



# City Research Online

## City St George's, University of London

**Citation:** Alberto, L., Marshall, A. P., Walker, R. M., Pálizas, F. & Aitken, L. M. (2021). Sensitivity and specificity of a quick sequential [Sepsis-Related] organ failure assessment sepsis screening tool. *International Journal of Clinical Practice*, 75(12), e14874. doi: 10.1111/ijcp.14874

This is the accepted version of the paper.

This version of the publication may differ from the final published version. To cite this item please consult the publisher's version.

**Permanent repository link:** <https://openaccess.city.ac.uk/id/eprint/26808/>

**Link to published version:** <https://doi.org/10.1111/ijcp.14874>

**Copyright and Reuse:** Copyright and Moral Rights remain with the author(s) and/or copyright holders. Copies of full items can be used for personal research or study, educational, or not-for-profit purposes without prior permission or charge, unless otherwise indicated, provided that the authors, title and full bibliographic details are credited, a hyperlink and/or URL is given for the original metadata page and the content is not changed in any way. For full details of reuse please refer to [City Research Online policy](#).

**Sensitivity and Specificity of a quick Sequential [Sepsis-Related] Organ  
Failure Assessment Sepsis Screening Tool**

Running title: Accuracy of qSOFA sepsis screening

Laura Alberto (corresponding author)

School of Nursing and Midwifery, Menzies Health Institute Queensland, Griffith  
University, Brisbane, Australia

Email: [laura.alberto@alumni.griffithuni.edu.au](mailto:laura.alberto@alumni.griffithuni.edu.au), [lauramaria.alberto@gmail.com](mailto:lauramaria.alberto@gmail.com),  
[laura.alberto@usal.edu.ar](mailto:laura.alberto@usal.edu.ar)

Postal address: School of Nursing, Institute for Research in Medicine and Health Sciences,  
Universidad del Salvador, Av. Córdoba 1601, 7° PISO. (C1020ADM). CABA. Argentina

Phone: +54 9 11 4915 8403 | Email: [laura.alberto@usal.edu.ar](mailto:laura.alberto@usal.edu.ar)

ORCID: [0000-0002-7961-9898](https://orcid.org/0000-0002-7961-9898)

Andrea P. Marshall

School of Nursing and Midwifery, Menzies Health Institute Queensland, Griffith  
University, Australia

Gold Coast University Hospital, Gold Coast Hospital and Health Service, Gold Coast,  
Australia

Email: [a.marshall@griffith.edu.au](mailto:a.marshall@griffith.edu.au)

ORCID: [0000-0001-7692-403X](https://orcid.org/0000-0001-7692-403X)

Rachel M. Walker

School of Nursing and Midwifery, Menzies Health Institute Queensland, Griffith  
University, Australia

Division of Surgery, Princess Alexandra Hospital, Brisbane, Australia

Email: [r.walker@griffith.edu.au](mailto:r.walker@griffith.edu.au)

ORCID: [0000-0002-6089-8225](https://orcid.org/0000-0002-6089-8225)

Fernando Pálizas

Intensive Care Units, Clínicas Bazterrica and Santa Isabel, Ciudad de Buenos Aires,

Argentina

Email: [palizasfernando@gmail.com](mailto:palizasfernando@gmail.com)

ORCID: [0000-0003-3681-8974](https://orcid.org/0000-0003-3681-8974)

Leanne M. Aitken

School of Health Sciences, City, University of London, London, UK

School of Nursing and Midwifery, Griffith University, Brisbane, Australia

Email: [leanne.aitken.1@city.ac.uk](mailto:leanne.aitken.1@city.ac.uk)

ORCID: [0000-0001-5722-9090](https://orcid.org/0000-0001-5722-9090)

## **ACKNOWLEDGEMENTS**

We acknowledge Ms Silvina Bravo (Director of Nursing, Clínica Bazterrica) and Dr Alejandra Di Leo Lira (Medical Director, Clínica Bazterrica) for granting access to the study site and supporting all study activities. Special thanks to Ms Maria Marta Ayala, Mr Alberto Sotomayor (Nurse Unit Managers, Clínica Bazterrica), and Mr David Sanz (Clínica Bazterrica Director of Nursing, Executive Assistant) for assisting the data collector with computing facilities and help to manage the study. Thanks to Dr Carlos Martin (Internal Medicine Director, Clínica Bazterrica) and his team, to the Nurse Unit Managers from specialty areas and the nurses from the study wards for supporting the data collection. Special thanks to the administrative, audit and security staff (Clínica Bazterrica) for granting access to the site after hours. Thanks to Ms Brooke Musty for assisting with data entry. We also acknowledge Dr Ian Hughes (Gold Coast University Hospital, Gold Coast Health) for his advice on data management, and Dr Manu Shankar-Hari (Kings College London) for reviewing the manuscript.

## **AUTHOR CONTRIBUTIONS**

LA had full access to all the data in the study and takes responsibility for integrity of the data and the accuracy of the analysis. LA, APM, RMW and LMA contributed to the concept and study design. LA and FP collected data. LA, AM and FP provided administrative, technical and material support. LA conducted the statistical analysis. All authors provided further input to the analysis and interpretation of data, revised the manuscript for important intellectual content and approved the final manuscript. AM, RMW, FP and LMA supervised the study process.

## **FUNDING SOURCE**

This study is part of the principal investigator PhD study at Griffith University and was supported by PhD Scholarships (Griffith University International Postgraduate Research Scholarship, Griffith University Postgraduate Research Scholarship and Completion Assistance Postgraduate Research Scholarship)

## **DISCLOSURES**

The authors declare that there is no conflict of interest related to this work.

# **Sensitivity and Specificity of a quick Sequential [Sepsis-Related] Organ Failure Assessment Sepsis Screening Tool**

Running title: Accuracy of qSOFA sepsis screening

## **Abstract**

**Aim:** There is limited evidence on the diagnostic accuracy of a quick Sequential [Sepsis-Related] Organ Failure Assessment (qSOFA) sepsis screening (SS) tool in developing nation health settings. The aim of this study was to test the diagnostic accuracy of a qSOFA-based SS tool, and the predictive validity of the qSOFA score in hospital ward patients from Argentina.

**Methods:** Prospective observational study. Patients ( $\geq 18$  years, without sepsis) were recruited within 24-48 hours of admission to a 169-bed tertiary referral private hospital in Buenos Aires. The index test was the qSOFA-based SS tool, and the reference standard sepsis diagnosed at discharge blindly evaluated with reference to the Sepsis-3.

**Results:** In 1151 patients (median age 69.9 [IQR, 29.0]); 47 (4.1%) had sepsis, 413 (35.9%) had infection and 691 (60.0%) other diagnoses at discharge. The qSOFA-based SS tool (index test) had moderate sensitivity (60%), good specificity (89%), a very low positive (19%) and very high negative (98%) predictive value for sepsis diagnosed at discharge according to the Sepsis-3 criteria (reference standard). For the same outcome, the qSOFA score in isolation had a reasonable predictive validity area under receiver operating characteristics curve 0.77 (95% CI 0.70-0.83)  $p < 0.001$ .

**Conclusion:** The qSOFA score could reasonably discriminate patients at risk of developing sepsis; qSOFA-based screening may be valuable where no screening criteria are in place.

**Kew words:** qSOFA, sensitivity, specificity, sepsis, screening, hospital ward, developing nation

**What's already known about this topic?**

- Sepsis is a major cause of morbidity and mortality, and a World Health Organization recognized global concern.
- Screening tools for the early recognition of sepsis has been predominantly tested in developed nations. Prospective studies reporting screening tools validated in hospital ward populations in developing nation health settings are scarce.

**What does this article add?**

- The quick Sequential [Sepsis-Related] Organ Failure Assessment (qSOFA) sepsis screening tool had moderate sensitivity and may be valuable where no screening criteria are in place.
- The qSOFA score could identify patients at risk of developing sepsis during their hospitalisation.
- Patients with suspected infection that score 1 qSOFA point should be assessed for indicators of organ dysfunction and should be closely monitored and treated according to clinical judgment.

