

Evolving sepsis definitions and their impact on Acute Medical Units

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Abstract

Background: There are currently several different definitions for sepsis. This study looked at what proportion of acute medical admissions were identified by the different definitions, what correlation they have, and how many patients would require a review with results in 1 hour.

Methods: Data on 212 admissions was collected, on time of admission and review, and number of patients with sepsis by each diagnostic criteria calculated.

Results: The NICE criteria identified 69% of admissions as requiring review within one hour, compared to 6% with qSOFA and 18% with previous sepsis definitions. The mean time to review was 1hr 18min, and only 50% of patients meeting the NICE criteria were reviewed within one hour.

Conclusions: The proposed NICE guidance will be challenging to implement with current resources.

Keywords

Sepsis, qSOFA, SIRS, NICE, Acute Medical Unit

Key points

- NICE and the International Consensus for Sepsis have recently released different definitions to try and identify patients at risk of dying from infection.
- Acute admissions should be 'screened' for infection as the cause of their deterioration.
- The patient cohorts identified by the different definitions are very different. The NICE guidelines identify 10 times the number of patients requiring a review within 1 hour compared to qSOFA. This places a significant resource implication on Acute Medical Units trying to identify septic patients on arrival.

Introduction

The definitions for sepsis are evolving, perhaps in recognition that the previous criteria of an infection causing a systemic inflammatory response syndrome (SIRS) did not identify all septic patients. One study in intensive care suggested that SIRS negative sepsis occurred in 1 in 8 patients.¹ The Third International Consensus Definitions for Sepsis and Septic Shock have suggested completely new criteria to screen for patients at risk of dying in hospital due to infection.² National Institute for Health and Care Excellence (NICE) have created new guidance for the management of sepsis in acute medical admissions. Their criteria utilise the SIRS criteria, but have added in additional components from the history to identify patients at higher risk of sepsis or with previously unrecognised symptoms consistent with infection.³ See Table 1 for definitions. The national Commissioning for Quality and Innovation (CQUIN) for 2015/16 currently uses the 2001 definition for sepsis and red flag sepsis.⁴

The International definitions have never been tested prospectively, but have been identified from an expert consensus process using databases, patient cohorts and original research, as likely to be beneficial in identifying septic patients. The draft NICE definitions are likely to be much more sensitive

than those of the systemic inflammatory response syndrome (SIRS) but may not be very specific. In particular, the NICE criteria require all patients at moderate to high risk of severe illness and death from sepsis to be seen, with results, and reviewed within 1 hour, so that Sepsis 6 can be delivered within 1 hour for those thought to have sepsis with organ failure (Figure 1). If these criteria are not very specific, that may generate an unmanageable demand on admitting services.

This study aimed to ascertain how many patients these new guidelines would identify as potentially septic and hence should have treatment within 1 hour of arrival on the Acute Medical Unit. The data were also used to see how the different definitions correlate, and whether they identified the same patients or different patient groups. The 30 day mortality of the cohort was used as a surrogate marker to determine how well the scoring systems identified critically unwell patients on arrival.

Methods

Data were collected prospectively on 212 admissions to the 51 bedded AMU which takes referrals from Primary Care, and the Emergency Department (ED). Patients with suspected acute stroke and acute coronary syndrome are sent directly to the alternative

