

Prognostic Accuracy of qSOFA, NEWS, SIRS Criteria for In-Hospital Mortality Among Patients with Suspected Infection Presenting to the Emergency Department in a Tertiary Hospital in Cebu City. A Prospective Study

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Abstract

Introduction: Sepsis has been redefined as a life-threatening organ dysfunction caused by a dysregulated host response to infection. The quick sepsis-related organ failure assessment (qSOFA) is a simple tool developed to prompt clinicians to consider patients at high risk for poor outcome. Studies have compared its utility with National Early Warning Score (NEWS) and the systemic inflammatory response syndrome (SIRS) criteria. These scoring systems may be utilized to prognosticate illness severity among patients with suspected infection and may be relevant in low- and middle-income settings where laboratory data are not readily available.

Objective: To determine and compare the accuracy of qSOFA, NEWS, and SIRS criteria in predicting in-hospital mortality in patients suspected to have infection presenting at the emergency department (ED)

Methods: This is a prospective cohort study. Patients ≥ 18 years old with suspected infection admitted to the ED between June 2018 to July 2018 were included in the study. SIRS, NEWS, and qSOFA scores were collected at presentation and patients were followed up until expired or discharged.

Results: A final population of 213 were included in the study with a mean age of 47 years (SD 21.2) and 124 (58.2%) females. The most common site of infection was respiratory (33.8%). Twelve patients (5.6%) died in-hospital. Among patients with $qSOFA \geq 2$, mortality rate was at 38% vs 3.5% for $qSOFA < 2$. Specificity for mortality was highest for qSOFA (96%). Sensitivity was highest for SIRS (75%). SIRS, qSOFA, and NEWS had no significant difference in predicting in-hospital mortality with an area under the receiver operating curve of 0.659, 0.711, 0.711 respectively.

Conclusion: SIRS, qSOFA, and NEWS have similar prognostic accuracy to predict mortality but have limited use when applied individually which brings into question the sole utility of qSOFA despite its high specificity. It is reasonable to further validate or develop new scoring systems with higher predictive accuracy appropriate across different populations.

Keywords: sepsis, qSOFA, SIRS, NEWS

Introduction

In 1991, sepsis was defined as a proven or suspected infection accompanied with two or more systemic inflammatory response (SIRS) criteria. The original conceptualization of sepsis as infection with at least 2 of the 4 SIRS criteria (fever $>38.0^{\circ}\text{C}$ or hypothermia $<36.0^{\circ}\text{C}$, tachycardia >90 beats/minute, tachypnea >20 breaths/minute, abnormal white blood cell count

$>12,000/\mu\text{L}$ or $< 4,000/\mu\text{L}$ or $>10\%$ immature [band] forms) focused solely on inflammatory excess. More than two decades later, sepsis has been redefined as a life-threatening organ dysfunction caused by a dysregulated host response to infection. The concept of SIRS has thus disappeared from this new definition of sepsis.¹

In 2016, the Sepsis-3 task force included a new tool derived specifically to prompt clinicians to consider possible sepsis with an increased risk for mortality. This model, called the Quick Sepsis-related Organ Failure Assessment (qSOFA) was found to be more accurate than SIRS and Sequential [Sepsis-related] Organ Failure

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Assessment (SOFA) for predicting adverse events outside the ICU.² Its main advantage is its simplicity in calculation and similar or higher in prognostic accuracy for mortality with other complex tests such as SOFA, Logistic Organ Dysfunction System (LODS) and Acute Physiology and Chronic Health Evaluation (APACHE) II, all of which predict accurately but their feasibility is hindered due to the requirement of multiple laboratory tests (bilirubin, creatinine, arterial oxygen, urea nitrogen, etc.) in calculation of the score.