## INTRODUCTION

Sepsis is an unresolved health issue, a major cause of morbidity and mortality world-wide. Sepsis affects almost 50 million people annually and, based on recent data 11 million will die.<sup>1</sup> In developing nations sepsis remains an under-investigated condition,<sup>2-4</sup> sepsis-related mortality is likely to be higher than in the developed world<sup>5,6</sup> although the true prevalence and consequences of sepsis remains unknown. Despite the impact of sepsis, effective screening methods in hospitalized patients are unclear, particularly in the developing world. This was confirmed by a recent systematic review that reported the majority of screening tools for sepsis were validated in the USA, with wide variation in their sensitivity and specificity.<sup>7</sup>

The clinical criteria to recognise sepsis has evolved. In 2016, the quick Sequential [Sepsis-related] Organ Failure Assessment (qSOFA) was introduced to prompt recognition of organ failure, in patients with suspected infection, and initiate treatment outside the intensive care.<sup>8,9</sup> Recently, a retrospective study reporting secondary analysis of data from nine developing nations found qSOFA could effectively discriminate infected patients at risk of death.<sup>10</sup> In contrast, based on studies predominantly from the developed world, reviewers found qSOFA had poor sensitivity for short term mortality;<sup>11</sup> and Sepsis-3 developers explained qSOFA is not a screening tool for sepsis as it was derived from data on symptomatic patients, and that screening intended to detect preclinical signs of disease.<sup>12</sup> In ward populations that develop sepsis in hospital, sepsis is more difficult to recognise, mortality is high, the use of hospital care is more intense<sup>13,14</sup> and is rarely investigated in developing settings. A tool based on the qSOFA could help screen early signs of sepsis. Therefore, the aim of this study was to test the diagnostic accuracy of a qSOFA-based sepsis screening (SS) tool within hospital ward patient population in a

developing nation. The predictive validity of the qSOFA score in the same population was also tested.

## **METHODS**

Prospective observational study conducted from April to November 2017, in five medical-surgical hospital wards of a 169-bed referral private hospital in Buenos Aires, Argentina. Ethics approval was gained from Griffith University Human Research Ethics; the Ethics Committee of Bio-Ethics Institute, Pontifical Argentine Catholic University; and the study site's Institutional Review Board. Patient informed consent was waived because the information collected was part of routine care. This study was designed and reported following the Standards for Reporting of Diagnostic Accuracy Studies.<sup>15</sup>

### **Setting**

The study wards comprised all general medical-surgical beds representing 55% (n = 94) of hospital beds. The remaining beds were dedicated to patients in paediatric, neonatal, obstetric, emergency department, coronary care and intensive care areas and not included in this study. Patients' health records were a combination of paper (vital signs, medication/fluid orders and medication administered registries) and electronic sources (routine physician/nursing reviews, plan/treatment provided, pathology reports).

### **Population, sample and recruitment**

Study participants were general hospitalized adults ( $\geq 18$  years). Patients were excluded if they were: admitted to and stayed in intensive, coronary, emergency or paediatric units; pregnant and/or receiving obstetrics care; receiving chemotherapy treatment, or bone marrow transplant; patients with acquired immune deficiency syndrome; or, receiving immunosuppressive therapy. Finally, patients who were being

palliated or who were not for resuscitation or had a sepsis diagnosis at the time of hospital admission were also ineligible.

The sample size was based on previous published sample sizes for diagnostic studies and administrative information. To achieve a 0.91 sensitivity, taking into consideration a 95% confidence interval (CI) lower limit of 0.88, a sample of 1,127 patients was recommended.<sup>16</sup> Because of the unknown prevalence of sepsis in the study setting, and an estimation of 15% based on an international report,<sup>17</sup> an additional 10% above the recommended sample was computed to ensure an adequate number of sepsis cases. This led to total target recruitment of 1,248 patients. Feasibility was confirmed with the admission of 761 eligible patients per month to the study wards during 2016.

Patients were recruited from the study wards within 24-48 hours of hospital admission. As wards differed in their patient diagnoses and numbers, the order of wards revised for daily recruitment was randomised (from first to fifth) using an online tool to optimise patient variation.<sup>18</sup> The list of admissions and the health records of each ward were reviewed for eligibility every day based on this randomization. Up to eight consecutive, eligible patients were recruited per day.

### **Data collection**

Data collected included: age, gender, medical insurance, hospital and intensive care unit (ICU) length of stay, comorbidities<sup>19</sup> qSOFA variables during all admission, source of confirmed or suspected infection, antibiotics, fluids and vasopressors administered, lactate value, culture reports and diagnosis at discharge. Data for qSOFA variables (Supporting Table 1) were collected from paper-based nursing vital sign charts and electronic nursing notes; where these variables were not documented, the information was collected from physicians' records. Diagnosis at discharge was assessed by an experienced intensivist

who, blinded to the qSOFA score, reviewed the electronic component of patients' health records with reference to the Sepsis-3 criteria,<sup>8,20</sup> and identified patients as having sepsis or septic shock. The Sepsis-3 criteria was preferred because it is the latest criteria for sepsis.<sup>8,20</sup> If during this process, the patient did not meet Sepsis-3 criteria,<sup>8,20</sup> he/she was classified as having infection or other diagnosis according to the information in the health records. All data were prospectively collected and entered into either of two secure forms a Microsoft<sup>®</sup> Excel (version 2016) file and REDCap 7.0.11<sup>©</sup> 2018 electronic data capture tools hosted at Griffith University.<sup>21</sup>

### **Data analysis**

Data were cleaned prior to analysis by randomly selecting 10% of participants and independently reviewing entered data against the case report form. The error rate was 0.01%. Continuous non-normally distributed data were analysed descriptively as medians and interquartile ranges (IQR), and categorical data as percentages. Discharge diagnosis groups were compared with Chi-Square and Kruskal-Wallis statistical procedures, where a  $p < 0.05$  was considered significant.

The index test was the qSOFA-based SS tool variable defined as a composite of the earliest qSOFA score  $\geq 2$  and any source of confirmed/suspected infection noted in the health record, or where antibiotics were administered. Previous evidence suggested that patients with suspected infection with qSOFA score  $\geq 2$  were more likely to have poor outcomes typical of sepsis.<sup>8,9</sup> To determine the earliest  $\geq 2$  (positive) or  $\leq 1$  qSOFA (negative) scores among all qSOFA sets during admission, a minimum of two out of three values -either respiratory rate (RR), systolic blood pressure (SBP) or altered mentation (AM)- were present per set. The reference standard was the diagnosis at discharge variable dichotomised; that is patients with sepsis and septic shock were grouped as "sepsis," and

patients with infection and other diagnoses were grouped as “no sepsis.” Then, the performance of the qSOFA-based SS tool was assessed against the reference standard using sensitivity, specificity, and predictive values. The predictive validity of the qSOFA score alone for sepsis diagnosis at discharge was examined using the area under the receiver operating characteristic curve (AUROC). All statistical analyses were conducted using IBM SPSS® Statistics for Windows Version 25 (Armonk, NY: IBM Corp).

## **RESULTS**

In 1,151 patients (median, age 69.9 [IQR, 29.0]; female, 619 [53.8%]), 47 (4.1%) had sepsis (including 11 with septic shock), 413 (35.9%) had infection and 691 (60.0%) other diagnoses at discharge (Table 1). Patients’ comorbidities are detailed in the Supporting Table 2. The most frequent sources of infection in patients with sepsis were pulmonary (40.4%) or urinary (38.3%) (Table 2). Infections classified at discharge are detailed in the Supporting Table 3. A total of 19,834 qSOFA sets were collected, among them 2,000 sets (10%) had one or more qSOFA individual variables (RR, SBP or AM) not documented (Supporting Figure 1); 213 (18.5%) patients had qSOFA  $\geq$  2 (Supporting Figure 2) and 145 (12.6%) met the qSOFA-based SS tool criteria (Figure 1). Cross tabulation of the qSOFA-based SS tool by sepsis diagnosed at discharge (Supporting Table 4) resulted in 60% sensitivity, 89% specificity, 19% positive predictive value (PPV) and 98% negative predictive values (NPV). The predictive validity of the qSOFA score in isolation for the same outcome was an AUROC, 0.77; 95% CI, 0.70-0.83;  $p < 0.001$  (Figure 2).

