and proportion of clinical signs with deterioration
Present signs of organ compromise at triage[a]		
No present	28 (13.9%)	10 (35.7%)
1 organ	67 (33.2%)	40 (59.7%)
Respiratory	16 (7.9%)	12 (75.0%)
Circulatory	43 (21.3%)	23 (53.5%)
Neurological	8 (4.0%)	5 (62.5%)
2 organs	70 (34.7%)	44 (62.9%)
Respiratory and Circulatory	24 (11.9%)	18 (75.0%)
Respiratory and Neurological	11 (5.4%)	5 (45.5%)
Circulatory and Neurological	35 (17.3%)	21 (60.0%)
3 organs (Respiratory, Circulatory and Neurological)	37 (18.3%)	27 (73.0%)
Shock index at triage		
1.00 – 1.25	125 (61.9%)	72 (57.6%)
1.26 – 1.50	54 (26.7%)	29 (53.7%)
1.51 – 1.75	11 (5.4%)	9 (81.8%)
1.76 – 2.00	9 (4.5%)	8 (88.9%)
> 2.00	3 (1.5%)	3 (100%)
Present SBP $\geq$ 90 mmHg at triage	132 (65.3%)	78 (59.1%)
Still SBP $\geq$ 90 mmHg within 6 hours	78 (38.6%)	45 (57.7%)
Deteriorate in SBP < 90 mmHg within 6 hours	54 (26.7%)	33 (61.1%)
Progress in septic shock	27 (13.4%)	18 (66.7%)

[a] Signs of organ compromise at triage include 1) respiratory compromise is respiratory rate $\leq$ 8 or $\geq$ 30 breaths/min and/or oxygen saturation $\leq$ 90%, 2) cardiovascular compromise is systolic blood pressure $\leq$ 90 mmHg, pulse rate $\leq$ 40 or $\geq$ 130 beats/min, and/or urine output $\leq$ 100 ml/4 hours, and 3) neurological compromise is acute alteration of conscious

Table 4.3 Number and percentage of severity of illness and proportion of clinical signs with deterioration in each group (n = 202) (cont.)

Characteristics of clinical signs	Total number of patients (n = 202)	Number and proportion of clinical signs with deterioration
Frequency of clinical deterioration to SBP < 90 mmHg within 6 hours	124 (61.4%)	76 (61.3%)
1 time	62 (30.7%)	34 (54.8%)
2 – 3 times	55 (27.2%)	36 (65.5%)
4 – 5 times	6 (3.0%)	5 (83.3%)
> 5 times	1 (0.5%)	1 (100%)
Duration of period at SBP < 90 mmHg within 6 hours	124 (61.4%)	76 (61.3%)
≤ 1 hour	42 (20.79%)	24 (57.14%)
> 1 – 2 hours	35 (17.33%)	23 (65.71%)
> 2 – 3 hours	19 (9.41%)	10 (52.63%)
> 3 – 4 hours	13 (6.44%)	6 (46.15%)
> 4 hours	15 (7.42%)	13 (86.67%)
Severity of illness		
The mortality in emergency department sepsis (MEDS) score at ED	17 (8.4%)	8 (47.1%)
Very low at 0 – 4	38 (18.8%)	13 (34.2%)
Low at 5 – 7	97 (48.0%)	63 (64.9%)
Medium at 8 – 12	35 (17.3%)	24 (68.6%)
High at 13 – 15	15 (7.4%)	13 (86.7%)
Very high at > 15		
Stage of sepsis within 6 hours[b]		
Sepsis	36 (17.8%)	15 (41.7%)
Sepsis with organ dysfunction	91 (45.0%)	57 (62.6%)
Sepsis with shock	75 (37.1%)	49 (65.3%)

[b] Stage of sepsis includes; 1) sepsis is two or more of SIRS criteria with shock index ≥ 1, 2) sepsis with organ dysfunction is sepsis with systolic blood pressure < 90 mmHg, oxygen saturation < 90%, and/or acute alteration of conscious, and 3) sepsis with shock is sepsis with systolic blood pressure < 90 mmHg after an initial fluid challenge of 20–30 ml/kg

4.2 The structure characteristics

From table 4.4, there were 11 hospitals including five tertiary or regional hospitals (45.5%) and six general hospitals (54.5%). All hospitals have an available hospital policy for sepsis (100%). Most of hospitals were presented the number of bed between 501 – 1,000 beds (54.5%), emergency cases at ED between 30,000 – 49,999 cases per year (63.6%), no data of sepsis cases at ED (54.5%), time to apply a sepsis policy at ED more than two years (72.7%) and the components of sepsis resuscitation bundle in policy that consisted of early fluid challenge and antibiotic management including and the achieved non-invasive and invasive monitoring (63.6%).

The proportions of clinical signs with deterioration between 6 – 72 hours since ED arrival were highest in hospitals which were tertiary or regional hospitals (69.1%) and presented the number of bed between 501 – 1,000 beds (66.9%), the emergency cases at ED between 70,000 – 99,999 cases per year (72.7%), sepsis cases at ED more than 30 cases per month (69.7%), time to apply a sepsis policy at ED between 13 months and two years (75.8%), and the components of sepsis resuscitation bundle in policy that consisted of early fluid challenge and antibiotic management including and the achieved non-invasive and invasive monitoring (65.0%).

When the sign of organ compromise at triage and severity of illness (MEDS score) at ED were divided into level of hospital, the tertiary or regional hospitals presented more patients with organ compromises at triage and high severity or MEDS sore $\geq$ 13 (90.2%, 111 cases from 123 cases; 28.5%, 35 cases from 123 cases respectively) than general hospitals (79.7%, 63 cases from 79 cases; 19.0%, 15 cases from 79 cases respectively).

When the triage practice was divided into level of hospital, the tertiary or regional hospitals presented more patients with no complete triage components (63.4%, 78 cases from 123 cases) than general hospitals (50.6%, 40 cases from 79 cases).

When the performance of sepsis resuscitation bundle divided into level of hospital, the tertiary or regional and general hospitals presented similar number of patients who achieved in all components of medical treatment and non-invasive monitoring (6.5%, 8 cases from 123 cases; 6.3%, 5 cases from 79cases respectively).

When a length of ED stay was divided into level of hospital, the tertiary or regional hospitals presented more patients with a length of ED stay more than six hours than general hospitals (27 cases and 6 cases respectively).

When general ward were divided into level of hospital, the general hospitals presented higher proportion of ICU and intermediate admission (30.4%, 24 cases from all 79 cases and 13.0%, 16 cases from all 123 cases respectively).

Table 4.4 Number and percentage of structure characteristics and patients and proportion of clinical signs with deterioration in each group

Structure characteristics	Total number of structures (n = 11)	Total number of patients (n = 202)	Number and proportion of clinical signs with deterioration
Level of hospital			
Tertiary or regional hospital	5 (45.5%)	123 (60.9%)	85 (69.1%)
General hospital	6 (54.5%)	79 (39.1%)	36 (45.6%)
Number of bed in hospital			
250 – 500	5 (45.5%)	69 (34.2%)	32 (46.4%)
501 – 1,000	6 (54.5%)	133 (65.8%)	89 (66.9%)
Emergency cases at ED (per year)			
30,000 – 49,999	7 (63.6%)	112 (55.4%)	63 (56.2%)
50,000 – 69,999	3 (27.3%)	57 (28.2%)	34 (59.6%)
70,000 – 99,999	1 (9.1%)	33 (16.3%)	24 (72.7%)
Sepsis cases at ED (per month)			
1 – 10	1 (9.1%)	17 (8.4%)	5 (29.4%)
11 – 20	1 (9.1%)	10 (5.0%)	4 (40.0%)
> 30	3 (27.3%)	99 (49.0%)	69 (69.7%)
No data	6 (54.5%)	76 (37.6%)	43 (56.6%)
Hospital policy for sepsis			
Available	11 (100%)	202 (100%)	121 (59.9%)
Not available	0 (0%)	0 (0%)	0 (0%)
Time to apply a sepsis policy at ED			
< 6 months	1 (9.1%)	14 (6.9%)	10 (71.4%)
6 – 12 months	1 (9.1%)	17 (8.4%)	5 (29.4%)
13 months – 2 years	1 (9.1%)	33 (16.3%)	25 (75.8%)
> 2 years	8 (72.7%)	138 (68.3%)	81 (58.7%)
Component of sepsis resuscitation bundle in policy			
Early fluid challenge and antibiotic management including the achievement of non-invasive monitoring	4 (36.4%)	59 (29.2%)	28 (47.5%)
Early fluid challenge and antibiotic management including the achievement of non-invasive and invasive monitoring	7 (63.6%)	143 (70.8%)	93 (65.0%)

Table 4.4 Number and percentage of structure characteristics and patients and proportion of clinical signs with deterioration in each group (cont.)

Structure characteristics	Total number of structures (n = 11)	Total number of patients (n = 202)	Number and proportion of clinical signs with deterioration
Tertiary or regional hospital	5 (45.5%)	123 (60.9%)	85 (69.1%)
Present signs of organ compromise at triage			
Present		111 (55.0%)	79 (71.2%)
No present		12 (5.9%)	6 (50.0%)
Triage practice			
No complete in any triage components		78 (38.6%)	58 (74.4%)
Complete in all triage components		45 (22.3%)	27 (60.0%)
Severity of illness (MEDS score) at ED			
Very low at 0 – 4		6 (3.0%)	5 (83.3%)
Low at 5 – 7		24 (11.9%)	10 (41.7%)
Medium at 8 – 12		58 (28.7%)	43 (74.1%)
High at 13 – 15		24 (11.9%)	18 (75.0%)
Very high at > 15		11 (5.4%)	9 (81.8%)
Performance of sepsis resuscitation bundle			
Not achieved in any components of medical treatment and non-invasive monitoring		115 (56.9%)	83 (72.2%)
Achieved in all components of medical treatment and non-invasive monitoring		8 (4.0%)	2 (25.0%)
Length of ED stay			
≤ 2 hours		35 (17.3%)	24 (68.6%)
> 2 – 4 hours		41 (20.3%)	29 (70.7%)
> 4 – 6 hours		20 (9.9%)	15 (75.0%)
> 6 – 12 hours		15 (7.4%)	9 (60.0%)
> 12 hours		12 (5.9%)	8 (66.7%)
Ward admission			
General ward		107 (53.0%)	77 (72.0%)
Intermediate care unit		8 (4.0%)	4 (50.0%)
Intensive care unit		8 (4.0%)	4 (50.0%)

Table 4.4 Number and percentage of structure characteristics and patients and proportion of clinical signs with deterioration in each group (cont.)

Structure characteristics	Total number of structures (n = 11)	Total number of patients (n = 202)	Number and proportion of clinical signs with deterioration
General hospital	6 (54.5%)	79 (39.1%)	36 (45.6%)
Present signs of organ compromise at triage			
Present		63 (31.2%)	32 (50.8%)
No present		16 (7.9%)	4 (25.0%)
Triage practice			
No complete in any triage components		40 (19.8%)	21 (52.5%)
Complete in all triage components		39 (19.3%)	15 (38.5%)
Severity of illness (MEDS score) at ED			
Very low at 0 – 4		11 (5.4%)	3 (27.3%)
Low at 5 – 7		14 (6.9%)	3 (21.4%)
Medium at 8 – 12		39 (19.3%)	20 (51.3%)
High at 13 – 15		11 (5.4%)	6 (54.5%)
Very high at > 15		4 (2.0%)	4 (100%)
Performance of sepsis resuscitation bundle			
Not achieved in any components of medical treatment and non-invasive monitoring		74 (36.6%)	35 (47.3%)
Achieved in all components of medical treatment and non-invasive monitoring		5 (2.5%)	1 (20.0%)
Length of ED stay			
≤ 2 hours		52 (25.7%)	23 (44.2%)
> 2 – 4 hours		20 (9.9%)	9 (45.0%)
> 4 – 6 hours		1 (0.5%)	1 (100%)
> 6 – 12 hours		5 (2.5%)	3 (60.0%)
> 12 hours		1 (0.5%)	0 (0%)
Ward admission			
General ward		55 (27.2%)	19 (34.5%)
Intermediate care unit		4 (2.0%)	3 (75.0%)
Intensive care unit		20 (9.9%)	14 (70.0%)

4.3 The process characteristics

4.3.1 EMS utilization

From table 4.5, there were 43 patients (21.3%) who arrived at ED with EMS utilization by most of them presented the severity of illness at medium level with MEDS score at 8 – 12 (24 patients) and received oxygen therapy and intravenous fluid (22 patients). The proportions of clinical signs with deterioration between 6 – 72 hours since ED arrival were highest in all groups of severity of illness at very high level with MEDS score more than 15 including no EMS utilization (88.9%), EMS utilization with no complete the modified Robson screening (100%), and EMS utilization with complete the modified Robson screening (80.0%). While the group of severity of illness at high level with MEDS score ≥ 13, who presented EMS utilization with complete the modified Robson screening, has lower the proportions of clinical signs with deterioration between 6 – 72 hours since ED arrival than no EMS utilization and EMS utilization with no complete the modified Robson screening (50.0%, 100% and 69.2 respectively for MEDS at 13 – 15; 80.0%, 100% and 88.9% respectively for MEDS at > 15).

4.3.2 Triage characteristics

From table 4.6, most patients were decided the triage level at emergent level (54.5%), not complete in any triage components (58.4%), and recorded vital signs with the average frequency ≤ 60 minutes within six hours since ED arrival in both cases of presenting SBP ≥ 90 mmHg (54 cases from all 78 cases) and SBP < 90 mmHg (41 cases from all 54 cases before SBP < 90 mmHg, 116 cases from all 124 cases during SBP < 90 mmHg, and 114 cases from all 124 cases after recovery to SBP ≥ 90 mmHg). The proportions of clinical signs with deterioration between 6 – 72 hours since ED arrival were highest in patients who were not completed in any triage components (67.2%). For cases presented SBP ≥ 90 mmHg at triage and then deteriorated to SBP < 90 mmHg within six hours, patients who were recorded vital signs in a period before SBP < 90 mmHg with the average frequency at > 1 – 2 hour (80%) and > 2 – 4 hours (100%) had higher proportions of clinical signs with deterioration between 6 – 72 hours since ED arrival than the average frequency ≤ 60 minutes (56.1%, 23 cases from 41 cases).