Prognostic accuracy between qSOFA and SIRS has been of much debate and abandoning the concept of SIRS might be premature. Furthermore, qSOFA was not compared to screening tools commonly implemented in clinical practice outside the ICU such as the National Early Warning Score (NEWS) which measures physiological parameters easily recorded at presentation. NEWS is a nationwide standardized system agreed by the Royal College of Physicians deemed practical and user friendly. Six physiological parameters form the basis of the NEWS and are all readily measured in patients, namely: respiratory rate, oxygen saturations, temperature, systolic blood pressure, pulse rate, level of consciousness. Once measured and recorded, the six physiological parameters had to be weighed and aggregated to derive the NEWS score. The weighting allocated to each physiological parameter for a specific level of disturbance was critical in defining the sensitivity of the final aggregate score as a trigger for a clinical response. Based on formal evaluation of the performance of the NEWS it was decided that a NEWS aggregate of 7 or more should trigger a high-level clinical alert, i.e., an emergency clinical review.³

It is widely asserted that early diagnosis and prompt initiation of treatment are associated with better outcomes. One of the main barriers to early treatment is the lack of diagnostic tools and this is aggravated by the fact that sepsis is an enigmatic syndrome with no gold standard for diagnosis. Identifying patients with infection who are at high risk for adverse events is an important approach to improving sepsis management. The initial assessment and quantification of acute-illness severity does not have to be complex. It should be practical and sufficient. Illness severity can be quantified by measurement of a combination of simple physiological parameters which are easily recorded during initial presentation or at bedside. In the setting of acute illness, these scoring systems have been shown to be good predictors of patient mortality.

In the absence of a gold standard test for sepsis, concern regarding early identification has led the Sepsis-3 Task Force to formulate screening tools to risk stratify patients according to severity. qSOFA is relatively new and is not very well studied, more so when compared to the older SIRS criteria and the widely used scoring system, NEWS. Furthermore, validation of these scoring systems in low- and middle-income settings are limited. Although these three scoring systems were designed with different aims at initial conceptualization, all may be utilized to

prognosticate illness severity in patients with suspected infection.

This study was therefore conducted to investigate the accuracy of these screening tools in predicting mortality at the emergency department level using parameters that are readily available.

Methodology

Study Design and Setting. This is a prospective cohort study conducted in Chong Hua Hospital, a 660-bed capacity, private tertiary hospital located in Cebu City.

Study Population.

Inclusion Criteria: Patients aged ≥ 18 years old admitted in the emergency room with suspected infection diagnosed by the treating emergency physicians, based on identification of an infectious source (clinical, microbiological, or radiological) or an equivocal presentation (e.g., febrile patient with inflammatory syndrome), whose most likely reason for admission was infection.

Exclusion Criteria: Any patient brought in from another hospital facility, were discharged against medical advice, or transferred to another hospital were excluded from the study. This also excluded patients who were later deemed without infection on the basis of clinical context.

Sample Size: A local study by Alejandria et al published in 2000 found that sepsis had a mortality rate of 23.5%.⁷ Deriving from this data, this study needed 141 samples to represent patients suspected to have infection presenting to the emergency department at risk for mortality.

Outcome Measures. The primary outcome of interest is to determine the accuracy of qSOFA, NEWS and SIRS criteria in predicting in-hospital mortality in patients suspected to have infection presenting at the emergency department. Secondary outcome measure is ICU/INT admission

Ethical Considerations. This study was approved by the Institution Review Board of Chong Hua Hospital (IRBI-9017-11).

Data Collection. All consecutive patients (288) admitted to the emergency department due to suspected infection during June to July 2018 were included in the study. Five patients who were transferred from another institution were excluded at the emergency department level. Among screened patients, the following data were extracted: age, sex, source of infection, vital signs, white blood cell count (WBC), and unit admitted. SIRS, qSOFA, and NEWS scores were calculated for each patient using physiological and laboratory parameters extracted on admission at triage. A score of 2 or more in SIRS and qSOFA, and 5 or more in NEWS were applied as threshold scores. Patients were then followed up until expired or discharged. Fifty-seven were ruled out to have infection, 12 went home against medical advice, and 1 transferred to another hospital and were excluded in the