## **DISCUSSION**

In this prospective study of over thousand medical-surgical adults from a developing nation, the tested qSOFA-based SS tool demonstrated moderate sensitivity,

high specificity, very low PPV and very high NPV. qSOFA score in isolation adequately discriminated sepsis diagnosis at discharge. The more common infections associated with sepsis were pulmonary and urinary, and the frequency of patients with sepsis was very low.

The diagnostic value of a 4-variable qSOFA-based screening tool (RR, SBP, AM and any confirmed/suspected source of infection) was examined in hospital ward population who developed sepsis in hospital. Screening variables were collected every admission day simulating screening in the real-world setting. This study design differs from others that examined the qSOFA prognostic value for ICU admission and mortality in patients with suspected infection or sepsis at admission,<sup>22,23</sup> although the epidemiological tools used in all studies were similar. The moderate sensitivity (60%) of the qSOFA-based SS tool was similar to that of a more complex sepsis surveillance tool developed by The Centers for Disease Control and Prevention for electronic health record systems use (The Adult Sepsis Event, which uses a simplified Sequential Organ Failure Assessment score named eSOFA).<sup>24</sup> Four of six eSOFA variables are laboratory indicators of organ dysfunction, which may be difficult to assess in settings where electronic resources are unavailable, or laboratory facilities are limited.

Index test positive patients had a very low probability of developing sepsis illustrated by the low PPV (19%). Predictive values have been rarely reported in qSOFA studies. Although for a different outcome, higher PPV (37%) for mortality was found for qSOFA positive patients outside intensive care.<sup>25</sup> Predictive values are highly dependent on the prevalence of the condition they intended to predict,<sup>26</sup> given a very low frequency of sepsis in our data (4.1%) this finding may not be useful.

Nineteen patients (40.4%) were index test false negatives (Table 2, Supporting Table 4); among them 18 scored 1 qSOFA point with the remaining scoring 0 (Table 2).

This misclassification was examined by retrospective analysis of qSOFA negative patients that developed sepsis as per Sepsis-2.<sup>27</sup> Researchers found those patients also developed hypothermia, and they hypothesised qSOFA may fail to identify impaired immune responses to infection.<sup>28</sup> Similarly, in a Brazilian study 13% of sepsis non-survivors scored  $\leq 1$  qSOFA point.<sup>23</sup> This suggests organ dysfunction must be investigated in patients with suspected/confirmed infection that scored 1 qSOFA point. Perhaps what made our qSOFA-based SS tool a moderate classifier of sepsis may be the tool's inability to capture dysfunctions evident in blood tests or other observations not included in the qSOFA parameters; although, this assumption merits further research.

There is growing evidence examining the predictive role of the qSOFA for sepsis diagnosis and poor outcomes. One Italian report highlighted better prediction performance for sepsis diagnosis (AUROC, 0.83; 95% CI, 0.74–0.89)<sup>29</sup> than ours (AUROC; 0.77; 95% CI, 0.70-0.83) when examined against Sepsis-3,<sup>8</sup> and a Chinese study showed slightly lower AUROC (0.75).<sup>30</sup> During the Coronavirus pandemic 2019 (COVID19), prediction of septic shock in patients represented an AUROC of 0.74.<sup>31</sup> On the other hand, qSOFA discrimination for mortality in various non-ICU settings has been widely examined. The AUROC reports ranged from 0.69 (95% CI, 0.67–0.70) outside ICU population,<sup>22</sup> 0.69 (95% CI, 0.67-0.72) in sub-Saharan Africa,<sup>32</sup> 0.70 (95% CI, 0.68-0.72) in nine developing countries,<sup>10</sup> 0.74 (95% CI, 0.66–0.81) in both emergency department and ward patients,<sup>33</sup> 0.75 in Brazil,<sup>23</sup> and 0.81 (95% CI, 0.80-0.82) in the Sepsis-3 study that used data from the USA and Germany.<sup>9</sup> In COVID19 patients AUROCs reported were 0.73 and 0.77 for in-hospital and 28-day mortality respectively.<sup>31,34</sup> Our findings, together with this evidence, reinforces the ability of the qSOFA score to discriminate either sepsis diagnosis or mortality in non-ICU, hospital ward populations in developed and developing nations, thereby providing further validation of this score.

It has been suggested that including qSOFA in a screening mechanism may lead to deferral of medical treatment and may miss patients at risk.<sup>22,23</sup> However, this assumption may be challenged when tools are implemented in hospital ward patients. A recent interrupted times series study reported a trend towards an improvement in the timing of treatment when qSOFA-based screening was implemented in patients who developed sepsis in hospital wards.<sup>35</sup> While it is known the sensitivity of qSOFA has been questioned, characteristics of a screening tool or scoring system do not always determine what happens in clinical practice. Researchers found that an early warning and response system for sepsis, which had poor sensitivity for a composite outcome (transfer to ICU, rapid response team activation or death) and sepsis diagnosis at discharge (17% and 22%) when implemented resulted in improved provision of treatment.<sup>7,36</sup> This evidence suggests that factors different than the sensitivity of a screening tool may play an important role when tools are introduced in clinical practice. Simplicity and setting characteristics may be important considerations for future research on screening for sepsis, particularly in settings where there are staffing and technology limitations.

Pulmonary, urinary and abdominal were the more common infections associated with a low frequency of sepsis. The types of infection causing sepsis were more like those reported in Brazil, Europe and the USA,<sup>37-39</sup> rather than those common in other developing nations in Africa and South East Asia.<sup>10</sup> The socioeconomic status and access to care of the studied population from a large urban city may explain these differences. However, the low frequency of sepsis (4.1%), measured against the Sepsis-3 criteria,<sup>8</sup> is surprising in the Argentinean setting. A similar percentage (6%) of hospitalizations with sepsis were reported in the USA where researchers used the Sepsis-3 criteria as part of electronic surveillance.<sup>40</sup> Although methodological differences may result in different frequencies,

our study provides an initial understanding of Sepsis-3<sup>8</sup> frequency in hospital wards in Argentina and may serve for future comparisons.

### **Implications for clinical practice and research**

Choosing a screening tool for sepsis is a complex decision for several reasons. There is no reference standard for the diagnosis of sepsis and available screening options are imperfect. Achieving a highly sensitive and specific tool would be ideal. However, identifying the adequate normal-abnormal point is an arbitrary decision, and when testing tools, sensitivity improves at the expense of specificity and vice versa.<sup>41</sup> In hospital ward settings it is difficult to identify subtle and non-specific clinical signs of organ disturbance due to infection. Thus, sensitivity should be prioritised in a screening mechanism, yet specificity should not be overlooked. The qSOFA-based SS tool has moderate sensitivity and high specificity and better represents the current knowledge of sepsis mechanism; importantly it allows the differentiation of patients with infection and inflammation from those presenting dysregulated host response to infection.<sup>42</sup> Clinicians must be reminded that every patient with infection has the potential to develop sepsis and eventually, every hospital ward patient is vulnerable to infection. Therefore, the suspicion of infection may be a valuable screening variable that is relevant for clinical practice. Although robust alerts for sepsis were studied,<sup>22,43</sup> contextual factors and resources available should not be underestimated and should be weighted in the decision making.

There are, however, questions future research should address to improve screening for sepsis. These include whether there is a clinical variable that can improve the qSOFA-based SS tool sensitivity, diverse populations to investigate, different methodological approaches and ways to use qSOFA. Recently, various systematic reviews have highlighted qSOFA strengths and limitations; included studies were largely secondary

analysis, interrogation of retrospective data, and studies predominantly produced in the developed world.<sup>11,44-46</sup> This evidence, while informative, may not be generalizable to the diverse developing settings; sepsis research should be representative of this diversity. In terms of methodological approaches, it has been proposed that in the absence of a reference standard the metrics such as sensitivity and specificity are not useful to evaluate parameters of sepsis; and, instead predictive validity and usefulness should be considered.<sup>47</sup> For example, researchers have evaluated the trajectories of qSOFA, that is repeated measures of the score in patients with infection; they seemed to improve prediction for sepsis.<sup>48</sup> This study, using electronic health records suggested repeated measurements of qSOFA allowed for monitoring of the patient deterioration/improvement, and may be of help where no-electronic resources are available. This study demonstrated a different use of the qSOFA score, considering the dynamic nature of the physiology. This understanding may provide alternatives to identify earlier signs of organ dysfunction and perhaps monitoring recovery. However, this is not a simple task, developing nations have limited or non-existent structures for health research. Thus, future research will require expansion of the current international collaborations, more active involvement of local expertise, governments, funding bodies and other interested stakeholders.