Table 4.5 Number and percentage of EMS utilization and proportion of clinical signs with deterioration in each group (n = 202)

EMS utilization	Total number of patients (n = 202)	Number and proportion of clinical signs with deterioration
EMS utilization		
No EMS utilization	159 (78.7%)	93 (58.5%)
MEDS score at 0 – 4	17 (8.4%)	8 (47.1%)
MEDS score at 5 – 7	34 (16.8%)	12 (35.3%)
MEDS score at 8 – 12	73 (36.1%)	47 (64.4%)
MEDS score at 13 – 15	26 (12.9%)	18 (69.2%)
MEDS score at > 15	9 (4.5%)	8 (88.9%)
EMS utilization with no complete the modified Robson screening	10 (5.0%)	8 (80.0%)
MEDS score at 8 – 12	6 (3.0%)	4 (66.7%)
MEDS score at 13 – 15	3 (1.5%)	3 (100%)
MEDS score at > 15	1 (0.5%)	1 (100%)
EMS utilization with complete the modified Robson screening	33 (16.3%)	20 (60.6%)
MEDS score at 5 – 7	4 (2.0%)	1 (25.0%)
MEDS score at 8 – 12	18 (8.9%)	12 (66.7%)
MEDS score at 13 – 15	6 (3.0%)	3 (50.0%)
MEDS score at > 15	5 (2.5%)	4 (80.0%)
EMS treatment		
No treatment	2 (1.0%)	1 (50.0%)
Oxygen therapy	16 (7.9%)	11 (68.8%)
Intravenous fluid	3 (1.5%)	2 (66.7%)
Oxygen therapy and intravenous fluid	22 (10.9%)	14 (63.6%)

Table 4.6 Number and percentage of triage characteristics, monitoring and proportion of clinical signs with deterioration in each group (n = 202)

Triage characteristics and monitoring	Total number of patients (n = 202)	Number and proportion of clinical signs with deterioration
Triage level		
Urgent	25 (12.4%)	14 (56.0%)
Emergent	110 (54.5%)	64 (58.2%)
Resuscitation	67 (33.2%)	43 (64.2%)
Triage components		
Assessment all vital signs[c]		
No	4 (2.0%)	3 (75.5%)
Yes	198 (98.0%)	118 (59.6%)
Assessment at least one organ function[d]		
No	4 (2.0%)	2 (50.0%)
Yes	198 (98.0%)	119 (60.1%)
Accuracy of triage acuity level[e]		
No	118 (58.4%)	79 (66.9%)
Yes	84 (41.6%)	42 (50.0%)
Emergent	31 (15.3%)	12 (38.7%)
Resuscitation	53 (26.2%)	30 (56.6%)
Triage practice		
No complete in any triage components	119 (58.4%)	80 (67.2%)
Complete in all triage components	83 (41.6%)	41 (49.4%)
The average frequency of vital signs monitoring within 6 hours		
Cases SBP ≥ 90 mmHg in all 6 hours	78 (38.6%)	45 (57.7%)
≤ 15 minutes	9 (4.5%)	6 (66.7%)
16 – 30 minutes	18 (8.9%)	9 (47.4%)
31 – 60 minutes	27 (13.4%)	15 (55.6%)
> 1 – 2 hours	15 (7.4%)	11 (73.3%)
> 2 – 4 hours	3 (1.5%)	3 (100%)
> 4 hours	6 (3.0%)	1 (16.7%)

[c] All vital signs including blood pressure, pulse rate, respiratory rate, and body temperature
[d] Organ function was neurological sign, pulse oximetric saturation, and urine output/ a last time of urination
[e] An accuracy of acuity level based on Emergency Severity Index which the criteria of resuscitation level are systolic blood pressure < 90 mmHg, oxygen saturation < 90%, and/or acute mental status deterioration to pain stimuli or unresponsive, and the criteria of emergent level are potential threat to life with hypoperfusion in sepsis including ≥ 2 SIRS criteria and presenting shock index ≥ 1.

Table 4.6 Number and percentage of triage characteristics, monitoring and proportion of clinical signs with deterioration in each group (n = 202) (cont.)

Triage characteristics and monitoring	Total number of patients (n = 202)	Number and proportion of clinical signs with deterioration
The average frequency of vital signs monitoring within 6 hours (Cont.)		
Case present SBP < 90 mmHg during 6 hours		
Before SBP < 90 mmHg (only case presents SBP ≥ 90 mmHg at triage)	54 (26.7%)	33 (61.1%)
≤ 15minutes	7 (3.5%)	4 (57.1%)
16 – 30 minutes	20 (9.9%)	11 (55.0%)
31 – 60 minutes	14 (6.9%)	8 (57.1%)
> 1 – 2 hours	10 (5.0%)	8 (80.0%)
> 2 – 4 hours	1 (0.5%)	1 (100%)
> 4 hours	2 (1.0%)	1 (50.0%)
During SBP < 90 mmHg	124 (61.4%)	76 (61.3%)
≤ 15minutes	50 (24.8%)	31 (62.0%)
16 – 30 minutes	43 (21.3%)	27 (62.8%)
31 – 60 minutes	23 (11.4%)	14 (60.9%)
> 1 – 2 hours	5 (2.5%)	3 (60.0%)
> 2 – 4 hours	2 (1.0%)	1 (50.0%)
> 4 hours	1 (0.5%)	0 (0%)
After recovery to SBP>90 mmHg for 4 times	124 (61.4%)	76 (61.3%)
≤ 15minutes	44 (21.8%)	24 (54.5%)
16 – 30 minutes	41 (20.3%)	27 (65.9%)
31 – 60 minutes	29 (14.4%)	18 (62.1%)
> 1 – 2 hours	7 (3.5%)	5 (71.5%)
> 2 – 4 hours	2 (1.0%)	2 (100%)
> 4 hours	1 (0.5%)	0 (0%)

4.3.3 Performance of sepsis resuscitation bundle

From table 4.7, for all 75 patients with sepsis and shock, there were 53.3% (40 cases from all 75 cases) who received fluid challenge at least 2,000 ml within three hours and 44% (33 cases from all 75 cases) who received vasopressor after fluid challenge at least 2,000 ml within six hours. Most patients were administered with antibiotic between more than one hour and three hours (50.0%). For non-invasive monitoring, most patients were achieved in mean arterial pressure (MAP) ≥ 65 mmHg (85.6%) and urine output ≥ 0.5 ml/kg/hr (57.9%) within six hours. While the invasive monitoring was little performed to monitor patients by only 9.9% and 2.0% were monitored with central venous pressure (CVP) and central venous oxygen saturation (ScvO2) respectively. Most patients in each stage of sepsis were not achieved in any components of medical treatment and non-invasive monitoring as following 35 cases from all 36 cases in sepsis, 89 cases from all 91 cases in sepsis with organ function, and 65 cases from all 75 cases in sepsis with shock. The proportions of clinical signs with deterioration between 6 – 72 hours since ED arrival were lowest in patients with all stages of sepsis who were achieved in all components of medical treatment and non-invasive monitoring including sepsis (0%, 0 case from 1 case), sepsis with organ function (0%, 0 case from 2 cases), and sepsis with shock (30%, 3 cases from 10 cases).

Table 4.7 Number and percentage of performance of sepsis resuscitation bundle and proportion of clinical signs with deterioration in each group (n = 202)

Performance of sepsis resuscitation bundle	Total number of patients (n = 202)	Number and proportion of clinical signs with deterioration
Fluid management within 3 hours		
Sepsis	36 (17.8%)	15 (41.7%)
< 500 ml	30 (14.9%)	15 (50.0%)
500 – 999 ml	5 (2.5%)	1 (20.0%)
1,000 – 1499 ml	0 (0%)	0 (0%)
1500 – 1999 ml	0 (0%)	0 (0%)
≥ 2000 ml	1 (0.5%)	0 (0%)
Sepsis with organ dysfunction	91 (45.0%)	57 (62.6%)
< 500 ml	48 (23.8%)	32 (66.7%)
500 – 999 ml	18 (8.9%)	12 (66.7%)
1,000 – 1499 ml	13 (6.4%)	8 (61.5%)
1500 – 1999 ml	6 (3.0%)	4 (66.7%)
≥ 2000 ml	6 (3.0%)	1 (16.7%)
Sepsis with shock	75 (37.1%)	49 (%)
< 500 ml	8 (4.0%)	7 (87.5%)
500 – 999 ml	10 (5.0%)	6 (60.0%)
1,000 – 1499 ml	8 (4.0%)	4 (50.0%)
1500 – 1999 ml	9 (4.5%)	8 (88.9%)
≥ 2000 ml	40 (19.8%)	24 (60.0%)
Vasopressor application within 6 hours in case of sepsis with shock		
Apply after fluid challenge at least 2,000 ml	34 (16.8%)	18 (52.9%)
Apply after fluid loading less than 2,000 ml	26 (12.9%)	19 (73.1%)
Apply without fluid loading/challenge	2 (1.0%)	2 (100%)
No application	13 (6.4%)	10 (76.9%)
Components of sepsis resuscitation bundle		
Fluid challenge with crystalloids at least 2,000 ml ≤ 3 hours		
Not achieved	155 (76.7%)	96 (61.9%)
Achieved	47 (23.3%)	25 (53.2%)

Table 4.7 Number and percentage of performance of sepsis resuscitation bundle and proportion of clinical signs with deterioration in each group (n = 202) (cont.)

Performance of sepsis resuscitation bundle	Total number of patients (n = 202)	Number and proportion of clinical signs with deterioration
Components of sepsis resuscitation bundle (cont.)		
Antibiotic administration		
≤ 1 hour	74 (36.6%)	41 (55.4%)
> 1 – 3 hours	101 (50.0%)	64 (63.4%)
> 3 hours	27 (13.4%)	16 (59.3%)
Non - invasive monitoring		
MAP[f] ≥ 65 mmHg ≤ 6 hours		
Not achieved	29 (14.4%)	25 (86.2%)
Achieved	173 (85.6%)	96 (55.5%)
Urine output ≥ 0.5 ml/kg/hr ≤ 6 hours		
No monitoring	30 (14.9%)	19 (63.3%)
Not achieved	55 (27.2%)	36 (65.5%)
Achieved	117 (57.9%)	66 (56.4%)
Invasive Monitoring		
CVP[f] 8-12 mmHg ≤ 6 hours		
No monitoring	182 (90.1%)	107 (58.8%)
Not achieved	1 (0.5%)	1 (100%)
Achieved	19 (9.4%)	13 (68.4%)
$ScvO_2$[f] ≥70% ≤ 6 hours		
No monitoring	198 (98.0%)	119 (60.1%)
Not achieved	2 (1.0%)	2 (100%)
Achieved	2 (1.0%)	0 (0%)
Performance of sepsis resuscitation bundle[g]		
Not achieved in any components of medical treatment and non-invasive monitoring	189 (93.6%)	118 (62.4%)
Sepsis	35 (17.3%)	15 (42.7%)
Sepsis with organ dysfunction	89 (44.1%)	57 (64.0%)
Sepsis with shock	65 (32.2%)	46 (70.8%)
Achieved in all components of medical treatment and non-invasive monitoring	13 (6.4%)	3 (23.1%)
Sepsis	1 (0.5%)	0 (0%)
Sepsis with organ dysfunction	2 (1.0%)	0 (0%)
Sepsis with shock	10 (5.0%)	3 (30.0%)

[f] MAP, Mean arterial pressure; CVP, Central venous pressure; $ScvO_2$, Central venous oxygen saturation
[g] Achievement in performance of sepsis resuscitation bundle consists of medical treatment and non-invasive monitoring including fluid challenge ≤ 3 hours, antibiotic administration ≤ 1 hour, and MAP ≥ 65 mmHg and urine output ≥ 0.5 ml/kg/hr ≤ 6 hours

4.3.4 Care model, length of ED and ward admission

From table 4.8, most patients were cared with the non-ED centric model (92.1%) by most of them presented the highest proportions of clinical signs with deterioration between 6 – 72 hours since ED arrival (60.8%). When the care model was divided into each stage of sepsis, a group of septic shock, who were cared with the ED centric model, had lower proportions of clinical signs with deterioration between 6 – 72 hours since ED arrival than who were cared with non-ED centric model (57.1% and 67.2% respectively). Most patients had a length of ED stay less than two hours (43.0%) and admitted at general ward (80.2%).

Table 4.8 Number and percentage of care model, length of ED and ward admission, and proportion of clinical signs with deterioration in each group (n = 202)

Others process characteristics	Total number of patients (n = 202)	Number and proportion of clinical signs with deterioration
Care model[h]		
The non-ED centric model	186 (92.1%)	113 (60.8%)
Sepsis	35 (17.3%)	15 (42.9%)
Sepsis with organ dysfunction	90 (44.6%)	57 (63.3%)
Sepsis with shock	61 (30.2%)	41 (67.2%)
The ED centric model	16 (7.9%)	8 (50.0%)
Sepsis	1 (0.5%)	0 (0%)
Sepsis with organ dysfunction	1 (0.5%)	0 (0%)
Sepsis with shock	14 (6.9%)	8 (57.1%)
Length of ED stay		
$\leq$ 2 hours	87 (43.1%)	47 (54.0%)
> 2 – 4 hours	61 (30.2%)	38 (62.3%)
> 4 – 6 hours	21 (10.4%)	16 (76.2%)
> 6 – 12 hours	20 (9.9%)	12 (60.0%)
> 12 hours	13 (6.4%)	8 (61.5%)
Ward admission		
General ward	162 (80.2%)	96 (59.3%)
Intermediate care unit	12 (5.9%)	7 (58.3%)
Intensive care unit	28 (13.9%)	18 (64.3%)

[h] The ED centric model is the achievement of all feasible components at ED including fluid challenge with crystalloid at least 2,000 ml $\leq$ 3 hours, antibiotic administration $\leq$ 1 hour, and MAP $\geq$ 65 mmHg before admission including within 6 hours if the length of ED stay > 6 hours. The non-ED centric model is no achievement in any feasible component at ED.