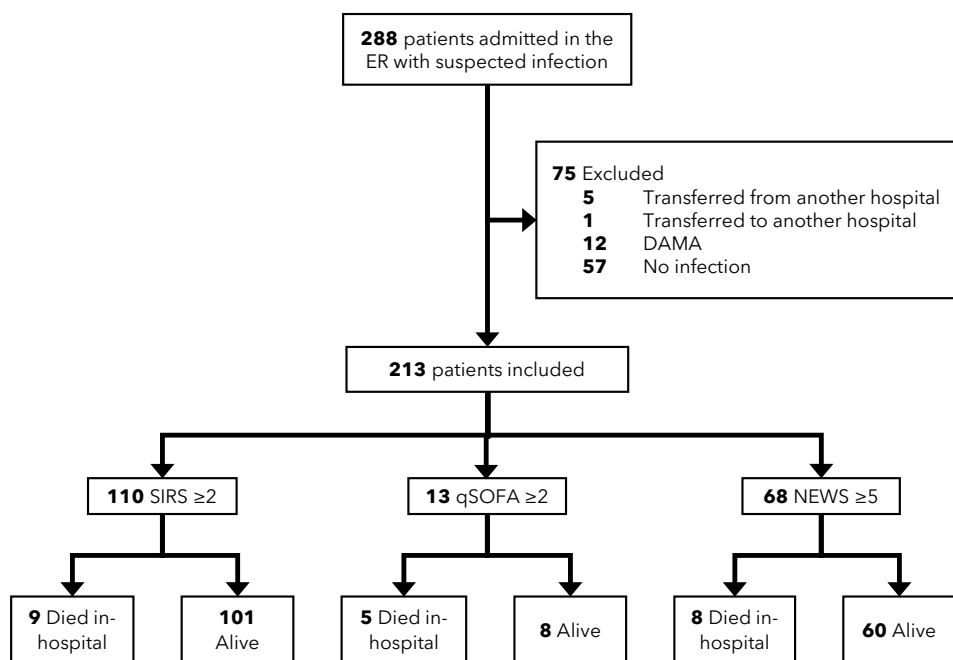


Figure 1. Flow Chart of Data Collection

study. A total of 213 patients were subjected for analysis (Figure 1).

Statistical Analysis. Patient age was presented as mean ± SD. Patient-related categorical variables (gender, unit admitted, mortality) were expressed as numbers and percentages.

To assess the performances of each scoring system in predicting in-hospital mortality and ICU/INT admission, sensitivity, specificity, positive predictive values, negative predictive values, positive and negative likelihood ratios

were calculated using a score of 2 or more for SIRS and qSOFA, and 5 for NEWS. Discriminatory power was determined by comparing the area under the receiver operating characteristic curve (AUROC) score.

Data were encoded using Microsoft Excel. All analyses were performed using SPSS ver 25 and MedCalc® ver 18.9.

Results

A final population of 213 was obtained from which the value of all 3 scoring systems on arrival were available. As

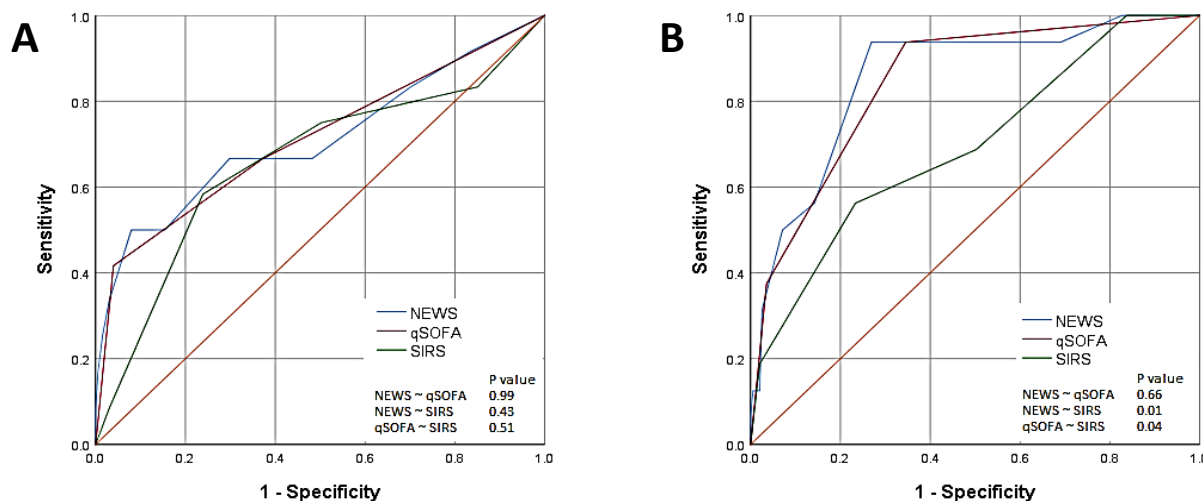


Figure 2. Receiver Operating Characteristic Curves for (A) In-hospital Mortality and (B) ICU/INT Admission