### **Limitations**

The limitations include that the qSOFA-based SS tool was based on clinician documentation of a known or suspected source of infection or administered antibiotics. This resulted in some cases where the infection was ruled-out at the time of the patient's discharge from hospital. However, this is a possible outcome for many screening tools used in clinical settings; patients are assessed for risk that may not be confirmed.<sup>49</sup> The unavailability of some data (RR, SBP, or AM) due to the fragmentation of data sources,

may have prevented some patients from scoring more qSOFA points to meet the screening tool criteria (Supporting Figure 1). Despite the diagnosis at discharge considering the Sepsis-3,<sup>8,20</sup> we did not collect the Sequential [Sepsis-Related] Organ Failure Assessment Score to better inform the reference standard. Given the setting characteristics, this would have contributed to additional data collection burden. Finally, the low frequency of sepsis and deaths, although good for the patients, prevented the evaluation of the qSOFA as a predictor of mortality.

## **CONCLUSION**

In this prospective study in a developing health setting the qSOFA-based SS tool had moderate sensitivity and high specificity for sepsis diagnosis at discharge in a hospital ward population. The qSOFA score demonstrated reasonable predictive validity for the same outcome. The qSOFA base screening might make a valuable contribution to a screening mechanism for sepsis where no screening tools are in place or where clinical resources are limited. Further research is needed to better understand screening for sepsis in developing nations.

## REFERENCES

1. Rudd KE, Johnson SC, Agesa KM, et al. Global, regional, and national sepsis incidence and mortality, 1990-2017: analysis for the Global Burden of Disease Study. *Lancet*. 2020;395(10219):200-211.
2. Fleischmann C, Scherag A, Adhikari NK, et al. Assessment of Global Incidence and Mortality of Hospital-treated Sepsis. Current Estimates and Limitations. *American Journal of Respiratory and Critical Care Medicine*. 2016;193(3):259-272.
3. Cheng AC, West TE, Peacock SJ. Surviving sepsis in developing countries. *Crit Care Med*. 2008;36(8):2487; author reply 2487-2488.
4. Machado FR, Azevedo LCP. Sepsis: A Threat That Needs a Global Solution. *Crit Care Med*. 2018;46(3):454-459.
5. Southeast Asia Infectious Disease Clinical Research Network. Causes and outcomes of sepsis in southeast Asia: a multinational multicentre cross-sectional study. *The Lancet Global health*. 2017;5(2):e157-e167.
6. Estenssoro E, Kanoore Edul VS, Loudet CI, et al. Predictive Validity of Sepsis-3 Definitions and Sepsis Outcomes in Critically Ill Patients: A Cohort Study in 49 ICUs in Argentina. *Crit Care Med*. 2018.
7. Alberto L, Marshall AP, Walker R, Aitken LM. Screening for sepsis in general hospitalized patients: a systematic review. *J Hosp Infect*. 2017;96(4):305-315.
8. Singer M, Deutschman CS, Seymour CW, et al. The Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3). *JAMA*. 2016;315(8):801-810.
9. Seymour CW, Liu VX, Iwashyna TJ, et al. Assessment of Clinical Criteria for Sepsis: For the Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3). *JAMA*. 2016;315(8):762-774.
10. Rudd KE, Seymour CW, Aluisio AR, et al. Association of the Quick Sequential (Sepsis-Related) Organ Failure Assessment (qSOFA) Score With Excess Hospital Mortality in Adults With Suspected Infection in Low- and Middle-Income Countries. *Jama*. 2018;319(21):2202-2211.
11. Fernando SM, Tran A, Taljaard M, et al. Prognostic Accuracy of the Quick Sequential Organ Failure Assessment for Mortality in Patients With Suspected Infection: A Systematic Review and Meta-analysis. *Annals of internal medicine*. 2018;168(4):266-275.
12. Singer M, Shankar-Hari M. qSOFA, Cue Confusion. *Annals of internal medicine*. 2018;168(4):293-295.
13. Jones SL, Ashton CM, Kiehne LB, et al. Outcomes and Resource Use of Sepsis-associated Stays by Presence on Admission, Severity, and Hospital Type. *Medical Care*. 2016;54(3):303-310.
14. Rothman M, Levy M, Dellinger RP, et al. Sepsis as 2 problems: Identifying sepsis at admission and predicting onset in the hospital using an electronic medical record-based acuity score. *J Crit Care*. 2017;38:237-244.
15. Cohen JF, Korevaar DA, Altman DG, et al. STARD 2015 guidelines for reporting diagnostic accuracy studies: explanation and elaboration. *BMJ open*. 2016;6(11):e012799.
16. Flahault A, Cadilhac M, Thomas G. Sample size calculation should be performed for design accuracy in diagnostic test studies. *Journal of clinical epidemiology*. 2005;58(8):859-862.
17. Rohde JM, Odden AJ, Bonham C, et al. The epidemiology of acute organ system dysfunction from severe sepsis outside of the intensive care unit. *Journal of hospital medicine*. 2013;8(5):243-247.
18. Urbaniak GC, Plous S. Research Randomizer (Version 4.0) [Computer software]. 2015; <http://www.randomizer.org/>. Accessed February 12, 2017.

19. Charlson M, Wells MT, Ullman R, King F, Shmukler C. The Charlson comorbidity index can be used prospectively to identify patients who will incur high future costs. *PLoS one*. 2014;9(12):e112479.
20. Shankar-Hari M, Phillips GS, Levy ML, et al. Developing a New Definition and Assessing New Clinical Criteria for Septic Shock: For the Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3). *JAMA*. 2016;315(8):775-787.
21. Harris PA, Taylor R, Thielke R, Payne J, Gonzalez N, Conde JG. Research electronic data capture (REDCap)--a metadata-driven methodology and workflow process for providing translational research informatics support. *Journal of biomedical informatics*. 2009;42(2):377-381.
22. Churpek MM, Snyder A, Han X, et al. Quick Sepsis-related Organ Failure Assessment, Systemic Inflammatory Response Syndrome, and Early Warning Scores for Detecting Clinical Deterioration in Infected Patients outside the Intensive Care Unit. *Am J Respir Crit Care Med*. 2017;195(7):906-911.
23. Machado FR, Cavalcanti AB, Monteiro MB, et al. Predictive Accuracy of the Quick Sepsis-related Organ Failure Assessment Score in Brazil. A Prospective Multicenter Study. *Am J Respir Crit Care Med*. 2020;201(7):789-798.
24. Rhee C, Zhang Z, Kadri SS, et al. Sepsis Surveillance Using Adult Sepsis Events Simplified eSOFA Criteria Versus Sepsis-3 Sequential Organ Failure Assessment Criteria. *Crit Care Med*. 2019;47(3):307-314.
25. Giamarellos-Bourboulis EJ, Tsaganos T, Tsangaris I, et al. Validation of the new Sepsis-3 definitions: proposal for improvement in early risk identification. *Clinical microbiology and infection : the official publication of the European Society of Clinical Microbiology and Infectious Diseases*. 2017;23(2):104-109.
26. McAdam AJ. Prevalence and Predictive Values: a Micro-Comic Strip. *Journal of Clinical Microbiology*. 2017;55(9):2566-2566.
27. Levy MM, Fink MP, Marshall JC, et al. 2001 SCCM/ESICM/ACCP/ATS/SIS International Sepsis Definitions Conference. *Intensive Care Med*. 2003;29(4):530-538.
28. Umemura Y, Ogura H, Gando S, et al. Assessment of mortality by qSOFA in patients with sepsis outside ICU: A post hoc subgroup analysis by the Japanese Association for Acute Medicine Sepsis Registry Study Group. *Journal of infection and chemotherapy : official journal of the Japan Society of Chemotherapy*. 2017;23(11):757-762.
29. Spoto S, Cella E, de Cesaris M, et al. Procalcitonin and MR-Proadrenomedullin Combination with SOFA and qSOFA Scores for Sepsis Diagnosis and Prognosis: A Diagnostic Algorithm. *Shock (Augusta, Ga)*. 2018;50(1):44-52.
30. Luo J, Jiang W, Weng L, et al. Usefulness of qSOFA and SIRS scores for detection of incipient sepsis in general ward patients: A prospective cohort study. *Journal of critical care*. 2019;51:13-18.
31. Jang JG, Hur J, Hong KS, Lee W, Ahn JH. Prognostic Accuracy of the SIRS, qSOFA, and NEWS for Early Detection of Clinical Deterioration in SARS-CoV-2 Infected Patients. *J Korean Med Sci*. 2020;35(25):e234.
32. Moore CC, Hazard R, Saulters KJ, et al. Derivation and validation of a universal vital assessment (UVA) score: a tool for predicting mortality in adult hospitalised patients in sub-Saharan Africa. *BMJ global health*. 2017;2(2):e000344.
33. Finkelsztein EJ, Jones DS, Ma KC, et al. Comparison of qSOFA and SIRS for predicting adverse outcomes of patients with suspicion of sepsis outside the intensive care unit. *Crit Care*. 2017;21(1):73.
34. Fan G, Tu C, Zhou F, et al. Comparison of severity scores for COVID-19 patients with pneumonia: a retrospective study. *Eur Respir J*. 2020.
35. Alberto L, Aitken LM, Walker RM, Palizas F, Marshall AP. Implementing a quick Sequential (Sepsis-Related) Organ Failure Assessment sepsis screening tool: an interrupted times

