

# **A comparison of the quick Sequential [Sepsis-related] Organ Failure Assessment score and the National Early Warning Score in non-ICU patients with/without infection**

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## **ABSTRACT**

**Objective:** The Sepsis-3 task force recommended the quick Sequential [Sepsis-Related] Organ Failure Assessment score (qSOFA) for identifying patients with suspected infection who are at greater risk of poor outcomes, but many hospitals already use the National Early Warning Score (NEWS) to identify high-risk patients, irrespective of diagnosis. We sought to compare the performance of qSOFA and NEWS in hospitalized, non-ICU patients with and without an infection.

**Design:** Retrospective cohort study.

**Setting:** Large UK General Hospital.

**Patients:** Adults hospitalised between 1<sup>st</sup> January 2010 and 1<sup>st</sup> February 2016.

**Interventions:** None

**Measurements and Main Results:** We applied the qSOFA score and NEWS to 5,435,344 vital signs sets (241,996 hospital admissions). Patients were categorised as having no infection, primary infection or secondary infection using ICD-10 codes. NEWS was significantly better at discriminating in-hospital mortality, irrespective of infection status (no infection, NEWS 0.831 (0.825-0.838) vs. qSOFA 0.688 (0.680-0.695); primary infection, NEWS 0.805 (0.799-0.812) vs. qSOFA 0.677 (0.670-0.685)). Similarly, NEWS performed significantly better in all patient groups (all admissions, emergency medicine admissions and emergency surgery admissions) for all outcomes studied. Overall, qSOFA performed no better, and often worse, in admissions with infection than without.

**Conclusions:** The National Early Warning Score outperforms the quick Sequential [Sepsis-Related] Organ Failure Assessment score, irrespective of infection status. These findings suggest that qSOFA should be re-evaluated as the system of choice for identifying non-ICU patients with suspected infection who are at greater risk of poor outcome.

## INTRODUCTION

The Sepsis-3 task force recommends the quick Sequential [Sepsis-Related] Organ Failure Assessment (qSOFA) score for identifying patients with suspected infection who are at greater risk of poor outcomes (1). qSOFA assigns one point for each of the following: systolic BP  $\leq 100$  mmHg; respiratory rate  $\geq 22$  breaths per min; altered mentation (Table 1) (1). Analysis of a large US database showed an area under the receiver operating characteristic (AUROC) curve for in-hospital mortality of 0.81 (95% CI, 0.80-0.82) for patients outside the intensive care unit (ICU) (2).

qSOFA is similar to the early warning scores (EWS) used on general wards to warn that a patient is at high risk of a serious adverse outcome, irrespective of underlying diagnosis (3-5). The UK's National Early Warning Score (NEWS) (6) allocates 0-3 points to each of seven clinical parameters (Table 1). NEWS performs well in a range of clinical settings in different countries (7-17) and is increasingly used as a frontline risk tool.

Introducing qSOFA to settings already using NEWS presents difficulties, as they include similar physiological variables but different weighting thresholds. Operating both is likely to introduce unnecessary duplication of staff effort, needless protocol complexity, confusion with respect to clinical practice and increased educational needs.

Recent publications demonstrate that, in patients with suspected infection, NEWS discriminates in-hospital mortality, ICU admission, and their combined outcome as well as or better than qSOFA (10,18,19). However, there is no published comparison in unselected hospital admissions to inform of a benefit to introducing qSOFA when NEWS is already used. Therefore, we compared the diagnostic performance of qSOFA and NEWS in non-ICU patients with and without a diagnosis of infection (hereafter termed "infection status") during their hospital stay, using a large database of routinely collected vital signs. We used a primary outcome of in-hospital death and four clinically relevant, secondary outcomes. To investigate the impact of reducing NEWS to the same three parameters in qSOFA, we also evaluated the performance of a simplified novel modification of NEWS - quick NEWS (qNEWS) (Table 1).

## **METHODS**

This retrospective study falls within local research ethics committee approval (08/02/1394) from the Isle of Wight, Portsmouth and South East Hampshire Research Ethics Committee.

### **Vital Signs database and its development**

A database was created of vital signs collected from consecutive patients aged  $\geq 16$  years admitted to a large UK hospital (<http://www.porthosp.nhs.uk/about-us>) on or after 1<sup>st</sup> January 2010 and discharged before 1<sup>st</sup> February 2016. Patients transferred directly on admission to critical care areas were excluded. Similarly, we excluded patients who (a) were discharged alive on the day of admission, or (b) had no observation set recorded in the 24 hours before discharge.