4.4 The outcome of clinical signs

From table 4.9, most patients presented the outcome of clinical signs with deterioration (59.9%), the highest level of national early warning score (NEWS) at 9 – 20 (46.0%), and presented the clinical deterioration within 24 hours (46.0%). The circulatory system was most of deterioration (55.4%) especially SBP < 90 mmHg (25.2%). The proportions of dead were highest in patients who presented clinical signs with deterioration between 6 – 72 hours since ED arrival (65.3%) especially in patients with deterioration in three systems of respiratory, circulatory and neurological (81.0%), presenting with acute alteration of conscious (84.6%), presenting the NEWS at 9 – 20 (75.3%), and time to present clinical signs with deterioration within 24 hours (67.7%).

Table 4.9 Number and percentage of clinical outcomes and proportion of dead in each group (n = 202)

Clinical outcomes	Total number of patients (n = 202)	Number and proportion of dead
No present clinical signs with deterioration between 6 –72 hours	81 (40.1%)	9 (11.1%)
The national early warning score (NEWS) at 72 hours		
0 – 4	62 (30.7%)	5 (8.1%)
5 – 6	11 (5.4%)	1 (9.1%)
7 – 8	6 (3.0%)	1 (16.7%)
9 – 20	2 (1.0%)	2 (100%)
Present clinical signs with deterioration between 6 – 72 hours	121 (59.9%)	79 (65.3%)
1 system	58 (28.7%)	30 (14.9%)
Respiratory	5 (2.5%)	5 (100%)
Circulatory	51 (25.2%)	23 (45.1%)
Neurological	2 (1.0%)	2 (100%)
2 systems	42 (20.8%)	32 (76.2%)
Respiratory and Circulatory	13 (6.4%)	7 (53.8%)
Respiratory and Neurological	2 (1.0%)	2 (100%)
Circulatory and Neurological	27(13.4%)	23 (85.2%)
3 systems (Respiratory, Circulatory and Neurological)	21 (10.4%)	17 (81.0%)
The national early warning score (NEWS) at time of clinical deterioration		
0 – 4	4 (2.0%)	0 (0%)
5 – 6	8 (4.0%)	1 (12.5%)
7 – 8	16 (7.9%)	8 (50.0%)
9 – 20	93 (46.0%)	70 (75.3%)
Present clinical signs with deterioration in respiratory system between 6–72 hours	41 (20.3%)	31 (75.6%)
Respiratory rate $\geq$ 30 breaths/min	19 (9.4%)	12 (63.2%)
Oxygen saturation $\leq$ 90 %	13 (6.4%)	11 (84.6%)
Respiratory rate $\geq$ 30 breaths/min and oxygen saturation $\leq$ 90 %	9 (4.5%)	8 (88.9%)

Table 4.9 Number and percentage of clinical outcomes and proportion of dead in each group (n = 202) (cont.)

Clinical outcomes	Total number of patients (n = 202)	Number and proportion of dead
Present clinical signs with deterioration in circulatory system between 6–72 hours	112 (55.4%)	70 (62.5%)
Systolic blood pressure ≤ 90 mmHg	51 (25.2%)	25 (49.0%)
Pulse rate ≥ 130 beats/min	10 (5.0%)	7 (70.0%)
Urine output ≤ 100 ml/4 hours	10 (5.0%)	4 (40.0%)
Systolic blood pressure ≤ 90 mmHg and pulse rate ≥ 130 beats/min	10 (5.0%)	6 (60.0%)
Systolic blood pressure ≤ 90 mmHg and urine output ≤ 100 ml/4 hours	20 (10.0%)	18 (90.0%)
Pulse rate ≥ 130 beats/min and urine output ≤ 100 ml/4 hours	1 (0.5%)	1 (100%)
Systolic blood pressure ≤ 90 mmHg, pulse rate ≥ 130 beats/min and urine output ≤ 100 ml/4 hours	10 (5.0%)	7 (70.0%)
Present clinical signs with deterioration in neurological system between 6–72 hours		
Acute alteration of conscious	52 (25.7%)	44 (84.6%)
Time to present clinical signs with deterioration in each system between 6 – 72 hours		
≤ 24 hours	93 (46.0%)	63 (67.7%)
Respiratory	4 (2.0%)	4 (100%)
Circulatory	38 (18.8%)	16 (42.1%)
Neurological	1 (0.5%)	1 (100%)
Respiratory and Circulatory	9 (4.5%)	7 (77.8%)
Respiratory and Neurological	1 (0.5%)	1 (100%)
Circulatory and Neurological	23 (11.4%)	19 (82.6%)
Respiratory, Circulatory and Neurological	17 (8.4%)	15 (88.2%)
25 – 48 hours	17 (8.4%)	10 (58.8%)
Respiratory	1 (0.5%)	1 (100%)
Circulatory	7 (3.5%)	5 (71.4%)
Neurological	0 (0%)	0 (0%)
Respiratory and Circulator	3 (1.5%)	0 (0%)

Table 4.9 Number and percentage of clinical outcomes and proportion of dead in each group (n = 202) (cont.)

Clinical outcomes	Total number of patients (n = 202)	Number and proportion of dead
Time to present clinical signs with deterioration in each system between 6–72 hours (Cont.)		
25 – 48 hours (Cont.)		
Respiratory and Neurological	1 (0.5%)	1 (100%)
Circulatory and Neurological	3 (1.5%)	3 (100%)
Respiratory, Circulatory and Neurological	2 (1.0%)	0 (0%)
49 - 72 hours	11 (5.4%)	6 (54.5%)
Respiratory	0 (0%)	0 (0%)
Circulatory	6 (3.0%)	2 (33.3%)
Neurological	1 (0.5%)	1 (100%)
Respiratory and Circulatory	1 (0.5%)	0 (0%)
Respiratory and Neurological	0 (0%)	0 (0%)
Circulatory and Neurological	1 (0.5%)	1 (100%)
Respiratory, Circulatory and Neurological	2 (1.0%)	2 (100%)

4.5 The multilevel logistic regression analysis

The analysis of multilevel logistic regression consisted of random intercept and no covariate model (model 1), random intercept model (model 2), random slope model (model 3), interaction effect model (model 4), model compared, and goodness of fit test for the best model.

4.5.1 Model 1: Random intercept and no covariate model

At first, the data was divided into two levels and then the assumption of multilevel analysis was tested of the intra-class correlation (ICC) coefficient with the data under random intercept and no covariate model. The result showed the standard deviation of system level at 0.549 (Table 4.10), so variance of between group was 0.301. Due to the logistic distribution for residual in patient level implied a variance of within group at $\pi^3/3$ or 3.29 (Snijders & Bosker, 2012). The value of ICC coefficient was 0.083 that calculated with the between-group variance divided by the sum of the between-group variance and the within-group variance (Guo, 2005). Therefore, there was a clustering effect influencing on clinical signs of patients with sepsis and the multilevel analysis was appropriate for this study following the acceptable ICC between 0.05 and 0.30 in previous multilevel research (Snijders & Bosker, 2012).

Table 4.10 Model 1: Random intercept and no covariate for the two-level model (n=202)

Variables	Estimate	SE	p-value
Fixed effect			
Intercept	-0.280	0.232	0.228
Random effect			
System level: S.D. (Intercept)	0.549	0.226	-
-2LL = -133.835 AIC = 271.670, BIC = 278.287			

4.5.2 Model 2: Random intercept model

Each variable was screened with random intercept model. There were five significantly variables at $p \leq 0.05$ (Appendix B: Table B1) including time to perceive symptom onset ($p = 0.051$), severity of illness ($p < 0.001$), level of hospital ($p = 0.003$), triage practice ($p = 0.020$), and performance of sepsis resuscitation bundle ($p = 0.011$). Then these variables were analyzed simultaneously in random intercept model for selecting variables. There were three significantly selected variables at $p \leq 0.05$ (Appendix B: Table B2) including severity of illness ($p < 0.001$), level of hospital ($p = 0.030$) and performance of sepsis resuscitation bundle ($p = 0.009$). Next, all significantly selected variables were analyzed simultaneously in random intercept for multilevel logistic regression model. The result of random intercept for multilevel logistic regression model was (Table 4.11);

$$\ln\left[\frac{\pi}{1-\pi}\right] = 0.606 - 0.168\ (\text{severity of illness}) + 1.024\ (\text{level of hospital}) + 2.213\ (\text{performance of sepsis resuscitation bundle})$$

Table 4.11 Model 2: Random intercept for multilevel logistic regression model (n=202)

Variables	$\hat{\beta}$	OR (SE)	p-value
Fixed effect			
Intercept	0.606	-	0.205
Severity of illness	-0.168	0.845 (0.039)	< 0.001*
Level of hospital			
Tertiary or regional hospital	-	1	-
General hospital	1.024	2.784 (1.087)	0.009*
Performance of sepsis resuscitation bundle			
Not achieved in any components of medical treatment and non-invasive monitoring	-	1	-
Achieved in all components of medical treatment and non-invasive monitoring	2.213	9.146 (6.834)	0.003*

Random effect	**Estimate**	**SE**
System level: S.D. (intercept)	0.328	0.247

-2LL = -118.259
AIC = 246.518, BIC = 263.059

* Significant at $p \leq 0.05$

4.5.3 Model 3: Random slope model

For consider the random slope model, there were analyzed the random slope with each variables including severity of illness (Appendix B: Table B3), performance of sepsis resuscitation bundle (Appendix B: Table B4), and level of hospital (Table 4.12). The random slope model with level of hospital was selected because this model presented the quality of fixed-effect model with the lowest values of AIC (Akaike information criterion) and BIC (Bayesian information criterion), and the quality of random effect model with the values of standard error at more than zero.

The random slope for multilevel logistic regression model was (Table 4.12);

$$\ln\left[\frac{\pi}{1-\pi}\right] = 0.545 - 0.160\text{ (severity of illness)} + 1.034\text{ (level of hospital)} + 2.235\text{ (performance of sepsis resuscitation bundle)}$$

Table 4.12 Model 3: Random slope for multilevel logistic regression model (n=202)

Variables	$\hat{\beta}$	OR (SE)	p-value
Fixed effect			
Intercept	0.545	-	0.248
Severity of illness	-0.160	0.852 (0.041)	0.001*
Level of hospital			
Tertiary or regional hospital	-	1	-
General hospital	1.034	2.813 (1.074)	0.007*
Performance of sepsis resuscitation bundle			
Not achieved in any components of medical treatment and non-invasive monitoring	-	1	-
Achieved in all components of medical treatment and non-invasive monitoring	2.235	9.349 (7.013)	0.003*

Random effect	Estimate	SE
System level:		
S.D. (intercept)	0.121	0.668
S.D. (Level of hospital)	0.423	0.378

-2LL = -118.094
AIC = 248.189, BIC = 268.038

* Significant at p ≤ 0.05

4.5.4 Model 4: Interaction effect model

From table 4.13, the interaction effect models were not significant between level of hospital and severity of illness (p = 0.393 for interaction effect with random intercept, p = 0.315 for interaction effect with random slope with level of hospital), and level of hospital and performance of sepsis resuscitation bundle (p = 0.571 for interaction effect with random intercept, p = 0.567 for interaction effect with random slope with level of hospital).

Table 4.13 Model 4: Interaction effect for multilevel logistic regression model (n=202)

Variables	$\hat{\beta}$	SE	p-value
Interaction effect: random intercept			
Level of hospital # Severity of illness	-0.079	0.092	0.393
Level of hospital # Performance of sepsis resuscitation bundle	-0.864	1.525	0.571
Interaction effect: random slope with level of hospital			
Level of hospital # Severity of illness	-0.091	0.090	0.315
Level of hospital # Performance of sepsis resuscitation bundle	-0.882	1.539	0.567

= interaction effect

4.5.5 Model compared

From table 4.14, the random slope model with level of hospital (model 3) was the best model because the average responses in fixed part allowed a variation on level of hospital in random part and the lowest log-likelihood was presented.

The results of best model were described for patients with sepsis who utilized the emergency health care system as following (Table 4.12); a one-unit increased in the severity of illness or MEDS score, the probability of clinical signs without deterioration between 6 – 72 hours since ED arrival decreased by 14.8% (OR = 0.852, p = 0.001). General hospital was more likely to promote the probability of clinical signs without deterioration between 6 – 72 hours since ED arrival by 2.813 times than tertiary or regional hospital (p = 0.007). Patients who achieved in all components of medical treatment and non-invasive monitoring were more likely to promote the probability of clinical signs without deterioration between 6 – 72 hours since ED arrival by 9.349 times than patients who did not achieve (p = 0.003). Conclusion, the best model was as follows;

$$\ln\left[\frac{\pi}{1-\pi}\right] = 0.545 - 0.160\ (\text{severity of illness}) + 1.034\ (\text{level of hospital}) + 2.235\ (\text{performance of sepsis resuscitation bundle})$$

Table 4.14 Model compared

Model	Log-likelihood	AIC	BIC	$\hat{\sigma}_u$
M1: Random intercept and no covariate model	- 133.835	271.670	278.287	$\hat{\sigma}_{u0} = 0.549$
M2: Random intercept model	- 118.259	246.518	263.059	$\hat{\sigma}_{u0} = 0.328$
M3: Random slope model	- 118.094	248.189	268.038	$\hat{\sigma}_{u0} = 0.121$ $\hat{\sigma}_{\text{level of hospital}} = 0.423$

4.5.6 Goodness of fit test for the best model

When the best model or random slope model was tested for goodness of fit with the scatter plots, the result showed that most observations of standard error ranged between 2 and -2 and only two observations exceeded 2 (Figure 4.1). It meant that the data of random slope model was significant associated with the outcome at 95% (z test, p $\leq$ 0.05). Conclusion, the multilevel logistic regression with random slope model has a goodness of fit to present the data for patients with sepsis in this study.

