Comparison of Diagnostic Accuracies of qSOFA, NEWS, and MEWS to Identify Sepsis in Older Inpatients With Suspected Infection

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ABSTRACT

Objectives To determine and compare the accuracies of qSOFA, NEWS and MEWS to identify sepsis in older inpatients with suspected infection.

Design Prospective diagnostic accuracy study

Setting and Participants Patients admitted to an Acute Geriatric Unit of an Italian University Hospital with at least one sepsis risk factor and suspected infection defined as antibiotic prescription and associated culture test during hospital stay.

Methods Sepsis diagnosis was defined as the presence on discharge documents of ICD-9-CM codes for severe sepsis, septic shock, or for infection and acute organ disfunction. For each patient, clinical parameters were evaluated at least twice daily throughout hospital stay; qSOFA, NEWS and MEWS were derived, and worst scores recorded. Positive cutoffs were set at ≥2, ≥7, and ≥5, respectively. Sensitivity, specificity, positive and negative predictive values (PPV and NPV, respectively), and positive and negative likelihood ratios, as well as areas under the receiver operating characteristic curve (AUROCs) were calculated.

Results Among 230 geriatric patients with suspected infection at risk for sepsis (median age 86 years, 49% female), 30.9% had a sepsis diagnosis. A qSOFA≥2 was recorded in 111 (48.3%) patients, a MEWS≥5 in 65 (28.3%) and a NEWS≥7 in 115 (50.0%). The qSOFA showed the highest sensitivity (81.7%, 95%CI 71.7%-89.5%), but low specificity (66.7%, 95%CI 59.1%-73.7%), resulting in a high NPV (89.1%; 95%CI 82.7%-93.8%) and poor PPV (52.3%, 95%CI 43.0%-61.4%). The AUROC for qSOFA was 0.76 (95%CI 0.69-0.83), comparable with that of NEWS (0.74, 95%CI 0.67-0.81, p=0.44) but significantly higher than that of MEWS (0.70, 95%CI 0.63-0.77, p=0.04).

Conclusions and implications

Repeated qSOFA determinations are useful to rule-out sepsis in geriatric inpatients with suspected infection, but poorly support its diagnosis due to low specificity. More complex MEWS and NEWS do not perform better. Implementation of clinical scores to reliably identify sepsis in older patients is urgently needed.

Introduction

Sepsis is a complex clinical syndrome that has been defined as a life-threatening organ dysfunction caused by a dysregulated host response to infection.[1,2] The incidence of sepsis is growing worldwide, both because of higher awareness among clinicians and because of increased patient complexity and prevalence of multidrug resistant microorganisms.[2–4] Older subjects are more prone to develop sepsis and to suffer its negative consequences, including disability and subsequent institutionalization, and death.[2,4–6] Sepsis is fatal in 30 to 60% of inpatients aged 65 years and older and in 40-80% of patients aged 80 years and older.[2,5] This excess mortality is probably due to the generally worse overall health and functional status of geriatric inpatients, with high levels of comorbidity, cognitive impairment, frailty and malnutrition.[3,5,7–9] Still, part of it may be accounted for by delayed diagnosis and treatment, because of low clinical suspicion and atypical and subtle presentation.[5,10,11]

The Sequential (Sepsis-related) Organ Failure Assessment (SOFA) has been proposed as a tool to identify and monitor organ dysfunction and clinically characterize patients with sepsis, with good performance both as a diagnostic and prognostic tool.[1,12] However, its application is complex, requiring laboratory test results, thereby hindering its prompt applicability and potential usefulness in patients outside intensive care units (ICU).[1,13] To overcome these limitations, the quick SOFA (qSOFA) has been proposed in the Sepsis-III consensus as a bedside tool to identify infected patients at risk for sepsis and death outside the ICU setting.[1,14] In the development of the qSOFA, the Task Force favored simplicity over accuracy, identifying cutoffs for three clinical parameters to be scored 1 point each: respiratory rate (RR) ≥22 breaths/minute, systolic blood pressure (SBP) ≤100 mmHg and altered mental status; a qSOFA score ≥2 points should prompt physicians to further investigate the presence of organ dysfunction and initiate or escalate therapy as appropriate.[1,14]