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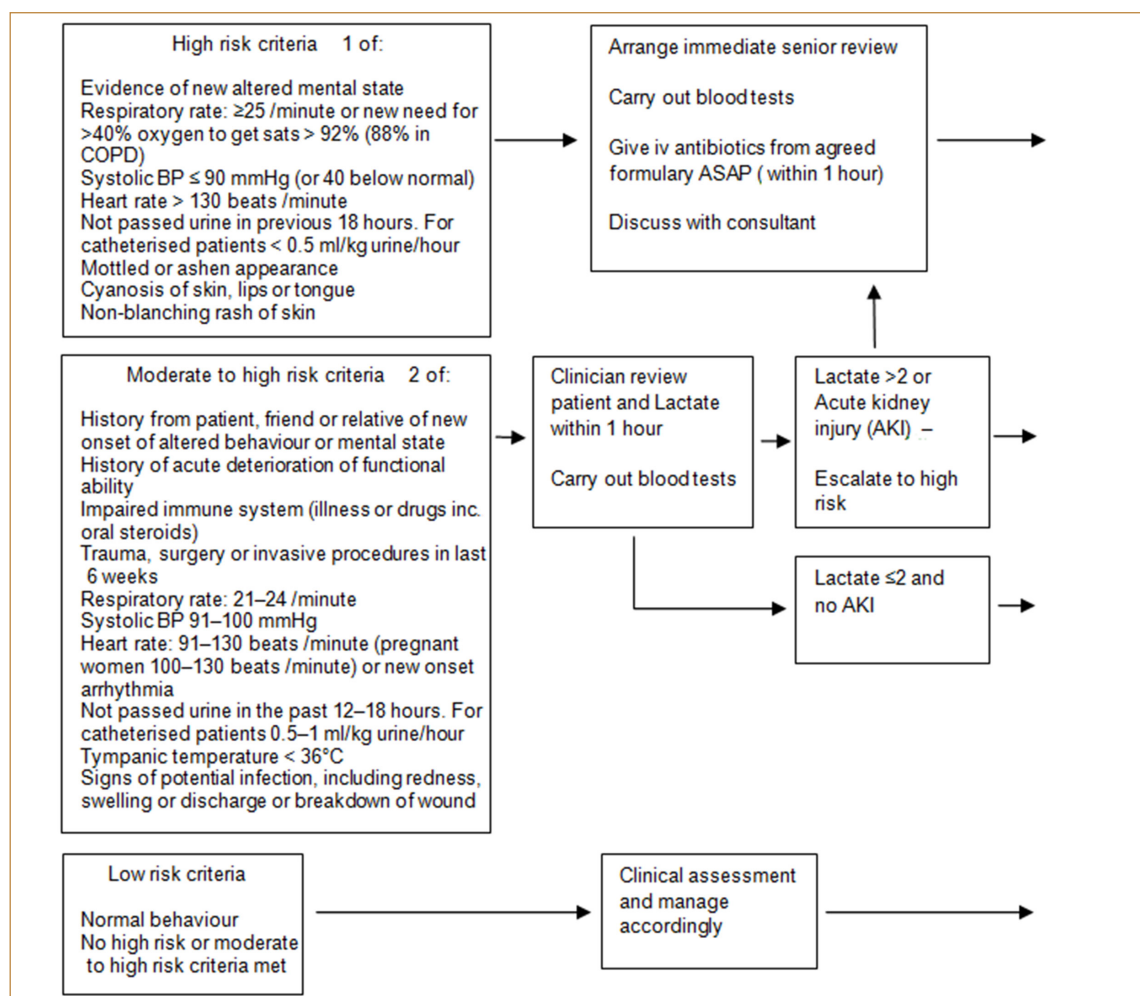


Figure 1. Part of risk stratification tool for adults with suspected sepsis adapted from NICE⁷

admitting areas. Patients referred from primary care have some basic information collected, including the referring reason (which may include infection) and documented on an admitting proforma. Admission observations are added to the proforma and used to calculate a National Early Warning score (NEWS). Patients with a NEWS score of 5 or more are triaged to be seen by medical staff more quickly. If 2 of more SIRS criteria or red flag criteria are triggered, they are also highlighted to the admitting doctors as potentially triggering sepsis, to ensure early review. Patients from ED are screened in ED for sepsis with doctors asked to consider sepsis in any patient with a NEWS score of 3 or more. Data were collected from consecutive patients admitted throughout the day, over a 15 day period, after the consultant post take ward round, when the results of initial investigations would be reviewed, and an admitting diagnosis completed. The admitting doctors were not aware of the data collection or reasons behind the study.

Data were collected on time of admission, time of review, admission diagnosis and serum lactate and time of antibiotic administration where appropriate.

The data were collected and analysed using Microsoft Excel.