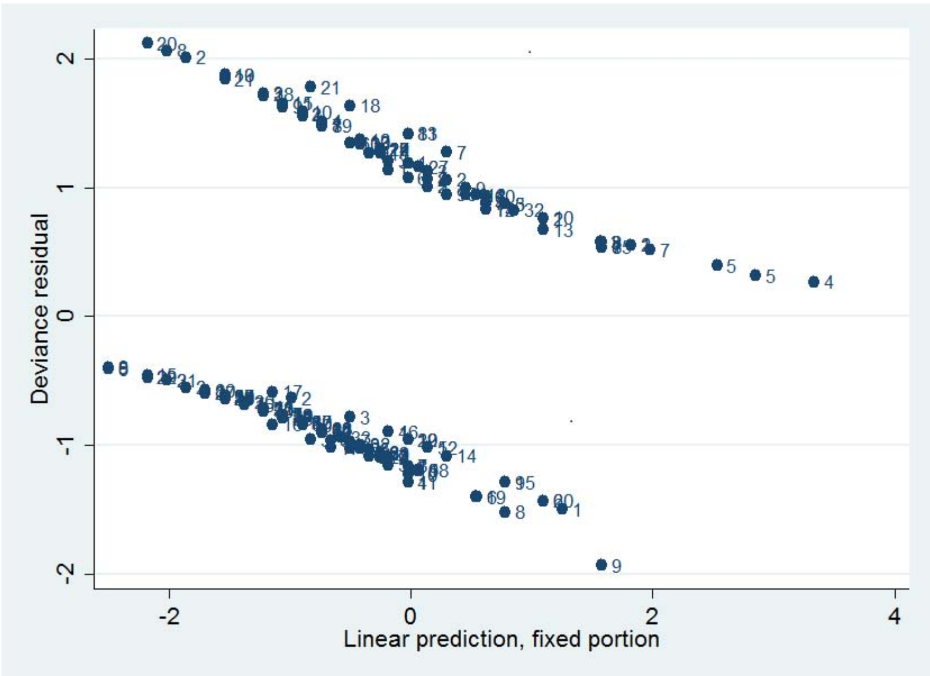

Figure 4.1 Scatter plot for goodness of fit test

CHARTER V
DISCUSSION

The research findings were discussed for the effectiveness of emergency health care system on clinical signs in patients with sepsis. They included prehospital and in-hospital phases. The discussion was presented to issues that related the patient characteristics, structure characteristics, process characteristics, the outcome of clinical signs in patients with sepsis, and the multilevel logistic regression analysis. The patient characteristics were discussed on five issues as follows; 1) most patients presented at least one organ compromise and at least medium level of severity of illness when arrived at ED, 2) many patients with sepsis delayed to seeking care after the clinical signs of organ compromise presented, 3) the elderly was a high risk to unrecognized clinical signs of present illness, 4) the outcome of clinical signs with deterioration presented in patients with sepsis who utilized the health service before arriving at ED, and 5) the early recognition with shock index $\geq$ 1 in patients with sepsis was effective. The structure characteristics were discussed on three issues as follows; 1) the higher workload in tertiary or regional hospitals related to the outcome of clinical signs with deterioration, 2) patients with sepsis needed process of nursing care in the policy, and 3) the tertiary hospitals demonstrated more access block in emergency department than the general hospitals. The process characteristics were discussed on practical performance of sepsis resuscitation bundle with factors of EMS utilization and triage practice. The outcome of clinical signs was discussed to consider nursing assessment for patients with sepsis within 72 dangerous hours. The multilevel logistic regression analysis was concluded the significant factors with the data related.

5.1 The patient characteristics

5.1.1 Most patients presented at least one organ compromise and at least medium level of severity of illness when arrived at ED.

Whereas the evidences showed that higher severity in sepsis related to higher mortality rate (Martin, 2012), most patients still presented at least one organ compromise (86.1%) with at least medium level of severity of illness or MEDS score $\geq$ 8 (72.7%) when arrived at ED. Signs of organ compromise based on following the society of critical care medicine (Sebat & Burg, 2010) as follows; 1) respiratory compromise is respiratory rate $\leq$ 8 or $\geq$ 30 breaths/min and/or oxygen saturation $\leq$ 90%, 2) cardiovascular compromise is systolic blood pressure $\leq$ 90 mmHg, pulse rate $\leq$ 40 or $\geq$ 130 beats/min, and/or urine output $\leq$ 100 ml/4 hours, and 3) neurological compromise is acute alteration of conscious.

Their proportions of clinical signs with deterioration between 6 – 72 hours since ED arrival were higher in more numbers of organ compromise and more severity of illness as following; 59.7% in one organ compromise, 62.9% in two organ compromises, 73.0% in three organ compromises, 64.9% in medium level of severity of illness, 68.6% in high level of severity of illness, and 86.7% in very high level of severity of illness. When clinical signs with deterioration presented, the proportion of dead was high at 65.3%. According to, a one-unit increased in severity of illness decreased by 14.8% in probability of clinical signs without deterioration between 6 – 72 hours since ED arrival ($p = 0.001$).

5.1.2 Many patients with sepsis delayed to seeking care after the clinical signs of organ compromise presented.

The clinical presentation of sepsis depended on the site of infection. Most patients presented the site of infection as follows; respiratory system (44.1%), urinary system (22.3%), gastrointestinal-abdominal system (17.3%), septicemia (12.4%), skin and soft tissue (3.0%), and central nervous system (1.0%). While alteration of conscious was a most chief compliant (45.5%), it was not dyspnea/tachypnea (30.7%). It implied the delay access because they were decided to seeking ED care when were worse with the neurological signs after a period of infection. According to, the longer of rank time of perceived symptom onset presented the higher proportion of clinical signs with deterioration between 6 – 72 hours since ED arrival exceptional the onset at 15 – 30 days in one case as following 54.2% for within 24 hours, 57.5% for 25 hours – 3 days, 69.7% for 4 – 7 days, and 91.6% for 8 – 14 days. If patients with sepsis decided to seeking care within first day of organ dysfunction, the survival rate will be more than seeking at next day as follows; 95.8% for within first day, 85.2% for 48 hours, and 72.3% for 7 days (Blanco et.al., 2008). The study of Rubulotta and colleagues (2009) showed that 88% of people in six developed countries never heard the sepsis term and 58% did not recognize the danger of sepsis.

5.1.3 The elderly was a high risk to unrecognized clinical signs of present illness.

The 65 years and older were a largest group in this study (55.9%). The previous studies found that they were a high risk group to unrecognized serious signs and symptoms and leading to delay access in ED (Rucker, Brennan, & Burstin, 2001) with complicated evaluation and management the illness due to a cognitive disorder and number of underlying disease (Samaras, Chevalley, Samaras, & Gold, 2010) . In this study, most patients had at least one underlying disease (78.2%) by 19.8% was patients with cerebrovascular disease. Many patients (22.3%) were notified only chief complaint without any abnormal symptoms in present illness by most chief complaint related to organ compromises including alteration of conscious (45.5%), dyspnea/tachypnea (30.7%), and fainting/syncope (7.4%). It may be the one-third of symptoms in present illness was unspecified to sepsis recognition such as loss of appetite (22.3%) and fatigue (8.9%). The proportions of clinical signs with deterioration between 6 – 72 hours since ED arrival in these chief complaints were 62.0%, 67.7%, and 53.3% respectively. According to the study of Freitas and colleagues (2008) found that the patients with sepsis, who were 61.1 ± 19.5 years, was significant delay diagnosed or intervention performed more than 48 hours after the onset of organ dysfunction than younger ($p = 0.05$) and the mortality rate increased when the duration of organ dysfunction prolonged to 2.6 ± 1.9 days ($p = 0.0001$).

5.1.4 The outcome of clinical signs with deterioration presented in patients with sepsis who utilized the health service before arriving at ED.

The 17.4% of patients had ever utilized health service before the latest ED arrival by 14.4 % utilized in one time and 3.0% utilized in two times. The out-patient department (6.9%) was more utilized than others including emergency department (4.5%), pharmacy service (4.5%), and primary care/private clinic (2.5%). Unfortunately, all of them presented the proportions of clinical with deterioration between 6 – 72 hours since ED arrival as follows; 44.4% for pharmacy service utilization, 40.0% for primary care/private clinic utilization, 57.1% for out-patient department utilization, and 88.9% for emergency department utilization.

5.1.5 The early recognition with shock index ≥ 1 in patients with sepsis was effective.

All patients, who had infectious disease with SIRS criteria and shock index ≥ 1, presented SBP ≥ 90 mmHg at 65.3% and SBP < 90 mmHg at 34.7% at triage. However, The 40.9% (54 cases from all 132 cases) of patients, who presented SBP ≥ 90 mmHg at triage, deteriorated in SBP < 90 mmHg within six hours since ED arrival by one-half (27 cases) progressed to septic shock. Most patients presented a hypoperfusion state within six hours as follows; sepsis with organ dysfunction including SBP < 90 mmHg, oxygen saturation < 90%, and/or acute alteration of conscious (45.0%) and sepsis with shock or persistent SBP < 90 mmHg after an initial fluid challenge of 20 – 30 ml/kg (37.1%). According the recent study presented that the shock index ≥ 1 predicted the state of hypoperfusion with hyperlactatemia with positive predictive value at 0.24, negative predictive value at 0.92, sensitivity at 0.48, and specificity at 0.81 in patients with infectious disease and SIRS criteria (Berger et al., 2013).

The rank of shock index between 1.00 – 1.25 (61.9%) was most presentation. The higher rank of shock index presented the higher proportion of clinical signs with deterioration between 6 – 72 hours since ED arrival as follows; 57.6% in shock index between 1.00 – 1.25, 53.7% in shock index between 1.26 – 1.50, 81.8% in shock index between 1.51 – 1.75, 88.9% in shock index between 1.75 – 2.00, and 100% in in shock index more than 2.00.

If they were recognized since triage and then were monitored continuously with a frequency at $\leq$ 60 minutes in a period of SBP $\geq$ 90 mmHg before deteriorated to SBP < 90 mmHg within six hours, the proportions of clinical with deterioration between 6 – 72 hours since ED arrival were lower than patients with monitoring more than 1 hour exceptional monitoring more than 4 hours in one case as follows; 57.1% for a frequency within 15 minutes, 55.0% for a frequency between 16 – 30 minutes, 57.1% for a frequency between 31 – 60 minutes, 80.0% for a frequency between more than 1 – 2 hours, and 100% for a frequency between more than 2 – 4 hours.

If they were recognized since triage and then were cared with the ED centric model, the proportions of clinical with deterioration between 6 – 72 hours since ED arrival were lower than patients who were cared with the non-ED centric model especially in patients with sepsis and shock (57.1% and 67.4% respectively). According to, the results of protocol-based standard therapy, that used the criteria of shock index for resuscitation in patients with sepsis and hyperlactatemia, demonstrated the rank of vital signs within normal criteria at 72 hours in patients with sepsis after receiving the therapy (Yealy et al., 2014).

5.2 The structure characteristics

5.2.1 The higher workload in tertiary or regional hospitals related to the outcome of clinical signs with deterioration.

The outcomes of clinical signs in patients with sepsis were significant different with level of hospital although all hospitals (100%) have an available of sepsis policy by the general hospital was more likely to promote the probability of clinical signs without deterioration between 6 – 72 hours since ED arrival by 2.813 times than tertiary or regional hospitals ($p = 0.007$). Conversely, the proportions of clinical signs with deterioration between 6 – 72 hours since ED arrival were highest in the tertiary/regional hospitals (69.1%) and their contexts including the number of bed in hospital between 501 – 1,000 beds (66.9%), emergency cases at ED between 70,000 – 99,999 cases, and sepsis cases at ED more than 30 cases (69.7%). According the study of Powell and colleagues (2010) found that a large number of beds at the hospital and the highest volume of patients with sepsis at the emergency department presented more mortality rate than a small number of beds ($p < 0.05$) and the lower volume ($p < 0.001$).

The tertiary or regional hospitals had presented not only higher numbers of patients who utilized the ED but also the higher severity of illness than the general hospitals. When the sign of organ compromise at triage and severity of illness or MEDS score at ED were divided into level of hospital, the tertiary or regional hospitals presented more patients with organ compromises and high severity or MEDS sore $\geq$ 13 (90.2%, 111 cases from 123 cases and 28.5%, 35 cases from 123 cases respectively) than general hospitals (79.7%, 63 cases from 79 cases and 19.0%, 15 cases from 79 cases respectively).

The high workload may influence the process of care in patients with sepsis since triage. When the triage practice was divided into level of hospital, the tertiary or regional hospitals presented more patients with no complete triage components (63.4%, 78 cases from 123 cases) than general hospitals (50.6%, 40 cases from 79 cases). The fact situation when the researcher collected the data, the numbers of physician and nurse at ED were not different in each shift between the tertiary/regional hospitals (one physician with teaching role and 5 – 8 nurses) and the general hospitals (one physician without teaching role and 5 – 8 nurses). Many nurses at the tertiary or regional hospitals had more than 30 shifts in a month. In addition, many general wards which consisted of 30 beds following the man-power, they showed the number of patients between 40 – 55 cases including intubated patients between 8 – 10 cases. According the final report (Srithamrongsawats et al., 2008) proposed that the service plan stressed on the development of structure capacity and the individual competency for excellent centers with inadequate consideration for man-power and supporting resources.

5.2.2 Patients with sepsis needed process of nursing care in the policy

Gaps of sepsis policy were identified when distinguished the changeable clinical signs in patients with sepsis. From all patients who presented SBP < 90 mmHg (124 cases) within six hours since ED arrival, there were the patients who presented SBP < 90 mmHg at triage (34.7%, 70 cases) or deteriorated in SBP < 90 mmHg later

(26.7%, 54 cases). They had a frequency of clinical deterioration to SBP < 90 mmHg between one to more than five times within six hours as follows; 62 cases for one time, 55 case for two and three times, 6 cases for four and five times, and 1 case for more than five times. The duration of period at SBP < 90 mmHg within six hours was as follows; one hour or less in 42 cases, between more than one and two hours in 35 cases, between more than two and three hours in 19 cases, between more than three and four hours in 13 cases, and more than four hours in 15 cases. Most patients were monitored with a frequency at $\leq$ 60 minutes within six hours as follows; 54 cases from all 78 cases in patients presented SBP $\geq$ 90 mmHg in all six hours, 41 cases from all 54 cases in a period of SBP $\geq$ 90 mmHg after triage before deteriorated to SBP < 90 mmHg, 116 cases from all 124 cases during a period of SBP < 90 mmHg, and 114 cases from all 124 cases after recovery to SBP $\geq$ 90 mmHg for four times. According the study of Carmona-Monge and collegues (2013) that demonstrated the workload of nurses caring for patients with sepsis was higher than others illness, including acute renal failure and acute coronary syndrome ($p < 0.01$). However, the nursing workload with changeable clinical signs for patients with sepsis in this study was only considered in non-invasive monitoring for changeable blood pressure.