Vital signs were documented at the bedside in real-time using handheld devices running Vitalpac™ software (The Learning Clinic, London) (20). Vitalpac™ was used throughout the general wards, but not in the ICU. Each vital signs observation set contained the necessary data items to calculate NEWS and qNEWS values. However, because qSOFA evaluates mental status using the Glasgow Coma Scale (GCS) (1) and the study hospital uses the AVPU scale ((alert (A); responds to voice (V); responds to pain (P); or unresponsive (U))), we categorised patients scoring V, P or U as having 'altered mental status' when calculating qSOFA scores. Vital signs sets for which any measurements were absent were excluded because a full set is required to calculate a NEWS value.

### **qSOFA, NEWS, qNEWS**

qSOFA and NEWS values were calculated for each vital signs set using the weightings described previously (1,6) (Table 1). We also calculated a 'quick NEWS' (qNEWS) value using only the systolic blood pressure, respiratory rate and AVPU components of NEWS, and the same weightings for each cut-off as in NEWS (Table 1).

**Categorisation of admissions:**

The categorisation of admissions into surgical and medical groups followed a previous method (9) and is described in Supplementary Table 1. Admissions were further categorized as “elective” or “non-elective”, as recorded in the hospital’s patient administration system (PAS). We analysed three datasets: (a) all admissions, (b) non-elective admissions to surgery, and (c) non-elective admissions to medicine.

**Patient comorbidity**

Patient comorbidity on admission was measured using Dr. Foster Intelligence’s modification of the Charlson Comorbidity index, as used by the National Health Service (NHS) (21).

**Categorisation of presence of infection:**

Patients’ infection status was assigned according to the presence/absence of Suspicion of Sepsis (SOS) ICD-10 codes relating to bacterial infection (22). During hospital admission, if a patient is transferred from one specialty to another, or from one consultant to another, a new ‘finished consultant episode’ (FCE) is generated. An admission has at least one FCE, but may have many. In our database, each FCE can contain up to eighteen diagnoses. Diagnosis one is the primary diagnosis. After inspection of the data and noting that diagnosis two appeared to have been used for subsidiary primary diagnoses, we decided to interpret it thus. Diagnoses three and higher (if present) are secondary diagnoses. Patients were considered to have had a primary infection if either diagnosis one or two of any FCEs contained an SOS ICD-10 code. Patients were considered to have a secondary infection if there was no primary infection but any of the secondary diagnoses of any FCEs contained an SOS ICD-10 code. Admissions with no associated SOS code were categorised to the “No Infection” group.

**Outcomes**

We studied a primary outcome of in-hospital death and four secondary outcomes: in-hospital death within 24 hours of a vital signs set; in-hospital death or ICU stay  $\geq 3$  days; in-hospital death or ICU admission from a ward; and ‘in-hospital death or ICU admission from a

ward' within 24 hours of a vital signs set. Outcome data were identified from the hospital PAS and ICU database. Where relevant, the maximum length of ICU stay (to account for multiple admissions in a single hospital stay) was calculated.

### **Observation selection methods**

Following a previous method (23), we constructed 10,000 random samples containing one vital signs observation set per admission. The observations were chosen by first randomly selecting a time during every admission, and then choosing the observation set closest to it. Vitalpac™ time-stamps observations automatically as they are entered at the bedside. We used the first and last observation dates and times to determine the time period from which to choose observations. To avoid biasing against selection of the first and last observation sets, we added to the beginning and end of the selection period a length of time equal to half of the mean time between observation sets for that patient episode. We truncated the analysis at the first ICU stay to avoid the inclusion of vital signs taken after ICU admission.

### **Statistical analysis**

All statistical analyses were undertaken using R v3.4 (R Core Team) (24). The ability of NEWS, qSOFA and qNEWS to discriminate outcomes were assessed using AUROC analyses. For each scoring system, the AUROC was calculated using the mean AUROC of the 10,000 samples; 95% confidence intervals were calculated from the distribution.

## RESULTS

### Characteristics of admissions

There were 751,804 patient admissions in the study period. After exclusions, (Figure 1) 241,966 admissions and 5,435,344 complete vital signs sets were studied. Only 59,300 of 6,298,191 (0.94%) sets were excluded because they were incomplete (Figure 1). Of the 241,996 admissions, 114,822 were non-elective medical and 47,592 non-elective surgical admissions. Patient demographics are shown in Table 2.

Of the all admissions group, 6798 (2.81%) were followed by in-hospital death, 2054 (0.85%) by ICU admission from the wards and 971 (0.40%) by ICU stays  $\geq 3$ d. There were more in-hospital deaths, ICU admissions and ICU stays  $\geq 3$ d for admissions with infection than for those without (odds ratios ranged from 1.75 to 15.55) Table 2. The 25 most common SOS diagnoses and 25 most common non-SOS diagnoses in the dataset, are shown in Supplementary Tables 2 and 3, respectively.