Lately, the qSOFA has been criticized because of its low sensitivity for the early recognition of sepsis,[15–20] particularly when not regularly repeated throughout hospital stay.[21] Some Authors have proposed for the same purpose to use the Modified and National Early Warning Scores (MEWS and NEWS) instead.[13,17,18,22,23] These scores have been originally developed to detect rapid clinical deterioration of hospitalized patients, irrespective of cause, and to prompt diagnostic and therapeutic interventions.[24–28] They have a wider range of scores and include other vital signs besides those included in the qSOFA, such as heart rate (HR) and body temperature (BT), both in MEWS and NEWS, peripheral oxygen saturation (SpO2) and need for oxygen supplementation (only in the NEWS).[24–26,28] These tools have been reported in some studies to be more accurate than the qSOFA for predicting adverse outcomes in patients with sepsis, with different thresholds performing differently in terms of sensitivity and specificity.[17–19,22,23] However, studies on these scores included generally younger, selected subjects, not fully representative of the population at risk for sepsis.[17–19,22,23] We thus aimed to determine and compare the accuracies of qSOFA, NEWS and MEWS to identify sepsis in older subjects with suspected infection at any time during hospital stay in a geriatric acute ward setting. The hypothesis was that all three clinical scores would have performed poorly in the detection of sepsis because of atypical presentation and of concurrent non-infectious causes for vital parameters' alteration.

METHODS

Study design and participants

This was a prospective diagnostic accuracy observational study that was conducted between 1st April 2019 and 31st October 2019 at A.O.U. Città della Salute e della Scienza di Torino, the main university teaching hospital in Piemonte, North-western Italy. Among all patients admitted to our Acute Geriatric Unit for any reason during the study period, we enrolled consecutive patients presenting at admission at least one risk factor for sepsis, defined

according to the National Institute for Health and Care Excellence (NICE) guidance; namely: age ≥75 years, impaired immune function (diabetes mellitus, previous splenectomy, hematologic diseases), long-term corticosteroid therapy, immunosuppressive or antineoplastic drug treatment, surgery or other invasive procedures in the previous 6 weeks, any breach of skin integrity (e.g. pressure ulcers), intravenous drug misuse, indwelling lines or catheters.[29] Study participants who had a suspected infection at admission or later on during hospital stay were evaluated using the index tests and included in the analysis as further detailed in the following sections. Suspected infection was defined according to the criteria published in the qSOFA validation study as the prescription of an oral and/or parenteral antibiotic therapy within a timeframe spanning from 24 hours before and 72 hours after the collection of a biological sample to perform a culture test.[14] The presence of sepsis was defined using discharge documents, as further detailed below.

The study was approved by the Hospital Ethics Committee (n.0069708/2019) and written informed consent was obtained for all patients. Study protocol is available at clinicaltrials.gov at registration number NCT04945889; results are reported according to the *Standards for Reporting Diagnostic accuracy studies* (STARD) 2015 reporting guidelines (See Supplement 1 for the STARD checklist).[30]

Descriptive variables

At the time of enrollment, age, gender and living condition (home vs long-term care facility) as well as history of hospitalization in the previous 3 months and presence of sepsis risk factors[29] were recorded. Each patient underwent a routine multidimensional geriatric evaluation including comorbidity, functional and cognitive status. Comorbidity was evaluated according to the Charlson Comorbidity Index.[31] Functional status was assessed using Katz's Basic Activities of Daily Living (BADL, range 0-6, higher scores indicating higher dependence),[32] and Instrumental Activities of Daily Living (IADL, range 0-14, lower scores

indicating lower autonomy).[33] Patients with BADL scores ≥1 (i.e., dependent in at least one function) were defined as dependent in BADL; patients scoring 9 or lower on IADL were defined as partially or completely not autonomous in IADL. Cognitive status was evaluated using the Short Portable Mental Status Questionnaire (SPMSQ, range 0-10, higher scores indicating higher levels of cognitive impairment); moderate to severe cognitive impairment was defined as a SPMSQ higher than 4.[34] For patients with suspected infection, timing from admission and suspected infection site were also retrieved from medical records.