Following the data of changeable clinical signs, the process of nursing care was a critical factor for supporting the caring in patients with sepsis. Normally, the international guideline stressed on medical treatment and clinical outcomes without the process of care (Dellinger et al., 2013). In the study, many settings were not identified too. However, some hospitals have been started to implement a policy with using a search out severity (SOS) score for appropriate monitoring clinical signs and supporting timely medical treatment for patients with sepsis. The mortality rate decreased from 47% to 37% when this score was implemented (Champunot, Kamsawang, Tuandoung, & Tansuphaswasdikul, 2012). Unfortunately, the 14.9% of patients with sepsis were not monitored urine output within six hours since ED arrival.

5.2.3 The tertiary hospitals demonstrated more access block in emergency department than the general hospitals.

The data implied that the tertiary or regional hospitals demonstrated more access block than general hospitals. The tertiary or regional hospitals presented more patients with a length of ED stay > 6 hours than general hospitals (22.0%, 27 cases from all 123 cases and 7.6%, 6 cases from all 79 cases respectively) by most patients who utilized the general hospitals had a length of ED stay $\leq$ 2 hours (65.8%, 52 cases from all 79 cases). When tha data of a length of ED stay and ward admission was analyzed with level of hospital. Most patients who utilized the tertiary or regional hospitals and general hospitals were admitted at general ward (87.0%, 107 cases from all 123 cases and 69.6%, 55 cases from all 79 cases respectively). The tertiary or regional hospitals presented to lower proportion of ICU or intermediate ward admission than general hospitals (13.0%, 16 cases from all 123 cases and 30.4%, 24 cases from all 79 cases respectively). The access block was associated with overcrowding condition and then leading to decreased compliance with the protocol and threatened to patient safety (Nugus et al., 2011).

5.3 The process characteristics: Practical performance of sepsis resuscitation bundle with factors of EMS utilization and triage practice

A rapidly sepsis recognition influenced the effective outcome by leading a timely performance of sepsis resuscitation bundle at ED. Generally, the performance of sepsis resuscitation bundle was started when sepsis was diagnosed (Dellinger et al., 2013). This performance also depended on many factors such as time to recognition, time to see physician, time to laboratory investigation, and time to diagnosis.

From this study, the achieved time of performance of sepsis resuscitation bundle was counted since time to triage or ED arrival. The results demonstrated that patients who achieved in all components of medical treatment and non-invasive monitoring in sepsis resuscitation bundle, including fluid challenge within three hours, antibiotic administration within one hour, and MAP $\geq$ 65 mmHg and urine output $\geq$ 0.5 ml/kg/hr within six hours, were more likely to promote the probability of clinical signs without deterioration between 6 – 72 hours since ED arrival by 9.349 times than patients who did not achieve ($p = 0.003$). Therefore, if triage nurse or EMS provider recognizes with alert team when patients with sepsis arrived at ED, the gap of time between triage and performance resuscitation bundle will be decreased.

Triage practice was a significant factor to promote the probability of clinical signs without deterioration between 6 – 72 hours since ED arrival when screened only a variable (p = 0.02) (Appendix B, Table B1). The result showed the proportion of clinical signs with deterioration between 6 – 72 hours since ED arrival was lower in patients with sepsis who were completed in all triage components (49.4%) than no complete (67.2%), especially the components of the assessment in all vital signs (59.6%) and the accuracy of triage acuity level (50.0%). When the triage acuity level was assigned, the timely process of care was stimulated following the triage acuity level that based on Emergency Severity Index (Gilboy, Tanabe, Travers, & Rosenau, 2012) as follows; immediately care for resuscitation level and 15 minutes for emergency level. Then a sepsis resuscitation bundle was performed rapidly in patients who were recognized sepsis.

An EMS utilization was not significant factor in this study (p = 0.300, EMS utilization with no complete the modified Robson screening; p = 0.799, EMS utilization with complete the modified Robson screening). It may because the effective of EMS utilization did not depend on only recognition with assessment but also need to sepsis notification for coordination and continuous care at ED. According the study of Band and colleauges (2011) presented that the arrival at ED with EMS induced the shorter time to treatment than non-EMS ($p \leq 0.001$) but not reduced the mortality rate (p = 0.16). While the study of Guerra and colleagues (2013) demonstrated that when the EMS provider recognized sepsis and notified at ED, the survival rate in patients with sepsis increased (p = 0.04) (Guerra et al., 2013). However, when EMS utilization was divided to MEDS score or severity of illness and considered score at least 8 or at least medium level, a group of EMS utilization with complete the modified Robson screening (65.5%, 19 cases from all 29 cases) showed a lower proportion of clinical signs with deterioration between 6 – 72 hours since ED arrival than no EMS utilization (67.6%, 73 cases from all 108 cases) and EMS utilization with no complete the modified Robson screening (80.0%, 8 cases from all 10 cases). Especially in patients with severity of illness at high level with MEDS score $\geq$ 13, who presented EMS utilization with complete the modified Robson screening, has lower the proportions of clinical signs with deterioration between 6 – 72 hours since ED arrival than no EMS utilization and EMS utilization with no complete the modified Robson screening (50.0%, 100% and 69.2 respectively for MEDS at 13 – 15; 80.0%, 100% and 88.9% respectively for MEDS at > 15).

5.4 The outcomes of clinical signs: To consider nursing assessment for patients with sepsis within 72 dangerous hours

During a first 72 hours, patients with sepsis need to close observation with nursing assessment in three organ systems including respiratory, cardiovascular and neurological systems. Because most patients (59.9%) presented the clinical signs with deterioration between 6 – 72 hours since ED arrival by most of them had the highest rank of national early warning score (NEWS) between 9 – 20 (46.3%). Their proportion of dead was 65.3%. Nursing care plan for assessment will be strict on a first 24 hours due to the highest occurrence of clinical signs with deterioration (46.0%, 93 cases from all 202 cases).

At first time of clinical signs with deterioration, one organ compromise was more found than two organ compromises and three organ compromises (58 cases, 42 cases, and 21 cases from all 121 cases respectively). The proportions of dead sequenced from lower to higher following the number of organ compromise as follows; one organ compromise (14.9%), two organ compromises (76.2%), and three organ compromises (81.0%). The sign of acute alteration of conscious presented higher the proportion of dead than respiratory and circulatory system (84.6%, 75.6%, and 62.5% respectively). Therefore, the early detection since the less number of organ compromise will save life in patients with sepsis.

5.5 The multilevel logistic regression analysis

Therefore, a best model was a random slope model with level of hospital which the significant factors were severity of illness (p = 0.001), level of hospital (p = 0.007) and performance of sepsis resuscitation bundle (p = 0.003). According the descriptive data as mentioned above, they were concluded as follows; 1) The severity of illness related to delay access, the older age, and the history of health care utilization; 2) The level of hospital, which was differentiated in workload and the situation of access block in emergency department, influenced the clinical outcomes differently; and 3) The performance of sepsis resuscitation bundle depended on triage practice, EMS utilization and process of nursing care.

CHAPTER VI
CONCLUSION AND RECOMMENDATIONS

This chapter consisted of two parts including conclusion and recommendations. The conclusion was the overview of results. The recommendations were proposed in the model of health service delivery for patients with sepsis, nursing practice, nursing education, and further study.

6.1 Conclusion

The study was a prospective descriptive correlational design. It was to explore factors in the system and patient levels influencing the clinical signs in patients with sepsis in the context of emergency health care system. Factors in patient level were severity of illness and time to perceive symptom onset. Factors in system level were level of hospital, sepsis policy, EMS utilization, triage practice, performance of sepsis resuscitation bundle, care model, length of ED stay and ICU admission. The multilevel logistic regression analysis was statistical used. The study was conducted from September 2014 to February 2015 in 5 tertiary or regional hospitals (45.5%) and 6 general hospitals (54.5%) in central region of Thailand. There were 202 patients in data analysis.

Most patients were 65 years of age and older (55.9%), male (52.0%), and presented marital status in couple (72.3%), education level at elementary school (50.5%), no monthly income (60.4%), and health service payment with universal coverage (72.8%). The proportions of clinical signs with deterioration were highest in patients who were 55 – 64 years (65.8%), male (63.8%), and single (72.2%), and had non-education level (61.9%), monthly income at 30,001 baht or more, and used social security insurance for health service payment (80.0%).

For health and illness, most patients had one underlying disease (37.1%) especially hypertension (35.1%) and time of perceive symptom onset within 24 hours

(41.1%) by perceive fever / chill as a most symptom in present illness (43.6%). Alteration of conscious was most of chief complaint (45.5%). Most site of infection was respiratory system (44.1%). About 17.4% of patients had ever utilized other health services before the latest ED arrival for the current illness. The proportions of clinical signs with deterioration were highest in patients who had four or more underlying diseases (75.0%), chronic liver disease (84.6%), time of perceive symptom onset between 8 – 14 days (91.6%), perceived dyspnea / tachypnea in present illness (67.6%) and chief complaint (67.7%), presented the site of infection at respiratory system (73.0%), and utilized ED before the latest ED arrival for the current illness (88.9%).

For the characteristics of clinical signs, most patients presented signs at least one organ compromise (86.1%) especially in two organs (34.7%) and shock index between 1.00 – 1.25 (61.9%) at triage. There were 132 patients (65.3%) who presented SBP $\geq$ 90 mmHg at triage and then 54 patients deteriorated with SBP < 90 mmHg by 27 patients progressed to septic shock. There were totally 124 patients (61.4%) who presented SBP < 90 mmHg within six hours since ED arrival. Most of them presented a period of SBP < 90 mmHg in one time (62 patients) and duration time $\leq$ one hour (42 patients). Most patients had a severity of illness at medium level with the score of the mortality in emergency department sepsis (MEDS) at 8 – 12 (48.0%) and presented the stage of sepsis with organ dysfunction (45.0%) within six hours since ED arrival. For clinical signs at triage, the proportions of clinical signs with deterioration were highest in patients who presented with three organ compromises (73.0%), shock index > 2.00 (100%), and a severity of illness at very high level as MEDS score > 15 (86.7%). For clinical signs during six hours since ED arrival, the proportions of clinical signs with deterioration were highest in patients who presented the stage of sepsis shock (65.3%) or deteriorated in septic shock later (66.7%), and a period of SBP < 90 mmHg with > five times (100.0%) and duration time > four hours (86.67%).

For the structure characteristics, all hospitals have an available hospital policy for sepsis (100%). Most of hospitals were presented the number of bed between 501 – 1,000 beds (54.5%), emergency cases at ED between 30,000 – 49,999 cases per year (63.6%), no data of sepsis cases at ED (54.5%), time to apply a sepsis policy at

ED more than two years (72.7%) and the components of sepsis resuscitation bundle in policy that consisted of early fluid challenge and antibiotic management including and the achieved non-invasive and invasive monitoring (63.6%). The proportions of clinical signs with deterioration were highest in hospitals which were tertiary or regional hospitals (69.1%) and presented the number of bed between 501 – 1,000 beds (66.9%), the emergency cases at ED between 70,000 – 99,999 cases per year (72.7%), sepsis cases at ED more than 30 cases per month (69.7%), time to apply a sepsis policy at ED between 13 months and two years (75.8%), and the components of sepsis resuscitation bundle in policy that consisted of early fluid challenge and antibiotic management including and the achieved non-invasive and invasive monitoring (65.0%). When the triage practice was divided into level of hospital, the tertiary or regional hospitals presented more patients with no complete triage components (63.4%, 78 cases from 123 cases) than general hospitals (50.6%, 40 cases from 79 cases). When the performance of sepsis resuscitation bundle divided into level of hospital, the tertiary or regional and general hospitals presented similar number of patients who achieved in all components of medical treatment and non-invasive monitoring (6.5%, 8 cases from 123 cases; 6.3%, 5 cases from 79cases respectively). When a length of ED stay was divided into level of hospital, the tertiary or regional hospitals presented more patients with a length of ED stay more than six hours than general hospitals (27 cases and 6 cases respectively). When general ward were divided into level of hospital, the general hospitals presented higher proportion of ICU and intermediate admission (30.4%, 24 cases from all 79 cases and 13.0%, 16 cases from all 123 cases respectively).

For EMS utilization, there were 43 patients (21.3%) who arrived at ED with EMS utilization by most of them presented the severity of illness at medium level with MEDS score at 8 – 12 (24 patients) and received oxygen therapy and intravenous fluid (22 patients). The proportions of clinical signs with deterioration were highest in all groups of severity of illness at very high level with MEDS score more than 15 including no EMS utilization (88.9%), EMS utilization with no complete the modified Robson screening (100%), and EMS utilization with complete the modified Robson screening (80.0%). While the group of severity of illness at high level with MEDS score $\geq$ 13, who presented EMS utilization with complete the modified Robson screening, has lower the proportions of clinical signs with deterioration between 6 – 72 hours since ED arrival than no EMS utilization and EMS utilization with no complete the modified Robson screening (50.0%, 100% and 69.2 respectively for MEDS at 13 – 15; 80.0%, 100% and 88.9% respectively for MEDS at > 15).

For triage characteristics, most patients were decided the triage level at emergent level (54.5%) and not complete in any triage components (58.4%). they were recorded vital signs with the average frequency ≤ 60 minutes within six hours since ED arrival in both cases of presenting SBP ≥ 90 mmHg (54 cases from all 78 cases) and SBP < 90 mmHg (41 cases from all 54 cases for before SBP < 90 mmHg, 116 cases from all 124 cases for during SBP < 90 mmHg, and 114 cases from all 124 cases for four times recording after recovery to SBP ≥ 90 mmHg). The proportions of clinical signs with deterioration were highest in patients who did not complete in any triage components (67.2%). For cases presented SBP ≥ 90 mmHg at triage and then deteriorated to SBP < 90 mmHg within six hours, the proportions of clinical signs with deterioration were high in patients who were recorded vital signs in a period before SBP < 90 mmHg with the average frequency at > 1 – 2 hour (80%) and > 2 – 4 hours (100%).