- series study. *International journal for quality in health care : journal of the International Society for Quality in Health Care*. 2020;32(6):388-395.
36. Umscheid CA, Betesh J, VanZandbergen C, et al. Development, implementation, and impact of an automated early warning and response system for sepsis. *Journal of hospital medicine*. 2015;10(1):26-31.
  37. Machado FR, Ferreira EM, Schippers P, et al. Implementation of sepsis bundles in public hospitals in Brazil: a prospective study with heterogeneous results. *Crit Care*. 2017;21(1):268.
  38. Torsvik M, Gustad LT, Mehl A, et al. Early identification of sepsis in hospital inpatients by ward nurses increases 30-day survival. *Crit Care*. 2016;20(1):244.
  39. Levy MM, Artigas A, Phillips GS, et al. Outcomes of the Surviving Sepsis Campaign in intensive care units in the USA and Europe: a prospective cohort study. *The Lancet Infectious diseases*. 2012;12(12):919-924.
  40. Rhee C, Dantes R, Epstein L, et al. Incidence and Trends of Sepsis in US Hospitals Using Clinical vs Claims Data, 2009-2014. *JAMA*. 2017;318(13):1241-1249.
  41. Fletcher RH, Fletcher SW, Fletcher GS. *Clinical epidemiology: the essentials*. 5th ed. Philadelphia: **Wolters Kluwer Health/Lippincott Williams & Wilkins**; 2014.
  42. Vincent JL, Opal SM, Marshall JC, Tracey KJ. Sepsis definitions: time for change. *Lancet*. 2013;381(9868):774-775.
  43. Smith GB, Prytherch DR, Meredith P, Schmidt PE, Featherstone PI. The ability of the National Early Warning Score (NEWS) to discriminate patients at risk of early cardiac arrest, unanticipated intensive care unit admission, and death. *Resuscitation*. 2013;84(4):465-470.
  44. Tan TL, Tang YJ, Ching LJ, Abdullah N, Neoh H-M. Comparison of Prognostic Accuracy of the quick Sepsis-Related Organ Failure Assessment between Short- & Long-term Mortality in Patients Presenting Outside of the Intensive Care Unit – A Systematic Review & Meta-analysis. *Scientific Reports*. 2018;8(1):16698.
  45. Song JU, Sin CK, Park HK, Shim SR, Lee J. Performance of the quick Sequential (sepsis-related) Organ Failure Assessment score as a prognostic tool in infected patients outside the intensive care unit: a systematic review and meta-analysis. *Crit Care*. 2018;22(1):28.
  46. Serafim R, Gomes JA, Salluh J, Povoia P. A Comparison of the Quick-SOFA and Systemic Inflammatory Response Syndrome Criteria for the Diagnosis of Sepsis and Prediction of Mortality: A Systematic Review and Meta-Analysis. *Chest*. 2018;153(3):646-655.
  47. Lamontagne F, Harrison DA, Rowan KM. qSOFA for Identifying Sepsis Among Patients With Infection. *Jama*. 2017;317(3):267-268.
  48. Kievlan DR, Zhang LA, Chang CH, Angus DC, Seymour CW. Evaluation of Repeated Quick Sepsis-Related Organ Failure Assessment Measurements Among Patients With Suspected Infection. *Crit Care Med*. 2018.
  49. UK National Screening Committee. Screening in the UK: making effective recommendations. In: Public Health England, ed2018.

**TABLE 1 Patients' characteristics by diagnosis at discharge**

<b>Patient's characteristics</b>	<b>Whole cohort</b>	<b>Sepsis</b>	<b>Infection</b>	<b>Other</b>	<b>p Value</b>
	<b>(n = 1,151)</b>	<b>(n = 47)</b>	<b>(n = 413)</b>	<b>(n = 691)</b>	
<b>Age, median (IQR)</b>	69.9 (29.0)	76.4 (21.3)	72.0 (28.8)	68.4 (29.6)	0.004
<b>Gender, n (%)</b>					
Male	532 (46.2)	27 (57.4)	204 (49.4)	301 (43.6)	0.049
Female	619 (53.8)	20 (42.6)	209 (50.6)	390 (56.4)	
<b>Medical insurance, n (%)</b>					
Private-prepaid	755 (65.6)	32 (68.1)	274 (66.3)	449 (65.0)	0.840
Social security	396 (34.4)	15 (31.9)	139 (33.7)	242 (35.0)	
<b>Type of admission, n (%)</b>					
Medical	701 (60.9)	32 (8.1)	285 (69.0)	384 (55.6)	<0.001
Surgical	450 (39.1)	15 (31.9)	128 (31.0)	307 (44.4)	
<b>Condition at discharge, n. (%)</b>					
Alive	1117 (97)	36 (76.6)	407 (98.5)	674 (97.5)	
DNR status, yes	29 (2.5)	9 (19.1)	5 (1.2)	15 (2.2)	
Deaths excluding DNR	7 (0.6)	3 (7.9)	2 (0.5)	2 (0.3)	
<b>CCI, median (IQR)</b>	2.0 (3.0)	3.0 (3.0)	3.0 (3.0)	2.0 (4.0)	<0.001
<b>Hospital LOS, median (IQR), days</b>	4.0 (4.0)	9.0 (11.0)	5.0 (4.0)	4.0 (3.0)	<0.001
<b>Use of higher level of care</b>					
ICU admission, n (%)	114 (9.9)	13 (27.7)	18 (4.4)	83 (12.0)	<0.001
ICU or CCU length of stay, median (IQR), days	1.4 (2.0)	7.8 (7.8)	2.5 (2.2)	1.1 (1.1)	<0.001
No use of OR, n (%)	656 (57)	31 (66.0)	274 (66.3)	351 (50.8)	
1 procedure in OR, n (%)	432 (37.5)	7 (14.9)	111 (26.9)	314 (45.4)	<0.001
≥ 2 procedures in OR, n (%)	63 (5.5)	9 (19.1)	28 (6.8)	26 (3.8)	
<b>Sepsis care</b>					
<b>Antibiotics administered, n (%)</b>					
Antibiotics	559 (48.6)	46 (97.9)	392 (94.9)	121 (17.5)	<0.001
No Antibiotics	592 (54.4)	1 (2.1)	21 (5.1)	570 (82.5)	
<b>Lactate</b>					
Lactate, median (IQR), mmol/L	1.8 (1.0)	1.9 (1.6)	1.7 (1.0)	1.8 (1.0)	0.153
Highest lactate, median (IQR), mmol/L	2.2 (3.1)	3.4 (3.3)	2.1 (1.3)	1.9 (1.5)	0.091
<b>Amount crystalloids, median (IQR), ml</b>	500 (500)	500 (1000)	500 (500)	1000 (500)	0.477
<b>Vasopressors initiated, n (%)</b>	10 (0.9)	8 (80.0)	0 (0)	2 (20.0)	
<b>≥ 1 culture, n (%)</b>	525 (45.6)	45 (95.7)	357 (86.4)	123 (17.8)	