During admission, a total of 44647 (18.5%) of all patient admissions had a primary and 21536 (8.9%) a secondary infection (Table 2). Similar proportions were seen for non-elective medical (24.3% and 11.9%) and non-elective surgical admission subgroups (22.8% and 8.0%).

The distribution of patients by age and infection status is shown in Supplementary Figure 1. Generally, the risk of having an infection – either primary or secondary – increased with patient age.

### Relationship between infection and scores

The distributions of qSOFA, NEWS and qNEWS values, and observed risk of in-hospital death by infection status are shown in Supplementary Figures 2a-c, respectively. For each of qSOFA, NEWS and qNEWS, in-hospital mortality increased with rising score value, irrespective of infection status. However, in-hospital mortality was significantly lower for admissions without infection for scores  $\leq 3$  (qSOFA),  $\leq 7$  (NEWS) and  $\leq 4$  (qNEWS). The relationships of qSOFA, NEWS and qNEWS values against the outcome of in-hospital death

within 24 hours of a vital signs set are shown in Supplementary Figures 3a-c.

Plots of qSOFA, NEWS and qNEWS values against the percentage of patient admissions with each infection status are shown in Supplementary Figures 4a-c. In general, for all three scores, an increasing score value was associated with a greater likelihood of a primary infection. A similar trend was seen for secondary infections. Observation sets with a qSOFA value between 1 and 2, NEWS value = 5, and qNEWS value = 4 were each associated with an approximately 50% risk of having an infection.

### **Performance of NEWS, qNEWS and qSOFA**

The AUROC values for NEWS, qNEWS and qSOFA for all 241,966 admissions are shown in Table 3, and for non-elective admissions to surgery and medicine in Table 4. Pictorial displays of the AUROC values for all scores and all outcomes are shown in Supplementary Figures 5a-c for three groups - all admissions (Figure 5a), non-elective admissions to medicine (Figure 5b) and non-elective admissions to surgery (5c). NEWS performed significantly better than qSOFA for all three patient groups and for all outcomes, irrespective of infection status. Considering the all admissions group and the primary outcome of in-hospital mortality, the AUROC (CI) value for NEWS was significantly higher (0.825 (0.821-0.829)) than for qSOFA (0.681 (0.676-0.686)).

For the all admissions group and primary outcome, qSOFA performed similarly in the no infection and primary infection groups (no infection, 0.688 (0.680-0.695); primary infection, 0.677 (0.670-0.685)), whereas NEWS performed better in the no infection group (no infection, 0.831 (0.825-0.838); primary infection, 0.805 (0.799-0.812)) (Table 3). Overall, qSOFA performed no better, and often worse, in admissions with infection than without.

Considering the all admissions group and the primary outcome, sensitivity (CI) was significantly higher for NEWS values of 5, 6 and 7 (46.6% (45.8-47.4%), 36.2% (35.4-37.0%) and 27.1% (26.4-27.9%)), respectively) than for qSOFA values of >2 (12.5% (12.0-13.1%)), but specificity (CI) was lower (NEWS 5 (95.9% (95.9-96.0%)), 6 (98.0 (98.0-98.1%)), 7 (99.1



(99.1-99.1%)); qSOFA >2 (99.7 (99.7-99.7%)). This relationship was unaltered by infection status.

NEWS consistently showed superior discrimination than qNEWS. However, overall, the performance of qNEWS was significantly better or the same as qSOFA across all groups and outcomes. Considering the all admissions group and the primary outcome, the AUROC value for qNEWS was higher than for qSOFA (0.701 (0.696-0.706) vs. 0.681 (0.676-0.686)).

To demonstrate the relationship between sensitivity against trigger rate (i.e., percentage of observations at, or above, a given score value) we plotted an EWS efficiency curve (25) for qSOFA and NEWS. We chose to compare qSOFA and NEWS for admissions with a SOS diagnosis using perhaps the most clinically useful of the outcomes we studied – in-hospital death within 24 hours of a vital signs set. The closer the efficiency curve is to the lower right corner, the higher the efficiency of the EWS (i.e., more outcomes are detected for a lower trigger rate). Supplementary Figure 6 shows that NEWS values of 5 and 7 are more efficient than a qSOFA score =2.