Index tests evaluation

According to hospital protocols, for every patient clinical parameters were assessed routinely twice daily throughout hospital stay, and whenever deemed necessary by attending healthcare professionals for clinical reasons, irrespective of hospitalization cause or enrolment in the present study. Such parameters included RR, SBP and HR, all assessed manually, as well as BT and SpO2, determined using electronic devices. Mental status alteration was defined as either a Glasgow Coma Scale (GCS) score <15,[35] or, since protocols in Italy frequently require the evaluation of patient mental status as Oriented, Disoriented, Agitated, or Sleepy (ODAS scale), as any worsening in this scale from the previous assessment. Parameters were recorded in clinical charts and used by the study investigators to score the three index tests, namely the qSOFA, MEWS and NEWS; positive cutoffs were pre-specified according to published validation studies at qSOFA ≥2,[14] MEWS ≥5,[24] and NEWS ≥7.[28] Determinations of single clinical parameters, but not index score calculations were directly available to attending physicians. For the determination of diagnostic accuracy measures, the worst among all measures recorded throughout hospital stay for each index test was considered.

Target condition diagnosis

Presence of sepsis was determined by study investigators reviewing discharge documents that were autonomously coded by attending senior geriatric medicine specialists. This was defined

as the presence of primary or secondary diagnosis International Classification of Diseases 9th revision, Clinical Modification (ICD-9-CM) codes at discharge of either severe sepsis or septic shock,[1] or, according to the Angus indirect method, as the simultaneous presence of codes for infection and at least one acute organ dysfunction.[2] Living status at discharge was also recorded.

Statistical analysis

The absolute and relative frequencies of dichotomous and categorical variables, and either mean and standard deviation or median and the 25th and 75th percentiles of continuous variables were calculated, as appropriate. Differences among patients with and without a diagnosis of sepsis at discharge were explored using the Chi square test for dichotomous and categorical variables, and the Mann-Whitney test for continuous variables. The sensitivities, specificities, positive and negative predictive values, and positive and negative likelihood ratios, as well as areas under the receiver operating characteristic curve (AUROCs) for all three index tests were calculated considering the worst recorded value throughout hospital stay. The AUROCs of the three index tests were compared using the paired-sample design option. Statistical analysis was performed using SPSS version 27 (IBM corporation); all tests were 2-sided and statistical significance was set at $P<.05$.

RESULTS

During the study period, 602 patients with at least one risk factor for sepsis were admitted; among the 580 patients that provided informed consent and were enrolled in the study, 230 had a suspected infection at any time during hospital stay (77.4% at admission and 22.6% later on) and were included in the analysis (see Figure 1 for the STARD study flowchart).

Baseline characteristics of the sample studied (50.7% women, median age 86 years, range 66-99 years) and stratified according to the presence or absence of sepsis diagnosis at discharge are presented in Table 1. Patients enrolled presented a high level of functional dependence,

with 62.6% of them dependent on more than 3 BADL functions and 87.4% partially or completely not autonomous on IADL; more than half of patients showed a moderate to severe cognitive impairment at SPMSQ and almost 20% were nursing home residents. Comorbidity burden was generally high, with a median Charlson Comorbidity Index of 3 and more than 1 patient out of 4 with at least another hospitalization in the previous 3 months.