<b>Infective agents, n (%)</b>				
≥ 1 fungi microbe	20 (1.7)	2 (12.8)	12 (2.9)	2 (0.3)
≥ 1 gram-negative bacteria	145 (12.6)	17 (36.2)	110 (26.6)	10 (1.4)
≥ 1 gram-positive bacteria	75 (6.5)	11 (23.4)	46 (11.1)	5 (0.7)
<b>Multiresistant bacteria</b>	35 (3.0)	2 (4.3)	29 (7.0)	4 (0.6)
<b>MRSA</b>	7 (0.6)	0 (0)	7 (1.7)	0 (0)
<b>ESBL producing bacteria</b>	26 (2.3)	2 (4.3)	20 (4.8)	4 (0.6)
<b>KPC producing bacteria</b>	2 (0.2)	0 (0)	2 (0.5)	0 (0)

Abbreviations: IQR, interquartile range; DNR, do not resuscitate; CCI, Charlson Comorbidity Index; LOS, length of stay; ICU, intensive care unit; CCU, coronary care unit; OR, operating room; mmol/L, millimoles per litre; ml, millilitre; MRSA, Meticillin-resistant Staphylococcus Aureus; ESBL, Extended-spectrum  $\beta$ -lactamase; KPC, Klebsiella Pneumoniae Carbapenemase.

**TABLE 2 qSOFA-based Sepsis Screening Tool Variables by Diagnosis at Discharge**

Screening tool variables	Whole cohort (n = 1,151)	Sepsis (n = 47)	Infection (n = 413)	Other (n = 691)	p value
<b>Source of confirmed or suspected infection, n (%)</b>					
Pulmonary	178 (15.5)	19 (40.4)	136 (32.9)	23 (3.3)	
Urinary	133 (11.6)	18 (38.3)	103 (24.9)	12 (1.7)	
Skin, soft tissues	120 (10.4)	2 (4.3)	109 (26.4)	9 (1.3)	
Abdominal	99 (8.6)	12 (25.5)	69 (16.7)	18 (2.6)	
Wounds	61 (5.3)	1 (2.1)	51 (12.3)	9 (5.3)	
Bone, joints	42 (3.6)	0 (0)	36 (8.7)	6 (0.9)	
Bacteraemia	17 (1.5)	7 (63.6)	9 (36.0)	1 (33.3)	
Devices, prosthesis	7 (0.6)	2 (18.2)	4 (16.0)	1 (33.3)	
Central line	6 (0.5)	0 (0)	5 (1.2)	1 (0.5)	
Esophageal, oral candidiasis	4 (0.3)	1 (9.1)	2 (8.0)	1 (33.3)	
Mastoiditis, otitis, parotid, tonsils	4 (0.3)	0 (0)	4 (16.0)	0 (0)	
Pelvis	4 (0.3)	0 (0)	4 (16.0)	0 (0)	
Viral infection	3 (0.3)	1 (9.1)	2 (8.0)	0 (0)	
Meningitis	2 (0.2)	1 (2.1)	1 (0.2)	0 (0)	
Endocarditis	2 (0.2)	0 (0)	2 (0.5)	0 (0)	
<b>Confirmed or suspected infection or antibiotics administered, n (%)</b>	587 (51%)	46 (97.9) †	405 (98.1)	136 (19.7)	
<b>qSOFA scores, n (%)</b>					
Score 0	317 (27.5)	1 (2.1)	84 (20.3)	232 (33.6)	
Score 1	621 (54)	18 (38.3)	235 (56.9)	368 (53.3)	<0.001
Score 2	196 (17)	23 (48.9)	87 (21.1)	86 (12.4)	
Score 3	17 (1.5)	5 (10.6)	7 (1.7)	5 (0.7)	
<b>qSOFA-based sepsis screening tool, n (%)</b>					
Positive	145 (12.6)	28 (59.6)	92 (22.3)	25 (3.6)	<0.001
Negative	1006 (87.4)	19 (40.4)	321 (77.7)	666 (96.4)	

Abbreviations: qSOFA, quick Sequential [Sepsis-Related] Organ Failure Assessment

Note: † This cell do not add the total (100%), the remaining patient did not have information related to infection or antibiotics, in the blind diagnosis was found with sepsis.

## **Figure 1 STARD flow diagram**

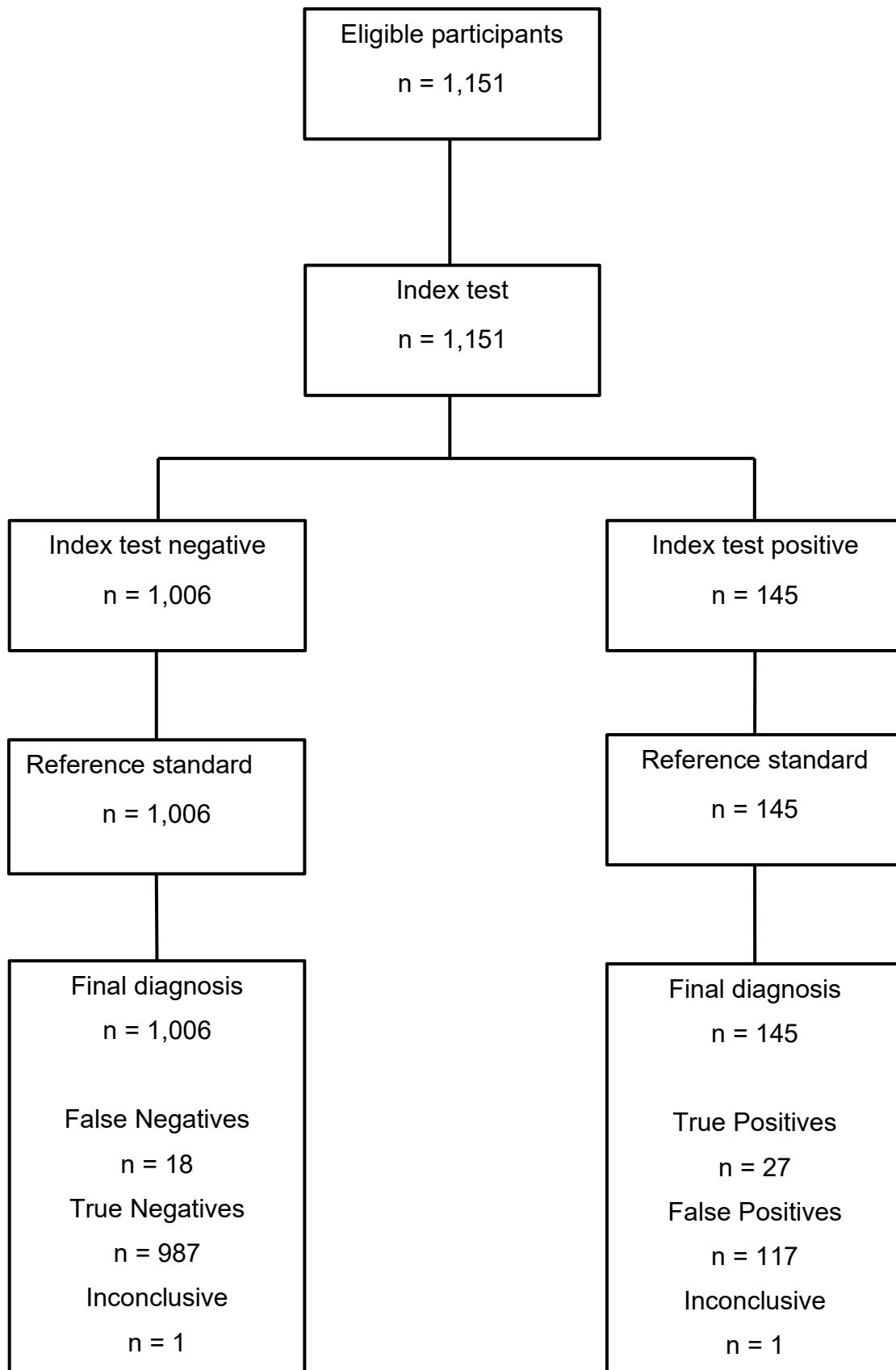
Abbreviation: qSOFA, quick Sequential [Sepsis-Related] Organ Failure Assessment

