



Original Article

Relationship between the prehospital quick Sequential Organ Failure Assessment and prognosis in patients with sepsis or suspected sepsis: a population-based ORION registry

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Aim: The quick Sequential Organ Failure Assessment (qSOFA) was proposed for use as a simple screening tool for sepsis. In this study, we evaluated the relationship between the prehospital use of qSOFA and prognosis in patients with sepsis or suspected sepsis using the population-based Osaka Emergency Information Research Intelligent Operation Network (ORION) registry, which compiles prehospital ambulance data and in-hospital information.

Methods: The study enrolled 437,974 patients in the ORION registry from January 1 to December 31, 2016. We selected hospitalized patients with sepsis or suspected sepsis using the appropriate codes from the International Classification of Diseases revision 10. We excluded patients with: (i) missing data (outcome, Japan Coma Scale, respiratory rate, and blood pressure); (ii) respiratory rate ≥ 60 /min; and (iii) blood pressure ≥ 250 mmHg. These measures were evaluated by ambulance personnel when they first contacted the patient in the prehospital setting. The primary end-point was discharge to death.

Results: In total, 12,646 patients (median age, 78 [interquartile range, 65–85] years; male, $n = 6,760$ [53.5%]) were eligible for our analysis. In a multivariable logistic regression analysis adjusted for confounding factors, the proportion of patients discharged to death was significantly higher for those evaluated as qSOFA positive (≥ 2 points) than qSOFA negative (≤ 1 point) (265/2,250 [11.78%] vs. 415/10,396 [3.99%]; adjusted odds ratio 2.91; 95% confidence interval, 2.47–3.43; $P < 0.0001$). The specificity and sensitivity were 83.4% and 39.0%, respectively, and the area under the receiver operating characteristic curve for qSOFA positive was 0.61.

Conclusions: The qSOFA evaluated by ambulance personnel in the prehospital setting was significantly associated with prognosis in patients with sepsis or suspected sepsis.

Key words: Emergency medical service, infection, qSOFA, survival

BACKGROUND

IN THE PREHOSPITAL setting, it is important for emergency medical service (EMS) personnel to recognize

critically ill patients early and transport them to the appropriate medical institution. Sepsis is an important disease that should be recognized early for EMS personnel.

In 2016, the Third International Consensus Definitions Task Force defined sepsis as “life-threatening organ dysfunction due to a dysregulated host response to infection”, and the quick Sequential Organ Failure Assessment (qSOFA) was proposed for use as a simple screening tool for sepsis, with sepsis being suspected at a score ≥ 2 points.¹ Due to its simplicity, qSOFA has high affinity in situations in which the examination environment is not prepared and in prehospital settings.² However, several studies in the prehospital setting have shown that there are large differences

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in its diagnostic and prognostic abilities due to the small and limited study groups examined.^{3–7} Therefore, the true assessment ability of qSOFA in the prehospital setting has not been fully clarified.

To resolve this issue, comprehensive regional analysis is required. Lane *et al.* reported that assessing the predicted risk for the modified version of the Systemic Inflammatory Response Syndrome score and qSOFA scores instead of classification accuracy reveals that the qSOFA score provides more information to clinicians about a patient's mortality risk, supporting its use in clinical decision-making by using a comprehensive regional database.⁸ However, there are still few such research reports.

The Osaka Prefecture Government has developed and introduced an information system for emergency patients transported by EMS personnel (the Osaka Emergency Information Research Intelligent Operation Network [ORION] system), which compiles prehospital ambulance records and in-hospital information such as diagnosis and prognosis.⁹ We thought that comprehensive regional analysis could be undertaken using this ORION registry. However, the ORION registry does not include all the evaluation items of the Systemic Inflammatory Response Syndrome score. Therefore, although qSOFA is a screening tool for sepsis, we decided to evaluate the prognosis in this study. We thought that qSOFA would be useful for Japanese EMS personnel who select hospitals according to their severity because the qSOFA score is a bedside prompt that could identify patients with suspected infection who are at greater risk for a poor outcome outside the intensive care unit.

In the present study, we attempted to evaluate the relationship between the prehospital use of qSOFA and prognosis in patients with sepsis or suspected sepsis using the population-based ORION registry.