Table I. Patient Characteristics

Characteristics	All (n=213)	ICU admission (n=16)	Dead (n=12)	Alive (n=201)	P Value
Sex, No. (%)					
Male	89 (41.8)	5 (31.3)	2 (16.7)	87 (43.3)	0.069
Female	124 (58.2)	11 (68.8)	10 (83.3)	114 (56.7)	
Age					
Mean (SD)	47 (21.2)	61 (19.2)	64 (15.6)	46 (21.1)	0.05
Severity of Illness (%)					
SIRS score ≥ 2	110 (51.6)	11 (68.8)	9 (75)	101 (50.2)	<0.096
qSOFA score ≥ 2	13 (6.1)	6 (37.5)	5 (41.7)	8 (4)	<0.001
NEWS score ≥ 5	68 (31.9)	15 (93.8)	8 (66.7)	60 (29.9)	<0.008
Outcome, No (%)					
In-hospital mortality	12 (5.6)	7 (43.8)	12 (100)	0	<0.001
ICU/INT admission	16 (7.5)	16 (100)	7 (58.3)	9 (4.5)	
Site of Infection, No (%)					0.012
Respiratory	72 (33.8)	8 (50)	5 (41.7)	67 (33.3)	
Urinary	41 (19.2)	4 (25)	2 (16.7)	39 (19.4)	
Abdominal	68 (31.9)	2 (12.5)	3 (25)	65 (32.3)	
Cutaneous	18 (8.5)	2 (12.5)	1 (8.3)	17 (8.5)	
Others	14 (6.5)	0 (0)	1 (8.3)	13 (6.5)	

Table II. Accuracy of qSOFA, NEWS, and SIRS score in predicting mortality

	SIRS	qSOFA	NEWS
Sensitivity, % (95% CI)	75 (43-95)	41 (15-72)	66 (35-90)
Specificity, % (95% CI)	50 (43-57)	96 (92-98)	70 (63-77)
Predictive value, % (95% CI)			
Positive	97 (95-98)	100 (99-100)	98 (96-99)
Negative	10 (4-22)	8 (5-12)	10 (5-20)
Likelihood ratio, % (95% CI)			
Positive	1.49 (1.0-2.1)	10.47 (4-27.2)	2.23 (1.4-3.5)
Negative	0.5 (0.2-1.4)	0.61 (0.4-1.0)	0.48 (0.2-1.1)
AUROC, % (95% CI)	0.659 (0.591-0.723)	0.711 (0.645-0.771)	0.711 (0.645-0.771)

Table III. Accuracy of qSOFA, NEWS, and SIRS score in predicting ICU/INT admission

Parameters	SIRS	qSOFA	NEWS
Sensitivity, % (95% CI)	69 (41-89)	38 (15-65)	93 (70-100)
Specificity, % (95% CI)	50 (43-57)	96 (93-99)	73 (66-79)
Predictive value, % (95% CI)			
Positive	96 (95-97)	100 (99-100)	99 (98-99)
Negative	8 (4-15)	8 (5-11)	38 (8-80)
Likelihood ratio, % (95% CI)			
Positive	1.37 (1.0-2.0)	11 (4-27.7)	3.48 (2.7-4.5)
Negative	0.63 (0.3-1.3)	0.65 (0.4-0.9)	0.086 (0.01-0.6)
AUROC, % (95% CI)	0.695 (0.629-0.756)	0.844 (0.788-0.890)	0.855 (0.801-0.900)

shown in *Table I*, mean age was 47 years (SD 21.2), 58.2% (n=124) were female, 41.8% (n=89) were male. The most common site of infection was respiratory (33.8%). Overall, 12 patients (5.6%) died in-hospital. The secondary outcome of admission to ICU/INT occurred in 16 patients (7.5%).

Accuracy comparison. Prognostic performances of the three scoring systems for in-hospital mortality are shown in *Table II*. Among patients with suspected infection, qSOFA was most specific (96%, 95% CI 92-98%) compared to SIRS and NEWS (50%, 70% respectively). However, qSOFA was the least sensitive scoring system (41%, 95% CI 15-72). NEWS had an intermediate specificity (70%, 95% CI 63-77) and sensitivity (66%, 95%

CI 35-90). SIRS was most sensitive (75%, 95% CI 43-95) but least specific (50%, 95% CI 43-57). NEWS and qSOFA have similar AUROC (0.711, 95% CI 0.645-0.771) but were not statistically significantly higher than SIRS (0.659, 95% CI 0.591-0.723) (NEWS, qSOFA P 0.99; NEWS, SIRS P 0.43; qSOFA, SIRS P 0.51) (*Figure 2A*).