## DISCUSSION

This study compared the ability of qSOFA and NEWS to discriminate in-hospital mortality and four other outcomes in admissions to non-ICU areas of a hospital. Irrespective of infection status, NEWS discriminated all outcomes significantly better than qSOFA. Sensitivity for NEWS values of 5-7 was significantly higher than for qSOFA values of  $\geq 2$ . Overall, qSOFA performed no better, and often worse, in admissions with infection than without. Even when NEWS was reduced to a version containing the same physiological variables as qSOFA – qNEWS – it performed significantly better or at least as well as qSOFA across all groups and outcomes.

The Sepsis-3 task force reported an AUROC value of 0.81 for qSOFA for mortality in non-ICU patients with suspected infection (2). Others have since described varying qSOFA performance in patients with suspected infection, with poor sensitivity for a range of outcomes being frequently observed (10,18,19,26-36). Two other studies demonstrate that qSOFA performs similarly in patients in whom infection has not been diagnosed or is not suspected, implying that qSOFA is not infection-specific and should simply be regarded as a general EWS (36,37).

In a few studies, qSOFA's performance has been compared with that of other EWS systems, e.g. the modified early warning score (MEWS) and NEWS, but only in patients with suspected or confirmed infection (10,18,38). Innocenti et al. found that MEWS and qSOFA discriminated 28-day mortality at ED admission similarly (38). However, Churpek et al. (10) reported that both NEWS and MEWS were *"...more accurate than qSOFA for predicting in-hospital mortality and ICU transfer..."*, with NEWS also performing significantly better than MEWS for in-hospital mortality (10). These relationships appear to be constant, irrespective of the criteria used to define 'suspicion of infection' (18).

That qSOFA performs similarly in patients with and without a primary infection is not surprising, as the abnormalities that cause raised qSOFA scores (and NEWS values) in infection also occur in ischemia, inflammation and trauma (39). That NEWS performs better than qSOFA, irrespective of the presence/absence of infection, should also be expected as

NEWS contains additional parameters known to be valuable in identifying high-risk patients.

NEWS and qSOFA do not diagnose infection; they merely identify patients with a high risk of adverse outcomes. In this respect, NEWS has already shown superior discrimination to other EWS systems (7, 8, 10) and the physiological components of Medical Emergency Team calling criteria (40). The current study now confirms NEWS's superiority over qSOFA. Consequently, there seems to be no benefit for hospitals already using NEWS to change to or introduce qSOFA. NEWS is already the recommended EWS for the UK (6), with the NHS (41), the Joint Royal Colleges Ambulance Liaison Committee and the UK Association of Ambulance Chief Executives (42) highlighting its use in the suspicion and management of sepsis. The current study results suggest that the Sepsis-3 task force should re-evaluate their recommendation to use qSOFA and reflect upon whether NEWS is a more appropriate score to use, even when infection is suspected.

This study has several strengths. It is a large multi-year study, with 241,966 completed admissions to a large general hospital. It studies over 5.4 million complete vital signs sets, each recorded in a standard manner as part of routine care using identical electronic devices (20). It is the first to compare the performance of qSOFA and NEWS in general ward patients with/without an infection diagnosis. It uses common, standardized, systems for measuring patient comorbidity (21) and categorising infection (22).

The study also has limitations. Whilst each vital signs set contained the data necessary to calculate a NEWS value, GCS score values were not available to calculate a qSOFA score and AVPU was used. This may have disadvantaged qSOFA compared to NEWS, as GCS is likely to be more sensitive than AVPU for mild altered mental status. We obtained the date/time of death/discharge from the hospital's PAS and these data are likely to be systematically late, such that the number of observations followed by death within 24 hours may have been underestimated.

We were unable to study data from the ED as these were unavailable; the operating characteristics of NEWS and qSOFA in the ED could vary from that obtained in other areas of

the hospital. However, we undertook a post-hoc analysis comparing the performance of qSOFA and NEWS for two admission groups: (a) those admitted from the ED to non-ICU ward areas of the hospital (n = 121,952), and (b) those admitted directly to non-ICU ward areas of the hospital, without attending the ED (n = 120,044) (Supplementary Table 4). The results are similar for the two groups suggesting that the route of admission is immaterial to the operating characteristics of NEWS and qSOFA.

Patients on an end-of-life (EoL) pathway could not be explicitly excluded, although we partially mitigated this by excluding those with no complete vital signs sets in the final 24 hours of their stay (it is hospital policy to cease the collection of complete sets of vital signs once a patient enters the EoL pathway). As it would not necessarily be anticipated that a patient would be subsequently managed on an EoL pathway at the time an EWS is applied, we repeated the analyses without excluding admissions where vital signs were not measured in the 24 hours prior to discharge (Supplementary Table 5). We included patients with Do Not Attempt Cardiopulmonary Resuscitation decisions, as such patients continue to receive normal care, including the measurement of vital signs. Finally, the study was conducted in a single site where the precursor of NEWS – ViEWS (25) - was developed and requires validation in independent data sets in various settings.