METHODS

Study design, population, and setting

THIS WAS A retrospective observational study using the ORION database.⁹ The study period spanned 1 year from January 2016 to December 2016. Osaka Prefecture is located in the western area of Japan, covers an area of 1,905 km², and has a population of 8.8 million. The proportion of male inhabitants was 48.1% and that of elderly people (aged ≥ 65 years) was 26.1% in 2015.⁹ There are 519 hospitals (106,273 beds) in Osaka Prefecture, of which 288 are emergency hospitals including 16 critical care centers that are designated to accept patients with life-threatening emergency conditions such as severe trauma and sepsis.⁹

We included all emergency patients registered in the ORION database. We selected hospitalized patients with sepsis or suspected sepsis using the International Statistical Classification of Diseases and Related Health Problems, version 10 (ICD-10) codes shown in Table S1. Each ICD-10 code was evaluated after hospital admission by physicians. We excluded those patients with: (i) missing data (outcome, Japan Coma Scale [JCS], respiratory rate, blood pressure); (ii) respiratory rate ≥ 60 /min; and (iii) blood pressure ≥ 250 mmHg. These were evaluated by ambulance personnel when they first contacted the patient in the prehospital setting.

This study was approved by the Ethics Committee of the Osaka University Graduate School of Medicine (No. 15003). Personal identifiers were removed beforehand from the ORION database, and thus the patients' right to informed consent was waived by this committee. This study was undertaken based on the ORION database under the present researchers' responsibility, and it differs from the statistics published by Osaka Prefecture. This research was not carried out by Osaka Prefecture. This study was written based on the STROBE statement to assess the reporting of cohort and cross-sectional studies.¹⁰ All methods were carried out in accordance with relevant guidelines and regulations.

Osaka Emergency Information Research Intelligent Operation Network

In January 2013, the Osaka Prefecture Government first developed and introduced an information system for emergency patients (the Osaka Emergency Information Research Intelligent Operation Network [ORION] system) that uses a smartphone app for hospital selection by on-scene EMS personnel and since then, it has been accumulating all ambulance records. Furthermore, since January 2015, medical institutions have registered information on the diagnosis and outcome of emergency patients transported to medical institutions, and the ORION system has merged these data with the respective ambulance records and smartphone app data. This report describes the ORION system and its profile of hospital information, EMS characteristics, and in-hospital diagnoses and outcomes.

Quick SOFA score

The qSOFA was introduced with the Sepsis-3 criteria. The score ranges from 0 to 3 with 1 point assigned for each of the following criteria met by the patient: systolic arterial blood pressure ≤ 100 mmHg, respiratory rate ≥ 22 breaths/min, or altered mental status.¹ For the prehospital evaluation

of mental status, Japanese EMS providers have adopted the JCS instead of the Glasgow Coma Scale since its introduction in 1974.¹¹ The JCS has four main grades (grade 0, alert; grade 1, possible verbal response without any stimulation, not lucid; grade 2, possible eye-opening, verbal and motor response upon stimulation; and grade 3, no eye-opening and coma upon stimulation). If the patient has an altered mental status, it will be judged as grade 1–3. Therefore, in this study, an evaluation other than JCS 0 (alert) was defined as “altered mental status” and was considered equal to a Glasgow Coma Scale score of ≤ 14 .

End-point

The primary end-point was discharge to death.

Statistical analysis

Patient characteristics and outcomes were evaluated between two groups using the Wilcoxon rank sum test for continuous variables and the χ^2 test or Fisher’s exact test for categorical variables. One-way ANOVA was used to evaluate the differences in mortality according to the qSOFA score. Multivariable analysis of the eligible patients was used to assess factors associated with the outcomes by using logistic regression models, and adjusted odds ratios (AORs) and their 95% confidence intervals (CIs) were calculated. Potential confounding factors (age [continuous value] and sex [male, female]) based on biological plausibility and previous studies were included in the multivariable analysis. To analyze the effectiveness of qSOFA positive/negative for predicting hospital mortality, we created a receiver operating characteristic (ROC) curve. A *P*-value of ≤ 0.05 was considered significant. All statistical analyses were undertaken using JMP Pro 13 (SAS Institute).