For performance of sepsis resuscitation bundle, the 53.3% and 44% of patients with sepsis and shock received fluid challenge at least 2,000 ml within three hours (40 cases from all 75 cases) and vasopressor after fluid challenge at least 2,000 ml within six hours (33 cases from all 75 cases) respectively. Most patients were administered antibiotic between more than one hour and three hours (50.0%). For non-invasive monitoring, most patients were achieved in mean arterial pressure (MAP) ≥ 65 mmHg (85.6%) and urine output ≥ 0.5 ml/kg/hr (57.9%) within six hours. While the invasive monitoring was little performed to monitor patients by only 9.9% and 2.0% were monitored with central venous pressure (CVP) and central venous oxygen saturation ($ScvO_2$) respectively. Most patients in each stage of sepsis were not achieved in any components of medical treatment and non-invasive monitoring as following 35 cases from all 36 cases in sepsis, 89 cases from all 91 cases in sepsis with organ function, and 65 cases from all 75 cases in sepsis with shock. The proportions of clinical signs with deterioration were lowest in patients with all stages of sepsis who were achieved in all components of medical treatment and non-invasive monitoring including sepsis (0 case from 1 case), sepsis with organ function (0 case from 2 cases), and sepsis with shock (3 cases from 10 cases).

For care model, most patients were cared with the non-ED centric model (92.1%) by most of them presented the highest proportions of clinical signs with deterioration (60.8%). When the care model was divided into each stage of sepsis, the proportions of clinical signs with deterioration between 6 – 72 hours since ED arrival in a group of septic shock, who were cared with the ED centric model, was lower than who were cared with non-ED centric model (57.1% and 67.2% respectively). Most patients had a length of ED stay less than two hours (43.0%) and admitted at general ward (80.2%).

For clinical outcomes, most patients presented the outcome of clinical signs with deterioration (59.9%) with the highest level of national early warning score (NEWS) at 9 – 20 (46.0%) within 24 hours (46.0%). The circulatory system was most of deterioration (55.4%) especially SBP $\leq$ 90 mmHg (25.2%). The proportions of dead were highest in patients who presented clinical signs with deterioration between 6 – 72 hours since ED arrival (65.3%) especially in patients with deterioration in three systems of respiratory, circulatory and neurological (81.0%), presenting with acute alteration of conscious (84.6%), presenting the NEWS at 9 – 20 (75.3%), and time to present clinical signs with deterioration within 24 hours (67.7%).

The results of multilevel logistic regression analysis were four models. Model 1 was presented a clustering effect influencing with ICC at 0.083 on clinical signs of patients with sepsis that the multilevel analysis was appropriate for this study. Model 2 and 3 were presented the analysis with three significantly selected variables including severity of illness ($p < 0.001$, $p = 0.001$), level of hospital ($p = 0.030$, $p = 0.007$) and performance of sepsis resuscitation bundle ($p = 0.009$, $p = 0.003$) for random intercept and random slope models respectively. Model 4 was demonstrated in no significant interaction effect model between level of hospital and severity of illness ($p = 0.393$ and $p = 0.315$ in random intercept and random slope respectively), and level of hospital and performance of sepsis resuscitation bundle ($p = 0.571$ and $p = 0.567$ in random intercept and random slope respectively). When compared model 1 – 3, the random slope model was the best for multilevel logistic regression in this study by presenting a goodness of fit with the scatter plots.

The results of best model were described for patients with sepsis who utilized the emergency health care system as following a one-unit increased in the severity of illness or MEDS score, the probability of clinical signs without deterioration between 6 – 72 hours since ED arrival decreased by 14.8% (OR = 0.852, p = 0.001). General hospital was more likely to promote the probability of clinical signs without deterioration between 6 – 72 hours since ED arrival by 2.813 times than tertiary or regional hospitals (p = 0.007). Patients who achieved in all components of medical treatment and non-invasive monitoring were more likely to promote the probability of clinical signs without deterioration between 6 – 72 hours since ED arrival by 9.349 times than patients who did not achieve (p = 0.003). This model was illustrated as follows;

$$\ln\left[\frac{\pi}{1-\pi}\right] = 0.545 - 0.160\ (\text{severity of illness}) + 1.034\ (\text{level of hospital}) + 2.235\ (\text{performance of sepsis resuscitation bundle})$$

6.2 Recommendations

The recommendations are proposed in the model of health service delivery for patients with sepsis, nursing practice, nursing education, and further study.

6.2.1 The model of health service delivery for patients with sepsis

The model of health service delivery for patients with sepsis (Table 6.1) is planned for an emergency situation of patients with sepsis and hypoperfusion. It explained following the data of discussion in timeline utilization in the emergency health service system including pre-hospital and in-hospital phases. Pre-hospital phase is public awareness for sepsis and EMS utilization. The achieved time in pre-hospital phase is within a first 24 hours of organ compromise presentation following the result of the lowest proportion of clinical signs with deterioration between 6 – 72 hours since ED arrival (54.2%) presented when time of perceived symptom onset $\leq$ 24 hours. According to the study of Blanco and colleagues (2008) revealed that when patients with sepsis decided to seeking care within first day of organ dysfunction, the survival rate will more than seeking at next day as follows; 95.8% for within first day, 85.2% for 48 hours, and 72.3% for 7 days. In-hospital phase was the policy in area of triage, emergency department, ward admission, and unit of quality assurance and control. The performance time at triage and emergency department is within four hours since ED arrival following the results of the lowest proportion of clinical signs with deterioration between 6 – 72 hours since ED arrival (< 50%) presented when a length of ED stay within four hours in general hospitals. The performance time at ward admission is within 72 hours since ED arrival following the dangerous period of changeable signs. The performance time at unit of quality assurance and control is every year for sustaining the quality of care in patients with sepsis following the result of proportion of clinical deterioration between 6 – 72 hours since ED arrival was dramatically changed from 6 – 12 months (29.4%) to 13 months – 2 years (75.8%) of time to apply a sepsis policy at ED.

6.2.1.1 Promote public awareness in symptoms of organ compromise when infectious disease suspected especially in elderly: The chief complaints for patients who were suspected sepsis, should be promoted to early sepsis recognition, are dyspnea/tachypnea (67.7%), fatigue (66.7%), alteration of conscious (62.0%), and fainting/syncope (53.3%) due to presenting more than 50% of the proportion of clinical signs with deterioration between 6 – 72 hours since ED arrival. The 65 years and older and care giver should be a target to promote the sepsis recognition because of a largest group of presenting sepsis (55.9%).

6.2.1.2 Determine dispatch guideline with signs and symptoms related sepsis and organ compromise: All chief complaints as mentioned above to promote in public awareness should be mixed in the process of dispatch for timely responding to recognition in patients with sepsis and promoting the assessment with using the modified Robson screening tool because there were 78.7% with no EMS utilization and 5.0% with no complete the modified Robson screening.

6.2.1.3 Determine sepsis assessment and notification in work instruction: The EMS utilization should be consisted of the process of assessment and notification. Because the results of EMS utilization with complete the modified Robson screening tool in patients with sepsis and a high severity level with MEDS score $\geq$ 13, who presented EMS utilization with complete the modified Robson screening, has tended to presented the lower proportions of clinical signs with deterioration between 6 – 72 hours since ED arrival than no EMS utilization and EMS utilization with no complete the modified Robson screening (50.0%, 100% and 69.2 respectively for MEDS at 13 – 15; 80.0%, 100% and 88.9% respectively for MEDS at > 15). Then the EMS providers notified to ED providers, the survival rate will increased ($p = 0.04$) (Guerra et al., 2013).

6.2.1.4 Stimulate to complete all components in triage practice: The result showed the proportion of clinical signs with deterioration between 6 – 72 hours since ED arrival was lower in patients with sepsis who were completed in all triage components (49.4%) than no complete (67.2%).

6.2.1.5 Determine sepsis fast track with consider SIRS criteria and shock index > 1 at triage and count the achieved time of performance of sepsis resuscitation since ED arrival: A policy of sepsis fast track since triage will promote the achieved time of sepsis resuscitation bundle especially fluid challenge within three hours and antibiotic administration within one hour. Especially the sepsis protocol is used the SIRS criteria with shock index ≥ 1 for early detection and closed monitoring in patients with infectious disease. Because the 40.9% of patients with infectious disease, who presented with SIRS criteria, shock index ≥ 1 and SBP ≥ 90 mmHg at triage, deteriorated in SBP < 90 mmHg within six hours since ED arrival by a half progressed to septic shock. Therefore, when the sepsis fast track is alerted at triage then the performance of sepsis resuscitation bundle is rapidly started, it is significant to promote the clinical signs without deterioration between 6 – 72 hours since ED arrival by 9.349 times than patients who did not achieve ($p = 0.003$).

6.2.1.6 Determine the sepsis protocol with identify nursing care with appropriate management when access block at ED: the results showed the patients with sepsis who were monitored with a frequency at ≤ 60 minutes within six hours (55.6%, 30 cases from 54 cases in case sustained SBP ≥ 90 mmHg; 56.1%, 23 cases from 41 cases in period before SBP < 90 mmHg) and had a length of ED stay was ≤ 4 hours in general hospitals (44.4%, 32 cases from 72 case) had lower proportions of clinical signs with deterioration between 6 – 72 hours since ED arrival than the patients with sepsis who were monitored with > 60 minutes within six hours (62.5%, 15 cases from 24 cases in case sustained SBP ≥ 90 mmHg; 76.9%, 10 cases from 13 cases in period before SBP < 90 mmHg) and had a length of ED stay was > 4 hours in both of general hospitals (57.1%, 4 cases from 7 cases) and tertiary or regional hospitals (68.1%, 32 cases from 47 cases).

6.2.1.7 Determine continuous monitoring with using a search out severity (SOS) score in work instruction and considering workload situation: Most patients with sepsis (59.9%) presented the clinical signs with deterioration between 6 – 72 hours since ED arrival with signs of organ compromise including respiratory, circulatory, and neurological systems. Therefore, a search out severity (SOS) score, which consists of the assessment with those signs of organ compromise with time varying from severity, should be appropriate to conduct nursing assessment for patients with sepsis. The workload should be appropriate to man-power for nursing care in patients with sepsis because it may interrupt the effective outcomes in the tertiary or regional hospitals. Especially for patients with septic shock, who should be close monitored due to the highest proportion of clinical signs with deterioration between 6 – 72 hours since ED arrival (65.3%).

6.2.1.8 Continuous review sepsis policy for sustaining the quality of care: The sepsis policy should be reviewed with education program in every year because the quality of policy drops after one year following the proportion of clinical deterioration between 6 – 72 hours since ED arrival was dramatically changed form 29.4% to 75.8% of time to apply a sepsis policy at ED between 6 – 12 months and 13 months – 2 years respectively.

Table 6.1 The model of health service delivery for patients with sepsis

Phase	Area	Health service delivery policy	Goal time
Pre-hospital phase	Public	1. Promote public awareness in symptoms of organ compromise when suspected infectious disease especially in elderly	Within 24 hour after organ compromise
	EMS	2. Determine dispatch guideline with signs and symptoms related sepsis and organ compromise 3. Determine sepsis assessment and notification in work instruction	

Phase	Area	Health service delivery policy	Performance time
In-hospital phase	Triage	4. Stimulate to complete all components in triage practice 5. Determine sepsis fast track with consider SIRS criteria and shock index ≥ 1 at triage and count the achieved time of performance of sepsis resuscitation since ED arrival	Within 4 hours since ED arrival
	Emergency department	6. Determine the sepsis protocol with identify nursing care with appropriate management when access block at ED	
	Ward admission	7. Determine continuous monitoring with using a search out severity (SOS) score in work instruction with considering workload situation	Within 72 hours since ED arrival
	Unit of quality assurance and control	8. Continuous review sepsis policy for sustaining the quality of care	Every year

6.2.2 Nursing practice

6.2.2.1 Use the shock index $\geq$ 1 in nursing assessment for patients with sepsis for early detection the unstable clinical signs with a frequency of monitoring $\leq$ 60 minutes because patients with sepsis and shock index $\geq$ 1 presented the 55.9% of clinical signs with deterioration between 6 – 72 hours since ED arrival.

6.2.2.2 Always follow-up appointment for continuous care after discharge patients with infectious disease from ED because the patients with sepsis, who had ever utilized the ED before the latest ED arrival, present a highest proportion of clinical signs with deterioration between 6 – 72 hours since ED arrival (88.9%).

6.2.3 Nursing education

6.2.3.1 Provide the knowledge of pathophysiology of sepsis for comprehensive practice since early detection and monitoring the clinical signs, and supporting the sepsis recognition in patients following the results that patients with sepsis and organ compromise had a high proportions (65.3%) of clinical signs with deterioration between 6 – 72 hours since ED arrival.

6.2.3.2 Provide the knowledge of assessment methods for the elderly who are suspected sepsis due to a high risk of sepsis (55.9%).

6.2.4 Further study

The pre-hospital phase of patients with sepsis is interesting for further study because the factors which influenced the access in patients with sepsis are unknown.

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APPENDICES

APPENDIX A
LIST OF HOSPITALS AND NUMBER OF CASES IN THE STUDY

Number	Hospital name	Number of cases
1	Thammasat university hospital	33
2	Faculty of Medicine Vajira hospital	33
3	Nakhonpathom hospital	14
4	Saraburi hospital	33
5	Chaoprayayomraj hospital	10
6	Pranangklao hospital	10
7	Klang hospital	10
8	Sing Buri hospital	17
9	Somdetphraphutthalertla hospital	22
10	Sukhothai hospital	10
11	Phraphutthabat Hospital	10
	Total	202

APPENDIX B

TABLES OF MULTILEVEL LOGISTIC REGRESSION ANALYSIS

B1 Random intercept model for screening variables (n=202)

Variables	$\hat{\beta}$	OR (SE)	p-value
Time to perceive symptom onset	- 0.005	0.995 (0.002)	0.051*
Severity of illness	- 0.157	0.855 (0.037)	< 0.001*
Level of hospital			
Tertiary or regional hospital	-	1	-
General hospital	1.023	2.783 (0.970)	0.003*
Sepsis policy			
No available	-	1	-
Available	0	1 (omitted[a])	-
EMS utilization			
No EMS utilization	-	1	-
EMS utilization with no complete the modified Robson screening	- 1.019	0.361 (0.28)	0.300
EMS utilization with complete the modified Robson screening	- 0.107	0.898 (0.379)	0.799
Triage practice			
No complete in any triage components	-	1	-
Complete in all triage components	0.742	2.101 (0.669)	0.020*
Performance of sepsis resuscitation bundle			
Not achieved in any components of medical treatment and non-invasive monitoring	-	1	-
Achieved in all components of medical treatment and non-invasive monitoring	1.780	5.930 (4.143)	0.011*

[a] omitted due to all hospitals have an available policy for sepsis

B1 Random intercept model for screening variables (n=202) (cont.)