Results

Of the 212 admissions, 45% were admitted from primary care, 55% from ED; the median age was 77 yrs (range 17 – 100 yrs).

Sepsis definitions and severity

Seventy two patients (34%) were referred with a possible diagnosis of infection; the diagnosis was thought to be infection in 59 patients (82%) after clinical examination and initial investigations. In addition, a further 14 patients were thought to have infection as their admitting diagnosis after initial assessment so that 34% of the sample had infection. For sepsis, 39 (18%) were captured by the 2001 definitions of SIRS secondary to sepsis; 13 (6%) were identified under the 2016 q-SOFA definition; 146 (69%) were highlighted as requiring review with results within 1 hour of arrival using the NICE guidelines. The correlation of the different sepsis screening definitions is shown in Figure 2.

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Table 1 Sepsis definitions

2001 Sepsis definitions	Sepsis = Infection causing ≥ 2 SIRS (systemic inflammatory response syndrome) • Temperature >38 or <36 °C • Heart rate >90 /min • Respiratory rate >20 /min • WCC $>12\ 000/\text{mm}^3$ or $<4\ 000/\text{mm}^3$
2014 Red Flag Sepsis – term introduced by UK Sepsis Trust using parameters from National Early Warning Score which are individually allocated a score of 3 to identify patients with sepsis and signs of critical illness. Requires immediate treatment	Severe sepsis – sepsis with organ failure Septic shock – sepsis induced hypotension, despite adequate fluid resuscitation • Heart rate $>131/\text{min}$ • AVPU $<$ alert • Respiratory rate $>25/\text{min}$
2016 NICE criteria⁶ for moderate to high risk with suspected sepsis (2 or more) • Bold indicates SIRS criteria • Requires review and results within 1 hour • Requires lactate $>2\text{mmol/L}$ or AKI to escalate to high risk for senior review and IV antibiotics within 1 hour	• Temperature >38 or <36 °C • Heart rate >90 /min • Respiratory rate >20 /min • WCC $>12\ 000/\text{mm}^3$ or $<4\ 000/\text{mm}^3$ • Systolic BP 91-100mmHg • Not passed urine 12-18 hours or 0.5-1.0ml/kg/hr • Signs of infection, redness or swelling • Altered behaviour or mental state • Acute deterioration in function • Rigors in the history • Impaired immune system (Diabetes mellitus, steroids, immunosuppressant drugs, chemotherapy) • Trauma or surgery within the past six weeks
2016 International Consensus Definitions for Sepsis and Septic Shock definition ⁵	Sepsis = life threatening organ dysfunction caused by a dysregulated host response to infection. Patients at risk identified by q(quick) SOFA, with 2 or more: • alteration in mental status • systolic blood pressure ≤ 100 mm Hg • respiratory rate $\geq 22/\text{min}$ Organ failure identified by SOFA (Sequential Organ Failure Assessment Score)

When the NICE criteria were triggered, 100 (68%) of these were as a result of the 'softer' history factors, and 33 (23%) by 2 history criteria alone. Of the 117 patients aged 75 or older, 76% triggered the NICE criteria.

The lactate was measured in just over half the patients, and was used with biochemical and oxygenation results to identify organ failure. The mean lactate was 2, of which 76 patients had lactate <2 , 13 patients lactate 2-4, and 13 patients had a lactate >4 . The traditional SIRS definition of sepsis and organ failure identified 14 patients, the 2016 definition of sepsis (with SOFA organ failure) identified 8 patients and the NICE guideline identified 42 patients with 2 risk criteria and organ failure. There was a very poor correlation of these patient groups.

Blood cultures were taken in 29%. Sepsis status or risk is sometimes divided into 3 categories: when blood cultures were not requested (151 patients),

requested and negative (56 patients) or positive (5 patients), reflecting whether the admitting doctor was concerned about sepsis. Blood cultures were taken in 34/39 (87%) patients with the SIRS criteria; 8/13 (62%) patients with qSOFA and 37/146 (25%) patients with NICE criteria. Of the 5 patients with positive blood cultures, all had an admitting diagnosis of infection and survived; none of the sepsis definitions recognised all the patients with positive blood cultures. There were 32 patients with a diagnosis made on the post-take ward round of infection in whom no blood cultures were taken, 6 of which had evidence of organ failure.