Prognostic performances for ICU/INT admission are shown in *Table III*. qSOFA was most specific (96%, 95% CI 93-99) but least sensitive (38%, 95% CI 15-65). NEWS scored the highest sensitivity (93%, 95% CI 70-100) with intermediate specificity (73%, 95% CI 66-79). SIRS had intermediate sensitivity (69%, 95% CI 41-89) and the lowest specificity (50%, 95% CI 43-57). AUROC for NEWS (0.855, 95% CI 0.801-0.900) and qSOFA (0.844, 95% CI

Table IV. Accuracy of scoring systems across different thresholds for mortality and ICU/INT admission

Score	Threshold	Mortality		ICU/INT Admission	
		Sensitivity	Specificity	Sensitivity	Specificity
qSOFA	0	100.00	0.00	100.00	0.00
	≥1	66.67	62.69	93.75	65.48
	≥2	41.67	96.02	37.50	96.45
	≥3	0.00	100.00	0.00	100.00
SIRS	0	100.00	0.00	100.00	0.00
	≥1	83.33	14.93	100.00	16.24
	≥2	75.00	49.75	68.75	49.75
	≥3	58.33	76.12	56.25	76.65
	≥4	8.33	97.01	18.75	97.97
NEWS	0	100.00	0.00	100.00	0.00
	≥1	91.67	16.42	100.00	17.26
	≥2	83.33	29.85	93.75	30.96
	≥3	66.67	51.74	93.75	73.10
	≥5	66.67	70.15	56.25	85.79
	≥6	50.00	84.58	50.00	92.89
	≥7	50.00	92.04	31.25	97.46
	≥8	33.33	97.01	12.50	97.97
	≥9	25.00	98.51	12.50	99.49
	≥10	16.67	99.50	6.25	100.00
	≥11	8.33	100.00	0.00	100.00
	≥15	0.00	100.00		

Table V. Classification According to Sepsis Criteria

	All No. (%) n=213	SIRS		qSOFA		NEWS	
		<2 n=103	≥2 n=110	<2 n=200	≥2 n=13	<5 n=145	≥5 n=68
In-hospital Mortality	12 (5.6)	3 (2.9)	9 (8.2)	7 (3.5)	5 (38.5)	4 (2.8)	8 (11.8)
ICU/INT admission	16 (7.5)	5 (4.9)	11 (10)	10 (5)	6 (46.2)	1 (0.7)	15 (22.1)

0.788-0.890) were similar and both statistically significantly higher relative to SIRS (0.629, 95% CI 0.629-0.756) ($p < 0.05$) (Figure 2B).

Across all scores, Youdin index showed an optimum threshold of ≥ 7 for NEWS (50% sensitivity, 85% specificity), ≥ 2 for qSOFA (42% sensitivity, 96% specificity), and ≥ 3 for SIRS (58% sensitivity, 76% specificity) (Table IV).

Discussion

The Sepsis-3 task force had estimated that patients with sepsis have an in-hospital mortality rate greater than 10%.¹ This study found that patients who scored positive for qSOFA, NEWS, and SIRS had an in-hospital mortality rate of 38%, 11.8%, and 8.2% respectively (Table V).

This prospective observational study found no statistically significant difference among SIRS, qSOFA, and NEWS in predicting in-hospital mortality. The Sepsis-3 task force has encouraged prospective validation of qSOFA in non-US health care settings to confirm its application since most of their data relied on extracted US databases. Initial studies were done in high-income countries and showed better accuracy of qSOFA compared to SIRS, but to apply these findings in low- or

middle-income countries, such as our setting, have not been robustly studied.^{4,5} Epidemiologic data for sepsis in low- and middle-income countries are scarce and low.⁹ Due to major differences in living conditions, financial status, and access to basic health care, challenges in efforts to improve outcome from sepsis may be encountered even before initial medical contact. To the best of the authors' knowledge, this is the only local study done prospectively to assess these sepsis scoring criteria in predicting mortality.

The findings of this study are consistent with initial studies that show that qSOFA has high specificity but low sensitivity to identify patients at a high risk of death.^{4,5} This is consistent with a meta-analysis by Maitra from 45 observational studies which showed that qSOFA is a poorly sensitive predictive marker for in-hospital mortality in patients with suspected infection.¹⁰ Hence, failure to meet a score of 2 or more for qSOFA should not lead to a deferral of treatment or work up or to a delay in medical care deemed necessary by practitioners.