In more than half of cases, patients presented only one risk factor for sepsis (range 1-5), in most instances represented by older age. One hundred and ninety-seven patients (85.7%) had a confirmed diagnosis of infection at discharge, mainly of the respiratory and urinary tracts (72 and 61 cases, respectively); in 24 patients the infection site was not specified. During a mean hospital stay of 10 days (range 1-50), 71 patients (30.9%) received a sepsis diagnosis, in 39 (55%) cases indirectly traceable in discharge documents according to Angus criteria; 13 patients had an ICD-9-CM diagnosis at discharge of severe sepsis, 19 of septic shock. Sepsis was more frequent among patients with higher levels of functional dependence and of cognitive impairment, and with a history of heart failure; urinary tract infections were significantly less frequent in patients with sepsis. During hospital stay, almost 20% of patients died; overall mortality was significantly higher in patients with a sepsis diagnosis at discharge (42% vs 8.2%, $p < 0.001$).

A qSOFA score of 2 or higher was recorded at least once in 111 (48.3%) patients, while a MEWS of 5 or more in 65 patients (28.3%) and a NEWS≥7 in 115 (50.0%). Accuracy measures of all clinical scores are reported in Figure 1 (contingency tables and receiver operating characteristic curves are available in Supplement 1). The AUROC for qSOFA was 0.76 (95% CI 0.69-0.83), comparable with that of NEWS (0.74, 95% CI 0.67-0.81, $p = 0.44$) but significantly higher than that of MEWS (0.70, 95% CI 0.63-0.77, $p = 0.04$).

Discussion

In the present study, we confirmed once more that sepsis is a frequent and severe complication among older subjects admitted to an acute geriatric unit, being present in almost one out of three (30.9%) patients with a suspected infection at any time during hospital stay, in 42% of cases eventually contributing to their death. Still, in accordance with previous reports, this condition may be underdiagnosed, since more than half of cases could be traced on discharge documents only by use of indirect methods.[2] Neither the number nor any type of sepsis risk factor was associated with sepsis in our sample, whereas septic patients showed a significantly higher prevalence of geriatric syndromes such as functional dependence and cognitive impairment.

In a population of high-risk older subjects admitted to an acute geriatric ward that had a suspected infection at admission or during hospital stay, the diagnostic accuracy of the worst among repeated qSOFA score determinations to detect sepsis was only fair (AUROC 0.76, 95% CI 0.69-0.83), mainly due to a poor specificity (66.7%, 95% CI 59.1%-73.7%). This is in contrast with previous reports of low sensitivity and high specificity of the qSOFA outside of the ICU setting including nursing homes,[15,16,20,27,36,37] and may be due to the frequent alteration of qSOFA parameters in acute older patients irrespective of sepsis.[5,10] In our sample, more than half of nonseptic patients were tachypnoic; this may be due to several non-infective conditions that could affect a population of older polimorbid patients, including for example congestive heart failure, acid-base disturbances, malignancies, musculoskeletal and neurological diseases. Mental status was altered in 70% of septic patients, but also in almost one out of four of nonseptic subjects. In the qSOFA validation study, the altered mental status was defined as a GCS <15,[14] but several studies have highlighted the difficulties of assessing the GCS in patients with cognitive impairment.[16,20,35] The use of other scales to evaluate mental status has been proposed,[38] and could help to increase qSOFA sensitivity possibly at the price of lower specificity. A reduced SBP was the least frequently altered parameter both in the nonseptic and