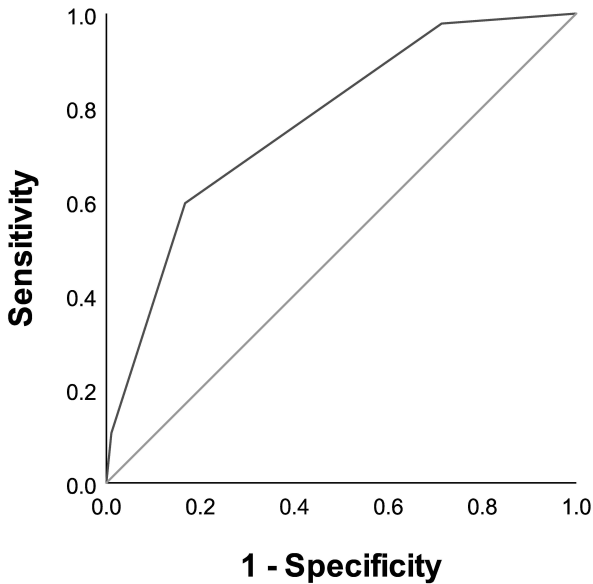
Note: Index test was the qSOFA-based sepsis screening tool variable. The reference standard was the sepsis diagnosis at discharge blindly defined according to Sepsis-3 criteria.

## **Figure 2 qSOFA score area under the receiver operating characteristic curve (AUROC) for sepsis diagnosis at discharge**

Abbreviation: qSOFA, quick Sequential [Sepsis-Related] Organ Failure Assessment

Note: 2 patients included in the sepsis group were clinically judged with sepsis during the blind diagnosis, although it was inconclusive the organ dysfunction observed in the chart review could have been related to the documented infection.





## Sensitivity and Specificity of a quick Sequential [Sepsis-Related] Organ Failure Assessment Sepsis Screening Tool

**Supporting Table 1. quick Sequential [Sepsis-Related] Organ Failure Assessment scoring**

	Score
Respiratory rate: $\geq 22$ /min	1
Systolic Blood Pressure: $\leq 100$ mmHg	1
Altered mentation was an acute, sudden deterioration in consciousness determined by one of the following [1,2]:	1
- a decrease of 2-points on the Glasgow Coma Scale	
- or the patient became disorientated to place	
- or time	
- or person	
- or assessed somnolent	
- or confused	
- or agitated	

### References

- [1] Gonzalez M, de Pablo J, Fuente E, et al: Instrument for detection of delirium in general hospitals: adaptation of the confusion assessment method. *Psychosomatics* 2004; 45:426-431.
- [2] Teasdale G, Maas A, Lecky F, et al: The Glasgow Coma Scale at 40 years: standing the test of time. *Lancet Neurol* 2014; 13:844-854.

**Sensitivity and Specificity of a quick Sequential [Sepsis-Related] Organ  
Failure Assessment (qSOFA) Sepsis Screening Tool**

**Supporting Table 2. Charlson Comorbidity Index frequency**

<b>Index Variables</b>	<b>Whole cohort (n = 1,151)</b>	<b>Sepsis (n = 47)</b>	<b>Infection (n =413)</b>	<b>Other (n = 691)</b>
HBP	524 (45.5)	21 (44.7)	187 (45.3)	316 (45.7)
Cancer	221 (19.2)	11 (23.4)	72 (17.4)	138 (20.0)
Metastases	42 (3.6)	3 (6.4)	11 (2.7)	28 (4.1)
COPD	190 (16.5)	4 (8.5)	88 (21.3)	98 (14.2)
Diabetes	159 (13.8)	9 (19.1)	65 (15.7)	85 (12.3)
Dementia	144 (12.5)	8 (17.0)	73 (17.7)	63 (9.1)
Myocardial infarction	129 (11.2)	10 (21.3)	46 (11.1)	73 (10.6)
Moderate to severe renal disease	104 (9.0)	8 (17.0)	47 (11.4)	49 (7.1)
Warfarin	101 (8.8)	7 (14.9)	31 (7.5)	63 (9.1)
Skin ulcer	92 (8.0)	7 (14.9)	57 (13.8)	28 (4.1)
Gastric or peptic ulcer	76 (6.6)	2 (4.3)	29 (7.0)	45 (6.5)
Heart failure	67 (5.8)	3 (6.4)	18 (4.4)	46 (6.7)
Peripheral vascular disease	36 (3.1)	2 (4.3)	14 (3.4)	20 (2.9)
Cerebrovascular accident	54 (4.7)	6 (12.8)	18 (4.4)	30 (4.3)
Depression	53 (4.6)	2 (4.3)	19 (4.6)	53 (4.6)
Hemiplegia	45 (3.9)	1 (2.1)	24 (5.8)	20 (2.9)
End organ damage from diabetes	12 (1.0)	1 (2.1)	5 (1.2)	6 (0.9)
Rheumatic	24 (2.1)	1 (2.1)	9 (2.2)	14 (2.0)
Chronic liver disease	16 (1.4)	0 (0)	6 (1.5)	10 (1.4)
HIV	13 (1.1)	1 (2.1)	6 (1.5)	6 (0.9)
Severe liver disease	7 (0.6)	2 (4.3)	0 (0)	5 (0.7)

Abbreviations: HBP, high blood pressure; COPD, chronic obstructive pulmonary disease; HIV, human immunodeficiency virus

**Sensitivity and specificity of a quick Sequential [Sepsis-Related] Organ Failure  
Assessment (qSOFA) Sepsis Screening Tool**

**Supporting Table 3. Infections classified at discharge**

<b>Infections</b>	<b>Whole cohort (n = 1,151)</b>	<b>Sepsis (n = 47)</b>	<b>Infection (n = 413)</b>
<b>Infections at discharge, n (%)</b>			
<b>1 Infection</b>	434 (37.7)	38 (80.9) *	396 (95.9) *
<b>≥ 2 Infections</b>	26 (2.3)	9 (19.1) *	17 (4.1) *
<b>Type of Infections at discharge, n (%)</b>			
Pulmonary or Respiratory Infections	145 (31.6)	16 (34.8)	129 (31.2)
Urinary tract infection	102 (22.2)	15 (32.6)	87 (21.1)
Cellulitis or soft tissues	59 (12.9)	0 (0)	59 (14.3)
Abdominal Infections	51 (11.1)	9 (19.6)	42 (10.2)
Surgical site infection	38 (8.3)	0 (0)	38 (9.2)
Joints, Prosthesis or Osteomyelitis	19 (4.1)	0 (0)	19 (4.6)
Bacteraemia or Catheter-related bloodstream infection	10 (2.2)	3 (6.5)	7 (1.7)
Viral infection	13 (2.8)	1 (2.2)	12 (2.9)
Gastrointestinal infection	12 (2.6)	1 (2.2)	11 (2.7)
HIV or Hepatitis	4 (0.9)	0 (0)	4 (1.0)
Other	6 (1.3)	1 (2.2)	5 (1.2)
<b>Type of concurrent infections in patients with ≥2 Infections at discharge, n (%)</b>			
Bacteraemia or Catheter-related bloodstream infection	7 (26.9)	6 (66.7)	1 (5.9)
Abdominal Infections	6 (23.1)	1 (11.1)	5 (29.4)
Cellulitis or soft tissues	5 (19.2)	0 (0)	5 (29.4)
Pulmonary or Respiratory Infections	4 (15.4)	1 (11.1)	3 (17.6)
Urinary tract infection	2 (7.7)	1 (11.1)	1 (5.9)
Gastrointestinal infection	1 (3.8)	0 (0)	0 (0)
Viral infection	1 (3.8)	0 (0)	1 (5.9)

Abbreviation: HIV, human immunodeficiency virus

Note: \* p value < 0.001 (difference between infection and sepsis groups)