Variables	$\hat{\beta}$	OR (SE)	p-value
Care model			
The non-ED centric	-	1	-
The ED centric	0.528	1.695 (0.928)	0.335
Length of ED	0.000	1.00 (0.000)	0.938
Ward admission			
General ward	-	1	-
Intermediate / Intensive care unit	-0.053	0.949 (0.405)	0.902

* Significant at $p \leq 0.05$

B2 Random intercept model for selecting variables (n=202)

Variables	$\hat{\beta}$	OR (SE)	p-value
Fixed effect			
Intercept	0.768	-	0.152
Time to perceive symptom onset	-0.005	0.995 (0.002)	0.056
Severity of illness	-0.172	0.842 (0.039)	< 0.001*
Level of hospital			
Tertiary or regional hospital	-	1	-
General hospital	0.874	2.396 (0.963)	0.030*
Triage practice			
No complete in any triage components	-	1	-
Complete in all triage components	0.629	1.877 (0.647)	0.068
Performance of sepsis resuscitation bundle			
Not achieved in any components of medical treatment and non-invasive monitoring	-	1	-
Achieved in all components of medical treatment and non-invasive monitoring	2.047	7.743 (6.099)	0.009*

Random effect	**Estimate**	**SE**
System level:		
S.D. (intercept)	0.345	0.249

* Significant at $p \leq 0.05$

B3 Random slope model with severity of illness (n=202)

Variables	$\hat{\beta}$	OR (SE)	p-value
Fixed effect			
Intercept	0.606	-	0.205
Severity of illness	-0.168	0.845 (0.039)	< 0.001*
Level of hospital			
Tertiary or regional hospital	-	1	-
General hospital	1.024	2.784 (1.087)	0.009*
Performance of sepsis resuscitation bundle			
Not achieved in any components of medical treatment and non-invasive monitoring	-	1	-
Achieved in all components of medical treatment and non-invasive monitoring	2.213	9.146 (6.834)	0.003*
Random effect	**Estimate**	**SE**	
System level: S.D. (intercept)	0.328	0.247	
Patient level: S.D. (severity of illness)	0.000	0.028	
-2LL = -118.259			
AIC = 248.518, BIC = 268.367			

* Significant at $p \leq 0.05$

B4 Random slope model with performance of sepsis resuscitation bundle (n=202)

Variables	$\hat{\beta}$	OR (SE)	p-value
Fixed effect			
Intercept	0.607	-	0.205
Severity of illness	-0.168	0.845 (0.039)	< 0.001
Level of hospital			
Tertiary or regional hospital	-	1	-
General hospital	1.024	2.784 (1.087)	0.009*
Performance of sepsis resuscitation bundle			
Not achieved in any components of medical treatment and non-invasive monitoring	-	1	-
Achieved in all components of medical treatment and non-invasive monitoring	2.213	9.146 (6.834)	0.003

Random effect	Estimate	SE
System level:		
S.D. (intercept)	0.328	0.247
S.D. (Performance of sepsis resuscitation bundle)	0.00	1.057

-2LL = -118.259
AIC = 248.518, BIC = 268.367

APPENDIX C
LIST OF EXPERTS

The five experts are listed for the content validity of research instruments as follows;

1. Jiraporn Srion, M.D.
Emergency Physicians,
Emergency Department, Faculty of Medicine Vajira Hospital, Navamindradhiraj University

2. Wimonwan Phonburee, M.S.N. (Adult Nursing)
Registered Nurse, Senior Professional Level,
Chief Nurse of Emergency Department, Sapphasitthiprasong Hospital

3. Shivakorn Srisomorn, B.Sc (Nursing & Midwifery)
Registered Nurse, Senior Professional Level,
Head Nurse, Emergency Department, Siriraj Hospital

4. Nittaya Puripun, M.S.N (Ambulatory Care)
Registered Nurse, Professional Level,
Head Nurse, Emergency Department, Lerdsin Hospital

5. Kannika Katsomboon, M.S.N. (Adult Nursing)
Registered Nurse, Professional Level
Lecturer, Boromarajonani College of Nursing Lampang

APPENDIX D
RESEARCH INSTRUMENT

Clinical and sociodemographic questionnaire

Instructor:

1. Data collection by interview patient or family in part I and II
2. Please tick √ in the box and fill in the blank corresponding the patient information

Part I Personal information of patient

1. Age …………….years

2. Gender
☐ Male ☐ Female

3. Marital status
☐ Single ☐ Couple ☐ Separate / window

4. Education level
☐ None ☐ Elementary school ☐ High school
☐ Diploma ☐ Bachelor's degree or higher

5. Monthly income
☐ None ☐ ≤ 10,000 Baht ☐ 10,001 – 20,000 Baht
☐ 20,001 – 30,000 Baht ☐ ≥ 30,001 Baht

6. Health service payment
☐ Self-payment ☐ Universal coverage
☐ Civil servants medical benefits scheme ☐ Social security insurance
☐ Others
………………………………………………………………………………..

Part II Health history and utilization

7. Underlying disease (can choose more than one answer)

- ☐ Cancer
- ☐ Cardiovascular disease
- ☐ Cerebrovascular disease
- ☐ Chronic lung disease
- ☐ Chronic kidney disease
- ☐ Chronic liver disease
- ☐ Congestive heart failure
- ☐ Diabetes
- ☐ Dyslipidemia
- ☐ Hypertension
- ☐ Human immunodeficiency virus infection
- ☐ No/Unknown underlying disease

8. Health service utilization for the current illness before the latest ED arrival (can choose more than one answer)

- ☐ None
- ☐ Pharmacy service………times
- ☐ Primary care / private clinic……times
- ☐ Out-patient department……times
- ☐ Emergency department………...times

9. Time of perceived symptoms onset (date/month/year/time)………………………….

10. First time to health service utilization (date/month/year/time)……………………...

11. Time to the latest ED arrival (date/month/year/time)……………………………….

12. What symptoms which urge the patient to go to ED? ………………………………

…………………………………………………………………………………………...

Organizational data- level of hospital

Instructor:

1. Data collection by interview the director or head nurse in part I and II, and observation with checklist about sepsis policy under the current situation.
2. Please tick √ in the box and fill in the blank corresponding the organizational data

Part I The hospital information and characteristics

Name of hospital…………………………………………………………………………...

Province……………………………………………………………………………………

1. Number of beds in hospital………………...

2. Level of hospital

☐ Regional or Tertiary hospital ☐ General hospital

3. What is the annual volume of ED (cases/year)?

☐ < 30,000 ☐ 30,000 to 49,999 ☐ 50,000 to 69,999

☐ 70,000 to 99,999 ☐ > 100,000

4. How many sepsis patients visit to ED monthly (cases/month)?

☐ 1 – 10 ☐ 11 – 20 ☐ 21 – 30

☐ > 30 ☐ No data

Part II Sepsis policy for resuscitation

5. Has the hospital or emergency department provided the sepsis policy?

☐ Yes ☐ No

<u>If the answer of question 5 is yes</u>, please continue to next table and questions at 6 - 13

Please tick √ in the box number 1 – 6 in the table corresponding the data of sepsis policy in the hospital or emergency department including protocol, education and continuous quality improvement

Protocol ☐ a. Instruction for “sepsis profile” or “clinical identification”: the systemic inflammatory response syndrome (SIRS) / severe sepsis / septic shock ☐ b. Instruction for “sepsis team” activation ☐ c. Instruction for sepsis treatment or management
Educational program ☐ d. Definition and clinical for identification of sepsis ☐ e. Sepsis resuscitation bundle as the timely and optimal therapy included fluid challenge with vasopressor in non-response, antibiotic, and the achievement of non-invasive monitoring or / and invasive monitoring
Continuous quality improvement ☐ f. An audit and feedback process such as monitoring sepsis performance and outcomes, evaluation meeting per monthly or more, and mortality case conference

6. Has all components (a – f items in the table above) of sepsis policy in the hospital or emergency department following the above table?

☐ Yes ☐ No

7. What in-hospital wards have a continuing care with sepsis policy after admission from ED?

☐ General ward and ICU ☐ General ward
☐ ICU ☐ No

8. Has the identification guideline for sepsis conditions at triage?

☐ Yes ☐ No

9. Who is the main in sepsis protocol in the ED? (If the answers are more than one, please sequence and ranging the number)

☐ ED physician (No.….) ☐ ED nurse (No.….)
☐ Internal medicine / Critical are physician (No.….)
☐ Other (No.….) ………………………………………………………………..

10. Who is the main in sepsis educational program in the ED? (If the answers are more than one, please sequence and ranging the number)

☐ ED physician (No.….) ☐ ED nurse (No.….)
☐ Internal medicine / Critical are physician (No.…)
☐ Other (No.….) ………………………………………………………………..

11. Who is the main in process of continuous quality improvement for sepsis in the ED? (If the answers are more than one, please sequence and ranging the number)

☐ ED physician (No.….) ☐ ED nurse (No.….)
☐ Internal medicine / Critical are physician (No.…)
☐ Other (No.….) ………………………………………………………………..

12. How long did apply the sepsis policy in ED?

☐ less than 6 months ☐ 6 to 12 months

☐ 13 months to 2 years ☐ more than 2 years

13. What are the components of sepsis resuscitation bundle consisted in the sepsis protocol of hospital?

☐ Early fluid challenge and antibiotic management

☐ Early fluid challenge and antibiotic management including the achievement of non-invasive monitoring: MAP $\geq$ 65 mmHg and/or urine output $\geq$ 0.5 ml/kg/hr

☐ Early fluid challenge and antibiotic management including the achievement of monitoring: MAP $\geq$ 65 mmHg and/or urine output $\geq$ 0.5 ml/kg/hr for non-invasive monitoring, and CVP 8-12 mmHg and/or $ScvO_2 \geq 70\%$ for invasive monitoring

☐ Others…………………………………………………………………………..

The emergency medical service (EMS) utilization

Instruction:
1. Data collection with checklist following the EMS record regarding the suggestion
2. Please tick √ in the box and fill the data corresponding each item

1. Use of EMS from home or resident to arriving to the ED
☐ Yes ☐ No

If the answer of question 1 is yes, please continue to question 2

2. EMS utilization with initial assessment
☐ Yes ☐ No

If the answer of question 2 is yes, please continue to next table and question 3 by tick √ in the box and fill the data corresponding to assessment in part I – III. For part III, please with √ in the box of etiology and signs consistent with infection at bottom of table following the data of patient.

Part	Data of assessment
Part I Clinical signs in the modified Robson screening tool	☐ 1. Pulse rate……………………………beats/min ☐ 2. Respiratory rate..……………………breaths/min ☐ 3. Body temperature..…………………ºC ☐ 4. Neurological sign…………………..(GCS or AVPU scale) ☐ 5. Blood glucose level……………..…...mg%
Part II The others clinical signs in the Robson screening tool	☐ 6. Blood pressure………………………………..mmHg ☐ 7. Pulse oximetric saturation (SpO2)………………% with room air / oxygen device…………………………. ☐ 8. Oliguria condition as not passed urine more than eight hours

Part	Data of assessment	
	Etiology	**Signs and symptoms**
Part III The history suggestion of new infection in the modified Robson screening tool	☐ Central nervous system	Headache / Neck stiffness / Photophobia; In combination with signs consistent with infection*
	☐ Respiratory tract	Cough / Dyspnea / Abnormal secretion / Chest discomfort or pain / Breathing difficulties / current treatment of pneumonia; In combination with signs consistent with infection*
	☐ Intra-abdominal and Gastrointestinal	Abdominal pain or tenderness / Abdominal distended / Diarrhea; In combination with signs consistent with infection*
	☐ Urinary tract	Abnormal urine color or odor without trauma / Frank or back or lower abdominal pain / current treatment of urinary tract infection; In combination with signs consistent with infection*
	☐ Skin, soft tissue, and bone (excluded chronic wound without the deteriorated status)	Red, swollen, warm, or painful soft tissue or joint without trauma / Bad smelling or purulent or black or deteriorated wound; In combination with signs consistent with infection*
	☐ Infected indwelling device	Redness, pain, or purulent secretions at site of catheters; In combination with signs consistent with infection*
	☐ Bacteremia	Unspecified fever / chill as related persons with feeling or temperature measure; In combination with signs consistent with infection*
***Signs consistent with infection** ☐ Fever ☐ Chills ☐ New-onset weakness ☐ Malaise ☐ Nausea ☐ Vomiting ☐ Alteration of conscious ☐ Hypotension (Systolic blood pressure <90 mmHg)		

3. Does the EMS assessment complete in the part I (1-5) and take some data in part III following the above table?

☐ Yes ☐ No

4. Treatment during EMS utilization …………………………………………………...

…………………………………………………………………………………………...

…………………………………………………………………………………………...

The mortality in emergency department sepsis (MEDS) score

Instruction:
1. Data collection with checklist following the medical and nursing record from the data of first time evaluation at ED.
2. Please circle the number and the range of number of points assigned to indicate the severity score of sepsis.