204 septic groups in our study; however, hypotension is a late sign of sepsis,[39] and relying on it to
205 diagnose this condition could negatively impact on prognosis.[40]. The low sensitivity of qSOFA
206 in identifying sepsis-related organ dysfunction and its low specificity in the geriatric population
207 make it unsuitable as a tool for screening and early identification of potentially septic
208 patients;[13,16,20,36,37] however, repeated negative qSOFA determinations could help to rule out
209 sepsis in this population due to its high NPV.
210 As previously reported, some authors have endorsed the use of Early Warning Scores to
211 identify septic patients with higher accuracy.[17,18,22,23] However, in our study both the more
212 complex NEWS and MEWS proved to be of little use: while the first showed an overall
213 performance that was comparable with that of the qSOFA, the MEWS showed even worse
214 accuracy measures. This may derive from the fact that Early Warning Scores have been
215 developed without the intent to be sepsis-specific, but to be high-sensitivity tools to recognize
216 situations at risk of rapid clinical deterioration and to prompt further measures to ensure patient
217 safety.[24–28] Moreover, both the NEWS and MEWS measure mental status using the Alert,
218 Verbal, Pain, Unresponsive (AVPU) scale, that does not consider the acute onset of confusion;
219 this limitation has been recently addressed by the development of the NEWS2, which adds to
220 the classic AVPU scale a "C" corresponding to the onset of an acute mental alteration.[41] The
221 better performance of the qSOFA over NEWS and MEWS in the present study could be thus
222 in part due to the inclusion of orientation in the mental status evaluation of the qSOFA only.
223 Moreover, just like the qSOFA, also Early Warning Scores rely on vital parameters with ranges
224 based on a young-adult population; whose values can be altered in the older population for a
225 variety of conditions (life-threatening or not), thus compromising the ability of these tools to
226 properly identify high-risk older inpatients.[10,25,42,43] The development of specific Early
227 Warning Scores for geriatric inpatients, taking into account the atypical and functional
228 presentation of disease in this population, would increase the sensitivity of present scores to

recognize clinically unstable situations, with the physician's experience to guide differential diagnosis. The Minnesota Hospital Association has recently proposed the "100-100-100 Early Detection Tool" (i.e., BT over 100°F – 37.7°C, HR >100 beats per minute, and SBP <100 mmHg)[44] to easily identify patients with suspected sepsis in the long term care setting, that proved a good screening tool with a fair to good sensitivity and specificity in a retrospective study on nursing home residents.[20] These characteristics are essential in a non-hospital setting, where sepsis is frequent, can go unnoticed and early detection and referral could help to save lives.[10,13,20] However, some Authors argue that this tool relies on the same nonspecific vital parameters as other tools such as qSOFA, NEWS and MEWS, and a high false positive rate could lead to potentially avoidable hospitalizations, diagnostic and therapeutic procedures, and related complications.[10,13]

The main strengths of the present study are represented by the reliable cohort of real-world geriatric inpatients enrolled, and by the standardized prospective collection of data, but the generalizability of its results may be hindered by the monocentric design. However, our sepsis prevalence figure reflects that reported in other studies,[8,17,45] and clinical score determination was performed following a standardized and easily reproducible protocol.

Even though we used a widely adopted definition of suspected infection, this might have led to the exclusion of patients with infection but without performance or with late performance of culture tests. Moreover, even if discharge diagnoses were made by experienced specialists, it cannot be excluded some degree of miscoding, also because discharge charts do not report temporal or causal relationships between infection and organ dysfunction. This could have led to overestimation of sepsis incidence and distortion of accuracy measures.

Lastly, the diagnostic performance accuracy measures were evaluated on the worse among repeated qSOFA determinations throughout hospital stay: this could mean that, even if a qSOFA score ≥2 proved to have a fair accuracy to recognize septic patients, it might do so

some time after the onset of sepsis-induced organ disfunction, thus making its clinical usefulness questionable.