**Sensitivity and Specificity of a quick Sequential [Sepsis-Related] Organ  
Failure Assessment (qSOFA) Sepsis Screening Tool**

**Supporting Table 4. Two by two table: quick Sequential [Sepsis-Related] Organ Failure Assessment Sepsis Screening Tool by Sepsis Diagnosed at Discharge**

		Reference Standard		
		Sepsis	No sepsis	Total
Index Test qSOFA-based Sepsis Screening Tool	Positive	28 <sup>£</sup>	117	145
	Negative	19 <sup>£</sup>	987	1,006
	Total	47	1,104	1,151

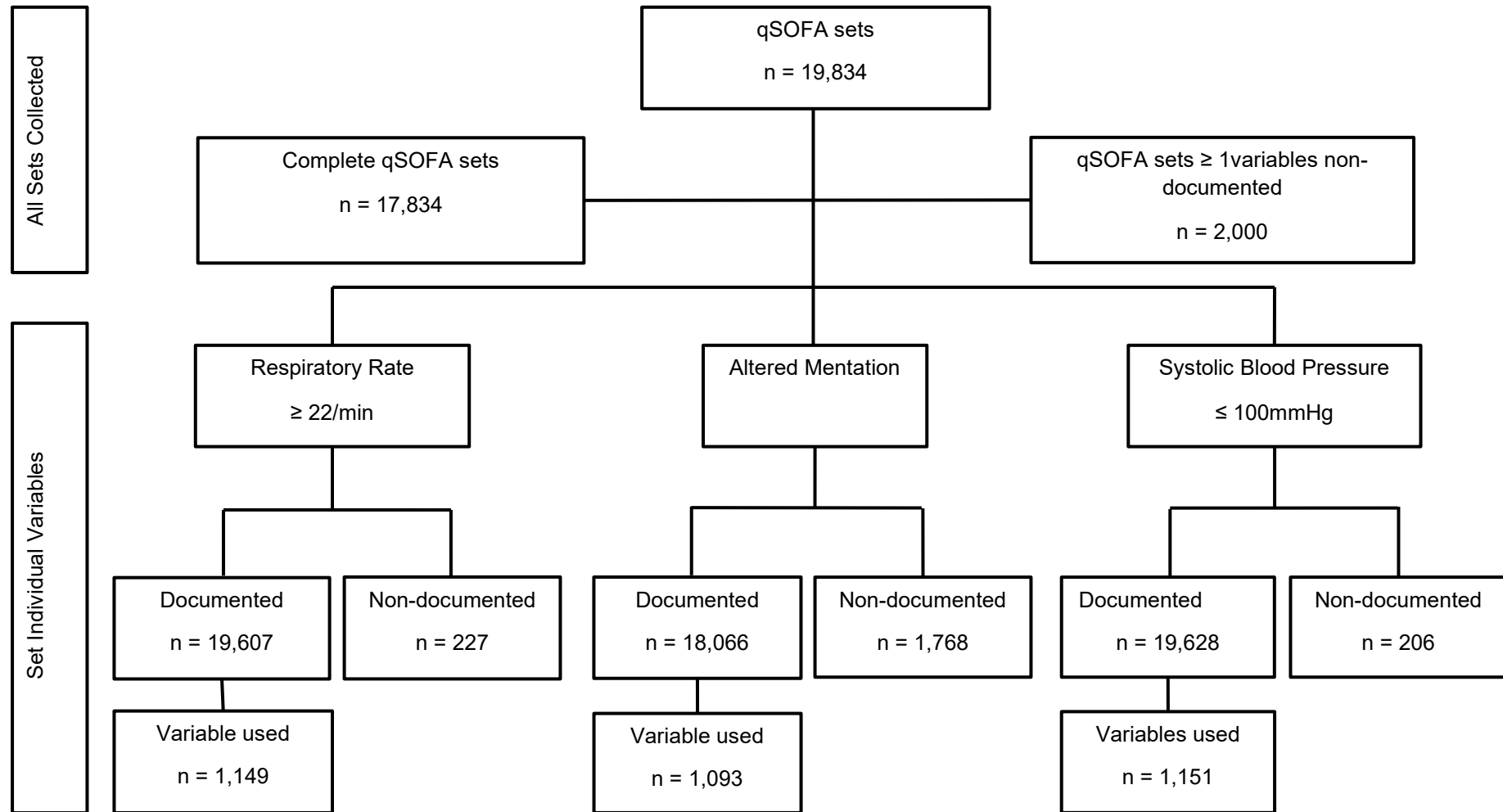
Abbreviation: qSOFA, quick Sequential [Sepsis-Related] Organ Failure Assessment

Note:

<sup>£</sup> 1 patient from this cell group was clinically judged with sepsis during the blind diagnosis, although it was inconclusive the organ dysfunction observed in the chart review could have been related to the documented infection

## Sensitivity and Specificity of a quick Sequential [Sepsis-Related] Organ Failure Assessment Sepsis Screening Tool

**Supporting Figure 1. qSOFA Flow Diagram of documented versus non-documented respiratory rate, systolic blood pressure and altered mentation variables in all patients**

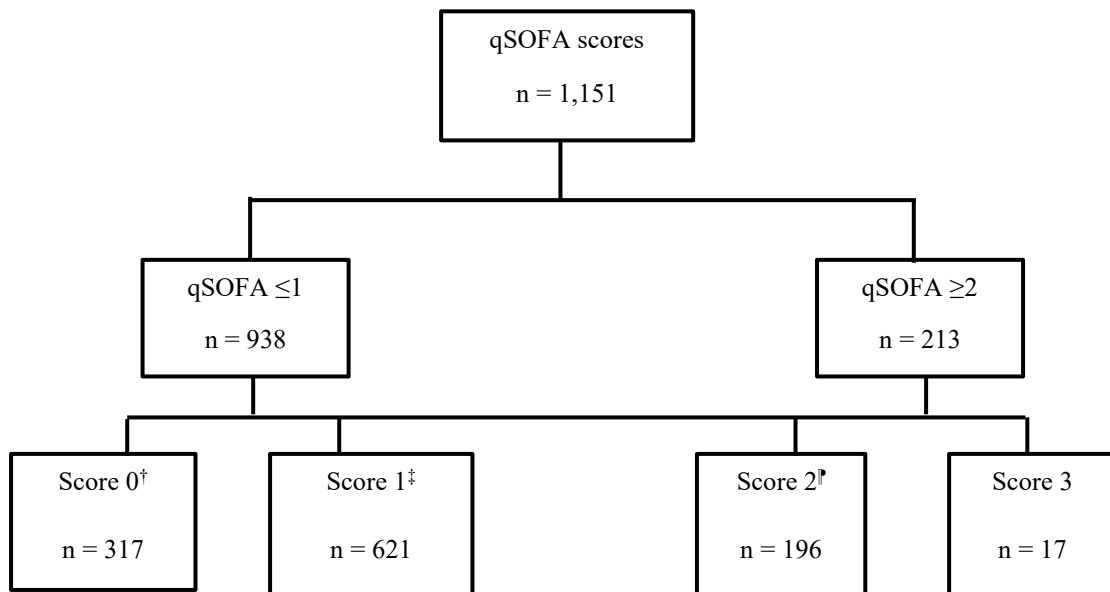


Abbreviation: qSOFA, quick Sequential [Sepsis-Related] Organ Failure Assessment

Note: A qSOFA set consisted of respiratory rate, altered mentation and systolic blood pressure assessed in one nursing observation. Variable used were either respiratory rate, altered mentation or systolic blood pressure present in the first qSOFA set chosen for the qSOFA-based sepsis screening tool, and they were one per patient.

**Sensitivity and Specificity of a quick Sequential [Sepsis-Related] Organ  
Failure Assessment Sepsis Screening Tool**

**Supporting Figure 2. Flow diagram of the earliest qSOFA score per patient chosen for the qSOFA-based sepsis screening tool**



Abbreviation: qSOFA, quick Sequential [Sepsis-Related] Organ Failure Assessment

Notes:

† 21 patients had altered mentation non-documented

‡ 2 patients had respiratory rate, and 32 had the systolic blood pressure non-documented

¶ 5 patients had altered mentation non-documented