It is reasonable to recommend a screening test for patients with suspected infection that has a higher sensitivity than specificity to reduce false negatives (delayed treatment) which is more hazardous than false

positives (overuse of antibiotics). In this study, SIRS had the highest sensitivity but the lowest specificity for mortality prediction compared to qSOFA and NEWS. This has been in keeping with previous studies.⁵ The concept of SIRS has been abandoned two decades after the first definition of sepsis. Presence of SIRS indicates activation of the innate immune system regardless of cause, i.e., infection and non-infectious cases such as myocardial infarction and trauma, thus it is known to be a non-specific marker of sepsis. However, results of this study showed that discrimination of its accuracy was similar and not inferior to NEWS nor qSOFA. The Sepsis-3 task force stressed that SIRS may still remain useful which was also seen in a study which showed similar discrimination of hospital mortality among infected patients outside the ICU setting to that with SOFA, a sepsis scoring tool from which qSOFA was derived.^{1,2}

From a clinical point of view, this statistically insignificant difference in accuracy may be of little value because the aim of these scoring systems is to screen and determine which patient with infection needs a higher level of care to prevent poor outcome. Hence, a test with a higher sensitivity may be more appropriate. In low- and middle-income countries, an important challenge in the sepsis management is the diagnosis at presentation: at the triage level and even prior to initial contact with a clinician. Outside the hospital, this has to be done through non-invasive methods and sensitive tests, more so in rural or far-flung areas where the first medical contact of a possibly septic patients is through nurses or midwives whose access to laboratory tests is limited. Compared to qSOFA and NEWS, SIRS score incorporates the value of the white blood cell count which delays identification of a possibly septic patient or may not even be feasible to obtain. Considering this factor, qSOFA may be more useful pre-hospital given that it is highly specific with only 3, non-invasive variables.

NEWS is widely used in emergency department settings and have been studied in comparison to other sepsis scoring systems.^{8,11} It can be assumed that the more variables are taken into account, the more likely it is to detect an abnormality. However, it is important to note that some parameters may be directly related to one another and in effect may be redundant i.e., respiratory rate, oxygen saturation, oxygen supplement. Hence, the use of such tests with numerous variables would expectedly lead to a more accurate result as seen in the study by Churpek et al which showed that NEWS was accurately superior to SIRS and qSOFA in predicting mortality.⁸ However, the study by Churpek used a NEWS threshold of 7 or more which is a high score trigger compared to this present study which used a medium score trigger (5 or an extreme variation in a parameter) which may explain the similar accuracy of NEWS to qSOFA and SIRS. On exploratory analysis, accuracy of NEWS ≥ 7 among patients included in this present study showed 50% sensitivity and higher specificity at 92% (*Table IV*), comparable to the findings in other studies.⁸

Conclusion

SIRS, qSOFA, and NEWS as predictors for in-hospital mortality have limited use when applied individually. The three scoring systems have similar accuracy, which brings into question the sole utility of qSOFA despite its recommendations. The goal of these scoring systems is to identify patients at risk for mortality hence a test with higher sensitivity would be more appropriate. SIRS, a concept which has disappeared in the new definition of sepsis, is equally accurate to qSOFA and NEWS hence its application should not entirely be abandoned.

Predicting outcome at early stages of sepsis is a challenging process. Although quick and feasible scoring systems are widely available, their utility should be applied with clinical judgement as no scoring system can represent a definition nor prediction of sepsis. It is reasonable to further validate or develop new scoring systems with higher predictive accuracy appropriate across different populations.

Limitations

This study has some limitations. First, this was conducted in a single-center, tertiary hospital and may not be generalizable especially in primary health care settings. Second, there were no data extracted on patient comorbidities, nosocomial infection, and their role in affecting the disease course. These factors may affect physiological response to sepsis and could have biased the results to a higher qSOFA score. However, it is likely that patients with sepsis will follow a linear trajectory of clinical deterioration, in the absence of medical intervention, prior to death. Third, patients who were discharged or transferred were not followed up and may possibly have been readmitted or died. This is because the Sepsis-3 authors have associated sepsis with mortality particularly only in in-hospital settings.

Disclosure. All authors declared no conflicts of interest.

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