Conclusions and Implications

Our study showed that having a qSOFA score persistently lower than 2 throughout hospital stay in geriatric inpatients with suspected infection allows to rule out sepsis with a relatively high degree of certainty, thanks to its high NPV. This comes at the cost of a high false positive rate; hence, the qSOFA should be seen more as a "red flag" to identify at risk patients rather than as a diagnostic tool in this population; clinical reasoning, including evaluation of functional manifestation of disease and geriatric syndromes should guide further diagnostic and therapeutic measures. At this purpose, the use of the more complex and time-consuming MEWS and NEWS does not provide a significant benefit over the simpler qSOFA. Development of easy to perform but reliable scores for the identification of sepsis in geriatric inpatients is urgently needed, perhaps as recently proposed by some Authors, including also widely available laboratory test measures.[46] Further development, validation and adoption of high suspicion tools such as the 100-100-100 Early Detection Tool for the referral of nursing home residents with suspected sepsis to the hospital is another key element for the successful management of this condition in the geriatric population.[13] Lastly, our study reported a strikingly high mortality rate among septic patients, but also in nonseptic patients; further studies will shed some light on the real impact of sepsis and of sepsis treatment on the prognosis of geriatric inpatients, taking into account relevant prognostic modifiers such as disability, frailty and dementia.

Conflict of Interest

The Authors report no conflicts of interest with the present study.

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430 **Table 1.** Clinical characteristics of the overall study sample and compared according to the

431 absence or presence of a diagnosis of sepsis at discharge.

Characteristic	**Overall sample (n=230)**	**No sepsis at discharge (n=159)**	**Sepsis at discharge (n=71)**	***P* value***
Age (years) median (IQR)	86 (81-89)	85 (80-89)	87 (83-90)	0.10
Female sex, No. (%)	113 (49.1%)	75 (47.2%)	38 (54%)	0.37
Nursing home resident, No. (%)	45 (19.6%)	30 (18.9%)	15 (21%)	0.69
Hospitalization in the previous 3 months, No. (%)	63 (27.4%)	46 (28.9%)	17 (24%)	0.43
ADL dependent (≥1 lost function), No. (%)	190 (82.6%)	126 (79.2%)	64 (90%)	0.04
IADL partially/not autonomous (<10/14), No. (%)	201 (87.4%)	134 (84.3%)	67 (94%)	0.03
Moderate/severe cognitive impairment at SPMSQ (>4/10 errors), No. (%)	120 (52.2%)	74 (46.5%)	46 (65%)	0.01
Selected chronic conditions				
Charlson comorbidity index, median (IQR)	3 (2-5)	3 (2-5)	3 (2-4)	0.90
Charlson comorbidity index >5, No. (%)	35 (15.2%)	25 (15.7%)	10 (14%)	0.75
Diabetes mellitus, No. (%)	50 (21.7%)	35 (22.0%)	15 (21%)	0.88
Heart failure, No. (%)	64 (27.8%)	37 (23.3%)	27 (38%)	0.02
Coronary artery disease, No. (%)	41 (17.8%)	31 (19.5%)	10 (14%)	0.32
Chronic obstructive pulmonary disease, No. (%)	42 (18.3%)	29 (18.2%)	13 (18%)	0.99
Chronic kidney disease, No. (%)	58 (25.2%)	43 (27.0%)	15 (21%)	0.34
Malignancy, No. (%)	49 (21.3%)	39 (26.0%)	10 (14%)	0.05
Risk factors for sepsis				
Number of risk factors for sepsis, median (IQR)	1 (1-2) (1-5)	1 (1-2)	2 (1-2)	0.49
Age ≥75 years, No. (%)	219 (95.2%)	149 (93.7%)	70 (99%)	0.18
Immune depression, No. (%)	66 (28.7%)	46 (28.9%)	20 (28%)	0.91
Long-term systemic corticosteroid use, No. (%)	19 (8.3%)	15 (9.4%)	4 (6%)	0.44
Immunosuppressive drug use/chemotherapy, No. (%)	5 (2.2%)	2 (1.3%)	3 (4%)	0.17
Surgery/invasive procedures in the previous 6 weeks, No. (%)	8 (3.5%)	6 (3.8%)	2 (3%)	>.99
Breach of skin integrity, No. (%)	30 (13.0%)	19 (11.9%)	11 (16%)	0.46
Parenteral drug misuse, No. (%)	1 (0.4%)	1 (0.6%)	0	>.99
Indwelling venous catheter, No. (%)	9 (3.9%)	7 (4.4%)	2 (3%)	0.73
Urinary catheter, No. (%)	26 (11.3%)	19 (11.9%)	7 (10%)	0.64
Infection site				
Respiratory tract, No. (%)	72 (31.3%)	40 (31.7%)	32 (45.1%)	0.06
Urinary tract, No. (%)	61 (26.5%)	46 (36.5%)	15 (21.1%)	0.03
Gastrointestinal tract, No. (%)	24 (10.4%)	15 (11.9%)	9 (12.7%)	0.87
Soft tissues, No. (%)	15 (6.5%)	13 (10.3%)	2 (2.8%)	0.09
Endocarditis, No. (%)	1 (0.4%)	1 (0.8%)	0	>.99
Unknown, No. (%)	24 (10.4%)	11 (8.7%)	13 (18.3%)	0.05
Clinical scores (worst values registered during hospital stay)				
qSOFA score ≥2, No. (%)	111 (48.3%)	53 (33.3%)	58 (82%)	<.001
qSOFA score, median (IQR)	1 (1-2)	1 (1-2)	2 (2-2)	<.001
qSOFA score				<.001
0	28 (12.2%)	25 (15.7%)	3 (4%)	
1	91 (39.6%)	81 (50.9%)	10 (14%)	
2	86 (37.4%)	45 (28.3%)	41 (58%)	
3	25 (10.9%)	8 (5.0%)	17 (24%)	