## **Conclusions**

In this single centre study, NEWS was a significantly better discriminator than qSOFA for identifying non-ICU patients at greater risk of poor outcomes, irrespective of infection status. Overall, qSOFA performed no better and often worse in admissions with infection than without, suggesting that qSOFA should be regarded as no more than another non-specific, but poorly performing, EWS. For hospitals already using NEWS, there seem to be no benefit to changing to or adding qSOFA, even when infection is suspected. The Sepsis-3 task force recommendation to use qSOFA as the system of choice for identifying patients with suspected infection at greater risk of poor outcomes requires re-evaluation. Hospitals seeking a high-performing EWS for identifying patients at high risk of adverse outcomes from any underlying condition, including infection, should consider introducing NEWS.

## LEGENDS FOR FIGURES

### Figure 1

Data flow diagram for the study.

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## **Supplemental Digital Content (in order of its citation in the manuscript)**

**Supplementary Table 1:** Categorisation of admissions

**Supplementary Table 2:** Twenty-five most common infection diagnoses in database

**Supplementary Table 3:** Twenty-five most common non-infection diagnoses in database

**Supplementary Figure 1:** The distribution of patient age, categorised by no infection code, or primary and secondary infection codes at any point during an admission.

**Supplementary Figure 2.** The distribution of quick Sequential [Sepsis-related] Organ Failure Assessment (qSOFA) (Figure 2a), National Early Warning Score (NEWS) (Figure 2b) and quick National Early Warning Score (qNEWS) (Figure 2c) values and observed risk of observed risk of in-hospital death categorised by no, primary and secondary infection codes at any point during an admission.

**Supplementary Figure 3.** The distribution of quick Sequential [Sepsis-related] Organ Failure Assessment (qSOFA) (Figure 3a), National Early Warning Score (NEWS) (Figure 3b) and quick National Early Warning Score (qNEWS) (Figure 3c) values and observed risk of death within 24h of an observation set categorised by no, primary and secondary infection codes at any point during an admission.

**Supplementary Figure 4.** Plot of qSOFA (Figure 4a), NEWS (Figure 4b) and qNEWS (Figure 4c) values and percentage of admissions with primary infection, secondary infection and no infection.

**Supplementary Figure 5.** Pictorial display of the area under the receiver operator characteristics curve (AUROC) values for quick Sequential [Sepsis-related] Organ Failure Assessment (qSOFA) score, the National Early Warning Score (NEWS) and the quick National Early Warning Score (qNEWS) for all admissions (Figure 5a), non-elective admission to medicine (Figure 5b) and non-elective admission to surgery (Figure 5c) for a range of outcomes.

**Supplementary Figure 6.** Efficiency curves for quick Sequential [Sepsis-related] Organ Failure Assessment (qSOFA) score and National Early Warning Score (NEWS) for the primary outcome of in-hospital death in a) all admissions b) admissions with infection c) admissions without infection. These plot workload (trigger rate) against the sensitivity (both as percentages) of qSOFA and NEWS. Each point on the efficiency curve for each score

represents a score value from 0 to 3 (for qSOFA) and 0 to 20 (for NEWS), starting with a value of 0 at the top right. Trigger rate =  $([\text{true positive} + \text{false positive}] / [\text{true positive} + \text{false positive} + \text{true negative} + \text{false negative}])$ . The closer the efficiency curve is to the lower right corner, the higher the efficiency of the test (i.e., more outcomes are detected for a lower trigger rate).

**Supplementary Table 4:** Area under the receiver operator characteristics curve for quick Sequential [Sepsis-related] Organ Failure Assessment (qSOFA) score, the National Early Warning Score (NEWS) and the quick National Early Warning Score (qNEWS) for a range of outcomes. A comparison of performance between direct admissions and those via the emergency department (ED).

**Supplementary Table 5:** Area under the receiver operator characteristics curve for quick Sequential [Sepsis-related] Organ Failure Assessment (qSOFA) score, the National Early Warning Score (NEWS) and the quick National Early Warning Score (qNEWS) for a range of outcomes for all admissions, including those where there were no vital signs observations taken in the 24 hours prior to discharge.

**Supplementary Table 6:** Sensitivity, false positive rates and positive predictive values at each threshold of NEWS/qSOFA for the primary outcome of in-hospital mortality.