RESULTS

Patient characteristics

FIGURE 1 shows the patient flow in this study. During the study period, 437,974 emergency patients were registered in ORION. Among them, 174,990 patients were hospitalized. Twenty seven thousand nine hundred seventy-seven patients were selected as patients with sepsis or suspected sepsis using the appropriate ICD-10 codes (Table S1). We excluded the following patients: (i) JCS, “missing data” ($n = 13,447$); (ii) respiratory rate, “missing data” or “ ≥ 60 /min” ($n = 14,624$); (iii) blood pressure, “missing data” or “ ≥ 250 mmHg” ($n = 14,331$); and (iv) outcome at hospital discharge, “missing data” ($n = 48$). Finally,

12,646 patients were eligible for our analysis. Among them, 680 (5.4%) died in the hospital.

Patient characteristics are shown in Table 1. Compared to the patients with qSOFA score ≤ 1 , those with a qSOFA score ≥ 2 were more likely to be older and female and to have a lower level of consciousness, higher respiratory rate, and lower systolic blood pressure.

Comparison of mortality by items included in qSOFA score

Figure 2 shows the mortality by items included in qSOFA. The proportion of patients discharged to death was significantly higher in those with altered mental status (344/4,332 [7.94%] vs. 336/8,314 [4.04%]; $P < 0.0001$), with respiratory rate ≥ 22 /min than < 22 /min (365/3,945 [9.25%] versus 315/8,701 [3.62%]; $P < 0.0001$), and with systolic blood pressure ≤ 100 mmHg than > 100 mmHg (172/1,510 [11.39%] versus 508/11,136 [4.56%]; $P < 0.0001$).

Comparison of mortality by qSOFA score

Figure 3 shows the mortality by qSOFA score. Mortality increased with increasing qSOFA score (0, 128/5,430 [2.36%]; 1, 287/4,966 [5.78%]; 2, 201/1,929 [10.42%]; 3, 64/321 [19.94%]; $P < 0.0001$).

Comparison of mortality by qSOFA positive or negative

Table 2 shows the mortality by qSOFA positive (score ≥ 2) or negative (≤ 1) as determined by a multivariable logistic regression model. The proportion of patients discharged to death was significantly higher for qSOFA positive than negative (265/2,250 [11.78%] vs. 415/10,396 [3.99%]; AOR 2.91; 95% CI, 2.47–3.43; $P < 0.0001$). For qSOFA positive/negative, the specificity and sensitivity were 83.4% (9,981/[9,981 + 1,985]) and 39.0%, (265/[265 + 415]), respectively. The area under the ROC curve of qSOFA positive/negative was 0.61 (Fig. 4).

DISCUSSION

FROM OUR ANALYSIS of the population-based ORION registry in Osaka, Japan, this study revealed that the proportion of patients discharged to death was significantly higher for qSOFA positive than negative in patients with sepsis or suspected sepsis evaluated by EMS personnel in the prehospital setting. To our knowledge, this is the largest report using a population-based registry to have assessed the association of prognosis in patients with sepsis