Respiratory rate ≥22 breaths/min, No. (%)	138 (60.0%)	87 (54.7%)	51 (72%)	0.01
Systolic blood pressure ≤100 mmHg, No. (%)	90 (39.1%)	48 (30.2%)	42 (53%)	<.001
Altered mental status, No. (%)	110 (47.8%)	60 (37.7%)	50 (70%)	<.001
MEWS ≥5, No. (%)	65 (28.3%)	34 (21.4%)	31 (43.7%)	0.001
MEWS, median (IQR)	3 (2-5)	3 (2-4)	4 (3-6)	<.001
NEWS ≥7, No. (%)	115 (50.0%)	62 (39.0%)	53 (74.6%)	<.001
NEWS, median (IQR)	6.5 (4-9.25)	5 (3-8)	9 (6-12)	<.001
Clinical outcomes of hospital stay				
Length of hospital stay, days, median (IQR)	10 (7-15)	10 (6-14)	11 (7-17)	0.33
All-cause death during hospital stay, No. (%)	43 (18.7%)	13 (8.2%)	30 (42%)	<.001

Abbreviations: IQR, interquartile range; ADL, activities of daily living; IADL, instrumental activities of daily living; SPMSQ, Short Portable Mental Status Questionnaire; qSOFA, quick Sequential Organ Failure Assessment; MEWS, Modified Early Warning Score; NEWS, National Early Warning Score

*p values were calculated according to the Mann-Whitney test for continuous variables and the Chi square test or Fisher exact test for dichotomous or categorical variables, as appropriate. Statistically significant values are underlined