Characteristic	Points assigned	
	Yes	No
Predisposing		
Age > 65 year	3	0
Nursing home resident	2	0
Terminal illness (metastatic cancer)	6	0
Infection		
Lower respiratory infection (Bronchitis, Pneumonia)	2	0
Response		
Band > 5%	3	0
Organ dysfunction		
Tachypnea (respiratory rate > 20 breaths/min) or hypoxemia (pulse oximetric saturation < 90%),	3	0
Septic shock (systolic blood pressure < 90 mmHg after an initial fluid challenge of 20–30 ml/kg)	3	0
Platelet count < 150,000 cells/mm3	3	0
Alteration of conscious	2	0
Total score		0
Summary point range		
Very low	0 – 4	
Low	5 – 7	
Moderate	8 – 12	
High	13 – 15	
Very high	> 15	

Profile of emergency health care delivery

Instruction:
1. Data collection with checklist following the medical and nursing record.
2. Please tick √ in the box and fill the data corresponding each part.

Part I Triage practice from triage record
1. The patient is assessed with triage practice before or at first time of physician exam at bedside
☐ Yes ☐ No

If the answer of question 1 is yes, please continue fill chief complaint and the data in next table with answering the question number 2
Chief

Complaint:…………………………………………………………………………......

Triage components	Assessment data
1. Evaluated vital signs[a] ☐ 1.1 Complete four vital signs ☐ 1.2 Not complete vital signs	☐ Blood pressure………………………………mmHg or MAP…………………………………...mmHg ☐ Pulse rate…………………………...…….beats/min ☐ Respiratory rate……………….............breaths/min ☐ Body temperature………………………………..ºC
2. Evaluated signs of organ dysfunction[b] ☐ 2.1 Evaluate one or more signs ☐ 2.2 No evaluate	☐ Level of conscious by description or evaluate with GCS or AVPU ……………..……………….... ☐ Oxygenation with pulse oximetric saturation (SpO2)………% in ☐ room air ☐ on oxygen ☐ ice……………………….l/m Approach urine output……………………………...
3. Sepsis alert ☐ 3.1 Alert with triage level ☐ 3.2 No sepsis alert with triage level at urgent / less urgent / non-urgent	☐ Sepsis alert code ☐ Higher acuity of triage level at emergent / resuscitation

[a] MAP, mean arterial pressure = [(2 X diastolic) + SYSTOLIC]/3
[b] GCS, Glasgow coma scale; AVPU, Alert, Verbal response, Pain response, Unresponsive; SpO2, the oxyhemoglobin saturation measured by pulse oximetry

2. Are the triage components performed in this patient including complete four vital signs (1.1) , evaluate one or more organ dysfunction signs (2.1), and alert with triage level (3.1) following the above table?

☐ Yes ☐ No

Part II Identification at first time of investigation

Diagnosis (infectious disease)…………………………………………………………...

Identification	Physiological parameters and laboratories
Sepsis (≥ 2 items of 1 - 4)	☐ 1. Body temperature >38°C or <36°C ☐ 2. Pulse rate > 90 beats/min ☐ 3. Respiratory rate > 20 breaths/min or partial pressure of carbon dioxide in arterial blood (PaC02) <32 mm Hg ☐ 4. Increased or decreased white blood cell count as >12,000/mm^3 or <4,000/mm^3 respectively or band >10%
Sepsis with suspected hypoperfusion[c] (5+6 / 5+7 / 5+6+7)	☐ 5. ≥ 2 items of 1 – 4 or two or more SIRS criteria ☐ 6. Serum lactate level ≥ 4mmol/L ☐ 7. Shock index ≥ 1, as the ratio of heart rate to systolic blood pressure at ED more than one
Severe sepsis[d] (at least 1 item of 8 –15)	☐ 8. Systolic blood pressure < 90 mmHg or MAP < 70 mmHg or a decrease in systolic blood pressure > 40 mmHg ☐ 9. Urine output < 0.5 ml/kg/hr for at least 2 hours despite adequate fluid challenge ☐ 10. PaO_2/FiO_2 < 200 in patients with pneumonia or PaO_2/FiO_2 < 250 in patients without pneumonia ☐ 11. Serum lactate level ≥ 4mmol/L ☐ 12. Serum creatinine level > 2 mg/dl (without chronic kidney disease) ☐ 13. Coagulation abnormalities or blood coagulation for international normalized ratio (INR) > 1.5 or activated partial-thromboplastin time (aPTT) > 60 sec ☐ 14. Platelet count < 100,000 /mm^3 ☐ 15. Total plasma bilirubin > 2 mg/dl (without chronic liver disease)
Septic shock (16)	☐ 16. Systolic blood pressure < 90 mmHg after an initial fluid challenge of 20 - 30 ml/kg

[c] SIRS, the systemic inflammatory response syndrome that consists of the criteria of sepsis identification in the number of 1 – 4

[d] PaO_2/FiO_2, The ratio of partial pressure arterial oxygen and fraction of inspired oxygen

3. Is this patient identified sepsis with suspected hypoperfusion (5+6 / 5+7 / 5+6+7) following the above table?

☐ Yes ☐ No

Part III The monitoring and treatment in ED within six hours

Time	Physiological parameters						Treatment
	Blood pressure (mmHg)	Pulse rate (beats/ min)	Respiratory rate (breaths/ min)	Oxygen saturation (%)	Body temperature (°C)	Neurological sign (AVPU)	
Time to triage ………							
Time.........							
Time.........							
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Part IV Sepsis resuscitation bundle

Time of presentation at ED ……………………………………………………………..

Time of ED disposition………………………………………………………………….

Estimated time for 3 hours after time presentation ……………………………………..

Estimate time for 6 hours after time presentation…..…………………………….........

Sepsis resuscitation bundle	Performance (since time of ED presentation)
Medical treatment Fluid challenge with crystalloids at least 2,000 ml within 3 hours and vasopressor application in non-response case with systolic blood pressure < 90 mmHg after fluid challenge within 6 hours	Fluid challenge ☐ Perform fluid challenge at least 2,000 ml within 3 hours ☐ No perform fluid challenge at least 2,000 ml within 3 hours Total fluid management (ml) within 3 hours ……………………………………………………… Duration triage time to fluid challenge (minutes)… …………………………………………………….. Vasopressor ☐ Perform vasopressor application within 6 hours after Fluid challenge ☐ Perform vasopressor application without Fluid challenge ☐ No vasopressor application within 6 hours Identify name of vasopressor………………………
Broad spectrum antibiotic administration within 3 hours	☐ Perform antibiotic administration within 1 hour ☐ Perform antibiotic administration > 1 - 3 hours ☐ Perform antibiotic administration > 3 hours ☐ No antibiotic administration Identify name of antibiotic…………………………

Sepsis resuscitation bundle	Performance
<u>Non-invasive monitoring</u> The achieved MAP[a] ≥ 65 mmHg within 6 hours The achieved urine output ≥ 0.5 ml/kg/hr within 6 hours : body weight ………………………kg estimated urine output …………...ml/hr	☐ Achieved ≤ 6 hours: MAP =……… ☐ Not achieved ≤ 6 hours : MAP =… ☐ No record within 6 hrs ☐ Record within 6 hrs ☐Achieved ≤ 6 hours ………..ml/hr ☐ Not achieved ≤ 6 hours …...ml/hr
<u>Invasive monitoring</u> The achieved central venous pressure (CVP) 8-12 mmHg within 6 hours The achieved central venous oxygen saturation ($ScvO_2$) ≥70% within 6 hours	☐ No investigation within 6 hrs ☐ Investigate within 6 hrs ☐Achieved ≤ 6 hours………mmHg ☐Not achieved ≤ 6 hours…..mmHg ☐ No investigation within 6 hrs ☐ Investigate within 6 hrs ☐ Achieved ≤ 6 hours…………% ☐ Not achieved ≤ 6 hours……..%

[a] MAP, mean arterial pressure = [(2 X diastolic) + SYSTOLIC]/3

4. Which the component group of sepsis resuscitation bundle is achieved in the patient?

Sepsis resuscitation bundle (since time of ED presentation)	The achieved performance
1. Fluid challenge with crystalloids at least 2,000 ml within 3 hours	☐ not achieved performance in any components at 1 – 4 ☐ achieved performance in all components at 1 – 4
2. Broad spectrum antibiotic administration within 1 hour	
3. The achieved mean arterial pressure ≥ 65 mmHg within 6 hours	
4. The achieved urine output ≥ 0.5 ml/kg/hr within 6 hours	

Part V Care model

<table>
<tr><th>Care model</th><th>Achievement of feasible components</th></tr>
<tr><td>☐ The ED centric model
(All feasible components of the sepsis resuscitation bundle are completed on time at ED)</td><td rowspan="2">▪ Fluid challenge with crystalloid at least 2,000 ml ≤ 3 hours at ED
☐ Achieved
☐ Not achieved
▪ Antibiotic administration ≤ 1 hours at ED
☐ Achieved
☐ Not achieved
▪ The achieved MAP ≥ 65 mmHg before admission including within 6 hours if the length of ED stay > 6 hours
☐ Achieved
☐ Not achieved</td></tr>
<tr><td>☐ The non-ED centric model
(Some or all feasible components of the sepsis resuscitation bundle are not completed on time at ED)</td></tr>
</table>

5. Is care model used in this patient following the above table?
☐ The ED centric model ☐ The non-ED centric model

Part V Admission and discharge

6. Time of admission (date/month/year/time)..…………………………………………

7. Time of ICU or ward disposition (date/month/year/time)……………………………

8. Length of ED stay (hours and minutes)………………………………………………

9. Characteristics of ward admission

☐ General ward

☐ ICU/ Intermediate ward within 6 hours after first presentation

☐ ICU/ Intermediate ward more than 6 hours after first presentation

☐ Other………………………………………………………………………………

10. Discharge status

☐ Death

☐ Discharge to home or resident

☐ Transfer to another hospital (time of transfer)……………………………………

☐ Institutionalization

☐ Other …………………………………………………………………………...

11. Length of hospital stay (days and hours)……………………………………………

The detection of clinical deterioration

Instruction:

Part I Data collection with the parameter of blood pressure, pulse rate, respiratory rate, oxygen saturation, body temperature, neurological signs, and urine output every 4 hours between 6 – 72 hours since presentation at ED.

Part II Detect the clinical signs with deterioration in Part I, following the criteria of the society of critical care medicine including the signs of respiratory, circulatory, and/or neurological compromises. The data of clinical signs with deterioration was collected when the clinical signs were worse than the data at 6 hours.

Part III Calculate the national early warning score (NEWS). For the patients with clinical deterioration in part II, the NEWS is calculated with the data at first time of deterioration. For the patients without clinical deterioration in part II, the NEWS is calculated with the data at 72 hours. Please consider the score of NEWS in part III for special condition as follows;

1. Body temperature If patients receive antipyretic drug within 4 hours, the score bases on the latest body temperature before antipyretic drug use.

2. Level of conscious If patients receive the sedative drug and they are not consciousness, the score of level of consciousness bases on clinical of conscious before sedative use.

3. Level of conscious For the intubated patients, if they are alert or fully awake, oriented and able to converse reasonably, the score is zero point or alert level.

4. Please tick √ in the box and fill the data corresponding the data of part I, II, III and time to collection.

Part I Monitoring between 6 – 72 hours

Time	The parameters						Urine output	Note
	Blood pressure (mmHg)	Pulse rate (beats/min)	Respiratory rate (breaths /min)	Oxygen saturation (%)	Body temperature (°C)	Level of consciousness (AVPU)		
After six hours of ED arrival Time ……….								
Time ………...								
Time …………								
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Time …………								
Time …………								

A=alert, V=verbal response, P=pain response, U=unresponsive

Part II Present clinical signs with deterioration with the signs of respiratory, circulatory, and/or neurological compromises following the society of critical care medicine between more than 6 – 72 hours after ED arrival. The data of clinical signs with deterioration was collected when the clinical signs were worse than the data at 6 hours.

☐ No
☐ Yes (Select and identify the deteriorated signs with time present)
 ☐ The signs of respiratory compromises
  ☐ Respiratory rate ≤ 8 or ≥ 30 breaths/min …………
  ☐ Oxygen saturation ≤ 90% …………………………
 ☐ The signs of cardiovascular compromises
  ☐ Systolic blood pressure ≤ 90 mmHg or decrease > 40 mmHg ………………………………………
  ☐ Heart rate ≤ 40 or ≥ 130 beats/min………………..
  ☐ Urine output ≤ 100 ml/4 hours ……………………
 ☐ The signs of neurological compromise
  ☐ Sudden alteration of conscious ……………………

Part III The NEWS
Time to collect data ☐ First time of clinical deterioration …………………………
 ☐ 72 hours ……………………………………………………

Physiological parameters	score							Score
	3	2	1	0	1	2	3	
1. Respiratory rate (breaths/min)	≤ 8	-	9 – 11	12 – 20	-	21 - 24	≥ 25	
☐ Without mechanical ventilation		-			-			
☐ With mechanical ventilation	-	-	-	-	-	-	Yes	
2. Oxygen saturations (%)	≤ 91	92 – 93	94 – 95	≥ 96	-	-	-	
☐ Non-COPD					-	-	-	
Oxygen saturations (%)	≤ 91	-	-	> 91	-	-	-	
☐ COPD case		-	-		-	-	-	

Physiological parameters	score							Score
	3	2	1	0	1	2	3	

3. Use oxygen device or supplement	-	Yes	-	No	-	-	-	
4. Body temperature($^{\circ}$C)	≤ 35.0	-	35.1 – 36.0	36.1 – 38.0	38.1 – 39.0	≥ 39.1	-	
All patients		-					-	
5. Systolic blood pressure (mmHg)	≤ 90	91 – 100	101 – 110	111 – 219	-	-	≥ 220	
☐ No vasopressure drug					-	-		
☐ On vasopressure drug	Yes	-	-	-	-	-	-	
6. Heart rate (beats/min)	≤ 40	-	41 – 50	51 - 90	91 - 110	111 - 130	≥ 131	
All patients		-						
7. Level of consciousness[a]	-	-	-	A	-	-	V, P or U	
☐ No underlying limited conscious	-	-	-		-	-		
Level of consciousness	-	-	-	V, P or U	-	-	P or U	
☐ Have underlying limited conscious	-	-	-	No changed level of conscious	-	-	Progre-ssive deterioration	
Total score (1 – 7)								

[a] 1. A = alert, V = verbal response, P = pain response, and U = unresponsive

BIOGRAPHY

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