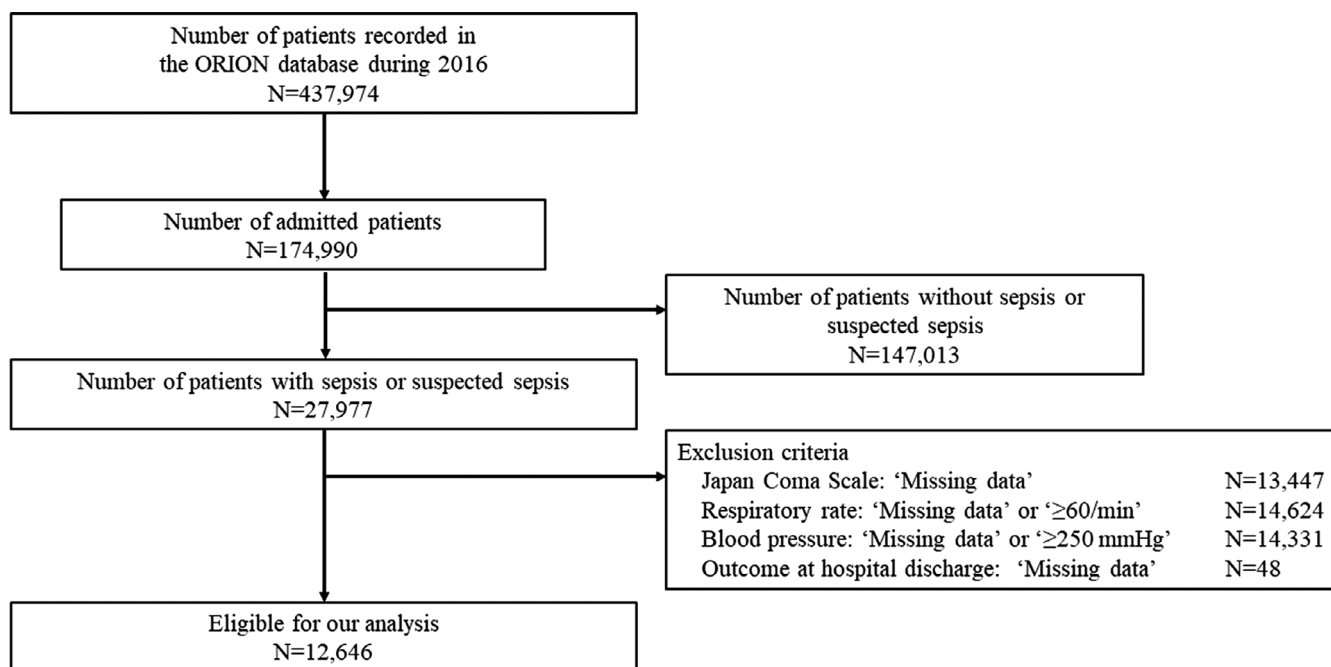


Fig. 1. Patient flow in this study. ORION, Osaka Emergency Information Research Intelligent Operation Network.

Table 1. Characteristics of patients with sepsis or suspected sepsis

Characteristic	qSOFA score ≥ 2 <i>n</i> = 2,250	qSOFA score ≤ 1 <i>n</i> = 10,396
Age, years	81 (70–87)	77 (63–85)
Sex, male	1,139 (50.6)	5,621 (54.1)
Japan Coma Scale		
0 (alert)	276 (12.3)	8,425 (81.0)
I (delirium, confusion, senselessness)	1,376 (61.2)	1,606 (15.4)
II (stupor, lethargy, hypersomnia, somnolence, drowsiness)	354 (15.7)	257 (2.5)
III (deep coma, coma, semicoma)	244 (10.8)	108 (1.0)
Respiratory rate	24 (24–30)	20 (18–20)
Systolic blood pressure	110 (93–140)	137 (120–156)
Dead	265 (11.78)	415 (3.99)

Data are expressed as median (interquartile range) or number (%).
qSOFA, quick Sequential Organ Failure Assessment.

or suspected sepsis with qSOFA evaluated in the prehospital setting. Our findings not only provide basic epidemiological information on sepsis patients but could help to improve the emergency medical system in prehospital settings and the prognosis of these patients by immediately recognizing their severity and selecting the appropriate hospital for treatment.

From the assessment of mortality by items included in qSOFA, the proportion of patients discharged to death was significantly higher in those with altered mental status positive than negative, with respiratory rate ≥ 22 /min than < 22 /min, and with systolic blood pressure ≤ 100 mmHg than > 100 mmHg (Fig. 2). Mortality also increased with increasing qSOFA score (Fig. 3). These results were similar to those of previous reports.^{2,5} Seymour *et al.* reported a study using the University of Pittsburgh Medical Center healthcare system in southwestern Pennsylvania including all medical and surgical encounters in the emergency department, hospital ward, and intensive care unit. The proportion of patients discharged to death was significantly higher in those with altered mental status positive than negative (1,495/7,574 [20%] vs. 1,677/66,879 [3%]; AOR 4.31; 95% CI, 3.96–4.69), with respiratory rate ≥ 22 /min than < 22 /min (2,496/29,055 [9%] vs. 676/45,398 [1%]; AOR 3.18; 95% CI, 2.89–3.50), and with systolic blood pressure ≤ 100 mmHg than > 100 mmHg (2,383/29,784 [8%] vs. 789/44,669 [2%]; AOR 2.61; 95% CI, 2.40–2.85). Among patients with serum lactate ≥ 4.0 mmol/L, those with qSOFA