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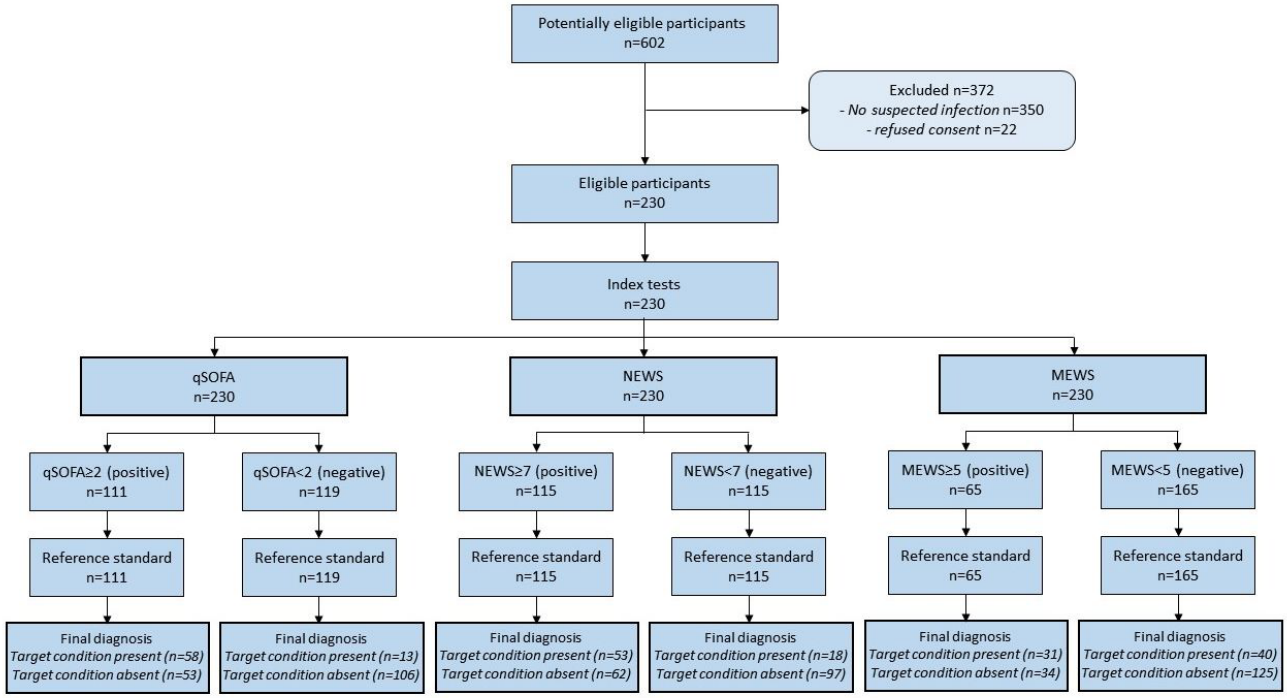
Figure 1 Modified STARD flowchart and diagnostic accuracy measures for the three index tests, presented as point estimates and their 95% confidence intervals.

Abbreviations: AUROC = area under the receiver operating characteristics curve, MEWS = Modified Early Warning Score, NEWS = National Early Warning Score, qSOFA = quick Sequential Organ Failure Assessment



Diagnostic accuracy measures for qSOFA score ≥ 2	
Sensitivity	81.7% (71.7%-89.5%)
Specificity	66.7% (59.1%-73.7%)
Positive predictive value	52.3% (43.0%-61.4%)
Negative predictive value	89.1% (82.7%-93.8%)
Positive likelihood ratio	2.45 (1.92-3.13)
Negative likelihood ratio	0.28 (0.17-0.45)
AUROC	0.76 (0.69-0.83)

Diagnostic accuracy measures for NEWS ≥ 7	
Sensitivity	74.6% (63.8%-83.8%)
Specificity	61.0% (53.3%-68.4%)
Positive predictive value	46.1% (37.1%-55.2%)
Negative predictive value	84.3% (77.0%-90.2%)
Positive likelihood ratio	1.91 (1.51-2.43)
Negative likelihood ratio	0.42 (0.27-0.63)
AUROC	0.74 (0.67-0.81)

Diagnostic accuracy measures for MEWS ≥ 5	
Sensitivity	43.7% (32.5%-55.3%)
Specificity	78.6% (71.8%-84.5%)
Positive predictive value	47.7% (35.8%-59.7%)
Negative predictive value	75.8% (68.9%-81.9%)
Positive likelihood ratio	2.04 (1.37-3.04)
Negative likelihood ratio	0.72 (0.58-0.89)
AUROC	0.70 (0.63-0.77)