The 30 day mortality was 7% (14 patients) of which 5 patients were admitted with a diagnosis of infection, 5 patients had a lactate greater than 2 on arrival, and 5 had other evidence of organ failure (See Table 2).

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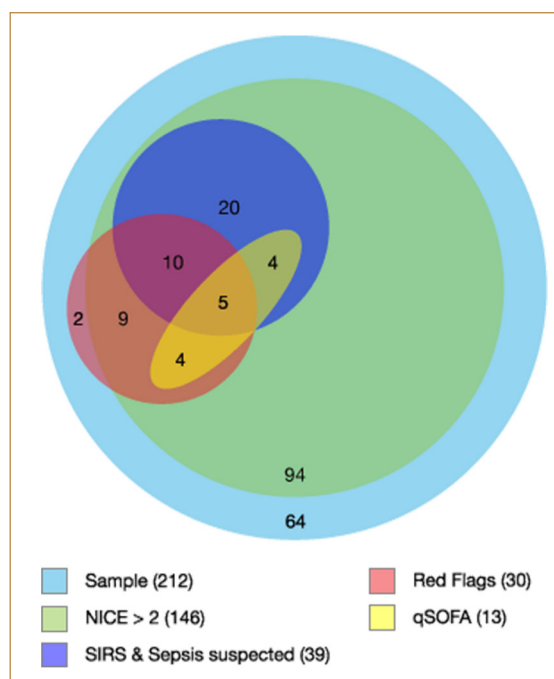


Figure 2. Venn diagram showing numbers of patients meeting different sepsis criteria

Time to review

For the 186 patients where the time of review was recorded, the mean time to review by doctor was 1hr 18min, with little difference for AMU and ED doctors (1hr 21min and 1hr 14min respectively). The time to be seen by a doctor in ED or AMU is shown in figure 3.

For patients with a lactate greater than 4, the mean time to review was 30 mins, suggesting that patients who were more unwell were prioritised appropriately. Those triggering the SIRS criteria which are highlighted on the GP admitting proforma were seen slightly sooner than average at 50 mins, as were those referred with a possible infection at 52 minutes, compared to those who would have been identified with the NICE criteria with the average time 1 hour 20 mins.

Discussion

Initiating treatment for all patients with suspected sepsis within 1 hour of arrival is a challenging target

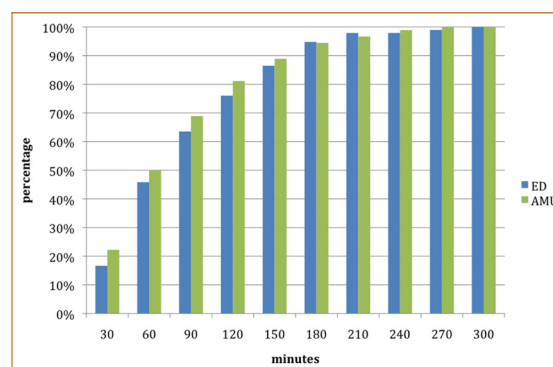


Figure 3. Cumulative time to be seen in minutes by a doctor

to achieve, requiring completion of multiple steps: meeting the patient, obtaining a set of observations, recognising the possibility of infection, taking blood and cultures, prescribing and administering antibiotics. Ensuring that resources are targeted to those individuals who are most in need requires triage patients based on the information available at the time of admission.