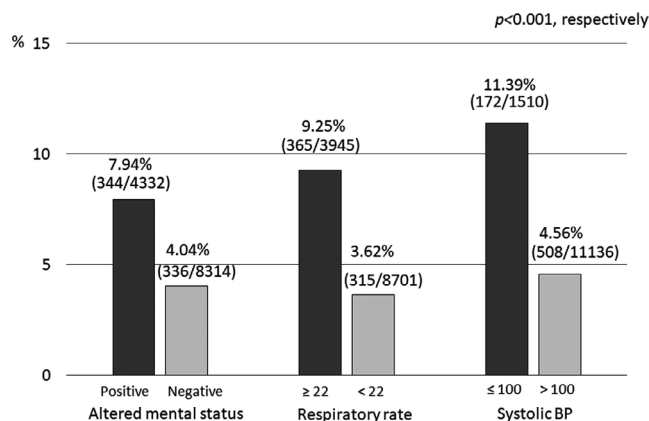


Fig. 2. Comparison of mortality among patients with sepsis or suspected sepsis by items included in the quick Sequential Organ Failure Assessment. Discharge to death was significantly higher in patients with altered mental status positive than negative, with respiratory rate ≥ 22 /min than < 22 /min, and with systolic blood pressure (BP) ≤ 100 mmHg than > 100 mmHg.

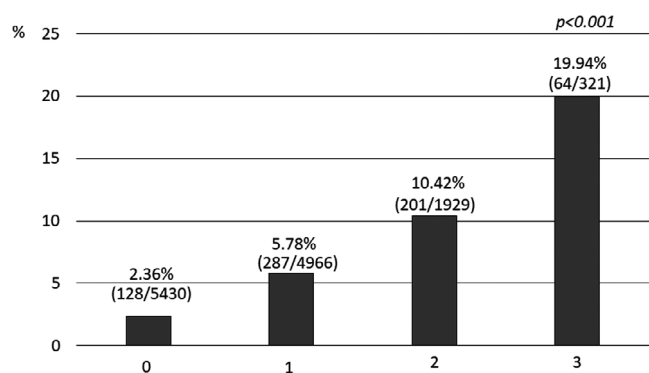


Fig. 3. Comparison of mortality among patients with sepsis or suspected sepsis by quick Sequential Organ Failure Assessment (qSOFA) score. Mortality increased with increasing qSOFA score.

Table 2. Outcomes at hospital discharge of patients with sepsis or suspected sepsis: logistic regression analysis by quick Sequential Organ Failure Assessment (qSOFA) positive (score ≥ 2) or negative (≤ 1)

	% (n/N)	Crude OR	95% CI	P-value	Adjusted OR [†]	95% CI	P-value
qSOFA score ≤ 1	3.99 (415/10,396)	Reference			Reference		
qSOFA score ≥ 2	11.78 (265/2,250)	3.21	2.74–3.77	< 0.0001	2.91	2.47–3.43	< 0.0001

Odds ratios (ORs) were calculated for qSOFA score ≥ 2 versus ≤ 1 .
 CI, confidence interval.
[†]Adjusted for age and sex.

score of 1 have a mortality of 7% compared to those with a qSOFA of 3 with a mortality of 43%.² Miyamoto *et al.*⁵ reported from study among patients transported by physician-staffed helicopter that the in-hospital mortality rates among patients with qSOFA scores of 0, 1, 2, and 3 were 5/411 (1%), 69/797 (9%), 71/541 (13%), and 24/100

(24%), respectively ($P < 0.0001$ for trend). These results were different from regional comprehensive prehospital data, but the effect of qSOFA score on mortality has also been clarified in this population-based study.

The present multivariable logistic regression model showed that qSOFA positive was associated with discharge