Many hospitals use the SIRS criteria and/or the NEWS score to start this triage process. Indeed, patients with observations that trigger these parameters are often referred to the medical team as “patients who trigger sepsis”, whether or not it is infection that is driving the physiological response. It is clear that the SIRS criteria by themselves are too sensitive for sepsis. In a recent analysis of a large US database, Churpek et al. reported that almost half of the 270,000 patients in hospital on regular wards met the SIRS criteria at one time or another.⁵

Whilst technically the NICE criteria relate to patients diagnosed with sepsis, these criteria are frequently being used to screen patients, in order to identify those that may be septic. Patients who meet the NICE criteria thereby need to be seen within the hour, in order to find out if it is sepsis that is causing the patient’s deterioration – in which case they will need treatment. Similar arguments relate to the qSOFA definition which should be applied to patients with infection. Proving that a patient has deteriorated due to infection within 1 hour of arrival is difficult; conversely almost all patients could have

Table 2. Recognition of patients who subsequently died

	SIRS	qSOFA	NICE
Pneumonia – decision not to treat (LOS 2 days)	✓		✓
COPD + new diagnosis Lung Cancer (LOS 14 days)			✓
Septic shock + failure to respond to therapy (LOS 3 days)	✓	✓	✓
Pneumonia (LOS 4 days)	✓	✓	✓
Multi-organ failure, initially treated for sepsis (LOS 8 days)		✓	✓
Non-infective causes (n = 9)	3 ✓	1 ✓	8 ✓

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infection as the cause of their deterioration unless there is a clear alternative diagnosis – which requires taking a history and examination. Furthermore, many of the older patients admitted on the acute medical take will present with non-specific symptoms due to infection.

The strength of this study is it is a pragmatic look at an unselected group of admission of acutely unwell adults, and reflective of the work typically carried out on Acute Medical Units across the UK. Scoring systems exist for a variety of clinical conditions, including acute coronary syndrome and gastro-intestinal bleeding; however in most cases these conditions require a diagnosis to be made before they can be applied. Guidelines which only become relevant when a diagnosis of sepsis has been clearly established are unhelpful, and guidelines which apply to possible infection affect almost all of the Acute Take.

The results of this study show that the different sepsis tools identify different populations. With the small numbers involved, and no gold standard with which to compare the definitions of sepsis, it is difficult to establish which is better – but no single definition correlated with mortality, positive blood culture or a high lactate. As predicted, the proposed NICE definition identified the largest number patients needing screening within 1 hour. This target was not achieved in 50% of these patients. Older patients represented a particular challenge, with higher proportions of those over 75 requiring 1 hour review; this has particular implications for service planning given the rising proportion of older patients being admitted on the acute medical take. By contrast the 2016 definition of sepsis identified the fewest patients to screen for organ failure; of those 62% had organ failure, but it also failed to identify some very sick patients. Of the 36 patients with organ failure identified by the SOFA criteria, 16 had suspected infection as the cause, but the qSOFA initial screening would have only identified 4 of these patients (25%).

There are some limitations to these data. Patients admitted directly to ITU/HDU from ED and those discharged prior to the post take ward round were not included; this may have impacted on the proportions of patients identified by the different scoring systems. The presence of organ failure was only calculated for patients in whom the necessary tests had been undertaken; given that not every patient had an arterial blood gas or lactate measurement, the actual number of patients with organ failure may have been under-reported.

The 2016 criteria may ultimately prove successful in identifying patients with a high mortality, in whom time critical interventions make a considerable difference, but requires other (non-sepsis) parameters to identify the critically ill patients which it misses. The NICE guidelines may identify every patient who has the potential to deteriorate, but the low specificity of these criteria may dilute resources too thinly. There are some studies which are starting to compare SIRS, NEWS and qSOFA for sepsis. The increase of the SOFA score >2 had more prognostic accuracy for in-hospital mortality than the SIRS criteria or the qSOFA score.⁶ The NEWS detected sepsis patients with an adverse outcome before qSOFA and SIRS and was more accurate for predicting death and ICU transfer in a single centre in the US.⁷ The 2016 definition of sepsis and the NICE criteria for sepsis represent opposite ends of the sepsis/infection spectrum. This study highlights the dilemma facing Acute Medical Units in choosing the most appropriate tools to identify patients with suspected sepsis, given the current constraints on staffing and resources. Until data emerges on patient outcomes following use of the different scoring systems, this dilemma will remain unresolved.

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Conflicts of interest

There are no competing interests.

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