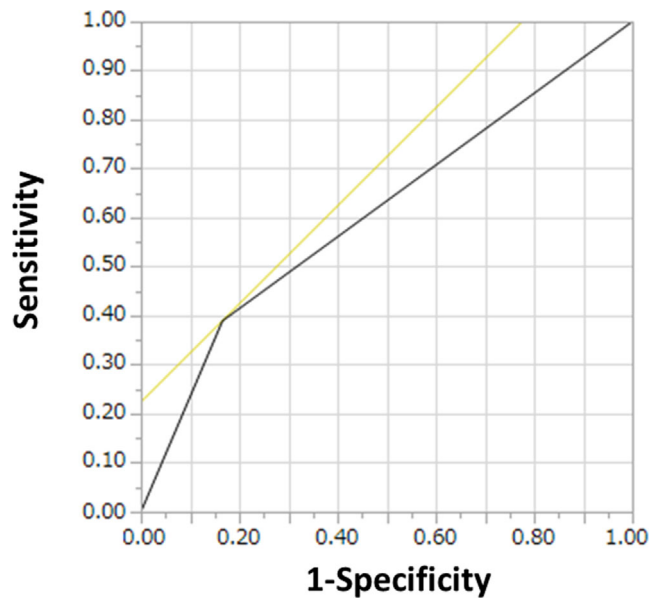


Fig. 4. Area under the receiver operating characteristic curve (AUC) of quick Sequential Organ Failure Assessment (qSOFA) positive/negative among patients with sepsis or suspected sepsis. With qSOFA positive/negative, the specificity and sensitivity were 83.4% and 39.0%, respectively. The AUC of qSOFA positive/negative was 0.61.

to death in patients with sepsis or suspected sepsis (Table 2). However, the specificity and sensitivity of qSOFA positive/negative were 83.4% and 39.0%, respectively, and the area under the ROC curve was 0.61 (Fig. 4). Several previous reports on the prehospital setting reported the sensitivity to prognosis outcome to be low.^{3–5} We thought that the initial or worst clinical data used could affect the ability to predict the prognosis of qSOFA. Most of the studies reporting the high prognostic ability of qSOFA have used “worst value” in the emergency room in their calculation.^{12–14} In contrast, most of the studies that used the “initial value” in the emergency room for the calculation reported that the predictive power of qSOFA for prognosis was not high,^{4,12,15–18} and we think that our research also shows low ability because the prehospital information in Japan uses the initial value. Therefore, we think that it is important to measure vital signs repeatedly and to pay attention to the changes in vital signs when using qSOFA in the prehospital setting. It could help EMS to immediately recognize a patient’s severity and select the appropriate hospital for treatment. It could also lead to improvement of emergency medical systems, such as the development of an early warning system for EMS personnel or a system for selecting the hospital to transport to, using qSOFA.

Nevertheless, the results of this study have great significance because qSOFA can be easily used in the prehospital setting, and it reflects the prognosis to some extent. The need to recognize septic patients in the prehospital setting is

being emphasized more and more. The Surviving Sepsis Campaign taskforce published a new revision of the sepsis bundle (hour-1 bundle), which recommended the complete initiation of resuscitation and treatments of patients with sepsis within 1 h from the time of triage in the emergency department.^{19,20} Once EMS providers identified patients with sepsis or suspected sepsis, the prehospital qSOFA score was an effective tool in estimating mortality. It is important to use qSOFA properly after fully understanding its inspection characteristics. Furthermore, as the population ages and the number of patients with sepsis increases throughout the world,²¹ if EMS personnel can identify suspected sepsis patients using qSOFA and start initial resuscitation in the prehospital setting, patient prognosis might improve.

Our study has some limitations. First, patients were included based on ICD-10 codes, not accurate diagnoses of patients with sepsis. We also chose the ICD-10 code for the disease suspected to have caused the sepsis. Second, the cause of death was unknown and might not be sepsis. Third, we did not compare the prehospital qSOFA score with other severity or prehospital screening tools because the information recorded in the ORION registry is limited. Fourth, patients with a do-not-resuscitate indication prior to admission were not excluded. Finally, some factors other than qSOFA in the prehospital setting could affect prognosis. In the future, we would like to undertake further research to develop a prehospital screening system that overcomes these limitations.

CONCLUSIONS

THE QSOFA AS evaluated by EMS personnel in the prehospital setting was significantly associated with prognosis in patients with sepsis or suspected sepsis in a comprehensive regional analysis using a population-based ORION registry. It could help EMS to immediately recognize their severity and select the appropriate hospital for treatment.

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DISCLOSURE

APPROVAL OF THE research protocol: This study was approved by the Ethics Committee of the Osaka University Graduate School of Medicine (No. 15003).

Informed consent: N/A.

Registry and the registration no. of the study/trial: N/A.

Animal studies: N/A.

Conflict of interest: None.

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SUPPORTING INFORMATION

Additional Supporting Information may be found in the online version of this article at the publisher's web-site:

Table S1. List of ICD-10 codes for selection of patients with sepsis and suspected sepsis.